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ODESSA NATIONAL MEDICAL UNIVERSITY

Department of General and Clinical Pharmacology and Pharmacognosy

APPROVED

Vice-Rector for Scientific and Pedagogical Work
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METHODOLOGICAL RECOMMENDATIONS FOR LECTURES ON THE ACADEMIC DISCIPLINE

CLINICAL PHARMACY AND PHARMACEUTICAL CARE

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LECTURE 1. TOPIC

"Clinical Pharmacy: introduction to the discipline, subject, objectives, world experience of development, relationship with other disciplines. Clinical Pharmacology: basic principles and provisions"

Relevance of the topic: The study of clinical pharmacy is extremely relevant in modern conditions, as it ensures the effective and safe use of medicines, which improves the results of patient treatment. Clinical pharmacy combines knowledge of pharmacology, medicine and pharmaceutics, which allows you to optimize therapy and reduce the risks of side effects.

Justification of relevance:

• Improving treatment outcomes: Clinical pharmacists develop and implement individual therapeutic regimens, taking into account the characteristics of each patient and a specific disease, which leads to a better clinical effect.

• Reducing side effects: They help identify and prevent undesirable drug reactions, control drug interactions, which reduces risks for patients.

• Rational use of resources: Clinical pharmacy contributes to the optimization of drug costs, ensuring their effective use and preventing unjustified costs.

• Support for physicians and other healthcare professionals: Clinical pharmacists provide advisory assistance to physicians and other healthcare professionals on issues of rational pharmacotherapy, contributing to the improvement of their qualifications.

• Development of evidence-based medicine:

Clinical pharmacy is an important component of evidence-based medicine, as it is based on scientific research and clinical data, which ensures the validity of decisions made.

• Improving the quality of life of patients:

Thanks to clinical pharmacy, patients receive more effective and safe treatment, which improves their general condition and quality of life.

Thus, clinical pharmacy is an important component of the healthcare system, which contributes to improving the quality of medical care and achieving positive patient treatment outcomes.

Purpose: To familiarize HES with the basic principles and provisions of clinical pharmacy and pharmaceutical care; modern requirements for practical and theoretical training of a pharmacist in accordance with the rules of good clinical practice, effective and safe pharmacotherapy; provide basic rules for choosing and selecting the appropriate dose, route of administration, and timing of drug use both when prescribed by a doctor and when responsible self-medication is used; explain the importance of monitoring the effectiveness and safety of drug use in a given patient.

To familiarize the HES with the basic principles and provisions of clinical pharmacology and the importance of the discipline in selecting personalized pharmacotherapy.

Key concepts (list of questions):

Clinical pharmacy is an integrative applied science that combines pharmaceutical and clinical aspects of knowledge about drugs. Its main task is to create reliable theoretical foundations and methodological approaches to the rational use of drugs.

Clinical pharmacology is a science that studies the effect of drugs on the body of a healthy and sick person.

A medicinal substance (active ingredient, substance) is any substance or mixture of substances that is intended for use in the production of a medicinal product and during this use becomes its active ingredient.

A medicinal product is a substance or mixture of substances used for the prevention, diagnosis, treatment of diseases, or changes in the state and functions of the body and is permitted by the relevant authorities for use within the country and in accordance with current legislation.

Over-the-counter drugs - OTC drugs or OTC drugs (English Over the Counter - without a prescription) - a large group of drugs that a patient can buy for self-medication directly at a pharmacy (and some drugs - and not only at a pharmacy) without a doctor's prescription.
Pharmacodynamics - a section of pharmacology that studies the biochemical effects and physiological actions of drugs, studies the mechanisms of action of drugs, the relationship between the concentration of medicinal substances and the effect achieved by them, studies possible pharmacological effects.
Pharmacokinetics - a section of pharmacology that studies the intake (routes of administration), absorption (absorption), distribution, transformation (biotransformation) of drugs in the body, their removal (excretion, elimination) from the body, as well as the dependence of the effectiveness and tolerability of drugs depending on these processes.
Pharmacogenetics - a science that studies the hereditary reactions of the body to the effects of a certain drug.

Lecture content (lecture text)

Clinical pharmacy is a branch of pharmacy that deals with optimizing pharmacotherapy, increasing the effectiveness and safety of patient treatment. It includes the development and implementation of clinical guidelines, consulting doctors and patients on the use of medicines, monitoring adverse reactions, etc.

Definition:

Clinical pharmacy is a discipline that combines knowledge of pharmacology, clinical medicine and pharmaceutical practice to ensure the safe and effective use of medicines in medical practice. It is aimed at optimizing pharmacotherapy and improving patient treatment outcomes.

Principles:

• Patient-centered: Clinical pharmacy puts the needs of the patient and their safety first.

• Evidence-based medicine: Decisions on the use of medicines are made on the basis of scientific evidence and clinical trials.

• Teamwork: Clinical pharmacists work closely with physicians, nurses, and other members of the healthcare team to provide a comprehensive approach to treatment.

• Continuing education: Clinical pharmacists must continually update their knowledge and skills to stay abreast of the latest developments in pharmacology and clinical medicine.

• Ethics: The activities of a clinical pharmacist are based on the principles of medical ethics, such as respect for the patient, confidentiality, and responsibility.

Tasks:

• Optimization of pharmacotherapy: Selecting the most effective and safe drugs, determining optimal doses and dosing schedules.

• Prevention and control of side effects: Monitoring adverse drug reactions, providing recommendations for their reduction and prevention.

• Counseling physicians and patients: Providing information about drugs, their uses, interactions with other drugs, and possible side effects.

• Participation in the development of clinical guidelines: Implementation of pharmacotherapy standards based on the principles of evidence-based medicine.

• Clinical trials of drugs: Participation in conducting clinical trials, analysis and interpretation of results.

• Pharmacoeconomic studies: Assessment of the economic effectiveness of various methods of pharmacotherapy.

• Pharmaceutical monitoring: Control over the quality and safety of drugs at all stages of their circulation.

• Education and awareness: Conducting educational activities for health professionals and patients on the rational use of drugs.

Questions for self-control on the topic:

1. Definition of the subject - clinical pharmacy, history of development in the world in Ukraine.
2. The fundamental difference between clinical pharmacy and pharmacology, clinical pharmacology, pharmacotherapy.
3. The main goals of clinical pharmacy.
4. The main tasks of clinical pharmacy:
 clinical testing of new pharmacological agents;
 clinical research and reassessment of old drugs;
 development of methods for the effective and safe use of drugs;
 organization of information services and advisory assistance of various specialists;
 training of students and doctors.
5. The main concepts of clinical pharmacy:
 medicinal substance.
 medicinal product - brand names, generic names - advantages and disadvantages, the concept of bioequivalence;
 the concepts of "chemical name", "international non-proprietary name", "trade name", "brand name" of drugs.
 OTC drug;
6. Medical monitoring: concepts, conditions that determine the need for medical monitoring.
7. Clinical pharmacology: definition of the discipline.
8. Clinical pharmacodynamics: definition, basic concepts.
9. Clinical pharmacokinetics: definition, basic concepts.
10. Pharmacotoxicodynamics: definition, basic concepts.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacy (pharmaceutical care): a textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
3. Clinical Pharmacy: A Textbook for Students of Pharmaceutical Faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
4. Clinical Pharmacology: A Textbook / Ed. O.M. Bilovol. – Vinnytsia: Nova Knyga, 2021. – 544 p.

LECTURE 2. TOPIC

"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of respiratory diseases (bronchial asthma, COPD, infectious diseases)"

Relevance of the topic: Respiratory system diseases, bronchial obstruction syndrome - a serious medical and social problem. According to epidemiological studies, 5% of the adult population and 15% of children have bronchopulmonary pathology with this syndrome. Bronchial obstruction syndrome occurs at a fairly early age and accompanies the patient throughout life, significantly worsening its quality, in our region it is the main cause of mortality in pulmonology.

Purpose: To familiarize the HES with the anatomical and physiological features of the bronchopulmonary system, the main etiological and pathophysiological features of the onset and progression of the main inflammatory and bronchoobstructive diseases of the respiratory system, the main symptoms in the corresponding nosoforms that require the intervention of a doctor or can be corrected by a pharmacist, to familiarize with the existing standards for providing pharmacotherapeutic care for acute viral obstructions, pneumonia, bronchial asthma, chronic obstructive pulmonary disease, etc.

Basic concepts (list of questions):

Symptom – a certain sign of a disease.

Syndrome – a set of symptoms united by a similar pathogenesis and characteristic of a certain disease.

Bronchoobstructive syndrome – a clinical symptom complex, the leading symptom of which is expiratory shortness of breath, which occurs as a result of restriction of air flow in the bronchi, caused by bronchospasm, edema and dyscrinia.

Bronchial asthma – a chronic inflammatory disease of the respiratory tract, caused by a significant number of cells and inflammatory mediators, which leads to bronchial hyperreactivity, manifested by wheezing, shortness of breath, cough, tightness in the chest.

Chronic obstructive pulmonary disease – a disease characterized by partial irreversible restriction of air flow in the respiratory tract, provoked by an abnormal inflammatory reaction of lung tissues to various pathogenic factors and gases.

Pneumonia is an acute infectious disease of predominantly bacterial etiology, characterized by focal lesions of the respiratory tract and insufficiency of intra-alveolar exudation.

Acute respiratory viral infections are a group of viral infections (the most common pathogens are influenza viruses, parainfluenza viruses, adenoviruses, rhinoviruses, coronaviruses, etc.), characterized by predominant damage to the mucous membranes of the respiratory tract and conjunctiva.

Broncholytics are substances and drugs that cause relaxation of bronchial smooth muscles.

Antiviral, antibacterial drugs are drugs for the etiotropic treatment of infectious and inflammatory diseases of the respiratory tract.

Lecture content (lecture text)

Broncholytics are a pharmacological group of symptomatic drugs that directly relieve bronchospasm and are used in the treatment of bronchial asthma and chronic obstructive pulmonary disease and some other diseases. This group does not include drugs that affect the causes of bronchospasm, such as antihistamines, corticosteroids, antivirals, antimicrobials, and others.

These include drugs that block bronchospasm in various ways:

 β2-adrenoceptor agonists
 Nonspecific β-agonists (beta-agonists, β-adrenomimetics)
 Orciprenaline, Isoprenaline
 Specific β2-agonists (beta-two-agonists, β2-adrenomimetics, β2-adrenoceptor agonists):
 short-acting: salbutamol, fenoterol, terbutaline, hexoprenaline, clenbuterol
 long-acting (prolonged) action: salmeterol, formoterol
 for oral administration: saltos
 M-cholinoreceptor antagonists (M-cholinoleptics, cholinolytics, anticholinergics) - ipratropium bromide, tiotropium bromide
 Xanthine derivatives - myotropic antispasmodics

Broncholytics are available in the form of inhalers, tablets, syrups and solutions for injection. Inhalers (and their subspecies, nebulizers) are the most popular.

Beta2-agonists (BDA)

They occupy a central place among the means of symptomatic control of asthma, as they have pronounced bronchodilator activity and, when used correctly, cause a minimum number of side effects.

Selective beta-two-agonists (BDA) have been used since 1970. The first drug from this group was salbutamol, which rightfully received the status of the "gold standard" in the BDA line. After salbutamol, it was worth introducing other beta-two-agonists into clinical practice, in particular fenoterol (berotec). The emergence of inhaled prolonged beta-two-agonists (salmeterol, formoterol) significantly expanded the possibilities of asthma therapy. The most effective way to administer BDA is inhalation. Its important advantage is the possibility of direct delivery of the drug to the target organ, as a result of which the therapeutic effect of the bronchodilator quickly occurs with minimal side effects.

Among the currently known delivery devices for BDA:

 most often (almost 70% of cases) metered-dose aerosol inhalers - DAI are used;
 metered-dose powder inhalers - DPI are used less often;
 even less often - nebulizers.

Pharmacodynamics

 Stimulation of beta-adrenoreceptors leads to activation of adenylate cyclase, resulting in an increase in the content of intracellular cAMP. Then there is a decrease in the intracellular calcium concentration, which leads to relaxation of the smooth muscles of the bronchial tree. BDA are universal bronchodilators, since they eliminate bronchoconstriction regardless of its genesis and mechanisms.
 BDA have a bronchoprotective effect, which is manifested by a slight decrease in the remodeling of the bronchial tree in obstructive lung diseases.
 In addition, BDA inhibit the release of mediators from inflammatory cells, limit capillary permeability, prevent the development of bronchial mucus edema-stasis.
 Reduce cholinergic reflex bronchoconstriction.
 Modulate mucus production and optimize mucociliary clearance.
 Long-term course use of Saltos significantly improves the patency of the entire bronchial tree. The maximum broncholytic effect at the level of small bronchi develops by the end of the second week of therapy. Along with the pronounced broncholytic effect, only Saltos among all BDAs has a significant bronchoprotective effect.
 Frequent regular use of inhaled BDAs can lead to the development of tolerance (desensitization) to them, which, unlike tachyphylaxis, develops gradually, over several days or weeks and is associated with the transition of receptors to an inactive state.
 It should be remembered that the selectivity of BDAs is always relative and dose-dependent. It has been established that the selectivity decreases clinically significantly with an increase in the dose of the drug or the frequency of its administration during the day. This must be taken into account in the treatment of acute asthma, especially when stopping the asthmatic status, when the patient inhales 5-10 or more daily doses of the drug for several hours.

 Clinically important is the question of the presence of BDA anti-inflammatory effect. This question still remains open. In addition, regular use of BDAs can mask the increasing exacerbation, thereby supporting the start or intensification of true anti-inflammatory therapy conducted by the central nervous system.
 A link has been established between an increased risk of death in patients with asthma and the use of high doses of inhaled BDA. It is believed that patients receiving high doses of BDA (more than 1.4 aerosol cans per month) certainly and, above all, need increased anti-inflammatory therapy.

Short-acting BDA (BDak)

Salbutamol (salben. salgim, saltos)

Currently the most popular bronchodilator. This is a classic short-acting BDA.

F. st. - for salbutamol-DAI, containing 200 doses of 100 mcg each.

- for salben - DPI Cyclohaler complete with a capsule containing 200 doses of the drug, 200 mcg of active substance each

- salgim in bottles containing 5 or 10 ml of 0.1% salbutamol solution for inhalation via a nebulizer.

Pharmacodynamics of salbutamol preparations

 Salbutamol is a selective beta-two-agonist, due to which it has a pronounced bronchodilator effect. The short-acting drug stops and prevents bronchial spasm, that is, it is the drug of choice for situational symptomatic control of asthma.
 Reduces the release of histamine and other biologically active substances from mast cells.
 Increases the excitability, frequency and strength of heart contractions.

Pharmacokinetics

The therapeutic effect of short-acting salbutamol after inhalation with DAI begins in 1 - 3 minutes and lasts up to 3 - 4 hours. The broncholytic effect of salben appears in 4 - 5 minutes; the maximum is reached by 40 - 60 minutes, and the duration of action of the drug is 4 - 5 hours. The response to inhalation of salgim through a nebulizer is usually observed after 10-15 minutes, and the effect lasts 4-6 hours.

Indications for use

- Relief ("on demand") and prevention of bronchospasm. Usually, bronchodilator therapy of patients with asthma begins with the appointment of salbutamol. The drug is less effective in CHOL and COPD.

Dosage regimen

Salbutamol preparations, with the exception of Saltos, are used only "on demand".

Adults 1 - 2 inhalations of salbutamol no more than 3-4 times a day.

Children over 2 years old 1 inhalation of salbutamol from 1 to 3 times a day.

Salben is used 1 - 2 inhalation doses per reception from 1 to 4 times a day.

When using Salgim, the starting dose = 2.5 mg every 4 - 6 hours during the first 2 days of treatment or until the clinical picture stabilizes.

If control of asthma is not achieved when using the above doses of salbutamol preparations, then anti-inflammatory therapy should be intensified.

Side effects and overdose symptoms

Impaired heart rhythm, decreased blood pressure, headache, restlessness, anxiety, muscle tremor.

Fenoterol (berotec, berotec N)

F. st. - for berotec - freon-based DAI, containing 200 doses of 100 mcg each.

- for berotec N - freon-free DAI, containing 200 doses of 100 mcg each. The drug contains small amounts of ethanol and citrates, which give it a light alcoholic and lemon flavor.

Pharmacodynamics

 Similar to that of salbutamol. In terms of therapeutic efficacy, it surpasses salbutamol. Therefore, with insufficient effect from salbutamol, the patient is transferred to berotec. However, returning to salbutamol for such patients is practically excluded.

 It is successfully combined with ipratropium bromide. There is a combined drug called berodual.

Results of comparative controlled studies
As a result of the conducted studies, it was found that Berotec in both forms - freon and freon-free DAI - had practically the same effect on FZD indicators in patients with asthma. At the same time, Berotec N was 2 times more effective than simple Berotec.
Indications for use
- Relief and prevention of bronchospasm, especially in patients with asthma
Dosage regimen
To relieve attacks of bronchospasm, 1 dose is prescribed. If necessary, after 5 minutes, inhalation can be repeated.
Side effects
In this regard, Berotec is more active than salbutamol.
From the CNS: minor tremor, dizziness, headache, nervousness.
From the cardiovascular system: tachycardia and other cardiac rhythm disturbances, angina attacks, increased systolic blood pressure.
Also possible: cough, nausea, vomiting, weakness, muscle pain.
Long-acting BDA (LDA)
Currently available inhaled BDA (formoterol, salmeterol) have their effect for 12 hours with almost equivalent bronchodilator effect.
Clinical studies indicate the feasibility of earlier appointment of IBD.
When using formoterol more than 2 times a week "on demand" it is necessary to add IGC to the treatment. Currently, it is recommended to use IBD only in patients who are simultaneously receiving IGC.
Salmeterol (Serevent)
F. st. - DAI, contains 60 or 120 doses of 25 mcg of salmeterol in each
- DPI with rotadisks, each of which contains 4 doses of 50 mcg of active substance.
Pharmacodynamics
- This is a highly selective BDA of prolonged action.
- Provides long-term control of asthma in patients with daily symptoms.
- Improves the quality of life, in particular, improves the quality of sleep in patients with asthma
- In therapeutic doses, it does not affect the cardiovascular system.
Pharmacokinetics
The onset of action is noted 5-10 minutes after inhalation. The bronchoncolytic effect lasts for 12 hours after a single inhalation.
Indications for use
- Regular long-term treatment of patients with clinically significant reversible bronchial obstruction.
- Nocturnal asthma.
Method of application
Adults, the contents of one rotadisk or 2 inhalations 2 times a day
Children aged 4 years and older - 1 - 2 inhalations 2 times a day.
Side effects
 Rarely tremor, usually transient and decreases during treatment
 Overdose symptoms
 Tremor, headache, palpitations, possible heart rhythm disturbances.
Formoterol (Foradil Aerolizer, Oxis Turbuhaler)
F. st. - Turbuhaler inhaler contains 60 doses of 4.5 or 9 mcg.

- capsules, each of which contains 12 mcg of powder for inhalation, complete with DPI "Aerolizer".

Pharmacodynamics

 This is a powerful selective BDA with a pronounced bronchodilator effect

 The rapid onset of bronchodilator action (within 1-3 minutes) allows for effective relief of acute bronchial obstruction. In this regard, formoterol does not outperform salbutamol.

 The drug lasts up to 12 hours

 It does not affect the effects of short-acting NSAIDs, which allows them to be used additionally against the background of basic therapy with formoterol. This is confirmed by the results of numerous clinical studies.

 In comparative studies with salbutamol, no significant differences in the duration of action per hour were found.

 Side effects of formoterol are dose-dependent and reach a clinically significant level only in doses significantly exceeding therapeutic ones, which indicates the high safety of the drug.

 When using therapeutic doses, the drug does not accumulate.

 In patients with COPD, in terms of its effect on FEV1, foradil in doses of 12 and 24 mcg 2 times a day significantly exceeds the effect of ipratropium bromide.

At the same time, unlike anticholinergics, formoterol in both doses causes a surprisingly significant improvement in the quality of life. In addition, against the background of treatment with formoterol, the percentage of "unfavorable days" is significantly lower than when using ipratropium bromide. The frequency of adverse events was comparable in all studied groups.

 It should be especially emphasized that formoterol, like other IBDAPs, potentiates the effects of GCs. The results of clinical studies have shown that adding formoterol to basic asthma therapy has a greater effect compared to theophylline with a significantly lower risk of side effects.

Indications for use

- Relief and prevention of bronchospasm attacks, including nocturnal asthma. In fact, formoterol is necessary for every asthma patient in any situation.
- Formoterol is indicated for patients with moderate and severe asthma as a basic anti-asthmatic therapy in combination with inhaled and/or systemic GCs.
- In COPD, formoterol improves lung function, reduces the frequency and severity of exacerbations.

Mode of application

Adults inhaled via Turbuhaler 4.5-9 mcg 1-2 times a day

Adults inhaled via Aerolizer 12-24 mcg (contents of 1-2 capsules) 1-2 r/s.

Side effects

It should be used with caution in coronary artery disease, cardiac arrhythmias, thyrotoxicosis, diabetes mellitus.

Patients with asthma should continue anti-inflammatory GC therapy after starting treatment with formoterol, without changing the dosage regimen of the latter.

Saltos

F. Art. - osmogenic tablets, each of which contains 7.23 mg of the active substance, cold.

Pharmacodynamics

The prolonged preparation of salbutamol is used mainly for the prevention of episodes of bronchospasm, especially at night.

Combined BDA (BDA + IGK)

Seretide Multidisk (salmeterol + fluticasone propionate)

Contains two active ingredients: salmeterol xinafoate (SC) and fluticasone propionate (FP)

F. st. – DPI "Multidisk", inside which there is a foil tape with 60 uniformly placed cells, each of which contains one dose of the drug in the form of a powder for inhalation.

Seretide Multidisk is available in the following dosages:

. 50 mcg SC + 100 mcg FP in one dose; 60 doses.

- 50 mcg SC + 250 mcg FP in one dose, 60 doses. 'f
- 50 mcg SC + 500 mcg FP in one dose; 60 doses.

Pharmacodynamics
 Effective control of asthma using an inhaler.
 Reduction in the severity of symptoms from the first day of treatment.
 Ability to control asthma with lower doses of IGC.
High safety profile.
 Unique delivery system with an accurate dose counter.
 Convenient dosing regimen: 1 inhalation 2 times a day.
 Increased compliance of patients with asthma.
 Improved quality of life of patients with asthma.
 Reduced cost of treatment compared to the simultaneous use of salmeterol and fluticasone in separate inhalers.
Indications for use
- Patients receiving maintenance therapy with BDAp and IGC.
- Patients in whom symptoms of the disease persist on the background of IGC therapy.
- Patients who regularly use bronchodilators, for whom IGC therapy is additionally indicated.
Dosage regimen
The starting dose of Seretide Multidisk is determined based on the dose of fluticasone propionate recommended for asthma of this severity.
Adults and adolescents from 12 years of age and older: one inhalation (50 mcg salmeterol + 100/250/500 mcg fluticasone) 2 times a day.
Children from 4 years of age and older: one inhalation (50 mcg salmeterol + 100 mcg fluticasone) 2 times a day.
Side effects
Similar to those of salmeterol and fluticasone.
Symbicort (formoterol + budesonide)
This is a combination in one inhaler Turbuhaler IGC budesonide and prolonged-release BDA formoterol.
F. st. - DPI Turbuhaler contains 60 doses, each of which contains 4.5 mcg formoterol + 80 or 160 mcg budesonide.
Pharmacodynamics
 Rapid relief of asthma symptoms, which occurs within 1 - 3 minutes after inhalation.
 Long-term control of the disease.
 Possibility of a single dose during the day.
 Flexibility of dosing using the same inhaler.
 Increased compliance, as patients note immediate relief of the condition after inhalation of Symbicort, which encourages them to systematically continue treatment.
 Turbuhaler is an effective and convenient drug delivery system in the BLS.
Indications for appointment
- Patients who are simultaneously receiving maintenance therapy BDAp and IGC.
- Patients who have symptoms of the disease on the background of IGC therapy.
- Patients who regularly use bronchodilators, for whom IGC therapy is additionally indicated.
Clinical efficacy
Symbicort has undergone a number of clinical trials abroad. It has been established that compared to IGC, Symbicort significantly reduces asthma symptoms, the frequency and duration of exacerbations, and improves FZD indicators. Compared to budesonide, Symbicort gives the patient 2 additional months a year not only without daytime, but even without nighttime symptoms of asthma. Treatment with Symbicort compared to treatment with budesonide and formoterol through separate inhalers leads to a faster increase and stabilization of peak flowmetry indicators.

In terms of the speed of onset and severity of the bronchodilator effect, Symbicort surpasses the combination containing salmeterol 50 mcg + fluticasone 250 mcg.
Dosage regimen
Adults, including HDP, and adolescents from 12 years and older - 1-2 inhalations (from the ras-spouse 1 dose = 160/4.5 mcg) 2 times a day. After achieving optimal control of asthma symptoms, the dose can be reduced to the minimum effective = 1 inhalation 1 time a day.
Side effects. Similar to those of budesonide and formoterol. The most common are tremor and tachycardia. These symptoms are usually moderately pronounced and disappear after a few days of treatment. Less common are headache, tremor, candidiasis of the oral pharynx, cough, hoarseness of the voice.
Biasten (salbutamol + budesonide)
F. st. - DPI Cyclohaler, containing 100 or 200 doses of the drug, each of which contains 200 mcg of salbutamol and 100 mcg of budesonide.
This is a combined drug that has anti-inflammatory and bronchodilator effects in the treatment of patients with asthma. This allows you to reduce the severity symptoms, as well as the frequency and severity of exacerbations of the disease. The broncholytic effect occurs quickly, within 1 - 3 minutes. after inhalation, and persists for 5-7 hours after taking a single dose.
Biasten is indicated for basic therapy of asthma. It combines well with virtually any anti-asthmatic drugs. Special caution is not required in people with heart rhythm disorders and hypokalemia.
The use of the drug allows you to achieve high compliance, as well as reduce the cost of basic therapy compared to the separate use of two inhalers.
The drug is recommended to be used 1 inhalation 3 times a day or 2 inhalations 2 times a day. After achieving optimal control of asthma symptoms, the dose can be reduced, up to taking 1 times a day.

XANTHINES

1. Short-acting drugs:
• Theophylline (Eufillin).
2. Long-acting drugs:
I generation:
• Teopek.
• Teodur.
• Teotard.
• Systair.
• Teobiolong.
• Retafil.
• Ventax.
• Durophyllin.
II generation:
• Dilatran.
• Teodur-24.
• Eufilong.
• Unifil.
• Retafil-retard.
• Filocontin.
• Diffumal-24.
• Teo-24.

Currently, short-acting theophylline drugs are used to relieve bronchospasm, while long-acting TFs are being used for the systematic treatment of asthma. As monotherapy, long-acting TFs have low efficacy and are obviously not suitable for long-term maintenance therapy. At the same time, in those patients who failed to achieve control of asthma with IGC alone, the

combination of the latter with prolonged theophyllines can improve treatment results. It should be borne in mind that the combination of IGC with prolonged-acting TF is less effective than the combination of IGC with β2-AM, but much cheaper. The mechanism of action of xanthines has not yet been fully elucidated. It has been shown that methylxanthines non-selectively inhibit the III and IV isoforms of phosphoryl-diesterase (PDE), which contributes to the accumulation of cAMP in cells. PDE III predominates in the smooth muscles of the bronchi, while the IV isoform of the enzyme plays the greatest importance in inflammatory cells (mast cells, eosinophils, T-lymphocytes). As a result, phosphorylation of myosin light chain kinase occurs, followed by bronchodilation and inhibition of the release of inflammatory mediators.

In addition, drugs of this group are able to non-selectively block all subtypes of adenosine receptors. Adenosine, being an endogenous purine nucleotide, is considered a natural ligand that specifically interacts with adenosine receptors (A1, A2A, A2B, A3). Activation of type 1 adenosine receptors in the bronchi leads to an increase in bronchial tone, while type 2 receptors exert a bronchodilating effect. In asthma, the density of adenosine receptors in the bronchi changes with a predominance of A1 receptors and a significant decrease in the number of A2 adenosine receptors. Thus, the bronchodilating effect of xanthines is due to the blockade of A1 adenosine receptors and inhibition of PDE.

At the same time, when treated with xanthines for more than 3 weeks, the density and activity of A2-adenosine receptors in the bronchi increases.Blockade of adenosine receptors (especially types A2B and A3) on the surface of mast cells leads to a decrease in the release of inflammatory mediators. A certain role in the mechanism of action of xanthines may be played by antagonism with TNF-α, which is of great importance in severe asthma. These components of the mechanism of action of theophylline, apparently, mediate its slight anti-inflammatory effect (in low doses).

It is currently believed that with systematic use of theophylline, its ability to prevent the release of allergy mediators prevails over its direct bronchodilator effect.

TF is metabolized in the liver to caffeine and 3-methylxanthine, which also have pharmacological activity. The kinetics of this process is nonlinear, which does not allow for an accurate prediction of the dependence of the drug metabolism on the administered dose.

The therapeutic effect of TF is manifested in a narrow dose range (from 10 to 20 μg/ml), exceeding which leads to the development of side effects. Stable serum concentration of TF is determined by the dose, administration interval and clearance of the drug. Even in one patient, pharmacokinetic parameters may fluctuate depending on the severity of the condition, the duration of previous therapy with methylxanthines, etc., which requires pharmacokinetic monitoring based on serum concentration of TF

For the treatment of asthma, prolonged-acting TF preparations can be used, slowly releasing theophylline from the dosage form. In the latter, theophylline can be either in the form of microcapsules or layered on a carrier (soluble film). The initial dose of prolonged-acting TF preparations is 16 mg/kg per day or 400 mg/day (a lower dose is preferred). The therapeutic concentration of TF in the blood in this case is maintained at a constant level for up to 12-24 hours (depending on the generation of the drug), which allows them to be taken once (II generation) or twice (I generation) per day. From the standpoint of chronopharmacology, doped forms of TF II generation should be taken in the evening (at 18-19 hours), since the metabolism of xanthines is significantly slowed down at night.

In the relief of asthma attacks, the place of theophylline has not been definitively determined. It can be administered as a 2.4% solution of euphylline, 10 ml intravenously, slowly by jet or drip. If it is impossible to administer euphylline intravenously, it is administered intramuscularly (1 ml of a 24% solution). However, it should be borne in mind that the addition of short-acting theophylline to adequate doses of short-acting β2-AM may not provide an additional bronchodilator effect, although it stimulates the act of breathing. In addition, it has been shown that in terms of the severity of the bronchodilator effect, intravenously administered

euphylline is inferior to both short-acting β2-AM administered via a nebulizer and magnesium sulfate (intravenously 2 g (or 25 mg/kg) over 20 min).

Side effects, as a rule, appear at a serum concentration of TF more than 20 μg/ml:

 - from the nervous system - insomnia (usually disappears after 5-6 days), headache, tremor, unconsciousness. The most formidable complication is convulsions, when the mortality rate can reach 40% or more;

 - from the gastrointestinal tract - nausea, vomiting, abdominal pain, diarrhea;

 - from the cardiovascular system - tachycardia, heart rhythm disturbances, hypotension;

 - from the urinary system - polyuria. A new approach in the pharmacotherapy of broncho-obstructive diseases was the creation of selective PDE IV inhibitors - cilomilast (ariflo) and roflumilast. Their feature is high selectivity for some types of immunocompetent cells involved in the formation of inflammation in the respiratory tract and bronchial smooth muscles. In addition, the drugs contribute to the relaxation of bronchial smooth muscles, suppress excessive activation of nerve endings in the bronchopulmonary tissue, reducing the phenomena of bronchospasm.

The use of drugs that change the state of the bronchial tree has a multifunctional purpose, due to their influence on the pathophysiological mechanisms of vascular tone disorders, edematous syndrome, syndromes of heart rhythm and conduction disorders, etc. The use of these drugs in combined pathology with syndromic disorders is of great importance.

Questions for self-control on the topic:

1. Classification of bronchodilators by mechanism of action.
2. Mechanism of action and main pharmacological effects of adrenoreceptor stimulants.
3. Mechanism of action and main pharmacological effects of m-holinoblockers.
4. Mechanism of action and main pharmacological effects of phosphodiesterase inhibitors (methylxanthines).
5. Algorithm for choosing bronchodilators.
6. Monitoring the effectiveness and safety of bronchodilators.
7. Main pathogenetic mechanisms of SBO, which are the object of drug influence, which determine the development and course of bronchial obstruction syndrome.
8. Diseases and clinical syndromes, the development of which is accompanied by disorders of bronchial patency.
9. Basic principles of COPD pharmacotherapy.
10. The role of glucocorticoids in the treatment of patients with SBO, the rules for their appointment and withdrawal, taking into account pharmacodynamic and pharmacokinetic features.
11. The role of infection in the development of respiratory diseases.
12. Acute respiratory diseases - definition, etiology, pathogenesis, use of etiotropic drugs, characteristics of the main groups, pharmacokinetics, pharmacodynamics, main representatives, undesirable effects, choice of route of administration.
13. Acute bronchitis - definition, etiology, pathogenesis, classification, choice of antimicrobial drugs depending on the form, severity of the course and stage of the disease.
14. Pneumonia. Definition, diagnostic criteria, clinical classification and treatment depending on the type of pneumonia
15. Pharmacotherapy of complications of pneumonia.
16. Features of the use of antibiotics in respiratory diseases.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.

2. Clinical pharmacy (pharmaceutical care): a textbook for students. higher. med. (pharmac.) academic. conclusion / I.A.Zupanets, V.P.Chernykh, T.S.Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
3. Clinical Pharmacy: a textbook for students of pharmaceutical faculties / Ed. V.P.Chernykh, I.A.Zupanets, I.G.Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
4. Clinical Pharmacology: a textbook / Ed. O.M.Bilovol. – Vinnytsia: Nova Kniga, 2021. – 544 p.
5. Protocols of a pharmacist (pharmacist) / Ed. V.P.Chernykh, I.A.Zupanets, O.M.Lishchyshyna. – Kharkiv: Golden Pages, 2013. – 192 p.
6. Modern classifications and standards of treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Edited by prof. Yu.M.Mostovoy. – 25th ed., changes and additions. – Kyiv: Center of the State Clinical Hospital, 2018. – 792 p.

LECTURE 3. TOPIC
"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of arterial hypertension (essential and symptomatic)"

Relevance of the topic: Arterial hypertension, or high blood pressure, is a serious public health problem due to its high prevalence and ability to cause serious complications such as heart attack, stroke and kidney failure. It often develops asymptomatically, making it a "silent killer", and requires regular monitoring and treatment to prevent serious consequences.

Here are the main aspects of the relevance of arterial hypertension:

• Prevalence: Arterial hypertension is one of the most common chronic diseases in the world. According to WHO, more than 1.28 billion adults aged 30-79 have high blood pressure.

• Asymptomatic: Many people with hypertension are unaware of their condition, as the disease can develop without obvious symptoms, making it difficult to diagnose in time.

• Risk of complications: Uncontrolled hypertension can lead to serious complications, including heart attack, stroke, heart failure, kidney failure, vision loss, and other problems.

• Cause of premature death:

High blood pressure is the leading cause of preventable death worldwide, underscoring the importance of its detection and treatment.

• Impact on quality of life: Hypertension can significantly impair quality of life through physical and psychological consequences, as well as limitations in daily activities.

• Need for prevention and treatment: Early detection, regular monitoring, and adequate treatment of hypertension are key to preventing complications and maintaining health.

• Impact on cognitive function: Hypertension is also associated with an increased risk of cognitive impairment and dementia.

Purpose: To familiarize the HES with the definition, classification of arterial hypertension, etiological and pathophysiological factors of certain types of primary and secondary hypertension, the principles of classification of drugs for normalizing elevated blood pressure, the principles of choosing mono- and combined pharmacotherapy of arterial hypertension, methods of monitoring the effectiveness and safety of the proposed therapy.

Basic concepts (list of questions):

Arterial hypertension is a clinical condition characterized by an increase in systolic blood pressure of more than 140 mm Hg and/or diastolic blood pressure of more than 90 mm Hg.

Primary arterial hypertension is a disease characterized by a persistent increase in blood pressure in the absence of an obvious cause of its increase.

Secondary arterial hypertension is hypertension, the etiology of which can be established.

Systolic blood pressure – shows the pressure in the arteries at the moment when the heart

contracts and pushes blood into the arteries, it depends on the force of heart contraction.
Diastolic blood pressure – shows the pressure in the arteries at the moment of relaxation of the heart muscle and reflects the resistance of peripheral vessels.
Antihypertensive drugs – drugs that reduce systemic blood pressure and are used for permanent therapy of chronic arterial hypertension (ACE inhibitors, beta-blockers, alpha-blockers, thiazide diuretics, calcium antagonists, angiotensin 2 receptor antagonists).
Hypotensive drugs – drugs that reduce systemic blood pressure and are used to quickly reduce pressure in acute hypertensive conditions (loop diuretics, nitrates, myotropic antispasmodics, magnesium salts, neuroleptics, ganoglioblockers, etc.).

Lecture content (lecture text)

Pharmacotherapy of arterial hypertension includes several classes of drugs that are prescribed to lower blood pressure and prevent complications. The main groups of drugs are ACE inhibitors, angiotensin II receptor blockers, diuretics, calcium channel blockers and beta-blockers. The choice of a specific drug depends on the individual characteristics of the patient, concomitant diseases and the degree of increase in blood pressure.

The main classes of drugs for the treatment of arterial hypertension:

• Angiotensin-converting enzyme inhibitors (ACEIs): Enalapril, lisinopril, ramipril. They dilate blood vessels and lower blood pressure by preventing the formation of angiotensin II.

• Angiotensin II receptor blockers (ARBs): Valsartan, losartan, irbesartan. The action is similar to ACEIs, but they block angiotensin II receptors, but do not prevent its formation.

• Diuretics (water pills): Hydrochlorothiazide, indapamide. Reduce the volume of circulating blood, which leads to a decrease in blood pressure.

• Calcium channel blockers (CCBs): Amlodipine, verapamil, diltiazem. Relax the smooth muscles of the blood vessels, which leads to their expansion and a decrease in pressure.

• Beta-blockers: Metoprolol, bisoprolol, atenolol. Reduce the heart rate and force of heart contractions, which leads to a decrease in blood pressure.

Features of the treatment of arterial hypertension:

• Step therapy: Typically, treatment is started with one drug, and if the effect is insufficient, others are added.

• Fixed combinations: Can be effective for simplifying medication intake and improving blood pressure control.

• Integration with lifestyle modification: It is recommended to combine pharmacotherapy with a healthy diet, physical activity, alcohol and smoking restriction.

• Individual approach: The choice of drugs and their dosage are determined by the doctor, taking into account the characteristics of the patient and the presence of concomitant diseases.

The first goal of treatment is to reduce BP to <140/90 mm Hg in all patients; with a good course of treatment, blood pressure (BP) values should be aimed at 130/80 mm Hg or lower for most patients. For most patients under 65 years of age who are receiving BP-lowering drugs, a reduction in systolic blood pressure to 120-129 mm Hg is recommended. In patients under 65 years of age who are taking antihypertensive drugs:

• A reduction in systolic blood pressure to 120-129 mm Hg is recommended.

• Close monitoring of side effects is recommended

A diastolic blood pressure <80 mm Hg should be the goal for all patients with hypertension, regardless of risk or comorbidities

There are two main areas of therapy aimed at lowering blood pressure that have proven effectiveness: lifestyle changes and drug treatment.

Lifestyle changes can undoubtedly help lower blood pressure and reduce the risk of cardiovascular disease, but most patients with hypertension (hypertension) also require drug treatment. Currently, antihypertensive drug therapy is recommended in patients with stage 2 or 3 hypertension along with lifestyle changes. Patients with stage 1 hypertension and high risk of cardiovascular disease or with hypertension-mediated organ damage (HMOD) should also take drugs to lower blood pressure.

Recommended lifestyle changes that lower blood pressure include limiting salt intake, moderate alcohol consumption, increasing the amount of vegetables and fruits in the diet, losing weight and maintaining an ideal body weight, and regular physical activity. In addition, smoking has an acute, long-term pressor effect (increases blood pressure), which can cause an increase in daytime ambulatory blood pressure, but quitting smoking and other lifestyle changes are important not only for the treatment of hypertension, but also for the prevention of other cardiovascular diseases and cancer.

But it is worth remembering that a sharp change in lifestyle, in particular the diet, requires a balanced and responsible approach. A properly developed nutrition plan will not cause stress for the body, and will minimize the possible negative impact on health, therefore, we recommend that you perceive the diet as part of the treatment and seek help from a professional dietitian.

Limiting sodium intake

There is evidence to support a causal relationship between sodium chloride (table salt) intake and blood pressure, and excessive sodium intake (more than 5 g/day, e.g. one small spoonful of salt per day) has a pressor effect and is associated with an increased incidence of hypertension and increased systolic blood pressure (SBP). The reduction in blood pressure resulting from sodium restriction is more pronounced in black people, older patients, and those with diabetes, metabolic syndrome, and chronic kidney disease.

Moderate alcohol consumption

There is a well-known linear relationship between alcohol consumption and blood pressure levels, the prevalence of hypertension and the risk of developing chronic kidney disease. Excessive alcohol consumption has a strong pressor effect. Men with hypertension who drink alcohol are advised to limit their intake to 14 units per week and non-pregnant women to 8 units per week (1 unit is equivalent to 125 ml of wine or 250 ml of beer or 40 ml of spirits), with

alcohol-free days during the week.

Other dietary changes

Patients with hypertension should follow a healthy balanced diet containing vegetables, legumes, fresh fruit, low-fat dairy products, whole grains, fish and unsaturated fatty acids (especially olive oil) and limit their intake of red meat and saturated fatty acids. The Mediterranean diet includes many of these nutrients and foods, with moderate alcohol consumption (mainly wine with meals). Thus, following a healthy and balanced diet can help lower blood pressure and reduce the risk of cardiovascular disease.

Weight loss

Excessive weight gain is associated with hypertension, and losing weight to an ideal body weight reduces blood pressure. Currently, it is recommended that patients with hypertension and for the prevention of its occurrence maintain a Body Mass Index of 20-25 kg/m2 (under 60 years of age, slightly higher in older people) and a waist circumference of less than 94 cm for men and less than 80 cm for women.

Regular physical activity

Epidemiological studies show that regular aerobic physical activity can be beneficial both for the prevention and treatment of hypertension and for reducing the risk of cardiovascular disease and mortality. Endurance training (but not other types of exercise) lowers blood pressure more.

To prevent hypertension, adults are recommended to gradually increase aerobic physical activity to 300 min. per week or moderate-intensity exercise to 150 min. per week. An equivalent combination of these types of physical activity is also possible.

Smoking cessation

Smoking cessation is probably the most effective lifestyle change for the prevention not only of arterial hypertension, but also of other cardiovascular diseases, including stroke, myocardial infarction, and peripheral vascular disease.

Most patients with hypertension require drug therapy along with lifestyle changes to achieve optimal blood pressure control. Treatment of arterial hypertension is long-term (often lifelong).

Five main classes of drugs are currently recommended for the treatment of hypertension:

- angiotensin-converting enzyme inhibitors (ACEIs)
- angiotensin receptor blockers (ARBs)
- beta-blockers
- calcium channel blockers (CCBs)
- diuretics

Recommendations for the use of these groups of drugs are based on: (i) proven ability to lower blood pressure; (ii) evidence from placebo-controlled trials that they reduce the incidence of cardiovascular disease; and (iii) evidence that the benefits of their use outweigh the risks associated with it. Typically, initial therapy for hypertension involves the use of 1-2 drugs (combination therapy) from the above classes. Other classes of drugs used to lower blood pressure are less well studied, have a lesser blood pressure lowering effect, or are associated with a higher risk of side effects (e.g., alpha-blockers, centrally acting drugs, mineralocorticoid receptor antagonists). However, these drugs are also used to treat hypertension in special clinical situations or in the case of resistant hypertension.

Questions for self-control on the topic:

1. List the clinical and pharmacological principles of choosing and selecting drugs for arterial hypertension.
2. What principles are the basis for the classification of antihypertensive drugs?
3. Justify the appointment of diazepam for hypertensive crisis and indicate the criteria for assessing the effectiveness and safety of its use.

4. What hemodynamic changes occur in the body under the influence of propranolol? Name the drugs, simultaneous use with which is inappropriate, and explain why?
5. List the drugs and the main mechanisms that cause vasodilation.
6. What hemodynamic changes occur in the body under the influence of slow calcium channel blockers? Indications and contraindications for their appointment.
7. Explain the mechanism of the hypotensive effect of drugs that affect the humoral links of blood pressure regulation. Formulate indications and contraindications for their use.
8. Name the main undesirable effects of clonidine and the mechanisms of their occurrence, which must be taken into account in urgent and planned therapy of arterial hypertension.
9. Explain why, in a hypertensive crisis caused by pheochromocytoma, the patient should first be given phentolamine, then beta-blockers?
10. Name and explain the mechanisms of hemodynamic changes in the body after the administration of pentamine and other ganglioblockers.
11. What undesirable effects are inherent in ganglioblockers?

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M. Bilovol. – Vinnytsia: Nova Kniga, 2021. – 544 p.
3. Clinical Pharmacy (Pharmaceutical Care): A Textbook for Students of Higher Medical (Pharmaceutical) Schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: A Textbook for Students of Pharmaceutical Faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Modern Classifications and Standards of Treatment of Diseases of Internal Organs. Emergency Conditions in Therapy. Analyses: Normative Indicators, Interpretation of Changes / Ed. Prof. Yu.M. Mostovoy. – 25th ed., changes. and supplements – Kyiv: Center of State Library, 2018. – 792 p.

LECTURE 4. TOPIC

"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of ischemic heart disease, atherosclerosis, heart failure"

Relevance of the topic: Coronary heart disease (CHD) remains one of the most pressing problems of modern medicine due to its wide prevalence and high mortality. It is the main cause of death in many countries, including Ukraine, where it accounts for a significant share of the causes of death, as well as among the causes of disability.

The relevance of CHD is due to several factors:

• Widespread: CHD is one of the most common diseases in the world, especially among the adult population.

• High mortality: CHD is the main cause of death in many countries, including Ukraine, where tens of thousands of people die annually from the consequences of this disease.

• Disability: CHD can lead to myocardial infarction, heart failure and other complications that lead to disability of patients.

• Economic burden: Treatment and rehabilitation of patients with CHD require significant financial costs, which creates a significant economic burden on the healthcare system.

• The need for prevention and early diagnosis: Given the high prevalence and consequences of coronary heart disease, it is important to carry out preventive measures and timely diagnosis of the disease, which will improve the prognosis and quality of life of patients.

Thus, coronary heart disease is a pressing problem due to its prevalence, mortality, disability and economic impact on society. It is necessary to continue working to improve the prevention, diagnosis and treatment of this disease.

Purpose: To familiarize HES with the definition, classification of coronary heart disease, heart failure, etiological and pathophysiological factors of coronary heart disease, heart failure, atherosclerosis, principles of classification of drugs for normalizing coronary blood circulation, lipid metabolism disorders, cardiac activity status, principles of choosing mono- and combination pharmacotherapy, methods of monitoring the effectiveness and safety of the proposed therapy, prescribing drugs for the treatment of acute angina pectoris, acute myocardial infarction, acute heart failure.

Basic concepts (list of questions):

Hypoxia - a condition that occurs with a reduced oxygen content in the tissues
Lipidemic agents - drugs that reduce the level of lipids in the blood,
mainly cholesterol and/or triglycerides.
Ischemia - a decrease in blood supply to a body part, organ (heart) or
tissue due to a decrease or weakening of the arterial blood flow.
Ischemic heart disease (IHD) - acute or chronic heart damage,
caused by a decrease or cessation of oxygen and blood delivery to the myocardium due to the atherosclerotic process in the coronary vessels, which leads to a mismatch between coronary blood flow and the myocardial oxygen demand.
Angina - a condition whose symptoms are attacks of sudden pain (angina pain) in the chest due to acute insufficiency of myocardial blood supply - a clinical form of ischemic heart disease.
Acute coronary syndrome is a condition that occurs as a result of impaired coronary circulation due to instability of atherosclerotic plaque with local thrombus formation and changes in vascular reactivity and corresponding clinical symptoms and ECG changes (unstable angina, myocardial infarction).
Myocardial infarction is a form of coronary artery disease that occurs with the development of ischemic necrosis of a myocardial area due to absolute or relative insufficiency of its blood supply.
Antianginal drugs are drugs that increase blood flow to the heart or reduce oxygen demand and are used to treat coronary artery disease (nitrates, beta-blockers, calcium antagonists, sydnonimines).
Cardiotonic drugs are drugs that have a positive isotropic effect on the myocardium (glycoside - cardiac glycosides, non-glycoside - dopamine mimetics).
Antithrombotic drugs are drugs that affect the coagulation system. They are divided into three groups: direct and indirect anticoagulants, fibrinolytics, and antiplatelet agents.

Lecture content (lecture text)

Pharmacotherapy of coronary heart disease and atherosclerosis includes a wide range of drugs aimed at reducing the risk of complications and improving the prognosis. The main groups of drugs: antiplatelet agents, statins, beta-blockers, calcium channel blockers, ACE inhibitors and nitrates.

The main groups of drugs and their effects:

• Antiplatelet agents: Prevent the formation of blood clots by thinning the blood and reducing the risk of thrombosis. Examples: acetylsalicylic acid (e.g. aspirin), clopidogrel.

• Statins: Reduce the level of "bad" cholesterol (LDL) in the blood, which helps reduce atherosclerotic plaques. Examples: simvastatin, atorvastatin.

• Beta-blockers: Reduce the need for myocardial oxygen, slow the heart rate and lower blood pressure. Examples: bisoprolol, metoprolol.

• Calcium channel blockers: Dilate blood vessels, improving blood flow to the heart and lowering blood pressure. Examples: amlodipine, verapamil.

• ACE inhibitors: Lower blood pressure, protect the heart and blood vessels, and slow the progression of atherosclerosis. Examples: enalapril, lisinopril.

• Nitrates: Relieve chest pain (angina), dilate blood vessels, and improve blood flow. Examples: nitroglycerin, isosorbide dinitrate.

Additional drugs:

• Anticoagulants: Widely used to prevent and treat thrombosis, especially in atrial fibrillation and after myocardial infarction. Examples: warfarin, rivaroxaban, dabigatran.

• Diuretics: Used to lower blood pressure and reduce edema, especially in heart failure. Examples: furosemide, hydrochlorothiazide.

• Metabolic drugs: For example, L-carnitine can improve energy metabolism in the heart muscle.

It is important to remember:

• Treatment of coronary heart disease and atherosclerosis should always be comprehensive and include lifestyle changes (quitting smoking, healthy eating, physical activity, weight control).

• The selection of drugs and their dosage should be carried out by a doctor, taking into account the individual characteristics of the patient and the stage of the disease.

• Regular follow-up with a cardiologist and compliance with all doctor's prescriptions is key to achieving the best treatment results.

Ischemic heart disease is damage to the heart muscle, which occurs as a result of an imbalance between the delivery and metabolic need of the heart muscle for oxygen due to atherosclerosis, spasm, thrombosis of the coronary vessels (vessels that supply blood to the heart).

The main cause of narrowing of the lumen in the vessels, which leads to coronary heart disease, is atherosclerosis. Narrowing of the lumen in the vessels usually occurs due to the fact that cholesterol gets into them. It forms atherosclerotic plaques that "stick" to the walls of blood vessels, being a mechanical obstacle to normal blood flow. Plaques become unstable over time - they develop tears and cracks. In this case, the body triggers a protective mechanism, activating platelets, which form blood clots on the surface of the plaque. Risk factors for the development of coronary heart disease are male gender, age (the risk of coronary heart disease increases after the age of 40), hereditary predisposition (the presence of coronary heart disease, hypertension in family members), increased levels of cholesterol, triglycerides, uric acid in the blood, increased blood pressure, excess body weight, smoking, physical inactivity, psychoemotional stress, diabetes, weather dependence. The most common manifestation of coronary heart disease is angina. Angina is an acute attack of pain behind the sternum lasting 5-10 minutes. with irradiation to the left arm, left half of the chest, lower jaw, epigastric region. The pain is pressing or burning, often accompanied by fear of death, as a rule, occurs under the influence of physical or psycho-emotional stress. Men are more often affected after 40-45 years of age. The course of coronary artery disease can be complicated by the development of myocardial infarction, heart failure, rhythm and conduction disorders (blockades), etc.

If a patient is diagnosed with coronary artery disease, it is necessary to begin its treatment as soon as possible. Depending on the manifestations of coronary artery disease, the degree of vascular damage and the localization of pathological changes, the doctor chooses the most

optimal treatment method. The principles of treatment of coronary artery disease are divided into two main groups: therapeutic (with the help of drugs) and surgical methods of correction of the condition of the vessels. Treatment is carried out with the aim of eliminating symptoms and improving the patient's quality of life and to prevent complications. Treatment includes: patient education, lifestyle modification, drug therapy.

The following medications are used:

• beta-blockers (bisoprolol, nebivolol, metoprolol, etc.)

• short-acting nitroglycerin preparations in the form of sublingual tablets and sprays to relieve angina attacks;

• nitrates with a prolonged effect or isosorbide dinitrate (nitrosorbide, cardiket, etc.), preparations containing molsidomine (sydnofarm, advokard, etc.), trimetazidine, ranolazine, ivabradine are used;

• calcium channel blockers (verapamil, diacordin, nifedipine, etc.);

• statins (atorvastatin, rosuvastatin, etc.);

• antiarrhythmic drugs in case of heart rhythm disturbances;

• for the prevention of thrombosis - acetylsalicylic acid in small doses (aspirin-cardio, cardiomagnyl, etc.) or clopidogrel (Plavix, Agrel, etc.).

Taking these drugs helps to improve the blood supply to the heart muscle and the patient's quality of life, and his speedy return to everyday life. If vascular damage reaches critical stages, more radical treatment methods are used. In particular, these include: transmyocardial laser revascularization of the myocardium; percutaneous coronary interventional procedures (artery stenting, coronary artery bypass grafting, balloon angioplasty).

Questions for self-control on the topic:

1. Name the clinical and pharmacological criteria for choosing hypolipidemic agents.
2. What principles are the basis for the classification of hypolipidemic agents?
3. Bile acid sequestrants, their mechanism of action and adverse effects (cholestyramine, colestipol).
4. Principles of treatment of hyperlipidemia with niacin.
5. Statins - mechanism of action and application.
6. Comparative characteristics of fibrates.
7. List the clinical and pharmacological principles of selection and selection of drugs for coronary insufficiency.
4. What principles are the basis for the classification of antianginal drugs?
5. Explain the antianginal effect of nitrates, approaches to choosing a single dose and frequency of taking the drug.
6. Name the undesirable effects of nitrates and therapeutic measures when they occur.
7. Explain the antianginal effect of beta-blockers, approaches to choosing a single dose and frequency of taking the drug.
8. Explain the antianginal effect of slow calcium channel blockers, approaches to choosing a single dose and frequency of drug administration.
9. Explain the antithrombotic effect of anticoagulants, approaches to choosing a single dose and frequency of drug administration.
10. Explain the antithrombotic effect of antiplatelet agents, approaches to choosing a single dose and frequency of drug administration.

11. Explain the antithrombotic effect of antiplatelet agents, approaches to choosing a single dose and frequency of drug administration.
12. Principles of treatment of angina pectoris, acute myocardial infarction, acute heart failure.

List of sources on the topic:

1. Clinical pharmacology / Ed. Prof. M.I. Yabluchansky, Prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Ed. O.M.Bilovola. – Vinnytsia: Nova Kniga, 2021. – 544 p.
3. Clinical Pharmacy (Pharmaceutical Care): A Textbook for Students of Higher Medical (Pharmaceutical) Schools / I.A.Zupanets, V.P.Chernykh, T.S.Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: A Textbook for Students of Pharmaceutical Faculties / Ed. V.P.Chernykh, I.A.Zupanets, I.G.Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Modern Classifications and Standards of Treatment of Diseases of Internal Organs. Emergency Conditions in Therapy. Analyzes: Normative Indicators, Interpretation of Changes / Ed. Prof. Yu.M.Mostovoy. – 25th ed., amended and supplemented – Kyiv: Center of State Library, 2018. – 792 p.

LECTURE 5. TOPIC
"Principles of clinical and pharmaceutical approach to drug selection in rheumatological practice. Pain: pathophysiological aspects of pharmacotherapy"

Relevance of the topic: Joint diseases are a pressing problem in modern society, as they significantly affect the quality of life, leading to pain, limited mobility and loss of work capacity. The incidence of these diseases is increasing, especially among the elderly, but also among young people, which is associated with certain lifestyle factors.

Here are some key aspects of the relevance of joint diseases:

• Prevalence: Joint diseases, such as arthritis, arthrosis, osteochondrosis, are among the most common diseases in the world.
• Impact on quality of life: Pain, stiffness, limited mobility that accompany these diseases significantly worsen daily activities and overall health.
• Loss of work capacity and disability: In some cases, joint diseases can lead to loss of work capacity and disability, which creates social and economic consequences.
• Increasing incidence in young people: Joint diseases are increasingly occurring at a young age, which may be associated with certain lifestyle factors, such as sedentary work, insufficient physical activity, overweight, and poor nutrition.
• The need for early diagnosis and treatment: Early diagnosis and treatment of joint diseases help prevent disease progression and preserve joint function for as long as possible.
• Development of new treatment methods: Due to the relevance of joint diseases, new treatment methods are being actively developed, including kinesitherapy, drug therapy, surgical interventions, and others.

In view of the above, joint diseases are a serious problem that requires attention from society, the health care system, and each individual. Prevention, early diagnosis, and effective treatment are key factors in the fight against these diseases.

Purpose: To familiarize students with the pathophysiological aspects of the inflammatory process, stages, symptoms of the inflammatory process, biochemical changes that occur in inflammatory diseases of the joints and connective tissue, with the main approaches to the treatment of specific and nonspecific inflammatory diseases; to familiarize students with the concept of pain, types and classification of pain syndrome; to familiarize students with the clinical and pharmacological characteristics of anti-inflammatory and analgesic drugs.

Basic concepts (list of questions):

Inflammation is a typical pathological process, a complex protective reaction of the body to the action of harmful agents, which has developed over a long period of evolution and is a complex of tissue and vascular changes. This is one of the processes that underlies many diseases, different in nature. The biological significance of inflammation is to prevent the spread of pathogenic agents in the body, sometimes the inflammatory process contributes to their destruction. This is a local adaptive reaction of the body in response to damage. This cyclical reaction is completed by the elimination of the pathogenic cause, tissue regeneration and restoration of organ function. This is a complex local vascular-mesenchymal reaction to tissue damage caused by the actions of various agents. This reaction is aimed at destroying the agent that caused the damage and restoring the damaged tissue.

Pain is a kind of sensation that occurs as a result of strong irritation of the nervous system. It is a symptom of many diseases. Pain irritations are perceived by peripheral nerve receptors and transmitted along nerve conductors to the brain. Pain is a protective reaction of the body that arose in the process. Sometimes pain is the first sign of a disease or a signal of danger that threatens the body from the environment. In this regard, pain plays a positive role. But with excessive intensity and duration, pain turns into a painful phenomenon. This is due to the fact that prolonged strong irritation of peripheral receptors that perceive pain is accompanied by a constant flow of pain impulses to the corresponding brain centers. As a result, their activity is disrupted, which affects the work of many body systems.

Prostaglandins are biologically active substances that belong to unsaturated fatty acids; they are produced in many organs, participate in metabolic processes, realize the occurrence of inflammation and the effect of anti-inflammatory drugs.

Anti-inflammatory drugs are drugs used to treat the inflammatory process (non-steroidal, steroid, basic drugs).

Analgesia is a weakening of pain sensitivity due to pharmacological or other effects, which, as a rule, does not lead to the suppression of other types of sensitivity.

Analgesic drugs are drugs that reduce or eliminate pain; Narcotic drugs (morphine, fentanyl, promedol, omnopon) and non-narcotic drugs (ketanov, analgin, dexalgin) are distinguished.

Lecture content (lecture text)

Pharmacotherapy of joint and connective tissue diseases covers a wide range of drugs aimed at reducing pain, inflammation and slowing the progression of the disease. The main groups of drugs are nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, modifying drugs (disease-modifying antirheumatic drugs, or DMARDs) and biological agents.

Main groups of drugs:

• Nonsteroidal anti-inflammatory drugs (NSAIDs): The most common group of drugs for relieving pain and reducing inflammation. These include, for example, ibuprofen, diclofenac, naproxen.

• Glucocorticoids: Powerful anti-inflammatory drugs that can be used both orally and locally (intra-articularly). They can have serious side effects with prolonged use.

• Disease-modifying antirheumatic drugs (DMARDs): These drugs affect the immune system and help slow the progression of the disease, especially in autoimmune diseases such as rheumatoid arthritis. Examples include methotrexate, sulfasalazine, leflunomide.

• Biologic agents: Block certain parts of the immune response, which leads to a decrease

in inflammation. Used for rheumatoid arthritis and other autoimmune diseases. Examples include tumor necrosis factor (TNF) inhibitors.

Additional drugs:

• Pain relievers (analgesics): To relieve pain, especially in acute pain.

• Cartilage protectors (chondroprotectors): Recommended for osteoarthritis to support cartilage, although their effectiveness is still being studied.

• Topical drugs: Creams and ointments with NSAIDs or capsaicin for topical application to reduce pain and inflammation in the joints.

It is important to remember:

• Treatment of diseases of the joints and connective tissue should be comprehensive and individual, taking into account the type of disease, stage, presence of concomitant diseases and the general condition of the patient.

• Self-medication can be dangerous. Consult a doctor for advice and appointment of appropriate treatment.

• Regular exercise recommended by a doctor, as well as a healthy lifestyle, proper nutrition and maintaining a healthy weight are important components of treatment and prevention.

Diseases requiring pharmacotherapy:

• Rheumatoid arthritis: A chronic autoimmune disease that affects the joints and other organs.

• Osteoarthritis: A degenerative disease of the joints characterized by the destruction of cartilage.

• Systemic connective tissue diseases: A group of diseases that include lupus, scleroderma, dermatomyositis and others.

• Gout: Caused by excessive accumulation of uric acid in the joints.

• Ankylosing spondylitis: A disease that affects the spine and joints.

Questions for self-control on the topic:

1. Explain the classification of NSAIDs by chemical structure.
2. Describe the classification of modern NSAIDs taking into account the pharmacodynamic effect, the degree of its severity.
3. List the pharmacodynamic effects of NSAIDs and explain their clinical significance.
4. Explain the process of formation and functional purpose of prostaglandins.
5. Explain the mechanism of anti-inflammatory action of NSAIDs.
6. Explain the mechanism of antipyretic action of NSAIDs.
7. Describe the mechanism of analgesic effect of NSAIDs and compare it with the mechanism of action of narcotic analgesics.
8. Explain the mechanism of irritating action of NSAIDs on the mucous membranes of the stomach and intestines. Indicate drugs that prevent negative effects.
9. Explain the antithromboaggregation mechanism of NSAIDs and its clinical significance.
10. What is the general mechanism of action that unites Movalis, Mesulide, Celebrex? In what concomitant pathology is their use preferable?
11. Arrange NSAIDs according to the strength of anti-inflammatory action.
12. State the criteria for assessing the effectiveness of NSAIDs in patients with rheumatoid arthritis.
13. List the methods and criteria for determining the safety of NSAIDs treatment.
14. Modern classification of corticosteroids.
15. Basic principles of hormonal anti-inflammatory therapy.
16. Explain the mechanisms of the anti-inflammatory action of corticosteroids.
17. Explain the mechanisms of the effect of corticosteroids on carbohydrate metabolism and indicate what indications and contraindications may be in this regard.

18. Explain the mechanisms of water-electrolyte metabolism disorders that occur against the background of the use of corticosteroids and the complications associated with them, indications and contraindications to their use.

19. Explain the mechanisms and measures for the prevention of hormone resistance, tolerance and "withdrawal syndrome".

20. Explain the tactics of use and dosing regimen of GCS in conditions of asthmatic status. In what conditions is pulse therapy of GCS indicated.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M. Bilovol. – Vinnytsia: Nova Kniga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: a textbook for students of pharmaceutical faculties / Edited by V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Pharmacist's Protocols / Edited by V.P. Chernykh, I.A. Zupanets, O.M. Lischyshyna. – Kharkiv: Golden Pages, 2013. – 192 p.
6. Modern classifications and standards for the treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Edited by prof. Yu.M. Mostovy. – 25th ed., changes and additions. – Kyiv: Center of State Library, 2018. – 792 p.

LECTURE 6. TOPIC
"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of digestive diseases (ulcer disease, GERD, intestinal diseases)"

Relevance of the topic: Gastrointestinal tract (GIT) diseases are a very relevant problem in the modern world, as they occupy one of the leading places among the most common diseases. These diseases affect various organs of the GIT, including the stomach, intestines and can significantly affect the quality of life of people.

Reasons why GIT diseases are relevant:

• Prevalence: GIT diseases occur in people of all ages and social groups, and their prevalence is constantly increasing.

• Impact on quality of life: Symptoms of GIT diseases, such as abdominal pain, discomfort, indigestion, can significantly worsen a person's general condition and reduce their working capacity.

• Risk of complications: Untreated GIT diseases can lead to serious complications, such as ulcers, bleeding, inflammation and even cancer.

• Impact on other organs and systems: GIT diseases can affect the functioning of other organs and systems, such as the cardiovascular, endocrine and nervous systems.

• The need for a comprehensive approach to treatment: Effective treatment of gastrointestinal diseases requires a comprehensive approach, including diagnostics, treatment, nutritional correction and psychological support.

Given these factors, it can be concluded that gastrointestinal diseases remain a pressing problem that requires attention from medical professionals and society as a whole.

Purpose: To familiarize HES with the definition, classification of acid-dependent, inflammatory diseases of the gastrointestinal tract, etiological and pathophysiological factors of nosoforms, principles of classification of drugs for normalizing the production and level of gastric juice, motor function of the gastrointestinal tract, protective mechanisms of gastroprotection, principles of choosing mono- and combination pharmacotherapy, methods of monitoring the effectiveness and safety of the proposed therapy, prescribing drugs for the treatment of acute complications of gastrointestinal diseases.

Basic concepts (list of questions):

Acid-dependent diseases are a group of various diseases in the pathogenesis of which hypersecretion of acid in the stomach plays a decisive role (ulcer disease, gastritis, gastroesophageal reflux disease, etc.).

Gastroesophageal reflux disease (GERD) is a disease that is primarily associated with impaired motor function of the esophagus, weakening of the antireflux barrier of the lower esophageal clearance and slowing of gastric emptying, prolonged contact between the esophageal mucosa and acidic gastric contents.

Gastritis is an acute and chronic clinical condition characterized by an inflammatory process of the gastric mucosa of various origins.

Colitis is an inflammatory disease of the mucous membrane of the large intestine of various etiologies.

Enteritis is an inflammatory disease of the mucous membrane of the small intestine of various etiologies.

Peptic ulcer disease is a general name for a disease characterized by the formation of ulcers in the wall of the stomach or duodenum.

Nonspecific ulcerative colitis is a chronic autoimmune inflammatory disease of the colon and rectum with damage to the mucous membrane and submucosal layer of the intestine and the formation of ulcers.

Non-systemic antacids are drugs that reduce the acidity of gastric contents by neutralizing hydrochloric acid, are insoluble in water, are not absorbed in the gastrointestinal tract, do not cause changes in acid-base balance (almagel, phosphalugel, maalox, etc.).

Systemic antacids are drugs that quickly neutralize hydrochloric acid, are well soluble in water, are quickly absorbed, and with frequent use lead to the development of metabolic acidosis (sodium bicarbonate).

Gastroprotectors – drugs that protect the gastric mucosa from the damaging effects of pepsin and hydrochloric acid (sucralfate, colloidal bismuth). Acid-reducing drugs – drugs that, due to a certain mechanism of action, suppress the secretion of hydrochloric acid in the stomach (proton pump inhibitors, blockers of histamine type II receptors, M-cholinoblockers).

Lecture content (lecture text)

Pharmacotherapy of gastrointestinal (GI) diseases includes a wide range of drugs aimed at treating and alleviating the symptoms of various diseases of the digestive system.

Main groups of drugs and their use:

• To reduce the acidity of gastric juice:

Proton pump inhibitors (e.g., omeprazole), antacids (e.g., Almagel).

• To protect the gastric mucosa:

Bismuth preparations, histamine H2-receptor blockers.

• To treat heartburn and gastroesophageal reflux disease (GERD):

Proton pump inhibitors, antacids, prokinetics (e.g., domperidone).

• To treat diarrhea:

Loperamide, adsorbents (e.g., activated charcoal).

• To treat constipation:

Laxatives (e.g., bisacodyl, macrogol), osmotic laxatives.

• For the treatment of irritable bowel syndrome (IBS):

Antispasmodics, drugs to normalize intestinal microflora (probiotics), drugs that regulate intestinal motility.

• For the treatment of liver and biliary tract diseases:

Hepatoprotectors, choleretic drugs.

• For the treatment of pancreatitis:

Enzyme drugs (for example, pancreatin).

• For the treatment of infectious diseases of the gastrointestinal tract:

Antibiotics, antiviral drugs.

Important to remember:

• Self-treatment of gastrointestinal diseases can be dangerous. Before using any drugs, you should consult a doctor.

• For effective treatment, it is important not only to take medications, but also to follow a diet, nutrition regimen and lead a healthy lifestyle.

• Drugs for the gastrointestinal tract can have side effects, so it is important to carefully read the instructions and follow the doctor's recommendations.

Examples of commonly used medications: Activated charcoal (to treat diarrhea and flatulence), Loperamide (to stop diarrhea), Omeprazole (to reduce gastric acidity), No-shpa (to relieve spasms), Pancreatin (to improve digestion in pancreatitis).

Questions for self-control on the topic:

1. Classification of drugs used to treat peptic ulcer disease and hyperacid gastritis.
2. The role of risk factors in the pathogenesis of acid-dependent diseases.
3. Etiology and microbiology of inflammatory diseases of the gastrointestinal tract.
4. Antacids: classification, clinical and pharmacological aspects.
5. Antisecretory drugs: principles of classification.
6. M-cholinoblockers: classification, clinical and pharmacological features.
7. Drugs that block histamine H2 receptors: classification, clinical and pharmacological features.
8. Proton pump inhibitors: clinical and pharmacological features.
9. Gastrocytoprotectors:

A) Drugs that create mechanical protection of the mucous membrane (sucralfate (Venter); colloidal bismuth: de-nol);

B) Drugs that increase the protective function of the mucous barrier and the resistance of the mucous membrane to the action of damaging factors (prostaglandins and their synthetic derivatives: misoprostone (cytotec, cytotec).

10. Methods of research of gastroesophageal reflux disease, peptic ulcer disease, gastritis
11. Principles of combined therapy of peptic ulcer disease, gastroesophageal reflux disease, chronic gastritis.
12. Principles of etiotropic pharmacotherapy of chronic gastritis, enterocolitis, peptic ulcer disease.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacy (pharmaceutical care): a textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
3. Clinical Pharmacy: a textbook for students of pharmaceutical faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

4. Clinical Pharmacology: a textbook / Ed. O.M. Bilovol. – Vinnytsia: Nova Kniga, 2021. – 544 p.
5. Modern classifications and standards for the treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Ed. Prof. Yu.M. Mostovoy. – 25th ed., changes and additions. – Kyiv: Center of State Clinical Research, 2018. – 792 p.

LECTURE 7. TOPIC
"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of diseases of the hepatobiliary system"

Relevance of the topic: Liver and gallbladder diseases are a pressing problem of modern medicine, as they can lead to serious health consequences. The relevance of these diseases is due to their wide distribution, variety of causes and the possibility of transition to chronic forms.

Relevance of liver diseases:

• Prevalence: Liver diseases, such as viral hepatitis (A, B, C, D, E) and non-alcoholic fatty liver disease (NAFLD), are quite common worldwide.
• Dangerous consequences: Untreated liver diseases can lead to cirrhosis, liver cancer and liver failure.
• Increasing incidence of NAFLD: The prevalence of NAFLD is increasing due to the epidemic of obesity and metabolic syndrome.
• Impact on quality of life: Liver diseases affect the general health, work capacity and quality of life of patients.

Current Status of Gallbladder Disease:

• Gallstones: Gallstones are one of the most common gallbladder diseases.
• Complications: Gallstones can cause inflammation (cholecystitis), blockage of the bile ducts, and pancreatitis.

• Prevalence in Women: Gallbladder disease, including gallstones, is more common in women, especially those over the age of 45.
• Symptoms and Diagnosis: Early diagnosis and treatment of gallbladder disease is important to prevent complications.

Liver-Gallbladder Relationship:

The liver and gallbladder are closely linked. The liver produces bile, which is stored in the gallbladder and then enters the intestines to digest fats. Disturbances in the work of one of these organs can affect the functioning of the other, which often manifests itself in the form of pain in the right hypochondrium, nausea, digestive disorders and other symptoms. Liver and gallbladder diseases are an urgent problem that requires attention from medical professionals and patients. Timely diagnosis, treatment and prevention of these diseases contribute to maintaining health and improving the quality of life.

Purpose: To familiarize the HES with the definition, classification of inflammatory, dysmetabolic diseases of the organs of the hepatobiliary system, etiological and pathophysiological factors of nosoforms, principles of classification of drugs for normalizing bile production, liver function, motor function of the hepatobiliary system, protective mechanisms of hepatoprotection, principles of choosing mono- and combination pharmacotherapy, methods of monitoring the effectiveness and safety of the proposed therapy, prescribing drugs for the treatment of hepatic colic.

Basic concepts (list of questions):

Hepatitis – inflammatory liver diseases of various etiologies.
Hepatoses – liver diseases, which are based on metabolic disorders in hepatocytes and the development of dystrophic changes in liver cells (diabetes mellitus, alcoholism).
Pancreatitis – inflammatory diseases of the pancreas.
Cholecystitis – acute and chronic inflammatory diseases of the gallbladder.
Hepatoprotectors – drugs, which, as a result of studies, have been shown to have a positive effect on liver function, the ability to protect the liver parenchyma from any damage and diseases.
Colic – an attack of sharp pain in diseases of the abdominal cavity.
Hepatic colic – colic localized in the right hypochondrium, which is observed in cholelithiasis and cholecystitis.
Cholekinetics are antispasmodic drugs that relax the sphincter of the hepatopancreatic ampulla and promote the excretion of bile into the intestines (atropine, papaverine, etc.).
Choleretics are drugs that increase the formation of bile in the liver (allohol, holosas, etc.).
Cholestasis is a violation of the movement of bile in the form of stagnation in the bile ducts.

Lecture content (lecture text)

Pharmacotherapy of liver diseases includes a wide range of drugs aimed at protecting, restoring and improving liver function. These include hepatoprotectors, choleretic, anti-inflammatory, antiviral and antiparasitic drugs, as well as drugs that affect bile acid metabolism.

The main groups of drugs for the treatment of liver diseases:

- Hepatoprotectors:
- These drugs protect liver cells from damage, improve their function and promote regeneration. These include, for example, Essentiale Forte, Carsil, Heptral.
- • Choleretics:

- These drugs stimulate the formation and secretion of bile, which improves digestion and prevents bile stagnation. Among them are:
- • Choleretics: increase bile production, for example, Allochol, Hofitol.
- • Cholekinetics: improve bile outflow, for example, Magnesium sulfate.
- Anti-inflammatory:
- Used to reduce inflammation in the liver caused by various causes.
- Antiviral:
- Used to treat viral hepatitis, such as hepatitis C.
- Antiparasitic:
- Used to treat parasitic liver infections.
- Drugs for the treatment of cholestasis:
- Help dissolve gallstones and improve bile flow, such as Ursosan, Ursofalk.
- Drugs that affect bile acid metabolism:
- For example, Ursodeoxycholic acid (Ursosan), which helps improve the composition of bile and reduce its toxicity.
- Examples of drugs often used to treat the liver:
- • Hepatoprotectors:
- Essentiale forte N, Karsil, Heptral, Antral, Argitec, Heparizin, Silibor forte, Legalon.
- • Choleretics:
- Allohol, Hofitol, Galstena, Artihol, Holosas, Bonzhigar.
- • Others:
- Glutargin, Betargin, Ursosan, Ursohol, Essliver Forte, Thiotriazolin, Rafaholin Ts.
- It is important to remember:
- • Self-treatment of liver diseases can be dangerous. Before starting any medication, you should consult a doctor.
- • The choice of a specific drug depends on the type and stage of the disease, as well as the individual characteristics of the patient.
- • The treatment of liver diseases often requires an integrated approach, including diet, lifestyle changes and medication.

One of the most commonly used drugs for the treatment of liver diseases are **hepatoprotectors.** Despite the fact that the term "hepatoprotectors" is not used in most countries of the world, they are widely used in the treatment of patients with liver pathology. What drugs can be classified as hepatoprotectors? First of all, these are substances whose action is aimed at normalizing metabolism, increasing resistance to the action of pathogenic factors, normalizing functional activity and stimulating reparative and regenerative processes in the liver. There is no single classification of hepatoprotectors, therefore they are divided depending on their origin: hepatoprotectors of plant and animal origin, essential phospholipids, amino acids, vitamins and vitamin-like substances, antioxidants, combined agents.

• Hepatoprotectors of plant origin. The most numerous group of drugs of plant origin, which make up more than half of all hepatoprotectors available on the pharmaceutical market. Among plant hepatoprotectors, milk thistle preparations are the best studied. The hepatoprotective effect of drugs of this group is due to the antioxidant and antitoxic properties of silibinin. The main mechanism of action of phenolic compounds of plant hepatoprotectors is the ability to enter into reversible redox reactions in the body. Bioflavonoids also exhibit a capillary-stabilizing effect, stimulate the synthesis processes in the adrenal glands of glucocorticoids, stabilize cell membranes and increase their resistance and barrier function. Phenolic compounds of plants entering the body activate detoxification processes in the liver, increase the activity of a number of enzymes involved in the biotransformation of xenobiotics. The hepatoprotective effect of milk thistle preparations also consists in the stimulation of RNA polymerase of hepatocytes, which accelerates transcription and synthesis of rRNA, an increase in the number of

ribosomes, which contributes to the increase in the synthesis of structural and functional proteins, phospholipids, and the permeability of cell membranes decreases.

• One of the well-studied phytomediators used as a hepatoprotector is the artichoke. The flesh of the artichoke is also rich in inulin, which has a positive effect on carbohydrate and lipid metabolism. Due to the content of carotenoids, ascorbic acid, and bioflavonoids, artichoke preparations exhibit antioxidant properties. The diuretic effect of artichoke preparations has also been proven.

• The pharmaceutical market presents combined herbal preparations, but caution should be exercised in using hepatoprotectors of plant origin containing extracts of unknown, little-studied, non-pharmacopoeial plants.

• Phospholipid preparations have taken a significant place in the treatment of many human diseases, especially in the therapy of liver diseases. Phospholipids are part of the cell membranes of all organs and tissues. The development of any disease is accompanied by damage to the cell, primarily its membranes. From this point of view, interest in phospholipid preparations is significantly expanding and is limited not only to use in liver pathology, but also in disorders of lipid metabolism, diseases of many organs and systems. Phospholipids of food products, biologically active additives and preparations of essential phospholipids in the small intestine are exposed to the action of phospholipases of pancreatic juice - phospholipases A and B and are split into components - fatty acids, phosphorus, choline, serine, etc. After resynthesis in the wall of the small intestine, phospholipids enter the lymphatic vessels as part of chylomicrons, then through the thoracic lymphatic duct into the general bloodstream. In the human body, there are phospholipids that are inherent to the person, and in the organs - phospholipids that have the tissue specificity of the given organ. Enzymes responsible for the synthesis of phospholipids are located in the endoplasmic reticulum. Lipid vesicles from the endoplasmic reticulum move to the Golgi apparatus. Thus, phospholipids synthesized inside the cell are incorporated into the plasma membrane. One of the most important components of phosphatidylcholine is choline. In liver diseases, the need for choline and phospholipids is increased, so it is advisable to use essential phospholipid preparations.

• The average dose of essential phospholipid preparations should be at least 2 capsules 3 times a day during or immediately after meals for 2–5 months. The dose and duration of taking essential phospholipid preparations can be increased if necessary.

• Special attention should be paid to amino acid preparations when prescribing them as hepatoprotectors. Amino acids compete for absorption and with increased use of one amino acid, the absorption of others may be impaired and an amino acid imbalance may occur. The amino acid formula of each protein is genetically determined, and protein recovery will depend on the amount of the amino acid whose content is the lowest. An additional increase in any amino acid will increase the load on the liver and kidneys, which are involved in the processes of metabolism and excretion of unused amino acids.

• Special attention should be paid to amino acid preparations when prescribing them as hepatoprotectors. Amino acids compete for absorption and with increased use of one amino acid, the absorption of others may be impaired and an amino acid imbalance may occur. The amino acid formula of each protein is genetically determined, and protein recovery will depend on the amount of the amino acid whose content is the lowest. An additional increase in any amino acid will increase the load on the liver and kidneys, which are involved in the processes of metabolism and excretion of unused amino acids. Special attention is required by patients who have certain changes in the psycho-emotional sphere. This is due to the fact that amino acids are

sources of neurotransmitter synthesis. In some patients, when using amino acid preparations, the psycho-emotional state will improve, in others, on the contrary, it will worsen. The reaction of the central nervous system (CNS) will depend not only on the characteristics of the metabolic processes of the brain, but also on the presence of other components - vitamins and minerals, which are cofactors of amino acid metabolism in the nervous system. An example is the action of the amino acid glutamine, which is the main excitatory neurotransmitter of the CNS, and its excessive intake can cause increased nervousness and excitement. Glutamine is also a source for the synthesis of the main inhibitory neurotransmitter of the CNS, gamma-aminobutyric acid (GABA). The conversion of glutamine into GABA occurs in the presence of vitamin B6. With a deficiency of vitamin B6, glutamic acid - an excitatory mediator - is not converted into GABA, which leads to the accumulation of glutamine in the brain. Insufficient synthesis of GABA can cause mental stress, insomnia, depression, panic attacks, anxiety, tremors, and rapid heartbeat. These features should be taken into account when prescribing drugs containing the amino acid glutamine.

• Among the amino acids traditionally used in the treatment of liver diseases, a significant place is occupied by the amino acid methionine and the active form of methionine ademethionine (S-adenosyl-L-methionine). Ademethionine participates in three types of biochemical reactions: transmethylation, transsulfuration and synthesis of polyamines. Thanks to the above reactions, methionine participates in the synthesis of phospholipids, glutathione, polyamines, and serves as a precursor of such important substances as cysteine, taurine, coenzyme A. Thus, the therapeutic effect of ademethionine is due to the influence of a large number of biologically active substances that positively affect numerous processes in the liver, nervous system, connective tissue, etc. S-adenosylmethionine is the main biological donor of methyl radicals, synthesized from methionine, ATP in a reaction catalyzed by methionine-adenosyltransferase. DNA methylation reactions are regulated primarily by enzymes and intermediates that constitute the so-called one-carbon metabolism. This is a complex biochemical pathway (also known as the homocysteine cycle), regulated by the presence of B vitamins (folic acid, B6, B12) and choline. Elevated homocysteine levels in the blood are associated with increased development of atherosclerosis, thrombovascular complications, degenerative diseases.

• Adenosylmethionine has a positive effect on the liver due to its ability to be converted to choline and participate in the synthesis of phosphatidylcholine and glutathione. Choline is also a source of synthesis of acetylcholine, an important neurotransmitter of the synapses of the nervous system. Adenosylmethionine exhibits antidepressant properties in depression characterized by high histamine levels (histadelia), but it is contraindicated in depression and schizophrenia characterized by low histamine levels (histapenia). Ademetionine should be avoided in patients with congenital folate cycle disorders and hyperhomocysteinemia.

• The amino acid methionine is neurotoxic in excessive amounts. Ademetionine enhances the formation of methanol, formaldehyde, and formic acid. These substances, especially formaldehyde, can damage neurons in conditions of excessive methylation. Elevated methionine levels occur in patients with some forms of schizophrenia. In the intestine, methionine is a precursor of toxic metabolites — methyl mercaptan, methionine sulfoxide, which in patients with portosystemic encephalopathy negatively affect the brain.

• The most significant positive effect on the functional state of the liver and central nervous system is exerted by adenosylmethionine in patients with alcoholic liver disease. This group of patients has nutritional deficiencies, including deficiencies of methionine, choline, glutathione, and taurine. The amino acid taurine, which is synthesized from S-

adenosylmethionine, is the main amino acid in the processes of bile acid conjugation, which positively affects the processes of bile secretion and reduces the manifestations of cholestasis.

• Ursodeoxycholic acid. Ursodeoxycholic acid (UDCA) is a substance belonging to the group of hydrophilic bile acids with pronounced anticholestatic properties. The mechanisms of action of UDCA are due to the choleretic effect due to the displacement of the pool of toxic hydrophobic bile acids due to competitive capture by bile acid receptors in the ileum. As has recently been established, the cytoprotective effect on biliary epithelial cells is realized by preventing the release of cytochrome C from mitochondria, which, in turn, blocks the activation of caspases and apoptosis of cholangiocytes. UDCA reduces the saturation of bile with cholesterol by inhibiting its absorption in the intestine, reducing its synthesis in the liver and secretion into bile; increases cholesterol solubility; reduces the lithogenic index of bile.

• In primary biliary cirrhosis, UDCA is the drug of choice. The drug is pathogenetically justified for diseases accompanied by intrahepatic cholestasis: primary sclerosing cholangitis, chronic hepatitis with a cholestatic component (especially alcoholic and drug-induced), cystic fibrosis, biliary atresia, post-transplant and parenteral nutrition cholestasis. In addition, UDCA is used to dissolve cholesterol gallstones and biliary reflux gastritis. It should also be remembered that UDCA is a free acid, and entering the liver, it is transformed and conjugated. About 70% of UDCA binds to taurine in the liver, and the rest to glycine. Conjugated bile acids, unlike free ones, do not have a hepatotoxic effect. This mechanism should be taken into account in the absence of effect when using UDCA drugs. It is advisable to combine UDCA with S-adenosylmethionine or additionally use the amino acid taurine. A reduced level of taurine can be expected in patients who consume an insufficient amount of animal protein with food. The combination of UDCA with S-adenosylmethionine is the most optimal in the treatment of patients with liver diseases accompanied by intrahepatic cholestasis.

• Hepatoprotectors of organ (animal) origin. This group includes drugs that are obtained from animal liver as a result of sublimation and drying. Getting into the human body, the liver cell of cattle disintegrates in the gastrointestinal tract, and growth factors and amino acids, getting into the liver, act as regeneration stimulators. This effect was registered during the study of short-chain fatty acids and is explained by the action of growth factors and amino acids and other biologically active components that are rich in liver tissue and which these drugs contain. The effective effect of organ preparations is noted in patients with various liver pathologies. In cirrhosis, long courses of therapy are recommended - up to 12 months. At the same time, a decrease in the phenomena of encephalopathy is noted. In preparations containing liver extracts, there is a small amount of amino acids, but they are balanced.

• Complex hepatoprotectors. The creation of complex hepatoprotectors has its advantages, since they include several components that potentiate the effects of each other, which can give a more significant effect compared to the use of a single preparation. The most famous complex hepatoprotectors include the preparations Gepadif®, Gepamerz, etc.

• The therapeutic efficacy of the drug Gepadif® is due to the physiologically active substances of metabolic action that are part of the drug: carnitine orotate, carnitine hydrochloride, antitoxic fraction of liver extract, as well as vitamins of group B (B2, B6, B12). Carnitine — acts as a carrier of fatty acid complexes with coenzyme A (acyl-CoA) through the mitochondrial membrane. Fatty infiltration of the liver is the most frequent morphological sign in hepatitis of various genesis. The presence of a large number of free fatty acids in the hepatocyte cytosol leads to an increase in the processes of free radical oxidation of lipids with the formation of free radicals and reactive oxygen species, which, regardless of the cause of hepatitis (viruses, alcohol, drugs, etc.), lead to damage to all biological compounds with the

formation of a large number of toxic aldehydes, ketones, alcohols, isoprostanes, isoleukotrienes, etc. They are able to interact with nitrogenous bases of DNA, enzymes of its replication and repair, cause mutations and increase the risk of tumor development. DNA helix strand breakage and cell death are also possible. The development of hepatic steatosis is associated with carnitine deficiency, which leads to mitochondrial dysfunction. The presence of carnitine in the composition of the drug Gepadif® helps to improve energy metabolism, reduces fatty infiltration of the liver. Gepadif® can be recognized as the drug of choice in the treatment of patients with hepatic steatosis and steatohepatitis. Indications for the use of the drug Gepadif® are steatosis and steatohepatitis in patients with metabolic syndrome, type 1 and type 2 diabetes, obesity, atherogenic dyslipidemia, as well as in cases of carnitine deficiency.

• The antitoxic fraction of the liver extract contains essential and non-essential amino acids in a balanced amount, growth factors, which promotes the regeneration of liver cells. Riboflavin (vitamin B2), which is part of the Gepadif® preparation, is an active group of flavone enzymes that regulate redox processes in liver cells, contributing to the normal metabolism of protein, carbohydrate, and fat. Pyridoxine (vitamin B6) is involved in the metabolism of amino acids (especially tryptophan), the synthesis of glutamic acid, which regulates the function of the liver and nervous system. Vitamin B6 exhibits detoxification properties, is considered an antidote to some substances, such as isoniazid. Cyanocobalamin (vitamin B12) and vitamin B6 reduce fatty infiltration of the liver, reduce hyperhomocysteinemia.

• Adenine is a purine derivative that is part of nucleic acids, participates in the processes of protein synthesis and tissue regeneration. Adenosine is a nucleoside containing adenine and ribose, is a component of many enzymes, ATP and nucleic acids, participates in the formation of macroergic compounds (ATP, ADP, cAMP), protein synthesis, exhibits anti-inflammatory effects and is an inhibitory neurotransmitter.

• The effectiveness of treatment of patients with liver diseases primarily depends on the elimination of etiological factors - this is effective treatment of viral hepatitis, alcohol abstinence, reduction of toxic effects of drugs and environmental factors, correction of the state of the immune system, intestines, rational full-fledged nutrition, normalization of body weight. It is also advisable to use hepatoprotectors in the treatment, which are important means of correcting metabolic disorders, increasing the state of the antioxidant system, improving energy processes in hepatocytes. When choosing a hepatoprotector, one should take into account not only the characteristics of the course and stage of liver disease, but also the presence of concomitant pathology, and the features of the action of a particular drug.

Questions for self-control on the topic:

1. Hepatoprotectors: classification.
2. Preparations containing natural or semi-synthetic flavonoids of milk thistle: hepabene, legalon, karsil, hepatofalk-planta, silibor.
3. Preparations containing natural or semi-synthetic flavonoids of other plants: hofitol, LIV-52 (hepaliv).
4. Preparations containing essential phospholipids: essentiale.
5. Amino acid preparations: ademetionine (heptral), lipoic acid (thioctacid), hepa-merz (ornithine).
6. Mechanisms of action of various hepatoprotectors
7. Research methods in chronic hepatitis, cirrhosis of the liver, hepatoses.
8. Etiology, pathogenesis, clinic, chronic hepatitis, cirrhosis of the liver.
9. Hepatoses: etiopathogenesis, clinic.
10. Principles of combination therapy.
11. What processes do you expect to improve when using enzyme drugs?
12. What are the features of the pharmacodynamics of enzyme inhibitors?

List of sources on the topic:

1. Clinical pharmacology / Ed. Prof. M.I. Yabluchansky, Prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacy (pharmaceutical care): a textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
3. Clinical pharmacy: a textbook for students of pharmaceutical faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
4. Clinical pharmacology: textbook / Ed. O.M. Bilovol. –
Vinnytsia: Nova Knyga, 2021. – 544 p.
5. Modern classifications and standards for the treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Ed. Prof. Yu.M. Mostovoy. – 25th ed., changes and additions. – Kyiv: Center of State Clinical Research, 2018. – 792 p.

LECTURE 8. TOPIC
"PRINCIPLES OF CLINICAL AND PHARMACEUTICAL APPROACH TO THE SELECTION OF DRUGS FOR THE TREATMENT OF DISEASES OF THE URINARY SYSTEM AND BLOOD SYSTEM"

Relevance of the topic: Kidney disease remains a pressing issue due to its widespread prevalence and serious health consequences. Chronic kidney disease (CKD) is a global health problem characterized by progressive decline in kidney function and an increased risk of cardiovascular disease and death.

Here are some key aspects of the relevance of kidney disease:

• Prevalence: CKD affects a significant portion of the population, with its prevalence increasing with an aging population and the prevalence of risk factors such as diabetes and hypertension.

• Progression to renal failure: CKD can progress to end-stage renal failure, requiring dialysis or kidney transplantation, which places a great burden on the healthcare system and patients.
• Impact on other organs and systems: Kidney disease can affect the cardiovascular system, bones, immune system, and other organs, leading to complications and a reduced quality of life.
• High cost of treatment: Treatment of CKD, especially in the later stages, can be very expensive, including the costs of dialysis, transplantation, and treatment of complications.
• Reduced life expectancy and quality of life: CKD can significantly shorten life expectancy and impair its quality due to limitations in physical activity, psychological problems, and the need for constant medical supervision.
• The need for prevention and early diagnosis: Early detection and treatment of CKD can slow the progression of the disease and improve the prognosis, so preventive examinations and screening are important.

Blood diseases remain a pressing problem in modern medicine, as they can have a significant impact on human health and life. These diseases range from anemia to leukemia, and their timely diagnosis and treatment are critically important.

The relevance of blood diseases is due to several factors:
• Prevalence: Blood diseases, such as anemia, are quite common, especially among certain groups of the population, such as women of childbearing age.
• Life-threatening: Some blood diseases, such as leukemia or severe anemia, can be fatal if left untreated.
• Impact on quality of life: Even less serious blood diseases can significantly impair quality of life, causing fatigue, weakness, shortness of breath, and other symptoms.
• Difficulty of diagnosis: Some blood diseases can have nonspecific symptoms, making them difficult to diagnose.
• Need for a comprehensive approach: Treatment of blood diseases often requires a comprehensive approach, including drug therapy, blood transfusions, and other treatments.
Main diseases of the blood system that require attention:
• Anemia: A decrease in the level of hemoglobin and red blood cells in the blood, which can be caused by iron, vitamin B12 or folic acid deficiency, as well as chronic diseases.
• Leukemia: A malignant blood disease characterized by excessive formation of leukocytes.
• Thrombocytopenia: A decrease in the number of platelets, which can lead to bleeding.
• Hemophilia: A hereditary disease characterized by a blood clotting disorder.

Diseases of the blood system are an urgent medical problem that require attention and a comprehensive approach. Timely diagnosis and treatment, as well as preventive measures, can significantly improve the prognosis and quality of life of patients.

Purpose: To familiarize the HES with the definition of diseases of the urinary system and blood system, etiological and pathophysiological factors of nosoforms, principles of classification of drugs for normalizing kidney function, hematopoietic system, principles of choosing mono- and combination pharmacotherapy, methods of monitoring the effectiveness and safety of the proposed therapy, and prescribing drugs for the treatment of renal colic.

Basic concepts (list of questions):

Pyelonephritis is a nonspecific inflammatory process with a predominant lesion of the renal glomeruli, mostly of bacterial etiology, characterized by damage to the renal pelvis (pyelitis), calyxes and renal parenchyma.

Glomerulonephritis is an inflammatory process of the kidneys, mainly of autoimmune origin, with a predominant lesion of the glomerular apparatus.

Diuresis is the process of formation and excretion of urine.

Diuretics are drugs that increase the excretion of salts and water with urine and reduce the fluid content in tissues and cavities (furosemide, torasemide, spironolactone, hypothiazide and others).

Renal colic is colic caused by stretching of the renal pelvis with urine due to impaired outflow.

Anemias are a group of clinical and hematological syndromes, the common point of which is a decrease in the concentration of hemoglobin in the blood, often with a simultaneous decrease in the number of erythrocytes.

Hemoglobin is a protein of erythrocytes, through which oxygen is transported from the lungs to the tissues, and carbon dioxide from the tissues to the lungs.

Hemoblastoses is a collective term for tumors that develop from hematopoietic cells.

Lecture content (lecture text)

Pharmacotherapy of kidney diseases includes a wide range of drugs used to treat and maintain kidney function. The main groups of drugs include diuretics, antibiotics, anti-inflammatory drugs, drugs for the treatment of renal failure, and others.

Main groups of drugs and their use:

• Diuretics:

Used to increase fluid excretion from the body, which can be useful for edema and some kidney diseases.

• Antibiotics:

Used to treat bacterial infections of the kidneys and urinary tract, such as pyelonephritis.

• Anti-inflammatories:

Help reduce inflammation in the kidneys and urinary tract, especially in glomerulonephritis and other inflammatory diseases.

• Kidney failure medications:

Used to maintain kidney function in cases of chronic kidney failure, including monitoring blood pressure, electrolyte levels, and more.

• Urinary calculi:

Used to treat urolithiasis by helping to dissolve stones and prevent their formation.

• Antispasmodics:

Used to relieve pain from renal colic by relaxing the smooth muscles of the urinary tract.

• Kidney support:

Includes dietary supplements and herbal remedies that help normalize kidney function, improve blood circulation, and protect kidney cells.

• Other medications:

Depending on the specific disease, other medications may be used, such as immunosuppressants for autoimmune kidney diseases.

Pharmacotherapy of anemia is aimed at eliminating the cause and restoring normal hemoglobin and red blood cell levels. Treatment may include iron supplements, vitamins (B12, folic acid), erythropoietins, immunosuppressants, or blood transfusions, depending on the type of anemia.

Types of anemia and their pharmacotherapy:

• Iron deficiency anemia:

• Iron supplements (oral or parenteral).

• Recommended iron supplements (ferrous sulfate, ferrous fumarate) and iron supplements (ferric hydroxide complex with polymaltose).

• In severe cases - blood transfusion.

Anemia caused by vitamin B12 and folic acid deficiency:

• Vitamin B12 (cyanocobalamin) and folic acid preparations.

Hemolytic anemia:

• Immunosuppressants (for the treatment of autoimmune forms).

• Spleen removal.

Anemia of chronic diseases:

• Treatment of the underlying disease.

• Erythropoietins (to stimulate the formation of red blood cells).

Aplastic anemia:

• Bone marrow transplantation.

Anemias associated with bleeding:

• Surgical intervention to stop bleeding.

Self-control questions on the topic:

1. Composition and physiology of blood, plasma, red blood cells, leukocytes and platelets.

2. Pharmacokinetic features of absorption, distribution and elimination of iron from the human body?

3. What chronic diseases lead to impaired iron absorption in the human body?

4. Features of iron consumption in the body of pregnant women?

5. Anemias - classification:

a) anemias that occurred due to blood loss;

b) anemias due to impaired erythropoiesis:

c) hemolytic anemias:

6. The main pathogenetic mechanisms that are the object of drug influence in anemia.

7. Means used for hypochromic anemias. Pharmacokinetics, pharmacodynamics of iron preparations. Comparative characteristics. Indications for use. Dosage regimen. Adverse effects. Poisoning with iron preparations and assistance measures (deferoxamine).

8. Pharmacological characteristics of drugs used for the treatment of hyperchromic anemias. Pharmacokinetics, pharmacodynamics. Adverse effects.

9. Erythropoietins. Biological role. Use of epoetin. Adverse effects.

10. Phytotherapeutic agents and preparations of animal origin used in anemia.

11. Clinical and pharmacological characteristics of antibiotics used for the treatment of infectious and inflammatory diseases of the urinary system.

12. Clinical and pharmacological characteristics of fluoroquinolones used for the treatment of infectious and inflammatory diseases of the urinary system.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.

2. Clinical pharmacy (pharmaceutical care): a textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden pages, 2011. – 704 p.
3. Clinical Pharmacy: A Textbook for Students of Pharmaceutical Faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
4. Clinical Pharmacology: A Textbook / Ed. O.M. Bilovol. – Vinnytsia: Nova Kniga, 2021. – 544 p.
5. Modern Classifications and Standards of Treatment of Diseases of Internal Organs. Emergency Conditions in Therapy. Analyses: Normative Indicators, Interpretation of Changes / Ed. Prof. Yu.M. Mostovoy. – 25th ed., changes and additions – Kyiv: Center of State Clinical Research, 2018. – 792 p.

LECTURE 9. TOPIC
"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of endocrine system diseases (diabetes mellitus, thyroid diseases)"

Relevance of the topic: Endocrine diseases are a pressing problem of modern medicine due to their wide impact on the general condition of the body and the high risk of developing complications. Disturbances in the endocrine system, which is responsible for the production of

hormones, can lead to a variety of diseases, including diabetes mellitus, thyroid disease, adrenal gland disease, and others.

The relevance of endocrine diseases is due to several factors:

• Wide range of effects: Endocrine diseases affect various body systems, including cardiovascular, nervous, reproductive, and others.

• High incidence: Diseases such as diabetes mellitus are highly prevalent in the world, and their number continues to grow.

• Socio-economic significance: Endocrine diseases often lead to disability, loss of work capacity, and an increased burden on the healthcare system.

• Risk of complications: Untreated endocrine diseases can lead to serious complications, such as heart attacks, strokes, kidney damage, and others.

• Reproductive disorders: Endocrine disorders can affect reproductive function in both men and women, causing infertility.

• Relationship with other diseases: Endocrine disorders can be a risk factor for the development of other diseases, such as cardiovascular disease, depression, and certain types of cancer.

• Iodine deficiency: In Ukraine, in particular, the problem of iodine deficiency remains relevant, which negatively affects the health of the thyroid gland and the intellectual development of the population.

Examples of endocrine diseases:

• Diabetes mellitus: A disease associated with impaired blood sugar levels.

• Thyroid disease: Hypothyroidism (insufficient thyroid hormones) and hyperthyroidism (excess thyroid hormones).

• Pituitary tumors: A neoplasm in the pituitary gland that can affect the production of various hormones.

• Adrenal gland diseases: For example, Cushing's syndrome or Addison's disease.

Therefore, the relevance of endocrine diseases is due to their widespread distribution, complexity and risk of complications, which requires attention to prevention, early diagnosis and effective treatment.

Purpose: To familiarize the HES with the definition of endocrine system diseases, etiological and pathophysiological factors of nosoforms, principles of classification of drugs for normalizing endocrine gland function, for replacement and pathogenetic pharmacotherapy, principles of choosing mono- and combination pharmacotherapy, methods of monitoring the effectiveness and safety of the proposed therapy, prescribing drugs for the treatment of diabetic coma, thyrotoxic crisis

Basic concepts (list of questions):

Hormones – biologically active substances that are synthesized and secreted by the glands of internal secretion.

Endocrine gland – a gland that secretes a secret (hormone) directly into the blood or lymph (thyroid gland).

Exocrine gland – a gland that secretes a secret through a duct onto the surface of the skin or mucous membrane (sweat, salivary glands).

Replacement therapy – used for deficiency of natural biogenic substances (hormones, enzymes, vitamins).

Thyroidogenic – caused by a decrease or increase in the secretory function of the thyroid gland.

Thyroiditis – inflammation of the thyroid gland.

Thyrotoxicosis – a pathological condition caused by the intake of an excessively large amount of thyroid hormones into the body; characterized by an increase in the basal metabolism, impaired function of the nervous and cardiovascular systems.

Thyrotropin – that which affects the thyroid gland.

Thyroxine – tetraiodothyronine – thyroid hormone, the deficiency of which leads to cretinism, myxedema, and excess – to thyrotoxicosis.

Triiodothyronine – thyroid hormone, in chemical structure and biological action close to thyroxine, but more active.

Diabetes mellitus – a group of endocrine diseases that develop due to absolute or relative (violation of interaction with target cells) insufficiency of the hormone insulin, which leads to hyperglycemia – a persistent increase in blood glucose levels.

Diabetes insipidus – an endocrine disease associated with a reduced content of the hormone vasopressin in the blood.

Steroid diabetes – extrapancreatic diabetes that develops with excessive content of glucocorticoids in the blood due to their increased secretion (Itsenko-Cushing's disease) or with prolonged use of their drugs.

Insulin is a protein-peptide hormone produced in basophilic insulocytes (beta cells) of pancreatic islets; regulates glucose utilization, stimulates glycogen formation, and inhibits gluconeogenesis.

Lecture content (lecture text)

Treatment of diabetes mellitus in the vast majority of cases is pathogenetic and aimed at eliminating the existing symptoms without affecting the cause of the disease, since the etiological treatment of diabetes has not yet been developed. The main tasks of the doctor in the treatment of diabetes mellitus are:

• Compensation of carbohydrate metabolism

• Prevention and treatment of complications

• Normalization of body weight

• Patient education

Compensation of carbohydrate metabolism is achieved in two ways: by providing cells with insulin, in different ways depending on the type of diabetes, and by ensuring a uniform supply of carbohydrates, which ensures adherence to the diet. Patient education plays a very important role in the compensation of diabetes mellitus. The patient must understand what diabetes is, how dangerous it is, what he should do in case of episodes of hypo- and hyperglycemia, how to avoid them, be able to independently control the level of glucose in the blood, and have a clear idea of the nature of the diet that is acceptable for him.

Diet therapy

Diet during diabetes is a necessary component of treatment, as is the use of sugar-lowering drugs or insulin. Without dieting, compensation of carbohydrate metabolism is impossible. It should be noted that in some cases during type 2 diabetes, only diet is enough to compensate for carbohydrate metabolism, especially in the early stages of the disease. In type 1 diabetes, dieting is vital for the patient, diet violation can lead to hypo- or hyperglycemic coma, and in some cases even to the death of the patient. The task of diet therapy during diabetes is to ensure a uniform and adequate intake of carbohydrates into the patient's body for physical activity. The diet should be balanced in terms of proteins, fats and calories. Easily digestible carbohydrates should be completely excluded from the diet, they can be consumed only in cases of hypoglycemia. During type 2 diabetes, there is often a need to reduce the calorie content of the diet to correct body weight.

The main concept in diabetes diet therapy is the bread unit (BSU). A bread unit is a conventional measure equal to 10–12 g of carbohydrates or 20–25 g of bread. There are tables indicating the number of BSUs in various foods. During the day, the number of BSUs consumed by the patient should remain constant; on average, 12–25 BSUs should be consumed per day, depending on body weight and physical activity. It is not recommended to consume more than 7 BSUs at one meal; it is advisable to organize food intake so that the number of BSUs in different snacks is approximately the same. It should also be noted that alcohol consumption can lead to delayed hypoglycemia, including hypoglycemic coma.

An important condition for the success of diet therapy is that the patient keeps a food diary. It records all the food consumed during the day, and calculates the number of bread units consumed during each meal and in total per day. Keeping such a food diary allows in most cases to identify the cause of episodes of hypo- and hyperglycemia, contributes to patient education, helps the doctor select an adequate dose of hypoglycemic drugs or insulin.

Oral hypoglycemic drugs

The structural formula of the central segment of sulfonamide drugs, additional compounds are added at the R1 R2 points, which provide different clinical effects of the drug.

This group of drugs is used mainly for the treatment of patients with type 2 diabetes. In type 1 diabetes, hypoglycemic drugs are ineffective.

According to the chemical composition and mechanism of action, hypoglycemic drugs can be divided into two groups - sulfonamides and biguanides.

Sulfonamide drugs are derivatives of sulfonylurea and differ from each other in additional compounds introduced into the main structure. The mechanism of hypoglycemic action is associated with stimulation of endogenous insulin secretion, suppression of glucagon synthesis, reduction of glucose formation in the liver during gluconeogenesis and increased sensitivity of insulin-dependent tissues to the action of insulin, due to increased efficiency of its postreceptor action.

This group of drugs is used in case of ineffectiveness of diet therapy, treatment begins with minimal doses under control of the glycemic profile. In some cases, an increase in the effectiveness of therapy is noted when combining several different sulfonylurea derivatives.

The following sulfonylurea drugs are distinguished:

• first generation - Tolbutamide, Carbutamide, Chlorpropamide;

• second and third generation - Glibenclamide, Glipizide, Gliclazide, Glikvidone, Glimepiride.

Biguanides are derivatives of guanidine. There are 2 main groups:

1. dimethylbiguanide (metformin)

2. butylbiguanide (adebit, silubin)

The mechanism of hypoglycemic action of this group of drugs is to enhance glucose utilization by muscle tissue by stimulating anaerobic glycolysis in the presence of endogenous or exogenous insulin. Unlike sulfonamides, they do not stimulate insulin secretion, but have the ability to potentiate its effect at the receptor and postreceptor levels, gluconeogenesis is also inhibited and carbohydrate absorption in the intestine is somewhat reduced. Biguanides also lead to a decrease in appetite and contribute to a decrease in body weight.

It should be noted that due to the accumulation of lactic acid, which is synthesized as a result of anaerobic glycolysis, the pH shifts to the acidic side and tissue hypoxia increases.

Treatment should begin with minimal doses of drugs, increasing them in the absence of compensation of carbohydrate metabolism and glycosuria. Often biguanides are combined with sulfonamide drugs in the absence of sufficient effectiveness of the latter. The indication for the appointment of biguanides is type 2 diabetes mellitus in combination with obesity. Given the possibility of developing tissue hypoxia, drugs of this group should be prescribed with caution to persons with ischemic heart disease.

In some cases, patients may experience a gradual decrease in the effectiveness of hypoglycemic drugs. This phenomenon is associated with a decrease in the secretory activity of the pancreas. This ultimately leads to the ineffectiveness of hypoglycemic drugs and the need for insulin therapy.

Insulin therapy

Insulin treatment is aimed at the maximum possible compensation of carbohydrate metabolism, prevention of hypo- and hyperglycemia and thus prevention of complications of diabetes mellitus. Insulin treatment is vital for patients with type 1 diabetes and can be used in some situations for patients with type 2 diabetes.

Indications for insulin therapy:

• Type 1 diabetes

• Ketoacidosis, diabetic hyperosmolar, hyperlactidemic coma.

• Pregnancy and childbirth in diabetes.

• Significant decompensation of type 2 diabetes.

• Lack of effect from other methods of treatment of type 2 diabetes.

• Significant weight loss in diabetes.

• Diabetic nephropathy.

There are a large number of insulin preparations that differ in duration of action (ultrashort, short, medium, prolonged), degree of purification (monopeak, monocomponent), species specificity (human, porcine, bovine, genetically engineered, etc.).

In many countries, insulins derived from cattle have been discontinued. This is due to the large number of side effects during their use. Quite often, allergic reactions, lipodystrophies, and insulin resistance develop when they are administered.

Insulin is available in concentrations of 40 IU/ml and 100 IU/ml. Insulin is distributed in 10 ml vials or 3 ml cartridges for syringe pens.

Despite the fact that insulins are divided by duration of action into short-acting and long-acting drugs, the duration of insulin action in different people is individual. In this regard, insulin therapy requires inpatient observation with control of blood glucose levels, and selection of insulin doses adequate to metabolism, diet, and physical activity. When selecting insulin therapy, one should strive for the maximum possible compensation of carbohydrate metabolism, the less significant the daily fluctuations in blood glucose levels, the lower the risk of various complications of diabetes.

In the absence of obesity and strong emotional stress, insulin is prescribed at a dose of 0.5 - 1 unit per 1 kilogram of body weight per day. Insulin administration is designed to simulate physiological secretion, in this regard, the following requirements are put forward:

• The dose of insulin must be sufficient to utilize glucose entering the body.

• The injected insulin must simulate basal secretion of the pancreas.

• The injected insulin must simulate postprandial peaks of insulin secretion.

Because of this, there is the so-called intensified insulin therapy. The daily dose of insulin is divided between long-acting and short-acting insulins. Long-acting insulins are administered mainly in the morning and evening and mimic the basal secretion of the pancreas. Short-acting insulins are administered after each meal containing carbohydrates, the dose may vary depending on the bread units consumed in a given meal.

An important role in the selection of a dose of short-acting insulin is played by the calculation of daily fluctuations in the need for insulin. Due to the physiological characteristics of the body, the need for insulin to absorb one bread unit varies during the day and can be from 0.5 to 4 units of insulin per one XO. To determine these indicators, it is necessary to measure the blood glucose level after the main meals, know the number of bread units consumed at this time, and the dose of short-acting insulin administered for this number of bread units. The ratio of the number of bread units to the number of insulin units is calculated. If the blood glucose level after a meal is higher than normal, then the next day the insulin dose is increased by 1-2 units and it is calculated how much the glycemia level has changed by 1 unit of insulin with the same amount of carbohydrates in this meal.

Knowledge of the individual need for insulin is a necessary condition for full compensation of carbohydrate metabolism in the treatment of diabetes with insulin therapy. Thanks to knowledge of the individual need for insulin per 1 bread unit, the patient can effectively and safely adjust the dose of short-acting insulins depending on the meal.

There is also a method of combined insulin therapy, when a mixture of short-acting and medium- or long-acting insulins is administered in one injection. This method is used in the labile course of diabetes mellitus. Its advantage is that it allows you to reduce the number of insulin injections to 2 - 3 per day. The disadvantage is the inability to fully simulate physiological insulin secretion and, as a result, the inability to fully compensate for carbohydrate metabolism.

Insulin is administered subcutaneously, using an insulin syringe, syringe pen or special pump-doser. Today in Ukraine the most common method of insulin administration is by syringe pens. This is due to convenience, less pronounced discomfort and ease of administration compared to conventional insulin syringes. The syringe pen allows you to quickly and practically painlessly administer the required dose of insulin.

The method of insulin administration using an insulin pump is more common in the USA and Western European countries, but even there it is available only to a small part of patients (on average 2-5%). This is due to a number of objective difficulties that largely offset the advantages of this method of insulin administration.

The advantages of this method include more accurate imitation of physiological insulin secretion (insulin preparations enter the blood throughout the day), the possibility of more accurate control of glycemia, the absence of the need to independently inject insulin (the amount of insulin administered is controlled by the pump), and the risk of acute and long-term complications of diabetes mellitus is also significantly reduced. The disadvantages include the complexity of the device, problems with its fixation on the body, complications from the constant presence in the body of the needle that delivers the mixture. There is also a certain difficulty in selecting an individual operating mode of the device. This method of insulin administration is considered the most promising, the number of people using insulin pumps is gradually increasing.

Questions for self-control on the topic:

1. Mechanisms of regulation of hormone synthesis.

2. Diabetes mellitus: classification, etiology, pathogenesis.

3. Clinical signs of type 1 and type 2 diabetes.

4. Main groups of drugs for replacement and pathogenetic therapy.

5. Classification of insulin preparations: clinical pharmacology.

6. Classification of oral hypoglycemic drugs.

7. Sulfonylurea derivatives - clinical and pharmacological characteristics.

8. Biguanides - clinical and pharmacological characteristics.

9. Alpha-glucosidase inhibitors – clinical and pharmacological characteristics.

10. Insulin sensitizers – glitazones – clinical and pharmacological characteristics.

11. Diabetic coma: signs, pharmacotherapy.

12. Indicate the mechanism of neurohumoral regulation of thyroid hormone synthesis.

13. Evaluate the molecular and biochemical mechanisms of the influence of thyroid hormones on metabolic processes in the body.

14. Highlight the pathogenesis of diffuse toxic goiter and other thyroid diseases with thyrotoxic manifestations.

15. Explain the pathogenesis of hypothyroidism (myxedema).

16. Name the modern classification of drugs used for hypo- and hyperfunction of the thyroid gland.

List of sources on the topic:

1. Clinical pharmacology / Edited by Prof. M.I. Yabluchansky, Prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.

2. Clinical pharmacology: textbook / Ed. O.M. Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.

3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.

4. Clinical pharmacy: textbook for students of pharmaceutical faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

5.Modern classifications and standards of treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Edited by prof. Yu.M.Mostovoy. – 25th ed., changes and additions – Kyiv: Center of the State Clinical Hospital, 2018. – 792 p.

LECTURE 10. TOPIC

"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of allergic diseases"

Relevance of the toipc: The relevance of allergic diseases is due to their widespread distribution and significant impact on human health. Allergies affect a large part of the population, and some forms, such as allergic rhinitis, can last throughout life. Allergic diseases are one of the most common reasons for seeking medical attention, which creates a significant burden on the healthcare system.

Reasons for the relevance of allergic diseases:

• Widespread: According to statistics, more than 40% of the world's population suffers from some type of allergy.

• Impact on quality of life: Allergic diseases can significantly worsen the quality of life, limit physical activity and social interaction.

• Increasing incidence: There is a tendency to increase the number of cases of allergic diseases, especially among children.

• Medical and socio-economic burden: Allergies require significant costs for diagnosis, treatment and prevention, and also affect labor productivity and social activity.

Main allergic diseases:

• Allergic rhinitis: Common in children and adults, can become chronic.

• Asthma: Allergy is one of the main causes of bronchial asthma.

• Atopic dermatitis: A skin disease that often occurs in childhood and may be accompanied by other allergic manifestations.

• Food allergy: Can lead to serious consequences, including anaphylaxis.

• Drug allergy: Must be carefully monitored to avoid serious consequences.

The importance of prevention and treatment:

• Timely diagnosis: Allows you to identify the allergen and take measures to avoid contact with it.

• Allergen-specific immunotherapy: An effective treatment method aimed at reducing sensitivity to the allergen.

• Preventive measures: Strengthening immunity, avoiding contact with allergens, a healthy lifestyle.

In this regard, the relevance of allergic diseases remains high, which requires attention from both medical professionals and the general public.

Purpose: To familiarize the HES with the definition of allergic diseases, hypersensitivity of the slow and immediate type, etiological and pathophysiological factors of nosoforms, the principles of classification of drugs for the prevention and treatment of allergic diseases, the principles of pathogenetic pharmacotherapy, the principles of choosing mono- and combination pharmacotherapy, methods of monitoring the effectiveness and safety of the proposed therapy, the appointment of drugs for the treatment of acute allergic conditions.

Basic concepts (list of questions):

Allergology is a section of immunology that studies the causes, clinical manifestations, diagnostics and treatment of allergic diseases and reactions.
Allergy is an increased sensitivity of the body to repeated exposure to an allergen.
Allergic reaction is hypersensitivity of the body's immune system with repeated exposure to an allergen on an organism previously sensitized to this allergen.
Exogenous allergens are allergens that enter the body from the outside.
Endogenous allergens are allergens that are formed in the body.
Drug allergy is a phenomenon of increased sensitivity to certain drugs, mainly with repeated use, the basis of which is the immune mechanism.
Antiallergic drugs are drugs that prevent allergic reactions or weaken them, causing hyposensitization.

Lecture content (lecture text)

Clinical pharmacology of antiallergic drugs studies the mechanisms of action, efficacy and safety of drugs used to treat allergic reactions. The main groups of antiallergic drugs include antihistamines, glucocorticosteroids, mast cell membrane stabilizers (cromones), vasoconstrictors and others.

The main groups of antiallergic drugs:

• Antihistamines: Block the action of histamine, which is one of the key mediators of the allergic reaction. There are I, II and III generation drugs. I generation drugs can cause drowsiness, so II or III generation drugs are often chosen.

• Glucocorticosteroids: Have a powerful anti-inflammatory effect and are used to reduce allergy symptoms, especially in severe cases of the disease.

• Mast cell membrane stabilizers (cromones): Prevent the release of histamine and other substances that cause inflammation. They are used mainly for the prevention of allergic reactions.

• Decongestants: Reduce swelling of the mucous membranes, relieving symptoms of nasal congestion. Used for allergic rhinitis.

• Anticholinergics: Can be used for allergic rhinitis to reduce runny nose.

• Antileukotrienes: Block the action of leukotrienes, other mediators of allergy. Used for allergic asthma and rhinitis.

• Monoclonal anti-IgE antibodies: Drugs that block the action of immunoglobulin E, which is responsible for the development of an allergic reaction. Used for severe cases of allergy.

Uses and mechanisms of action:

• Antihistamines block the H1 receptors that histamine acts on, preventing the development of allergy symptoms such as itching, redness, swelling, and runny nose.

• Glucocorticosteroids suppress the body's inflammatory response to the allergen, reducing swelling, redness, and other signs of inflammation.

• Cromones stabilize the membranes of mast cells, preventing the release of allergy mediators.

• Vasoconstrictors constrict the blood vessels in the nasal mucosa, reducing swelling and making breathing easier.

Important:

• Self-treatment of allergies can be dangerous. Before starting any anti-allergy drugs, you should consult a doctor.

• Pregnant and breastfeeding women should be especially careful when choosing anti-allergic drugs, as some drugs may be contraindicated.

• Long-term use of some antihistamines can lead to addiction and a decrease in their effectiveness.

Examples of drugs:

• Antihistamines: Loratadine, Cetirizine, Desloratadine, Claritin, Suprastin, Diazolin.

• Glucocorticosteroids: Betamethasone, Dexamethasone, Prednisolone.

• Cromones: Sodium cromoglycate.

• Antihistamines (Greek anti- — against + histos — tissue + Latin aminum — amine) — a specific group of antiallergic drugs, the pharmacological effect of which is the blockade of H-receptors (H comes from Histamine). There are several types of histamine receptors: H1, H2 and H3.

• H1-receptors are located in the smooth muscles of the bronchi, intestines, arteries, veins, capillaries, heart in the neurons of the CNS. H2-receptors are located in the parietal cells of the gastric mucosa, smooth muscles of the arteries, in the neurons of the CNS, heart, myometrium, mast cells, basophilic and neutrophil leukocytes, T-lymphocytes, in adipose tissue. H3-receptors are located in the neurons of the CNS, cardiovascular system, gastrointestinal tract, upper respiratory tract.

• Antihistamines that block H1 receptors (H1-histamine blockers) thereby eliminate or reduce such types of histamine effects as increased tone of smooth muscles of the bronchi, intestines, uterus; decreased blood pressure (partially); increased capillary

permeability with the development of edema; hyperemia and itching with intradermal administration of histamine or with the release of endogenous histamine in the skin. These effects are caused mainly by immediate-type allergic reactions, which are accompanied by acute exudation: allergic rhinitis, urticaria, angioedema, insect bites, allergic reactions to drugs, food allergies, serum sickness, dermatoses, para(pseudo)allergic reactions.

• Today, there are three generations of drugs in this group on the market:

• First-generation antihistamines (1940s) are non-selective histamine receptor blockers, the action lasts for 4–8 hours (diphenhydramine (diphenhydramine), promethazine (diprazin, pipolfen), chloropyramine (suprastin), mebhydrolin (diazolin), clemastine (tavegil), sequifenadine (fencarol), cyprofentadine (peritol), ketotifen (zaditen); dimetinden and clemastine - up to 12, mebhydrolin - up to 24 hours). They block m-cholinergic receptors in peripheral tissues, which leads to a decrease in the secretion of exocrine glands, an increase in the viscosity of secretions, including bronchial secretions, dryness of the mucous membranes of the oral cavity, a decrease in gastrointestinal motility and urinary tract tone, impaired accommodation, increased intraocular pressure and heart rate. Antiemetic and antiparkinsonian effects may develop, and some antipsychotics exhibit antidopamine, antitussive, and anxiolytic effects. Adverse effects from the gastrointestinal tract may include nausea, vomiting, diarrhea, decreased or increased appetite. The frequency of adverse reactions is reduced when antipsychotics are taken with food. They penetrate the blood-brain barrier and block the H1 receptors of the CNS, which is manifested by a sedative effect, drowsiness, decreased psychomotor activity, increased appetite, a feeling of lethargy, impaired coordination of movements, and a decrease in the ability to learn and concentrate. Sedation is most often caused by drugs of the diphenhydramine (diphenhydramine) group. The sedative effect is enhanced by alcohol and other substances that depress the CNS: tranquilizers, neuroleptics, sedatives, and some other drugs. Dizziness, ringing in the ears, apathy, fatigue, decreased visual acuity, diplopia, nervousness, insomnia, tremor are often possible. With prolonged use of A.p. their effectiveness (habituation) decreases. AP I generation is not recommended for use in the first 3 months of pregnancy, patients with glaucoma, benign prostatic hyperplasia, bronchial asthma, as well as elderly patients. A significant disadvantage is the appointment of these drugs several times a day.

• Antihistamines II generation (80s of the XX century) - terfenadine (Trexil), astemizole (Gismanol), loratadine (Cloritin), astemizole, acrivastine, cetirizine, ebastine - are distinguished by the absence of a sedative effect, effect on choline and serotonin receptors, interaction with alcohol and psychotropic drugs, habituation with prolonged use, as well as high affinity for H1 receptors. Receptor binding is long-lasting and non-competitive. These drugs are prescribed 1–2 times a day. However, terfenadine and astemizole have a significant side effect - an effect on the cardiovascular system (ventricular arrhythmias with prolongation of the Q–T interval on the ECG, tachycardia, which develops due to the blockade of potassium channels that control the repolarization of myocardial membranes). All second-generation antihistamines (except cetirizine and acrivastine) are prodrugs, the action of which is due to active metabolites formed in the liver by the CYP 3A4 isoenzyme of the cytochrome P450 system. They should not be used with drugs that are metabolized by the same enzyme systems: macrolide antibiotics (erythromycin, clarithromycin, oleandomycin, azithromycin), antifungal drugs (ketoconazole, itraconazole), the H2-receptor blocker cimetidine, some antiarrhythmic drugs (quinidine, procainamide, disopyramide), antidepressants (fluoxetine, sertraline and

paroxetine), as well as in cases of impaired liver function, which can lead to cardiotoxic effects (for terfenadine and astemizole).

• Third-generation antihistamines are active metabolites of second-generation drugs (fexofenadine - the active metabolite of terfenadine, norastemizole - astemizole, desloratadine - loratadine), providing an increased level of safety profile. They inhibit mediators of systemic allergic inflammation, including cytokines and chemokines, and reduce the expression of adhesion molecules, inhibit chemotaxis, activation of eosinophil granulocytes and the formation of superoxide radicals; reduce bronchial hyperreactivity. The use of third-generation antihistamines is most rational in long-term therapy of allergic diseases (perennial allergic rhinitis, seasonal allergic rhinitis or rhinoconjunctivitis with exacerbations lasting more than 2 weeks, chronic urticaria, atopic and allergic contact dermatitis). H2-receptor blockers (cimetidine, ranitidine, famotidine, nizatidine) are competitive antagonists of histamine. From a chemical point of view, they can be considered as derivatives of histamine. H2-receptors are associated with adenylate cyclase. From a chemical point of view, they can be considered as derivatives of histamine. H2 receptors are associated with adenylate cyclase. This is manifested in the fact that when histamine stimulates H2 receptors, intracellular cAMP increases, while the secretory activity of parietal cells of the gastric mucosa increases. In addition, when histamine stimulates H2 receptors, heart rate increases, a positive inotropic effect is noted in the heart; in unstriated muscles of arterial vessels, a decrease in tone is observed; in mast cells and basophilic leukocytes, degranulation is inhibited; in neutrophil leukocytes, chemotaxis is reduced, and the release of lysosomal enzymes is inhibited; in T lymphocytes, cytotoxic activity is reduced, and the production of a factor that inhibits macrophage migration is inhibited; in adipose tissue, fatty acid release is increased. By acting on H2 receptors of parietal cells, they reduce the secretion of hydrochloric acid. To a lesser extent, they inhibit the secretion of pepsin and gastromucoprotein (intrinsic Castle factor). These drugs have low lipophilicity, so they do not cross the blood-brain barrier well. H2-receptor blockers are used as antisecretory drugs for duodenal and gastric ulcers, hypergastrinemia, peptic (reflux) esophagitis, erosive gastritis, duodenitis. Unlike ranitidine, famotidine and nizatidine are more active, act longer (prescribed once a day) and have fewer side effects.

• H3-receptors were originally found on histaminergic neurons of the CNS in the form of presynaptic receptors that regulate the formation and release of histamine. H3-receptors as a target of pharmacological action are of less importance today. Histamine-containing neurons are mainly localized in the posterior hypothalamus. In addition to the inhibitory effect on histamine release, presynaptic H3 receptors are involved in the regulation of the production of some other mediators/modulators (acetylcholine, GABA, dopamine, glutamine, serotonin, norepinephrine), thus they also function as heteroreceptors. In addition to the CNS, H3 receptors are found in the gastrointestinal tract (their stimulation inhibits the secretion of hydrochloric acid in the stomach; they participate in the gastroprotective effect), in the cardiovascular system (activation of presynaptic H3 receptors inhibits the adrenergic effect), in the upper respiratory tract (anti-inflammatory effect). H3 receptor blockers include ciprofloxacin, clobenpropit, thioperamide, clozapine.

Self-test questions on the topic:

1. Classification of allergic reactions.
2. Etiology, pathogenesis, clinical manifestations of immediate-type allergic reactions.
3. Etiology, pathogenesis, clinical manifestations of delayed-type allergic reactions.
4. Classification of antiallergic drugs.
5. Glucocorticoids: clinical and pharmacological characteristics.

6. Classification of antihistamine drugs.
7. Type 1 histamine blockers: classification, clinical and pharmacological characteristics.
8. Mast cell membrane stabilizers: clinical and pharmacological characteristics.
9. Principles of pharmacotherapy of anaphylactic shock, angioedema, urticaria.
10. Measures and methods for preventing allergic reactions.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M.Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical Pharmacy (Pharmaceutical Care): A Textbook for Students of Higher Medical (Pharmaceutical) Schools / I.A.Zupanets, V.P.Chernykh, T.S.Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: A Textbook for Students of Pharmaceutical Faculties / Ed. V.P.Chernykh, I.A.Zupanets, I.G.Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Protocols of a Pharmacist (Pharmacist) / Ed. V.P.Chernykh, I.A.Zupanets, O.M.Lishchyshyna. – Kharkiv: Golden Pages, 2013. – 192 p.
6. Modern classifications and standards of treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Edited by prof. Yu.M.Mostovoy. – 25th ed., changes and additions. – Kyiv: Center of the State Clinical Hospital, 2018. – 792 p.

LECTURE 11. TOPIC
"Principles of clinical and pharmaceutical approach to the selection of drugs for the treatment of infectious diseases"

Relevance of the topic: Infectious diseases remain a pressing health problem worldwide, including in Ukraine. The increase in the number and scale of outbreaks, the emergence of new and adaptation of old infections, as well as insufficiently effective methods of treatment and prevention, create significant risks to public health.

Main aspects of the relevance of infectious diseases:

• Increase in the number of outbreaks: Current observations indicate an increase in the frequency and scale of outbreaks of infectious diseases, including pandemics.
• Emergence of new infections: New viral and bacterial infections are constantly emerging, which can pose a significant threat, such as COVID-19.
• Adaptation of pathogens: Infectious pathogens adapt to existing treatment methods, which leads to increased resistance to antibiotics and other drugs.
• Epidemiological risks: The unstable epidemiological situation in the world, caused by globalization and population movements, increases the risks of the spread of infections to new territories.
• Socio-economic consequences: Infectious diseases lead to significant socio-economic consequences, including increased health care costs, job losses, and reduced productivity.
• Public health threat: Infectious diseases can lead to serious health consequences, including disability and death, especially among vulnerable populations.
• Rising incidence of certain infections in Ukraine: Ukraine is experiencing an increase in the incidence of infections such as hepatitis A, chronic viral hepatitis B, and C.

Examples of infectious diseases that remain relevant:

• Viral hepatitis: Hepatitis A, B, and C continue to be a serious problem, especially due to the possibility of chronicity and the development of cirrhosis and liver cancer.
• Acute respiratory viral infections (ARI): Widespread seasonal epidemics of ARVI, including influenza, place a great burden on the health care system.
• Intestinal infections: Intestinal infections such as dysentery, salmonellosis, rotavirus infection remain relevant, especially among children.
• Tuberculosis: Despite advances in treatment, tuberculosis remains a serious problem, especially in the context of increasing antibiotic resistance.
• HIV/AIDS: Continues to be a global problem, although significant progress has been made in treatment and prevention.

Purpose: To familiarize HES with the basic principles of antibacterial therapy, the modern algorithm for selecting and selecting an antimicrobial drug for a specific patient, choosing a dosage regimen, route of administration, frequency of administration, duration of therapy; explain the importance of monitoring the effectiveness and safety of drug use in a given specific patient.

Basic concepts (list of questions):

Infection - penetration and reproduction of microorganisms in the human body with the subsequent development of various forms of their interaction - from carrier to severe disease.

Infectious process – a time-limited complex interaction of biological systems of micro- (pathogen) and macroorganism, which occurs under certain environmental conditions, manifests itself at the submolecular, subcellular, cellular, tissue, organ and organism levels and naturally ends either with the death of the macroorganism or its complete liberation from the pathogen.

Antibacterial drugs – drugs that kill bacteria or inhibit their vital activity and are used to treat bacterial infectious and inflammatory processes (antibiotics, fluoroquinolones, nitroimidazoles, etc.).

Antibiotics – specific products of the vital activity of microorganisms, plants or animal tissues that inhibit the growth and reproduction of other microbes, as well as tumor cells (penicillins, cephalosporins, macrolides, etc.). There are synthetic analogues of natural compounds.

Nitroimidazoles are synthetic antimicrobial drugs with high activity against anaerobic bacteria and pathogens of protozoal infections (metronidazole, tinidazole, etc.).

Nitrofurans are derivatives of furan, in which the hydrogen atom is replaced by a nitro group; they have a wide spectrum of antimicrobial action, based on their ability to inhibit the respiration of microbial cells; they are used as uroseptics (furagin, furamag, furadonin) and for intestinal infections (nifuroxazide).

Fluoroquinolones are a group of drugs that have pronounced antimicrobial activity due to the inhibition of two vital enzymes of the microbial cell - DNA gyrase and topoisomerase-4, disrupting the synthesis of DNA and RNA, which leads to the death of bacteria (norfloxacin, ofloxacin, ciprofloxacin, moxifloxacin, etc.). Broad spectrum of action.

Lecture content (lecture text)

The main principles of treating infectious diseases are: timely diagnosis, etiotropic therapy (impact on the pathogen), pathogenetic therapy (impact on the mechanisms of disease development), symptomatic therapy (elimination of symptoms), as well as preventive measures to prevent the spread of infection.

Etiotropic therapy includes the use of antimicrobial drugs, such as antibiotics (for bacterial infections), antiviral drugs (for viral infections) or antifungal drugs (for fungal infections). It is important to choose the right drug and adhere to the treatment regimen prescribed by the doctor. Untimely or inadequate treatment can lead to complications or the development of drug resistance of pathogens.

Pathogenetic therapy is aimed at correcting disorders that occur in the body as a result of infection. It may include: detoxification (cleansing the body of toxins), immunostimulation (increasing immunity), anti-inflammatory therapy and other measures aimed at restoring the normal function of organs and systems.

Symptomatic therapy is aimed at alleviating the symptoms of the disease. It may include: the use of antipyretics, analgesics, anti-inflammatory drugs and other drugs that help eliminate specific symptoms.

Preventive measures include: vaccination, compliance with personal hygiene rules (washing hands, using antiseptics), avoiding contact with sick people, safe nutrition, supporting immunity.

Rational treatment of an infectious patient consists in influencing all components of both the infectious process and the disease. First of all, measures are necessary against the causative agent of the disease, as well as its waste products, especially toxins. Thus, etiotropic therapy is used for many infectious diseases. Etiotropic treatment (from the Greek. aia - cause, Greek. tropos - path, direction), respectively, the term "etiotropic" is defined as directed against the cause of the disease, eliminating or weakening the effect of the factor that causes the disease. Etiotropic action can be directed at the pathogen and (or) its toxins. The indication for the use of etiotropic agents is the pathogenic effect on the macroorganism of such a pathogen, with which the macroorganism itself cannot cope, or under the influence of which the development of serious, often fatal complications is possible.

Etiotropic drugs can be conditionally divided as follows:

• nonspecific - which are able to act on a certain number of different pathogens;

• specific - which are able to act only exclusively against one pathogen (therapeutic serums, immunoglobulins, bacteriophages, etc.).

They are also divided into:

• chemotherapy drugs - antibiotics, sulfonamides, nitrofurans, 8-hydroxyquinoline derivatives, neuraminidase inhibitors, acyclovir group, etc.;

• biological drugs - interferons, DNase, etc.

In case of bacterial infectious disease, one should first of all try to use drugs with a bactericidal effect, and only in the absence of an effective bactericide for this infection, a drug with a bacteriostatic effect can be used. Despite the fact that synergism can be demonstrated in laboratory conditions using a number of combinations of antibacterial drugs, only in a few clinical conditions has it been proven that combined treatment is more effective than monotherapy. First of all, this applies to tuberculosis, sepsis and some others. It was also determined that combinations of antibiotics should not be used in situations where there may be mutual enhancement of the side effects of the drugs, and that simultaneous combinations of bactericidal and bacteriostatic drugs are absolutely unsuitable.

Conducting etiotropic therapy for infectious diseases caused by various pathogens

Currently, there are certain problems in conducting etiotropic therapy. Medicine has achieved the greatest success in the treatment of bacterial infectious diseases since the mid-1950s, when penicillin was discovered, but in the 21st century there has been a certain stagnation. Over the past 20 years, no new group of antibiotics has been created in the world. As a result of inadequate treatment with antibiotics and other antibacterial drugs in previous years without clear justification (powerful antibiotics were prescribed for mild forms of the disease, used for a short time, leading to the selection of resistant microorganisms and the formation of numerous medical complications), pathogens with serious resistance to these drugs have emerged (methicillin-resistant strains of staphylococci, multi-resistant tuberculosis bacilli, etc.). The gram-negative bacterium Acinetobacter and some strains of Klebsiella and Pseudomonas, which were previously classified as opportunistic pathogens, have acquired multidrug resistance. These bacteria cause a variety of diseases, such as nosocomial (hospital-acquired) pneumonia, infectious lesions of blood vessels, urinary tracts caused by catheterization, infectious lesions of the abdominal cavity and even meningitis in people who have received medical procedures related to the head and back, in particular, epidural anesthesia during childbirth. Isolated in 2010 in some countries of the world (India, Bangladesh, Great Britain, etc.) strains of Escherichia coli - carriers of a gene called NDM1 (New Delhi metallo-β-lactamase), are resistant to almost all known antibacterial agents.

The use of antiviral drugs is very limited. For many viral infectious diseases, there are no etiotropic agents. The most effective antiviral drugs are nucleoside analogues of the cyclovir series (acyclovir, ganciclovir, valacyclovir, etc.), although their effectiveness is significant only in a number of diseases caused by certain viruses of the herpesvirus family. However, they have not solved the problems of recurrence and chronicity of these diseases. Also, modern antiretroviral therapy for HIV infection shows some effectiveness in the early stages of this disease. Although the addition of HIV-associated diseases reduces patient survival. Today, drugs for the treatment of chronic viral hepatitis C, such as ribavirin, pegylated interferons, nucleotide analogues and their combinations (sofusbuvir, ledipasvir, dasabuvir, ombitasvir, paritaprevir, ritonavir, etc.), depending on the genotype of the virus that caused the disease, are highly effective. Neuraminidase inhibitors (oseltamivir, zanamivir, peramivir) also have a serious evidence base for the treatment of influenza.

An uncertain situation exists in the treatment of protozoal infections. The effectiveness of their respective etiotropic agents depends greatly on the type of pathogen and the stage of the process. With a large number of protozoal invasions, there are no effective drugs for treatment. Slow infections, prion diseases currently do not have an effective etiotropic solution, always ending unfavorably.

In some infectious diseases, for effective etiotropic treatment, in addition to antibacterial agents, antitoxic sera are necessarily used (in particular, diphtheria, gas gangrene). In some infectious diseases (botulism, tetanus), for effective etiotropic treatment, it is not antibacterial drugs at all that are of primary importance, but antitoxic sera and immunoglobulins.

Pathogenetic therapy

During the infectious process, the pathogen introduces numerous antigens, toxic substances, and aggression factors into the macroorganism, which causes the simultaneous development of many pathological reactions and processes. This should be taken into account when developing pathogenetic treatment for an infectious patient.

Detoxification treatment

To avoid additional effects of these factors on organs and systems, adequate detoxification treatment allows:

• activation of natural detoxification mechanisms,

• active forced methods of parenteral detoxification,

• use of extracorporeal methods of body cleansing.

Replacement therapy

In infectious diseases, it must strictly correspond to the losses of the macroorganism both quantitatively and qualitatively. In particular, in cholera, water and certain trace elements are lost due to profuse diarrhea and vomiting. Formed blood elements, plasma proteins are not lost. In this regard, replacement of losses should be carried out only with balanced salt solutions.

Anti-inflammatory therapy

In infectious patients, it should be prescribed according to strict indications only in those situations when its use is one of the decisive factors for recovery.

Use of drugs for reactivity correction

In infectious diseases, the body's reactivity is corrected (immunomodulators, immunity inducers, immunosuppressants, etc.), which must have strict indications and control of contraindications and side effects. Many drugs of this action have not shown their effectiveness, or do not have a sufficient international evidence base. If it is possible to prescribe them in certain situations, side effects, drug interactions should be carefully studied in advance, and the feasibility of such a prescription should be assessed - will their use lead to success or does the risk of side effects from their prescription exceed the level of common sense. You should also avoid prescribing an immunostimulating drug when the body's defenses are overexerted. There is also no reason to use a suppressive drug with weak protective reactions in cases of infectious diseases. Prescribing drugs with truly immunomodulatory action is also a great risk of encountering an inadequate response, which can lead to completely unpredictable consequences. It is necessary to avoid prescribing an immunostimulating drug when the body's defenses are overexerted, such as in the midst of infectious mononucleosis. There is also no reason to use an immunosuppressive drug with weak protective reactions in cases of infectious diseases (in particular, glucocorticosteroids in most acute viral diseases). Prescribing drugs with a truly immunomodulatory effect is also a great risk of encountering an inadequate response, which can lead to completely unpredictable consequences.

It is also necessary to carry out that part of pathogenetic therapy that is aimed at eliminating the pathogenic chain reactions that have arisen in the body. In this regard, it is important to restore the impaired functions of organs and systems, which means affecting some parts of the human body. Such treatment involves proper nutrition, the supply of sufficient vitamins, the use of heart drugs, drugs that act on the nervous system, etc., if necessary. Often, this type of treatment plays a leading role in the patient's recovery, especially when the person has already got rid of the pathogen. For example, after effective antibacterial and detoxification therapy for bacterial meningitis, active restorative treatment should be carried out in the future: nootropics, drugs that improve cerebral circulation, hyperbaric oxygenation, etc.

Symptomatic therapy

This is an effect on the symptom in order to reduce its severity. In particular, this is the appointment of non-steroidal anti-inflammatory drugs to reduce fever, headache, etc. The line between symptomatic and pathogenetic agents is not always easy to draw, since competently prescribed pathogenetic agents reduce the severity of the pathological symptom, and illogical symptomatic ones, temporarily reducing the severity of the symptom, aggravate the further clinical course of the disease.

General principles and measures of non-specific prevention

There are public and individual prevention of infectious diseases. Individual prevention involves compliance with the rules of personal hygiene in everyday life and at work, public includes a system of measures to protect the health of collectives. Measures to prevent infectious diseases can be conditionally divided into 2 large groups:

• general - state measures aimed at increasing material well-being, improving medical care, working conditions and recreation of the population, as well as sanitary-technical, agro-forestry, hydrotechnical and land reclamation measures, rational planning and development of settlements and much more that contributes to the elimination of infectious diseases.

• special - preventive measures carried out by specialists of medical and preventive and sanitary-epidemiological institutions. The system of preventive measures also includes international measures to prevent those dangerous infectious diseases that are regulated by the International Health Regulations (IHR) 2005.

The content and scale of preventive measures can be attributed directly to the focus of infection or extend to the entire district, city, region. When planning and implementing preventive measures, they are divided into 3 groups according to the place of application:

• measures regarding the source of infection, aimed at its neutralization (or elimination);

• measures regarding the transmission mechanism, carried out in order to break the transmission routes;

• measures to increase the immunity of the population;

Currently, all preventive measures against infectious diseases are also divided according to the executive action into 3 main groups:

• sanitary and hygienic,

• disinfection,

• disinsection.

Depending on the state of health, the presence of risk factors for the disease or pronounced pathology, 2 types of prevention are also considered:

• primary prevention - a system of measures to prevent the occurrence and impact of risk factors for the development of diseases (vaccination, rational work and rest regime, rational high-quality nutrition, physical activity, environmental protection, etc.). A number of primary prevention measures are carried out on a state scale.

• secondary prevention — a set of measures aimed at eliminating pronounced risk factors, which under certain conditions (stress, weakened immunity, excessive loads on any other functional systems of the body, etc.) can lead to the occurrence, exacerbation or recurrence of the disease. The most effective method of secondary prevention is medical examination as a complex measure of early detection of diseases, dynamic monitoring, targeted treatment, rational sequential recovery.

Specific prevention

In the system of anti-epidemic measures, it is the creation of the population's unfavorability to infectious diseases that occupies one of the most important places. Specific prevention (immunoprophylaxis) of infectious diseases is a traditional scientifically substantiated means of reducing morbidity and eliminating infectious diseases. The WHO strategy for reducing mortality and morbidity from infectious diseases, primarily among children, provides for the mandatory implementation of effective specific immunization of the population. The implementation of immunization programs has led to significant successes in the fight against infectious diseases. In particular, as a result of immunoprophylaxis on a global scale, smallpox was completely eliminated.

• Acquired artificial active immunity, which makes it possible for a person to be immune to a certain disease, is formed in the human body as a result of immunization with vaccines or toxoids, while the body forms specific immune reactions to antigens that are part of the vaccines.

• Acquired artificial passive immunity occurs as a result of the introduction of antibodies into the body in the form of immune serums, immunoglobulins, convalescent plasma, which almost immediately protect against infection. Such immunity is less stable and not as long-lasting as active.

During the primary immune response to the introduction of the vaccine, a certain number of "long-lived" T- and B-lymphocytes (immunological memory cells) are formed, which store information about the antigen and, upon its repeated entry into the body (revaccination), cause the formation of a secondary immune response. The secondary immune response is characterized by a higher affinity of antibodies (i.e. the strength of the bond between antigen and antibody) and the presence of mainly IgG and IgA antibodies, which are formed faster and more intensively. Revaccination is the basis for achieving long-term and intense immunity against most infectious diseases. The interval between vaccinations should not be less than one month.

The immune response to the introduction of vaccines develops in three phases:

• the latent phase lasts from the moment of the introduction of the vaccine until the appearance of specific antibodies, cytotoxic cells and effectors of delayed-type hypersensitivity in the blood and can last from several days to two weeks;

• the growth phase is characterized by an increase in antibody and T-lymphocyte titers

and can last from 4 days to 4 weeks. A rapid increase in the level of specific antibodies occurs with the introduction of a live measles vaccine (the first 3-4 days). This allows the use of a measles vaccine for emergency prophylaxis of measles in contact persons in the focus within 3 days after contact with the patient;

• the phase of antibody decline occurs after reaching the maximum antibody titer, and at first relatively quickly, then slowly over several years or decades. If the decrease in protective antibodies reaches a critical level and at this time infection with the corresponding pathogen occurs, then the development of the disease is possible.

With repeated administration of a certain antigen, the latent phase and the growth phase are shortened, and the decline phase becomes longer. Vaccination can consist of a series of vaccine administrations with a minimum interval. Revaccination, as a rule, consists of the administration of a single dose of vaccine. Live viral vaccines are designed to multiply the vaccine (attenuated) virus in the cells of the vaccinated body, which creates stable immunity after the first administration of the vaccine. Scheduled vaccination is an effective means of controlling many infections. At the same time, a significant epidemiological effect can be obtained only when at least 95% of the relevant population groups are covered by vaccination.

Medical immunobiological preparations used for immunoprophylaxis are divided into:

• vaccines - preparations made from microorganisms, their antigens and toxins:

• vaccines made from microorganisms are divided into live and inactivated (killed). There are also vaccines from antigenic components of microorganisms (chemical polysaccharide, subunit vaccines, toxoids) and genetically engineered (recombinant) vaccines. Genetic vaccines (DNA vaccines) and synthetic vaccine preparations are under development.

• toxoids (toxoids) are produced in the form of monopreparations (diphtheria, tetanus, staphylococcal, etc.) and associated preparations (diphtheria-tetanus). The introduction of toxoids produces only antitoxic immunity, which, however, does not provide complete protection against infection and does not prevent the occurrence of bacterial carriage. To achieve intense antitoxic immunity, at least two vaccinations and revaccination with preparations of this group are required. At the same time, their prophylactic effect reaches 96-100% and persists for several years. An important feature of toxoids is also that they ensure the preservation of long-term immunological memory, so when administered a second time to people who were vaccinated 10 or more years before, there is a rapid formation of antitoxic antibodies in high titers (by the type of secondary immune response).

• serums, immunoglobulins - in this case, antibodies are already "ready for action". These preparations are made from the blood of hyperimmunized animals (heterogeneous serums or immunoglobulins) or people (homologous or allogeneic) who have suffered an infectious disease in the past, or from the blood of specially immunized volunteers. Currently, the following antiviral and antibacterial drugs are used for emergency prevention and treatment: heterogeneous anti-tetanus, anti-botulinum serum, normal immunoglobulin for the prevention of viral hepatitis A and B, measles, rubella, whooping cough, anti-staphylococcal, anti-influenza, anti-rabies immunoglobulins, etc. Before administering heterogeneous serums or immunoglobulins, the individual sensitivity of the body to a foreign protein is necessarily determined by an intradermal test. Immune protection is provided immediately with intravenous administration of such drugs or 4-24 hours after intramuscular administration. The most active effect is manifested in the first day after administration of the drug, but can persist for up to 2 weeks or more. The ability of drugs of this group to quickly provide immune protection also determines the area of their application. They are used for emergency prophylaxis of contact persons, prevention of certain diseases due to specific possibilities of infection (tetanus, rabies, etc.), for the treatment of certain diseases (tetanus, gas gangrene, diphtheria, etc.).

Questions for self-control on the topic:

1. List the etio-pathogenetic mechanisms of action of antibiotics.

2. Name the main classifications of antibiotics.
3. List the main groups of antibiotics that have bactericidal or bacteriostatic action.
4. Give the classification of penicillins, cephalosporins, aminoglycosides, tetracyclines.
5. Name the criteria that determine the choice of an antibiotic for the treatment of an infectious process.
6. List the criteria for the effectiveness of the action of antibiotics.
7. Indicate the stages of assessing the action of an antibiotic in the temporal aspect. The doctor's tactics at these stages.
8. What organs and systems are involved in the elimination of antibiotics and the significance of this process?
9. What features of the body should be taken into account when prescribing antibiotics?
10. Name the clinical and laboratory indicators that characterize the function of the kidneys and liver. What is their significance when choosing an antibiotic?
11. What are the features of prescribing antibacterial therapy in terms of preventing allergic complications
12. List the undesirable effects of antibiotic therapy, methods of their prevention and treatment.
13. Name the general properties of penicillins and cephalosporins. What is the practical significance of this in treating patients and choosing combination therapy?
14. What are the features of the pharmacokinetics and pharmacodynamics of lincomycin?
15. Principles of selecting and prescribing antibacterial drugs during pregnancy and lactation.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by om.m. Bilovol. – Vinnytsia: Nova Kniga, 2021. – 544 p.
3. Clinical Pharmacy (Pharmaceutical Care): A Textbook for Students of Higher Medical (Pharmaceutical) Schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: A Textbook for Students of Pharmaceutical Faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Modern Classifications and Standards of Treatment of Diseases of Internal Organs. Emergency Conditions in Therapy. Analyses: Normative Indicators, Interpretation of Changes / Ed. Prof. Yu.M. Mostovoy. – 25th ed., changes and additions. – Kyiv: Center of State Library, 2018. – 792 p.

LECTURE 12. TOPIC "ANTIBIOTICS: CLINICAL PHARMACOLOGY OF MODERN GROUPS OF ANTIBIOTICS"

Relevance of the topic: Antibiotics are essential for their vital role in treating bacterial infections, but overuse and misuse are leading to the development of drug resistance, a serious health threat.

Antibiotics remain essential for the treatment of many serious bacterial infections, such as pneumonia, meningitis and sepsis, and for preventing complications after surgery and in patients with certain medical conditions. However, overuse and misuse of antibiotics, especially for viral infections such as influenza and the common cold, is leading to the development of antibiotic resistance.

Antibiotic resistance, or the resistance of bacteria to antibiotics, is a serious problem because it makes it harder to treat infections, increases mortality and the cost of treatment. According to the WHO, antibiotic resistance is one of the ten greatest threats to humanity and is predicted to lead to a significant increase in mortality in the coming years.

Causes of antibiotic resistance:

• Overuse of antibiotics, especially for viral infections, where they are not effective.

• Incorrect prescription of antibiotics without a doctor's prescription.

• Non-compliance by patients with the course of treatment, which leads to the fact that bacteria are not completely destroyed and can develop resistance.

• Use of antibiotics in livestock and fish farming.

What to do to overcome antibiotic resistance:

• Consult a doctor for a prescription for antibiotics only in cases of bacterial infections.

• Strictly adhere to the prescribed course of treatment.

• Do not self-medicate and do not use antibiotics to treat viral infections.

• Raise public awareness about the problem of antibiotic resistance.

Antibiotics are an important tool in the fight against bacterial infections, but their responsible use is critical to maintaining their effectiveness in the future.

Purpose: To familiarize the HES with the basic principles of antibacterial therapy, the modern algorithm for selecting and selecting modern groups of antibiotics for a specific patient, choosing the dosage regimen, route of administration, frequency of administration, duration of therapy; explain the importance of monitoring the effectiveness and safety of antibiotic use in a given specific patient.

Basic concepts (list of questions):

Antibiotics are drugs used to combat bacterial infections. They either kill bacteria (bactericidal antibiotics) or inhibit their reproduction (bacteriostatic antibiotics), helping the body fight the infection.

Cephalosporin antibiotics of 4-5 generations are broad-spectrum antibiotics used to treat bacterial infections. 4th generation cephalosporins, such as cefepime, have improved activity against gram-negative bacteria, including some strains resistant to beta-lactamases. Fifth-generation cephalosporins, such as ceftobiprole and ceftaroline, have an extended spectrum of activity, including methicillin-resistant Staphylococcus aureus (MRSA).

Carbapenem antibiotics are a class of β-lactam antibiotics that have a β-lactam ring in their structure that is not directly linked to a thiazolidine ring. There are three generations of carbapenems: 1st - imipenem, thienames, 2nd - meropenem, 3rd - ertapenem.

Monobactam antibiotics are a group of beta-lactam antibiotics that have bactericidal

activity. The only monobactam currently available is aztreonam. They are effective against aerobic gram-negative bacteria, including some strains of Pseudomonas aeruginosa.

Glycopeptide antibiotics are a class of antibiotics that contain a glycosylated cyclic or polycyclic nonribosomal peptide. In addition to the glycosidic and peptide parts, glycopeptides can contain acyl residues of various lengths. Such glycopeptides are sometimes referred to as lipoglycopeptides (e.g., teicoplanin). A feature of all glycopeptides is that they inhibit the biosynthesis of peptidoglycan, the main component of the bacterial cell wall, which is vital for their survival. Important glycopeptide antibiotics include the anti-infective antibiotics vancomycin, teicoplanin, and telavancin.

Antibiotics – streptogramins – a group of natural antibiotics and their derivatives produced by bacteria of the genus Streptomyces. Each streptogramin consists of 2 completely separate chemical compounds, the first group of these compounds (streptogramins A) are macrolactone molecules containing many unsaturated bonds, and include: pristinamycin IIA, pristinamycin IIB, dalfopristin (a semi-synthetic derivative of pristinamycin IIB).

Antibiotics - oxazolidinones are a class of antibiotics used to treat infections caused by gram-positive bacteria, in particular those resistant to other antibiotics, such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE). The most famous representative of this group is linezolid.

Lecture content (lecture text)

Antibiotics (Greek anti - against + bios - life) - products of vital activity (or their synthetic analogues and homologues) of living cells (bacterial, fungal, plant and animal origin), which selectively inhibit the functioning of other cells - microorganisms, tumors, etc. This group includes hundreds of drugs of different chemical structure, which differ in the spectrum and mechanism of action, side effects and indications for use. The term "A." was proposed by S.A. Vaksman (1942). The division of A. into groups by predominant activity is based on the classification of pathogens of infectious diseases. There are A. with antibacterial, antiprotozoal, antifungal and antitumor activity. The activity of A. is not constant, but decreases over time, which is due to the formation of resistance; Resistant pathogens pose a danger not only to the patient from whom they are isolated, but also to many other people, even those separated by space and time.

Classification of antibiotics. Traditionally, antibiotics are divided into natural (penicillins, lincomycin, vancomycin, etc.), semi-synthetic (products of modification of natural molecules: amoxicillin, clindamycin, cefazolin, etc.). The accepted division into groups, classes and generations (generations) is of great importance in terms of understanding the mechanism of action, spectrum of activity, features of pharmacodynamics and pharmacokinetics, the nature of undesirable side reactions, selectivity of action.

Classification of antibiotics by mechanism of action:

• inhibitors of cell wall synthesis of microorganisms (β-lactams, vancomycin);

• Antibiotics that disrupt the molecular organization and function of cell membranes (polymyxins, antifungals, aminoglycosides, cyclic lipopeptides);

• Antibiotics that inhibit protein and nucleic acid synthesis - inhibitors of protein synthesis at the ribosomal level (chloramphenicols, tetracyclines, macrolides, lincosamides, aminoglycosides, oxazolidinones);

• RNA polymerase inhibitors (ansomacrolides).

By chemical structure:

• β-lactams (penicillins, cephalosporins, carbapenems, monobactams);

• aminoglycosides;

• macrolides (erythromycin, clarithromycin, roxithromycin, azithromycin, spiramycin, josamycin, midecamycin);

• chloramphenicols;

• tetracyclines;

• lincosamides (lincomycin, clindamycin);

• fusidic acid;

• ansamacrolides (rifampicin);

• polymyxins;

• polyenes (nystatin, levorin, amphotericin B).

By spectrum of antimicrobial action:

• Antibiotics that act mainly on gram-positive and gram-negative cocci and gram-positive bacilli - corynebacteria, clostridia (first-generation cephalosporins, phenoxymethylpenicillin, bicillin, penicillinase-resistant penicillins (oxacillin, methicillin), macrolides (midecamycin, azithromycin, roxithromycin), vancomycin, lincomycin);

• Antibiotics active against gram-positive and gram-negative bacteria (chloramphenicol, tetracyclines, aminoglycosides, semi-synthetic penicillins (ampicillin, carbenicillin, azlocillin), second-generation cephalosporins);

• Antibiotics, with predominant activity against gram-negative bacteria (third-generation cephalosporins);

• anti-tuberculosis: Antibiotics (streptomycin, rifampicin, florimycin);

• antifungal: Antibiotics (nystatin, griseofulvin, amphotericin B).

Questions for self-control on the topic:

1. List the etio-pathogenetic mechanisms of action of antibiotics.
2. Name the main classifications of antibiotics.
3. List the main groups of antibiotics that have bactericidal or bacteriostatic action.
4. Give the classification of penicillins, cephalosporins, carbapenems, glycopeptides, streptogramins.
5. Name the criteria that determine the choice of an antibiotic for the treatment of an infectious process.

6. List the criteria for the effectiveness of the action of antibiotics.
7. Indicate the stages of assessing the action of an antibiotic in terms of time. The doctor's tactics at these stages.
8. What organs and systems are involved in the elimination of antibiotics and the significance of this process?
9. What features of the body should be taken into account when prescribing antibiotics?
10. Name the clinical and laboratory indicators that characterize the function of the kidneys and liver. What is their significance when choosing an antibiotic?
11. List the undesirable effects of antibiotic therapy, methods of their prevention and treatment.
12. Principles of selection and prescription of antibacterial drugs during pregnancy and lactation.

List of sources on the topic:

1. Clinical pharmacology: a textbook / Ed. O.M. Bilovol. – Vinnytsia: Nova Knyga, 2021. – 544 p.
2. Clinical pharmacy: a textbook for students of pharmaceutical faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
3. Modern classifications and standards of treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Ed. Prof. Yu.M. Mostovoy. – 28th ed., changes and additions. – Kyiv: Center of the State Library, 2023. – 792 p.

LECTURE 13. TOPIC
"Neurosis and stress: principles of choosing drugs"

Relevance of the topic: Stress is a pressing problem for many people, especially in the conditions of modern life and challenges such as war, economic difficulties, and other social factors. Constant stress can negatively affect physical and mental health, leading to various diseases and a decrease in the quality of life.

The relevance of stress can be considered from several perspectives:

• Increasing the frequency and intensity of stressful situations: The modern world is characterized by a high rate of change, an increase in the amount of information, competition and uncertainty, which leads to an increase in stress factors.

• Negative health consequences: Prolonged stress can cause serious diseases such as cardiovascular diseases, diabetes, depression, as well as sleep problems, reduced immunity and others.

• Decreased productivity and quality of life: Stress can affect cognitive functions, concentration, memory, as well as emotional state, which leads to a decrease in productivity at work, in school and in everyday life.

• The importance of psychological support: Awareness of the relevance of stress encourages people to find ways to overcome it and develop stress-resistance skills, as well as to seek help from psychologists and other specialists.

It is important to understand that stress can be both a negative and a positive factor:

• Short-term stress can be beneficial: It can mobilize the body, improve attention, increase immunity and motivation.

• It is necessary to distinguish between acute and chronic stress: Acute stress is a short-term reaction to a stimulus, and chronic stress is a long-term condition that can negatively affect health.

Currently, in conditions of war, the relevance of stress in Ukraine is extremely high:

• Studies show that the majority of Ukrainians experience stress and nervousness: According to the results of a survey conducted by Gradus Research, 77% of Ukrainians experience stress and severe nervousness, and another 52% experience anxiety and tension.

• It is important to provide support and assistance to people suffering from the effects of stress: Psychological support and the development of stress-management programs are important tasks during this period.

In conclusion, the relevance of stress lies in its prevalence, negative health consequences, and the importance of developing stress tolerance and psychological support. In the context of the war in Ukraine, this issue is becoming particularly acute, so systemic measures are needed to help people suffering from stress.

Purpose: To familiarize the HES with the basic principles of therapy aimed at reducing the impact of neurotic and stressful factors on the body, the modern algorithm for selecting and selecting drugs for a specific patient that suppress the functions of the CNS, choosing the dosage regimen, route of administration, frequency of administration, duration of therapy; to explain the

importance of monitoring the effectiveness and safety of the use of relevant drugs in a specific patient.

Basic concepts (list of questions):

Neurosis is a group of functional psychogenic disorders of the nervous system, characterized by asthenic, obsessive or hysterical manifestations, as well as a temporary decrease in mental and physical performance. These disorders arise as a result of excessive psycho-emotional stress, stress and psychological trauma, but are not accompanied by organic brain damage.

Stress is the body's natural reaction to any demands or changes, which may be physical, emotional or psychological. It is a non-specific reaction that helps to adapt to new circumstances. Stress can be both positive, for example, motivating to achieve, and negative, when it becomes excessive and prolonged, affecting mood, physical and mental health.

The central nervous system is the part of the nervous system consisting of the brain and spinal cord, and is responsible for processing information and controlling body functions. The central nervous system is a complex and vital system that controls almost all functions of the body. It consists of:

• Brain: Responsible for thinking, memory, emotions, movement, perception, and many other processes.

• Spinal cord: Transmits signals between the brain and other parts of the body and controls some reflexes.

The CNS works closely with the peripheral nervous system, which consists of nerves that extend beyond the brain and spinal cord. Together, they form the nervous system that connects the body to the outside world and coordinates all of its functions.

Tranquilizers – also known as anxiolytics or anti-anxiety drugs – are psychotropic medications used to reduce anxiety, emotional tension, and mental agitation. They relieve symptoms of fear, worry, and sleep disorders, but do not treat the causes of these conditions.

What tranquilizers do:

• Reduce anxiety and tension: Tranquilizers affect the central nervous system by reducing the activity of certain neurotransmitters, which leads to calmness.

• Eliminate fear and anxiety: They help reduce the intensity of these emotions, improving the patient's psychological state.

• Improve sleep: Tranquilizers can have a sedative effect, making it easier to fall asleep and improving the quality of sleep.

Antidepressants are a group of medications used to treat depression and other mental disorders, such as anxiety disorders. They affect chemical processes in the brain, regulating the levels of neurotransmitters such as serotonin, norepinephrine, and dopamine, which affects mood and emotional state.

• Purpose: Antidepressants are prescribed to treat depression, anxiety disorders, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and other mental illnesses.

• Mechanism of action: They affect neurotransmitters in the brain that are responsible for mood and emotions. Antidepressants generally help restore the balance of these chemicals, improving mood and reducing symptoms of depression and anxiety.

• Different types of antidepressants: There are different groups of antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), and others.

Psychosedative drugs are a group of psychotropic drugs that affect the central nervous system, reducing its activity and causing a calming effect. They can be used to reduce anxiety, emotional

tension, agitation, and other mental disorders.
• Mechanism of action: Psychosedative drugs affect various parts of the brain, including the cortex, limbic system, striatum, thalamus, hypothalamus, and reticular formation. They enhance inhibitory processes or suppress excitatory processes in the central nervous system.
• Uses: Psychosedative drugs are used to treat various mental disorders, such as anxiety, insomnia, and psychosis, and to reduce emotional tension and agitation in mentally healthy people.
• Classification: Psychosedative drugs may include:
• Neuroleptics (antipsychotics): used to treat psychoses, including schizophrenia, and help eliminate delusions, hallucinations, and other symptoms of psychosis.
• Tranquilizers: reduce anxiety and tension, have a sedative effect.
• Sedative drugs: have a calming effect, can be used to treat insomnia and other disorders.

Lecture content (lecture text)

Pharmacotherapy of neuroses and stress involves the use of various drugs to relieve symptoms and improve psychological state. The main groups of drugs are sedatives, anxiolytics, antidepressants, and tranquilizers, which are prescribed as needed. Psychotherapy also plays an important role in the treatment of these conditions.

Drug treatment:

• Sedatives: Calm the nervous system and reduce anxiety. These include, for example, drugs based on valerian and motherwort.

• Anxiolytics (anti-anxiety drugs): Help reduce anxiety, fear, and panic attacks.

• Tranquilizers: Widely used to reduce anxiety, excitement, and fears.

• Antidepressants: Used for depression and sleep disorders, helping to stabilize mood and improve emotional state.

• Nootropics: Can improve cognitive function and concentration.

• B vitamins: Help reduce irritability and improve the functioning of the nervous system.

Non-drug treatment:

• Psychotherapy: Helps identify and resolve the internal causes of neurosis.

• Physical therapy, relaxation massage, hardening: Can be useful for anxiety disorders.

• Diet: A diet rich in omega-3 fatty acids is useful for maintaining brain health. You should limit the use of caffeine, alcohol and sweets.

• Daily regimen: It is important to adhere to a sleep and wakefulness regimen, as well as avoid excessive physical and emotional stress.

Important to remember:

• Self-medication can be harmful, so if symptoms of neurosis or stress appear, you should consult a doctor for professional help and determine the appropriate treatment.

• Treatment of neurosis and stress is often complex and may include both drug therapy and psychotherapy and lifestyle changes.

Neurosis is a nervous system failure that occurs as a result of the depletion of its capabilities. The causes of such a disorder can be quite a lot of different factors: from severe stress to climacteric changes in the body.

Usually, such diseases are treated comprehensively. Not only medications for neurosis are needed, but also psychotherapy. Modern pharmaceuticals offer a variety of medications for neurosis, but before taking them, you need to consult a specialist. Only a doctor can choose the most effective drugs for the nervous system that will help in the treatment of a particular patient. And it is most convenient to order online and purchase the best drugs for neurosis at affordable prices at the pharmacy "We wish you health".

A variety of drugs for the treatment of the nervous system

In the presence of such anxiety states, the doctor can prescribe a variety of medical products, taking into account the patient's condition. The most popular are drugs for the treatment of neurosis in capsules and tablets, but there are also other forms of drugs:

• drops;
• syrups;
• solutions for injections;
• powders;
• granules;
• herbal preparations;
• syrups, etc.

Modern manufacturers produce medical products that are designed for different conditions of patients. For example, with a minor form of the disease, it is best to use herbal preparations. They are available in the form of teas in bags, so they are very convenient to use.

More serious disorders require longer and more effective treatment, so for convenience, medications in drops or granules are used. Injection solutions are prescribed for the most severe forms.

Categories of drugs for neurosis

Medicines for the treatment of neurosis are divided into several varieties. In modern drug therapy of such disorders, the following types are used:

• antidepressants - can be activating or sedative (overcome panic, fear, depression). Sleeping pills are prescribed for severe sleep disorders. Tablets are taken before bedtime, the course is no more than one month;
• tranquilizers – provide muscle relaxation, prevent seizures, have a hypnotic effect;
• neuroleptics – have an antipsychotic effect, relieve irritability, fear;
• nootropics – overcome apathy, saturate the brain with oxygen, remove toxins.

Phytopreparations (herbal remedies). Preparations based on medicinal plants (valerian, lemon balm, St. John's wort) can be used as auxiliary means.

Questions for self-control on the topic:

1. Anatomical and physiological aspects of the nervous system.
2. Functions of the CNS.
3. Functions of the peripheral nervous system.
4. General information about the etiology, pathogenesis of vascular diseases of the CNS.
5. Main clinical and diagnostic characteristics of CNS diseases.
6. Main clinical and diagnostic characteristics of peripheral nervous system diseases.
7. Stress: etiology, pathogenesis, treatment.
8. Neurosis: etiology, pathogenesis, treatment.
9. The main subjective signs of diseases of the nervous system, in which symptomatic treatment is possible.
10. Justification for the appointment of etio-pathogenetic therapy of diseases of the nervous system.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Ed. O.M.Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmac.) schools / I.A.Zupanets, V.P.Chernykh, T.S.Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical pharmacy: textbook for students of pharmaceutical faculties / Ed. V.P.Chernykh, I.A.Zupanets, I.G.Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Protocols of a pharmacist (pharmacist) / Ed. V.P. Chernykh, I.A. Zupanets, O.M. Lischyshyna. – Kharkiv: Zoloti storyni, 2013. – 192 p.

6. Modern classifications and standards of treatment of diseases of internal organs. Emergency conditions in therapy. Analyses: normative indicators, interpretation of changes / Edited by prof. Yu.M. Mostovoy. – 25th ed., changes and additions. – Kyiv: Center of State Clinical Laboratory, 2018. – 792 p.

LECTURE 14. TOPIC
"Pharmaceutical care: definition, principles, role of pharmacist in the implementation of pharmaceutical care"

Relevance of the topic: Pharmaceutical care is extremely relevant in modern conditions, as it is aimed at ensuring the rational and safe use of medicines by patients, which leads to improved treatment outcomes and reduced risks of side effects.

The relevance of pharmaceutical care is due to several factors:

• The growth of self-medication: More and more people are engaged in self-medication, and pharmaceutical care helps them correctly select and use medicines, avoiding errors and complications.

• The need for an individual approach: Each patient has unique needs and characteristics, and the pharmacist can provide individual recommendations for taking medicines, taking into account age, concomitant diseases, other medicines taken.

• Reducing the number of side effects: Pharmaceutical care helps to identify possible negative interactions between medicines and prevent them, which contributes to safer treatment.

• Increasing the effectiveness of treatment: Correct medication administration, as determined by pharmaceutical care, increases the chances of recovery and improvement of the patient's health.

• Reducing treatment costs: Avoiding side effects and more effective treatment lead to lower costs for medications and additional examinations.

• Strengthening the role of the pharmacist: Pharmaceutical care contributes to increasing the professional role of the pharmacist as a consultant and assistant to the patient in matters related to medicines.

• Improving the interaction between the doctor, pharmacist and patient: Pharmaceutical care contributes to closer interaction between these three parties, which positively affects the treatment process.

Therefore, pharmaceutical care is an important component of the modern health care system, ensuring the rational, safe and effective use of medicines for patients.

Purpose: To familiarize HES with the basic principles and provisions of pharmaceutical care; modern requirements for practical and theoretical training of a pharmacist in accordance with the rules of good clinical practice, effective and safe pharmacotherapy; provide basic rules for choosing and selecting the appropriate dose, route of administration, and timing of drug use both when prescribed by a doctor and when responsible self-medication; explain the importance of monitoring the effectiveness and safety of drug use in a given patient.

Basic concepts (list of questions):

Medicinal substance (active substance, substance) - any substance or mixture of substances that is intended for use in the production of a medicinal product and during this use becomes its active ingredient.

Medicinal product - a substance or mixture of substances used for the prevention, diagnosis, treatment of diseases, or changes in the state and functions of the body and permitted by the relevant authorities for use within the country and in accordance with current legislation.
Over-the-counter drugs - over-the-counter drugs or OTC drugs (English Over the Counter - without a prescription) - a large group of drugs that a patient can buy for self-medication directly at a pharmacy (and some drugs - and not only at a pharmacy) without a doctor's prescription.
Pharmacodynamics - a section of pharmacology that studies the biochemical effects and physiological actions of drugs, studies the mechanisms of action of drugs, the relationship between the concentration of medicinal substances and the effect achieved by them, studies possible pharmacological effects.
Pharmacokinetics - a section of pharmacology that studies the intake (routes of administration), absorption (absorption), distribution, transformation (biotransformation) of drugs in the body, their removal (excretion, elimination) from the body, as well as the dependence of the effectiveness and tolerability of drugs depending on these processes.
Pharmaceutical care is a comprehensive program of interaction between a pharmacist and a patient (pharmacist and doctor) throughout the entire period of medication therapy. The concept of self-medication, responsible self-medication is the use by a consumer of over-the-counter medications for the prevention and treatment of health disorders and to reduce the severity of subjective symptoms recognized by him/herself.

Lecture content (lecture text)

PHARMACEUTICAL CARE (P.c.) is a comprehensive program of interaction between a pharmacist and a patient (pharmacist and doctor) throughout the entire period of drug therapy, starting from the moment of dispensing the drugs until their complete cessation.

For the first time, the term "P.c." was formulated in the Tokyo Declaration, which was adopted by the Congress of the International Federation of Pharmacists in 1994. In the same year, the WHO defined the concept of GPP, an element of which is P.o. In the light of the requirements of GPP, the term "P.c." has become established as the name of the ideology of practice that defines the patient and society as the primary users of the pharmacist's activities. P.o. involves the involvement of a pharmacist in active activities to ensure health and prevent diseases among the population, the responsibility of a pharmacist to a specific patient for the result of treatment with pharmacological drugs, but must be carried out by a pharmacist in close cooperation with other health care professionals (doctors and nurses). The pharmacist is not only obliged to provide the patient with high-quality drugs and medical devices - the main task of his professional activity is to increase the effectiveness and safety of drug therapy for a specific patient. In pharmacy practice, there is often a need for F.c. patients, taking into account responsible self-medication, which necessitates the control of therapy for outpatients. Responsible self-medication is possible only in the event of the development of life-threatening symptoms and syndromes, which can be eliminated with the help of over-the-counter (OTC) drugs of various groups (antacids, laxatives, analgesics-antipyretics, antispasmodics, etc.). Throughout life, each person uses responsible self-medication, without consulting a doctor for "non-serious" symptoms - headache, heartburn after overeating or drinking alcoholic beverages, scratches, abrasions, cuts, runny nose, flatulence, constipation. In such cases, the role of a pharmacist as a consultant on drug therapy is paramount. A pharmacist in a pharmacy in the system of measures that determine the F.o. takes into account physiological, biopharmaceutical and pharmacoeconomic factors and gives recommendations for the use of drugs, their generic replacement.

The basis of the F.c. is the professional knowledge and experience of the pharmacist, the norms of professional medical and pharmaceutical ethics and deontology, the pharmacist's

friendly attitude to the patient and a responsible attitude to his duties. To implement the F.c. When dispensing over-the-counter drugs in a pharmacy, the pharmacist must: correctly assess the patient's problem (age, gender and individual characteristics of the person subject to F.o.; symptoms, duration of illness, medical history; find out whether the symptoms are associated with any serious health disorder and, if so, refer the patient to a doctor; in the case of a less serious problem, give advice); provide the patient with over-the-counter drugs and complete information about the action of the drug, its method of use, duration of treatment, combination with other drugs and food, possible side effects; advise the patient to seek further medical supervision.

Pharmaceutical care solves the main problems associated with the dispensing of drugs and is a close interaction between the pharmacist, doctor and patient throughout the entire period of drug therapy.

A pharmacist is one of the most accessible healthcare professionals who directly provides the consumer with objective information about the use of drugs to increase the effectiveness and safety of therapy for a particular patient. In particular, it provides the choice of the optimal dosage form and route of administration of the drug, advises on the rules for using different dosage forms, dosage features, interactions with other drugs, food, alcohol and nicotine, the optimal time of day for taking these drugs, possible adverse effects of drugs on the functions of human organs and systems, as well as on the storage conditions of this drug.

Nowadays, the role of a pharmacist in providing primary health care is difficult to overestimate, since the concept of self-medication is rapidly developing and the indications for the use of non-prescription drugs are constantly expanding. At the same time, the actions of a pharmacist must be in accordance with the rules and recommendations of good pharmacy practice, which is developed to ensure the proper quality of pharmaceutical services. Good pharmacy practice determines the role of a pharmacist in the health care system, in particular in promoting public health and preventing diseases, ensuring the safety of effective and rational treatment, identifying and solving problems in the use of drugs. Good pharmacy practice defines the role of the pharmacist in the healthcare system, in particular in promoting public health and disease prevention, ensuring the safety of effective and rational treatment, identifying and resolving problems with the use of medicines. The rules of good pharmacy practice aim to provide the population with high-quality, safe medicines and medical devices, provide timely and verified information about the medicine, promote a healthy lifestyle and disease prevention, familiarize with the rules for the rational use of prescription medicines, as well as provide information about the side effects of medicines and measures to assist in self-medication.

To provide proper pharmaceutical care for patients in a pharmacy, a pharmacist must have sufficient information about the treatment regimens of the most common diseases, and the basics of the rational use of medicines, advise the patient, have complete information about medicines, dosage forms and features of their use, the influence of age, gender, kidney and liver diseases, etc. on the pharmacodynamic effects of the drug. It is important to warn the patient about the possible negative effects of drugs on the body. The pharmacist establishes the most rational route and regimen of drug administration, prevents the prescription of incompatible drugs and controls polypharmacy in treatment.

Therefore, to ensure proper pharmaceutical care, the pharmacist must adhere to the following algorithm of actions:

• establishing the symptom for the treatment of which the patient decided to purchase this drug;

• questioning the patient whether this symptom is a manifestation of a disease that requires mandatory treatment to a doctor;

• determining the pharmacotherapeutic group of drugs that must be prescribed to this patient;

• choosing the optimal drug for the patient in this particular case from among the drugs of this group;

• providing the patient with appropriate information about the selected drug in a form accessible to him.

Thus, the key to proper pharmaceutical care is the pharmacist's professional knowledge and experience, compliance with the norms of professional pharmaceutical ethics, attitude to the patient and his duties.

Questions for self-control on the topic:

1. Definition of the subject - clinical pharmacy, history of development in the world in Ukraine.

2. The main tasks of clinical pharmacy:

 clinical testing of new pharmacological agents;

 clinical research and reassessment of old drugs;

 development of methods for the effective and safe use of drugs;

 organization of information services and advisory assistance of various specialists;

 training of students and doctors.

3. Basic concepts of clinical pharmacy:

 medicinal substance.

 medicinal product - brand names, generic names - advantages and disadvantages, the concept of bioequivalence;

 the concept of "chemical name", "international non-proprietary name", "trade name", "brand name" of drugs.

 OTC drug;

4. Medical monitoring: concepts, conditions that determine the need for medical monitoring.

5. Pharmaceutical care - definition of the term.

6. The role of pharmaceutical care in the development of the self-medication system.

7. The algorithm of actions of a pharmacist is the main goal of such an algorithm.

8. Self-medication is an essential part of the modern health care system.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.

2. Clinical pharmacy (pharmaceutical care): a textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others – Kh.: NFAU: Golden Pages, 2011. – 704 p.

3. Clinical pharmacy: a textbook for students of pharmaceutical faculties / Edited by V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

4. Protocols of a pharmacist / Edited by V.P. Chernykh, I.A. Zupanets, O.M. Lischyshyna. – Kharkiv: Zoloti storynych, 2013. – 192 p.

LECTURE 15. TOPIC
"Side effects of drugs: prevention and treatment. General principles of treatment of acute drug poisoning"

Relevance of the topic: According to WHO, adverse drug reactions occur in 0.4%-10-20% of hospitalized patients and in 2.5%-28% of outpatients. Mortality from adverse drug reactions is 5th in the world (after diseases of the cardiovascular system, lungs, oncological pathology, injuries). Thus, consideration of the topic is relevant for studying the course of clinical pharmacy and further practical activity of a pharmacist.

Purpose: To familiarize the HES with the main types of side effects, mechanisms of occurrence of side effects, acute and chronic toxicity of drugs, principles of detection, monitoring, prevention and treatment of negative consequences of drug use, explain the importance of monitoring the effectiveness and safety of drug use in a given patient.

Basic concepts (list of questions):

Side effect - characterized by the ability of a drug to cause an undesirable or harmful effect simultaneously with the main therapeutic effect.

Unpredicted side effect - an undesirable effect that develops rarely and is not always due to the pharmacological action of the drug, not previously described in the medical literature.

Predicted side effect - an effect that has a certain clinical picture and has been previously described in the medical literature.

Undesirable pharmacological effect - each substance causes a number of pharmacological effects characteristic of it. In each specific case, only certain effects of the drug are used, which are defined as the main effects. Other pharmacological effects are called undesirable, or side, effects.

Antidotes - various drugs that, interacting with the poison, neutralize it, reduce the toxic effect or contribute to its rapid elimination from the body.

Toxicity - the property of a substance to cause poisoning or death when entering the body in certain quantities.

Toxicodynamics is a section of toxicology that studies and examines the mechanism of toxic action, the patterns of development and manifestation of various forms of the toxic process.

Lecture content (lecture text)

Side effects of drugs, or side effects (English side effects) - any detection of undesirable, i.e. inappropriate for the purpose of pharmacotherapy, sometimes dangerous effects of drugs on

the body, which occurs in the range of therapeutic doses (recommended for treatment, diagnosis or prevention of diseases).

A side effect of drugs is the antipode of the main effect for which drugs are used. Side effects of drugs are heterogeneous in their detection and frequency of occurrence, therefore they require various methodological techniques. The frequency of S.D. reaches 20% in outpatient treatment, up to 5% of patients require hospitalization to treat its consequences. Most often in Ukraine, S.D. is registered when using antibacterial drugs, blood substitutes, anti-inflammatory, analgesic drugs, cardiological drugs, anesthetics, vitamins, and antitumor agents. But the statistics of S.D.L. sometimes reflects not so much the relevant properties of certain drugs, but the frequency of their use.

According to the international classification, the side effect of drugs is divided into reactions of type A, B, C and D. According to the mechanism of occurrence, it can be of non-allergic and allergic origin. Adverse drug reactions of non-allergic origin are mainly included in group A, occur most often (up to 75% of all cases). It is due to the pharmacological properties of the drug, is predictable, depends on the dose of the drug (directly proportionally), and can be studied experimentally. Similar types of side effects are most typical for non-selective drugs, and increasing selectivity helps to reduce Adverse drug reactions. For example, β1,2-adrenoceptor blockers - propranolol, oxprenolol, pindolol, etc. when used for hypotensive, antianginal, antiarrhythmic purposes (for these effects, blockade of β1-adrenoceptors in the myocardium is necessary), they often cause an increase in bronchial tone and secretion, which is due to blockade of β2-adrenoceptors. Cardioselective drugs: acebutolol, nebivolol, bisoprolol, etc. - usually devoid of this P.d.l. Indomethacin, acetylsalicylic acid and other NSAIDs - non-selective COX 1 and 2 types inhibit the synthesis of cytoprotective prostaglandins in the stomach, therefore often cause gastropathy (irritation of the mucous membrane). In contrast, selective and specific COX-2 inhibitors (nimesulide, meloxicam, celecoxib, etc.) cause gastropathy much less often. Diazepam is a tranquilizer that stimulates GABAergic processes due to the activation of benzodiazepine receptors, can cause unwanted drowsiness and muscle relaxation in the treatment of anxiety disorders, but the anxiolytic drug afobazole is devoid of this type of P.d.l. Drug dependence can be caused by drugs that cause euphoria or hallucinations - ketamine, etc. Infrequent manifestations of P.d.l. of a non-allergic nature include idiosyncrasy, i.e. congenital hypersensitivity to drugs. For example, in individuals with a genetic defect (low activity) of the cholinesterase enzyme in the blood, the depolarizing muscle relaxant dithylin can cause very long - up to several hours - relaxation of skeletal muscles with respiratory impairment. The causes and mechanisms of idiosyncrasy are studied by pharmacogenetics.

To S.D. include dangerous effects that occur when using drugs in pregnant women due to the penetration of drugs and/or their metabolites from the mother's vascular bed into the embryo or intrauterine fetus. This is an embryotoxic, teratogenic and fetotoxic effect. An embryotoxic effect is damage to the zygote or embryo located in the lumen of the fallopian tube or uterine cavity, i.e. before implantation - in the first 3 weeks after fertilization. Damage and even death of the embryo can be caused, in particular, by estrogenic, gestagenic hormonal drugs, deoxycorticosterone acetate, somatotropic hormone, salicylates, barbiturates, sulfonamides, cytostatics and a number of other xenobiotics, e.g. nicotine. Teratogenic effect (from the Latin teras - a monster) - the occurrence of malformations of internal organs, the central nervous system, limbs in the embryo, i.e. ugliness. The danger of teratogenic effects of drugs became obvious in the late 1950s. after about 7 thousand children were born in Western Europe to women who used the sedative and hypnotic drug thalidomide with malformations of the limbs (due to impaired collagen synthesis in bone tissue), gastrointestinal tract, hemangiomas on the face, etc. Teratogenic effects most often develop in the first trimester, especially from the beginning of the 4th to the end of the 8th week of pregnancy, that is, during the period of organ

formation. The specific type of defect depends on the duration of pregnancy - on which organs are formed and intensively formed during the use of the drug.

The likelihood of its development is determined not only by the drug used, but also by the age of the pregnant woman (the risk increases at the age of ≤17 or ≥ 35 years, when prenatal damage to the eggs is more common), the health status of the woman (especially diseases of the organs that eliminate drugs and their metabolites - the liver, kidneys, as well as the cardiovascular and endocrine systems), the genetic characteristics of the parents and the fetus, the dose of the drug, the duration of its use. Among the causes of congenital malformations, up to 25% are genetic disorders, about 10% - infections (cow rubella, influenza, etc.), radiation, injuries. In approximately 65% of cases, the causes remain unclear, and a significant part of them is explained by the action of drugs or xenobiotics. According to the degree of danger of teratogenic effects, drugs are divided into 3 groups (Table 2). It is important that teratogenic effects can occur not only as a result of transplacental entry of drugs (xenobiotics) into the fetus, but also as a result of their action on the father's body on the eve of conception, which can cause genetic abnormalities of sperm, impaired viability, and motility. Getting into the female genital tract with seminal fluid, the drug can act locally, disrupting the early stages of pregnancy.

Fetotoxic effect (from the Latin foetus - fetus) is an adverse effect of drugs on the condition of the fetus in utero (more often - in the last weeks of pregnancy) and the newborn. Thus, β2-adrenomimetics (partusisten), used to reduce the contractile activity of the uterus, provoke fetal hyperglycemia and, as a result, stimulation of insulin secretion, which is slowly excreted from the body of the fetus and newborn, contributing to hypoglycemia in the neonatal period. These drugs can also cause metabolic acidosis, hyperbilirubinemia, hypocalcemia, intestinal obstruction. Magnesium sulfate, which is also used for tocolytic purposes, due to the suppression of the fetal CNS can cause muscle weakness, respiratory and sucking disorders in the newborn. Aminoglycoside antibiotics (streptomycin, gentamicin, etc.) affect the inner ear, which can impair hearing up to deafness. Indomethacin and other NSAIDs, which inhibit the synthesis of prostaglandins, contribute to premature closure of the ductus arteriosus; this disrupts blood circulation and causes heart failure and even death of the fetus, and after birth provokes pulmonary hypertension in the child. In addition, drugs of this group, reducing urine formation in the fetus, reduce the amount of amniotic fluid, which inhibits motor activity and delays the development of the child, and also easily cause bleeding in the fetus and newborn. When using drugs by breastfeeding mothers, it is possible to detect P.d.l. in a child whose body the drug enters with breast milk. In particular, anticoagulants in such cases can cause bleeding, sulfonamides - hemolysis.

One of the types of side effects of drugs is mutagenicity, i.e. the ability to cause changes in hereditary information — mutations — in germ and somatic cells. The study of the mutagenicity of new APIs and excipients is carried out at the stage of preclinical studies of the safety of their use using a set of methods on various test objects. In particular, chromosomal aberrations or micronuclei in mammalian bone marrow cells and gene mutations in microorganisms or Drosophila are recorded, and before the second phase of clinical trials, the ability of the drug to induce mutations in mouse germ cells (dominant lethal test) is studied. In case of ambiguous results in individual tests, the level of chromosomal aberrations in peripheral blood lymphocytes of patients receiving the drug is examined. Original drugs created by chemical, biotechnological, genetic engineering and other methods, in particular from raw materials of natural origin, are tested for mutagenic activity. New fixed combinations of medicinal substances with structural similarity of components with known mutagens, carcinogens or their metabolites also require testing for mutagenicity. The conclusion about the presence of mutagenic properties in the studied medicinal product is made if the mutagenic effect is registered in at least one test. Dangerous manifestations of S.D. also include carcinogenic effect (from Latin cancer - cancer), that is, the ability to cause malignant tumors. It

is closely related to the mutagenic properties of drugs. Clinical trials and introduction into production of new medicinal products and excipients are carried out with the availability of results of assessment of its potential carcinogenic properties. Newly created medicinal products intended for use as therapeutic and prophylactic, cosmetic, repellent, contraceptive, for use in long repeated courses, in pediatric practice, during pregnancy and breastfeeding, for non-prescription release are subject to mandatory experimental testing for carcinogenicity. Carcinogenicity studies are very important if the drugs have cytostatic, hormone-like properties, or the ability to stimulate cell proliferation. In addition, such studies are necessary if there is clinical and epidemiological data on the carcinogenic risk when using their analogues in medical practice, in the case of mutagenic properties or the ability to covalently bind to DNA.

Side effects of drugs can be primary and secondary. Primary is a direct consequence of the drug's effect on a specific target (nausea, epigastric pain and other manifestations of dyspepsia when the gastric mucosa is irritated). Secondary side effects occur indirectly (e.g. hypovitaminosis during antibiotic therapy due to suppression of the intestinal microflora that synthesizes vitamins). Side effects of an allergic nature manifest themselves in the form of sensitization of the body due to the antigenic properties of drugs and/or their metabolites, complexes of drugs with blood proteins, components of cell membranes, etc. with the subsequent development of allergic reactions. The most allergenic drugs include, in particular, antibiotics, blood substitutes, vitamins. Allergic manifestations of side effects are dose-independent: their severity does not always correlate with the dose of the drug, and even a low dose can cause a very severe reaction up to anaphylactic shock. Allergic reactions of type I (urticaria, angioedema, rhinitis, bronchospasm, anaphylactic shock) are quite often caused by penicillins, sulfonamides; type II - metamizole, or analgin (agranulocytosis), methyldopa (hemolysis), quinidine (thrombocytopenia); type III (so-called serum sickness - urticaria, joint pain, lymphadenopathy, fever) - penicillins, sulfonamides, iodides; type IV (contact dermatitis) - various drugs when applied topically. Cross-allergy is possible when a substance chemically similar to the one that caused sensitization is introduced into the sensitized organism, and therefore capable of interacting with immunoglobulins, inducing an allergic reaction. Cross-allergic reactions are caused, in particular, by β-lactam antibiotics (various representatives of penicillins, penicillins with cephalosporins), sulfonamides, sulfonylurea derivatives. For the prevention of allergic manifestations of P.d.l., careful collection of an allergic history and special tests are necessary. In terms of clinical manifestations, pseudoallergic reactions are close to allergic reactions, which are realized in the form of skin itching, urticaria and occur when taking drugs that have the properties of histamine liberators or complement system activators. Examples are morphine, tubocurarine, iodine-containing radiopaque contrast agents, ampicillin, vancomycin. The peculiarity of the mechanism of pseudoallergic reactions is that the release of histamine from mast cells is not due to sensitization and the participation of immunoglobulins, as in allergies, but to the activation of the complement system or the direct release of mediators of immediate hypersensitivity due to biochemical reactions. Without requiring sensitization, pseudoallergic reactions occur even with the first administration of a drug with the appropriate properties. Pseudoallergic reactions to ampicillin are especially likely in children with infectious mononucleosis or cytomegalovirus infection, manifesting as a spotty (less often papular) rash on the inner surface of the extremities, which usually disappears on its own within several days, despite further use of the drug. It is very difficult to clinically distinguish pseudoallergic reactions from allergic ones. When they appear, it is advisable to stop using the medication and use antihistamines. The main and P.d.l. must be considered in the context of the pathology for which the drug is intended. For example, the main effect of atropine, used for sinus bradycardia, is to accelerate the heart rate, and P.d.l. may manifest itself in the form of unnecessary suppression of gastric secretion in this case. But in a patient with gastritis with increased secretory function, the antisecretory effect becomes the main one, and tachycardia is a side effect. The causes and factors of the occurrence of P.d.l. may be associated with age (in children under 1 year of age and in old age, the risk usually increases), gender (it is observed more often

in women), and genetic characteristics of the patient. Among the factors contributing to the manifestations of P.d.l., it is necessary to note the state of health. In particular, in patients with bronchial asthma, high bronchial reactivity provokes easy detection of a known side effect of β-adrenergic blockers - bronchospasm. In gout, hydrochlorothiazide and furosemide are much more likely to cause an increase in the level of uric acid in the blood than in the absence of this background pathology. The state of the organs of elimination of xenobiotics, primarily the liver and kidneys, is of great importance. In case of insufficiency of their function, a significant number of drugs are contraindicated or require a special dosage regimen. P.d.l. may increase when they are used against the background of bad habits - smoking or alcohol consumption. In particular, oral contraceptives are incompatible with smoking due to the increased risk of thrombosis of the vessels of the brain and heart. Alcohol sharply enhances the depression of the CNS by clonidine, neuroleptics, benzodiazepine tranquilizers, barbiturates and other depressants, increases the hepatotoxicity of paracetamol.

Food also matters. It can affect the pharmacokinetics or pharmacodynamics of many drugs and thus provoke PD. Thus, grapefruit or its juice contributes to the disruption of the metabolism of astemizole, nifedipine, cyclosporine and other drugs, therefore significantly increases the likelihood of PD. from the side of the heart rhythm. Low consumption of table salt slows down the excretion of bromides, which creates conditions for the manifestation of their PD. Foods and drinks rich in tyramine (cheese, smoked meat or fish, bananas, beer, etc.) contribute to a significant increase in the concentration of monoamines in the brain during the action of antidepressants of the MAO inhibitor group, therefore, the “cheese syndrome” is possible - hypertensive crisis, convulsions. There are many examples of dangerous combinations of drugs and food. There are known examples of the detection of P.d.l. when a patient, after using a certain drug, switches to using another one containing the same active substance in the same dose, but produced by a different manufacturer — the so-called multi-source LP (see Generic substitution). This is most often observed in treatment with antiepileptic drugs, β-adrenoceptor blockers, calcium channel blockers. The reasons for the manifestation of P.d.l. in such cases may be associated with differences in bioavailability and other pharmacokinetic parameters, the quality of the substance, the effects of excipients. The likelihood of P.d.l. increases with prolonged treatment: prolonged use of antibiotics significantly increases the risk of dysbiosis and other side effects, NSAIDs for joint diseases, hypoglycemic drugs for diabetes, etc. In tuberculosis, the hepatotoxicity of most drugs used in combination for several months is of great importance (especially pyrazinamide, isoniazid, rifampicin); if hepatitis develops, anti-tuberculosis drugs must be discontinued, which sometimes threatens the death of a seriously ill patient and requires the appointment of the least hepatotoxic streptomycin and ethambutol.

The factor for the development of S.D. may be the route and speed of drug administration, in particular, in cases of rapid creation of a high concentration of the drug in the blood - with intravenous administration, when the bioavailability is 100%. Due to the ability to release histamine with rapid intravenous administration, the glycopeptide antibiotic vancomycin causes a dangerous "red man" syndrome - redness of the face and upper half of the body with a decrease in blood pressure, tachycardia, pain behind the sternum, so its infusion should be done slowly drip - for at least 60 minutes. Side effects can occur and intensify with an unsuccessful combination of drugs in case of their incompatibility. In the body, it is realized due to pharmacokinetic or pharmacodynamic interaction. For example. Excessive bradycardia, cardiac conduction disorders, and decreased contractility are possible with simultaneous use of the calcium channel blocker verapamil and β-adrenergic receptor blockers (all of which inhibit the work of the heart and its conduction system), especially with parenteral administration. In this case, the side effects are mutually enhanced and potentiated. In the case of combining β-adrenergic receptor blockers and dihydropyridine calcium channel blockers, such as nifedipine, amlodipine, lacidipine, etc., which affect blood vessels more and less — on the heart, the risk of these manifestations of P.d.l. is practically absent. Sildenafil (Viagra) is especially prone to causing cardiovascular complications (collapse, heart failure) when combined with nitrates, since

both drugs increase the level of NO in the body, so their combined use threatens to potentiate nitroxidergic effects. The combination of antifungal drugs from the group of azoles (ketoconazole, itraconazole, etc.) and antiallergic drugs from the group of second-generation H1-histamine receptor blockers (astemizole, claritin, etc.) is extremely dangerous due to the increased risk of heart rhythm disorders. NSAIDs contribute to a decrease in the severity of the diuretic effect and an increase in the nephrotoxicity of diuretics. Levomycetin is extremely dangerous to use against the background of or after taking cytostatics or radiation therapy due to an increase in the risk of bone marrow suppression and liver function. In any case, it is advisable to refrain from polypharmacy, which significantly increases the likelihood of P.d.l. It is worth noting that back in 1853, Professor Goryaninov wrote about "the rule of pharmacology that you should know a lot, use as little as possible." To reduce the risk of P.d.l. use combined drugs containing a correcting component (loop or thiazide diuretics with potassium-sparing ones - furesis, triampur, moduretic; tetracycline in combination with nystatin), which is especially convenient from the point of view of compliance, or prescribe correctors separately (misoprostol to reduce gastric irritation of NSAIDs, cyclodol to reduce the risk of parkinsonism during treatment with typical neuroleptics - aminazine, haloperidol, etc.; pyridoxine together with isoniazid to reduce neurotoxicity). DD and herbal preparations, the use of which the patient often does not inform the doctor, can also cause side effects, in addition, they can interact with drugs and contribute to the development of P.d.l. For example, supplements containing ginkgo or garlic increase the risk of bleeding when using acetylsalicylic acid and other drugs that reduce the ability to clot. P.d.l. is one of the factors affecting compliance: if a drug causes side effects, the patient may refuse to use it. P.d.l. must be distinguished from the effects observed in overdose. In doses exceeding therapeutic, drugs cause toxic effects, the manifestations of which, taking into account the commonality of development mechanisms, often resemble P.d.l., but are more pronounced, i.e. the differences are quantitative. For example, an overdose of β-adrenoceptor blockers due to a sharp weakening of sympathoadrenal and predominance of parasympathetic influences on the conduction system is accompanied by significant disturbances in cardiac conduction up to complete atrioventricular blockade, while in the range of therapeutic doses these drugs only slightly slow down atrioventricular conduction. Insulin in high doses causes much deeper than in therapeutic doses, hypoglycemia and neuroglycopenia with the development of a comatose state. This manifestation of toxic action is used to treat schizophrenia in case of resistance to the action of neuroleptics. Sometimes toxic effects are qualitatively different from P.d.l. In therapeutic doses, salicylates can cause compensated respiratory alkalosis due to direct excitation of the respiratory center and increased formation of CO2 in the tissues. But with an overdose of salicylates, the development of metabolic acidosis is possible, as well as an increase in body temperature that is not typical for therapeutic doses.

Some states attribute the safety of drugs and DD, which are closely related to P.d.l., to the problems of national security. In Ukraine, since 1995, the Pharmacological Committee has been studying P.d.l. (since 1999, the Department of Pharmacological Supervision of the State Pharmacological Center, now the State Expert Center (see Pharmacological Supervision) of the Ministry of Health). The Order of the Ministry of Health of Ukraine dated 27.12.2006 No. 898 is in force, approving the procedure for monitoring adverse reactions to drugs. For the detection of side effects in all countries of the world, in particular, in Ukraine, the method of spontaneous reporting is of primary importance, which meets the requirements of the Law of Ukraine dated 04.04.1996 No. 123/96-VR "On Medicinal Products". Medical workers of all specialties voluntarily inform the relevant regulatory authorities - regional and national centers of the drug safety control service (pharmacological supervision). Pharmacological surveillance is a state system of collecting, scientific evaluation and control of information on adverse drug reactions in the conditions of their usual use in order to make appropriate regulatory decisions regarding drugs registered in the state. Such decisions can be made at the stage of clinical trials of drugs. The method of spontaneous reports is particularly effective in identifying adverse drug reactions caused by the pharmacological properties (mechanism of action) of drugs and immunoallergic

mechanisms. There is a special form of a report card containing information about the patient, a description of the adverse drug reaction (time of onset, drugs used, examination results, corrective measures, consequences). Medical institutions annually submit a general report on adverse drug reactions. Such delayed manifestations of side effects as hepatitis, retinitis, etc., reproductive defects, mutagenic, teratogenic, carcinogenic effects, which sometimes occur months or years after treatment, are especially difficult to detect and study. The problem of adverse drug reactions is extremely complex. Due to the multiplicity of mechanisms and manifestations of P.d.l., there are certain difficulties in its classification, detection, and prevention. Even the issues of terminology are ambiguous. For example, in scientific and reference literature, regulatory documents, it is often proposed to distinguish between P.d.l. and adverse reactions, although the criteria for each of these phenomena are not clear, and the clinical manifestations and correction measures actually coincide. Sometimes side effects are unusual and unexpected, so it is difficult to suspect their connection with the use of drugs. P.d.l. may resemble a spontaneous disease or occur after a long time after the use of drugs, and the clinical picture of the disease may be very complex and mask P.d.l. Further development of medicine and pharmacy will certainly contribute to improving knowledge about S.D.

To reduce S.D. necessary are continuous training of medical and pharmaceutical personnel, rational use of existing drugs, avoidance of polypharmacy, strict consideration of contraindications, health education and awareness of the dangers of self-medication by broad segments of the population, creation and introduction of safer new drugs, especially those that have a selective effect. In the prevention of S.D.. the role of pharmaceutical workers is especially important. When dispensing both over-the-counter and prescription drugs to a patient, the pharmacist acts as a consultant, therefore he must be well-versed in the issues of S.D. and drug compatibility. Any measures for timely prevention, detection and correction of S.D. are necessary and constitute the basis for increasing the safety of pharmacotherapy.

Questions for self-control on the topic:

1. Classification of side effects of drugs.
2. Toxic side effects.
3. Allergic reactions, classification, prevention, treatment.
4. Groups of drugs with antiallergic activity.
5. Dysbacteriosis, candidiasis: definition, mechanisms of development, prevention, treatment.
6. Withdrawal syndrome: mechanism of development, prevention.
7. Embryotoxicity, teratogenicity, fetotoxicity of drugs: examples, methods of prevention.
8. Carcinogenicity, mutagenicity of drugs: examples, prevention.
9. Clinical signs of acute and chronic drug intoxication.
10. Principles of treatment of drug poisoning.
11. The concept of antidote therapy, classification, mechanisms of action.
12. Examples of the most commonly used antidotes.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M. Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others – Kh.: NFAU: Zoloti storyni, 2011. – 704 p.
4. Clinical pharmacy: textbook for students of pharmaceutical faculties / Edited by V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

LECTURE 16. TOPIC
"The influence of drugs on changes in clinical, laboratory and functional indicators"

Relevance of the topic: According to WHO, adverse drug reactions occur in 0.4%-10-20% of hospitalized patients and in 2.5%-28% of outpatients. Mortality from adverse drug reactions is 5th in the world (after diseases of the cardiovascular system, lungs, oncological pathology, injuries). Thus, consideration of the topic is relevant for studying the course of clinical pharmacy and further practical activity of a pharmacist. This concerns the negative impact of drugs. However, in any case, when carrying out pharmacotherapy, it is necessary to control its effectiveness and again by studying the impact of drugs on changes in clinical and laboratory indicators.

Purpose: To familiarize the HEI with the main types of side effects, mechanisms of occurrence of side effects, acute and chronic toxicity of drugs, principles of detection, monitoring, prevention and treatment of negative consequences of drug use, explain the importance of monitoring the effectiveness and safety of drug use in a given patient; mechanisms and types of negative and positive effects of drugs on clinical and laboratory indicators.

Basic concepts (list of questions):

Side effect - characterized by the ability of a drug to cause an undesirable or harmful effect simultaneously with the main therapeutic effect.

Unpredicted side effect - an undesirable effect that develops rarely and is not always due to the pharmacological action of the drug, not previously described in the medical literature.

Predicted side effect - an effect that has a certain clinical picture and has been previously described in the medical literature.

Undesirable pharmacological effect - each substance causes a number of pharmacological effects characteristic of it. In each specific case, only certain effects of the drug are used, which are defined as the main effects. Other pharmacological effects are called undesirable, or side, effects.

Toxicity - the property of a substance to cause poisoning or death when entering the body in certain quantities.

Drug safety is a complex concept that includes ensuring the quality of drugs at all stages of their circulation, including production, transportation, storage and rational use in medical practice in order to eliminate or minimize the occurrence of toxic and side effects when used separately and simultaneously with other drugs or food components. According to the definition of the Ministry of Health of Ukraine (Order of September 25, 2009 No. 543), it is a characteristic of the drug, based on a comparative assessment of the benefits and potential harm that may be caused to the patient when using this drug. Safety is formed at the stage of pharmaceutical development, ensured during industrial production, studied at the stage of preclinical and clinical studies, assessed at the stage of registration, and safety monitoring is carried out throughout their entire life cycle.

Drug efficacy is the ability of a drug to achieve the desired therapeutic effect, i.e. to influence physiological processes in the body as predicted by its pharmacological action, and, as a result, to improve the patient's condition or treat a disease.

It includes:

• Therapeutic efficacy: achieving the desired clinical effect (for example, lowering fever, reducing pain, improving organ function).

• Pharmacokinetic efficacy: the ability of the drug to reach the site of action in the body in the required concentration and at the required time (depends on the absorption, distribution, metabolism and excretion of the drug).

• Pharmacodynamic efficacy: the ability of the drug to interact with targets in the body (receptors, enzymes, ion channels) and cause the desired biological responses.

In addition, the effectiveness of a drug may also depend on:

• Quality of the drug: compliance with established quality standards, absence of undesirable impurities, stability during storage.

• Pharmaceutical factors: the influence of excipients, dosage form and route of administration on the effectiveness of the drug.

• Individual characteristics of the patient: age, gender, genetic characteristics, concomitant diseases, taking other medications.

Thus, the effectiveness of a drug is a complex characteristic that reflects its ability to achieve the desired therapeutic effect, taking into account various factors that affect its action.

Lecture content (lecture text)

Especially sensitive to such effects:
hematopoietic organs,
endocrine system,
enzymes.

The effect of drugs on laboratory parameters occurs in two possible ways.

The first way is chemical, or physico-chemical ("analytical interference"). In this case, drugs or their metabolites interfere with the specific reaction of determining a particular substance.

An example of chemical interference is the distortion of the results of spectrophotometric analysis of 5-hydroxyindoleacetic acid in urine, which is carried out in an acidic environment, due to the use of phenothiazine drugs by patients.

Quinidine, tetracycline have fluorescence properties and interfere with the fluorometry of catecholamines in urine.

Riboflavin and carotene increase the optical density of solutions when determining bilirubin.

The second way is pharmacological ("pharmacological interference").

The mechanism of pharmacological interference includes changes in the pathological process under the influence of drugs, side effects of drugs on various functions of organs and

systems, toxic effects of drugs in case of their overdose.

Such an effect of drugs can cause shifts in laboratory parameters indirectly related to the main, expected effect.

Ascorbic and nalidixic acids can cause an increase in the level of total bilirubin in the blood serum.

In order to avoid undesirable consequences of the influence of drugs on the results of diagnostic clinical and laboratory tests as much as possible, the following Rules should be followed:

1. For a successful diagnostic examination, the prescription of any drugs should be canceled a week before taking biological samples for analysis.

2. When conducting a diagnostic clinical and laboratory examination, it is necessary to carefully collect a medical history.

3. If the patient is taking any drugs during the tests, this should be indicated in the referral.

4. If deviations from normal parameters are detected, before interpreting the results obtained on the basis of medical history, it is necessary to exclude the possibility of these deviations occurring under the influence of medications.

5. If it is impossible to exclude the influence of a drug on the analysis results, this drug should be canceled and the study repeated, and only then interpret the results obtained.

Questions for self-control on the topic:

1. Classification of side effects of drugs.
2. Toxic side effects.
2. Allergic reactions, classification, prevention, treatment.
3. Withdrawal syndrome: mechanism of development, prevention.
4. Embryotoxicity, teratogenicity, fetotoxicity of drugs: examples, methods of prevention.
5. Carcinogenicity, mutagenicity of drugs: examples, prevention.
6. Clinical signs of acute and chronic drug intoxication.
7. Principles of treatment of drug poisoning.
8. Mechanisms of drug influence on clinical and laboratory indicators.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Ed. O.M.Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A.Zupanets, V.P.Chernykh, T.S.Sakharova and others. – Kh.: NFAU: Golden pages, 2011. – 704 p.
4. Clinical pharmacy: textbook for students of pharmaceutical faculties / Ed. V.P.Chernykh, I.A.Zupanets, I.G.Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

LECTURE 17. TOPIC

"Tuberculosis of pulmonary and extrapulmonary localization: etiology, pathogenesis, clinical pharmacology of drugs with antituberculosis activity"

Relevance of the topic: Tuberculosis in Ukraine remains a serious public health problem. The incidence of tuberculosis, including relapses, in 2023 amounted to 19,851 cases, which is 7.3% more than in 2022. This is 48.4 cases per 100,000 population. The increase in incidence indicates the need to strengthen measures for the prevention, early detection and treatment of tuberculosis.

Key points about tuberculosis in Ukraine:

• General situation: Ukraine has one of the highest levels of tuberculosis incidence in the European region.

• Risk factors: The disease is more common among the unemployed, homeless, people below the poverty line, prisoners, as well as among migrants, military personnel, medical workers and workers in certain industries.

• HIV co-infection: A significant proportion of patients with tuberculosis are also infected with HIV, which complicates treatment and increases the risk of mortality.

• Drug-resistant tuberculosis: There are cases of drug-resistant tuberculosis in Ukraine, when conventional anti-tuberculosis drugs do not work.

• Treatment challenges:

The effectiveness of tuberculosis treatment in Ukraine, especially among patients with bacterial excretion, remains below WHO recommended indicators.

• Detection challenges: Early detection of tuberculosis remains a weak point, which leads to late diagnosis and detection of destructive forms of the disease.

• Social aspects: Stigmatization of tuberculosis patients and lack of sufficient awareness among the population about the disease are significant obstacles in the fight against tuberculosis.

• Importance of prevention: Increasing public awareness of tuberculosis, its symptoms, methods of prevention and treatment, as well as preventive vaccinations, is important to combat the spread of the disease.

Purpose: To familiarize the HES with the basic principles of anti-tuberculosis therapy, the modern algorithm for selecting and selecting modern groups of anti-tuberculosis drugs for a specific patient, choosing the dosage regimen, route of administration, frequency of administration, duration of therapy; to explain the importance of monitoring the effectiveness and safety of using specific pharmacotherapy in a given specific patient.

Basic concepts (list of questions):

Pulmonary tuberculosis is a form of tuberculosis that affects the lungs. This is an infectious disease caused by the bacterium Mycobacterium tuberculosis (Koch's bacillus), and most often begins in the lungs, making the patient contagious to others.

Key points:

• Causative agent: Pulmonary tuberculosis is caused by Mycobacterium tuberculosis (Koch's bacillus).

• Route of transmission: Usually transmitted by airborne droplets from person to person, especially when coughing, sneezing or talking.

• Symptoms: The main symptoms include cough (lasting more than 3 weeks), hemoptysis, chest pain, shortness of breath, weakness, weight loss, fever, night sweats.

Forms of pulmonary tuberculosis:

• Infiltrative pulmonary tuberculosis: Characterized by an inflammatory process in the lungs with the formation of infiltrates (foci of compaction).

• Miliary pulmonary tuberculosis: This is a generalized form in which the infection spreads throughout the body through the bloodstream, affecting various organs.

Extrapulmonary tuberculosis is a form of tuberculosis that affects organs and systems of the body other than the lungs. It can develop as a result of the spread of mycobacteria tuberculosis through the blood or lymph from a primary focus in the lungs, or the lesion can occur directly from a neighboring organ.

Features of extrapulmonary tuberculosis:

• Location: Can affect lymph nodes, pleura, bones and joints, genitourinary system, digestive system, central nervous system, skin, pericardium and other organs.

• Symptoms: Symptoms depend on the location of the localization and may be non-specific, which complicates diagnosis.

• Diagnosis: Includes clinical examination, radiography, computed tomography, bronchoscopy, as well as microscopic and bacteriological examination of diagnostic material (sputum, biopsy, exudate).

• Treatment: Is carried out with anti-tuberculosis drugs and usually lasts at least 6 months.

Common forms of extrapulmonary tuberculosis:

• Lymph node tuberculosis: Enlarged, thickened lymph nodes that may soften and form fistulas over time.

• Pleural tuberculosis: Fever, dry cough, sometimes shortness of breath, and chest pain.

• Bone and joint tuberculosis: Pain, swelling, and limitation of movement in a joint.

• Genitourinary tuberculosis: Often has subtle symptoms, such as frequent or painful urination, and in women, pelvic pain and menstrual irregularities.

• Central nervous system tuberculosis: Tuberculous meningitis with headache, photophobia, and impaired consciousness.

• Miliary tuberculosis: Multiple organ involvement, acute intoxication, and critical condition.

Mycobacterium tuberculosis (obsolete - "Koch's bacillus") is a bacterium that causes a significant number of cases of tuberculosis in humans. This bacterium was first described on March 24, 1882 by the German microbiologist Robert Koch, who later received the Nobel Prize in Physiology or Medicine for this discovery in 1905.

Morphology:

• Gr+ are thin, slightly curved polymorphic rods, while M. bovis are short, thick rods.
• length up to 8 microns, while in M. bovis - up to 2-3 microns
• acid-, alkali-, alcohol-resistant
• the cell wall has a high content of unsaturated fatty acids (mycolic acid), lipids, waxes (up to 40%)
• immobile
• do not form spores and capsules
• in the patient's body under the influence of HTZ can form filter and L-forms
• in smears-preparations are detected during microscopic examination after staining according to the Ziehl-Neelsen method
• in the cell during staining, tigeroidity is observed - alternation of acid-fast (Splenger grains) and non-acid-fast areas (Mucha metaphosphate grains)

Physiology: M. tuberculosis is an obligate aerobe, it is a weakly gram-positive acid-fast mycobacterium that stains according to Ziehl-Neelsen (acid-fast staining). Although most mycobacteria do not meet the criteria for being Gram-positive (i.e., they do not retain crystal violet stain), they, like Gram-positive bacteria, lack a second cell membrane and are classified as Actinobacteria or "high GC-content Gram-positive bacteria." Under favorable conditions, M. tuberculosis divides every 15 to 20 hours, which is extremely slow compared to other bacteria that typically divide several times per hour (for example, E. coli can divide approximately every 20 minutes). This bacterium can withstand mild disinfectants and survives in dry conditions for weeks.

Anti-TB drugs of the 1st line - According to clinical activity, PTZ are divided into 1st line drugs - drugs of the streptomycin group (aminoglycosides), isonicotinic (isoniazid, ftivazid, saluzid, larusan, etc.) and acetylsalicylic (PASK, bepask) acids.

Anti-TB drugs of the 2nd line - drugs of the 2nd line - antibiotics (kanamycin, amikacin, rifampicin, capreomycin), as well as pyrazinamide, ethionamide, ethambutol, ethoxide and other synthetic drugs. Treatment begins with 1st line drugs, and then, to prevent the resistance of mycobacteria of tuberculosis to drugs, 2nd line drugs are prescribed.

Lecture content (lecture text)

Anti-tuberculosis drugs are chemotherapeutic antibacterial drugs that inhibit the reproduction and development of mycobacteria tuberculosis (tuberculostatic effect) or cause their death (tuberculocidal effect). These include some synthetic drugs (isoniazid, ethambutol, ethionamide, prothionamide, pyrazinamide, sodium para-aminosalicylate, PASK, etc.) and antibiotics (streptomycin sulfate, rifampicin, cycloserine, kanamycin sulfate, etc.). The Treatment Committee of the International Anti-Tuberculosis Union in 1975 proposed the following classification of anti-tuberculosis drugs: group A (most effective) - isoniazid, rifampicin; group B (effective) - streptomycin, pyrazinamide, ethambutol, kanamycin, ethionamide, cycloserine, viomycin; group C (least effective) - PASK, thioacetazone. All antituberculosis drugs are divided into first-line drugs (main drugs) - derivatives of isonicotinic acid hydrazide (isoniazid, phtivazid, opiniazid, saluzid soluble); PASK derivatives (calcium benzamidosalicylate); antibiotics (streptomycin sulfate, streptosaluzid, pasomycin, rifampicin); second-line drugs (reserve drugs) - derivatives of isonicotinic acid thioamide (ethionamide, prothionamide); antibiotics (cycloserine, viomycin, capreomycin sulfate) and fluoroquinolones (lomefloxacin); drugs of different chemical groups (ethambutol, pyrazinamide, thioacetazone).

The mechanism of action of antituberculosis drugs differs depending on their chemical structure. Derivatives of isonicotinic acid hydrazide form chelate complexes with heavy metal ions, which are part of respiratory enzymes and thus inhibit mycobacterial respiration; disrupt the structure of phospholipids and the synthesis of mycolic acid in the cell membrane of mycobacteria. The tuberculocidal effect of derivatives of isonicotinic acid hydrazide is possible if the molecule contains a hydrazide group (isoniazid, ftivazid, opiniazid, saluzid soluble). PASK derivatives selectively compete with PABA, which is necessary for the growth and reproduction of mycobacteria (PASK, calcium benzamidosalicylate). First-line antibiotics inhibit protein synthesis at the ribosomal level or inhibit RNA synthesis of mycobacteria (streptomycin sulfate, streptosaluside, pasomycin, rifampicin). Derivatives of isonicotinic acid thioamide bind divalent metal ions, which are coenzymes, which leads to inhibition of the growth and development of tuberculosis bacillus (ethionamide, prothionamide). Second-line antibiotics inhibit the synthesis of mycobacterial cell wall components (cycloserine), protein (viomycin, capreomycin sulfate), inhibit the enzyme DNA hydrase (fluoroquinolones); drugs of different chemical groups inhibit RNA synthesis of tuberculosis pathogens (ethambutol, pyrazinamide, thioacetazone). These groups of drugs differ significantly in their antimicrobial spectrum. Tuberculostatic action is exerted by derivatives of isonicotinic acid hydrazide, PASK derivatives, isonicotinic acid thioamide derivatives, drugs of various chemical groups; tuberculocidal action is exerted by streptomycin sulfate, rifampicin (rifadin), fluoroquinolones (lomefloxacin). Drugs of the first row are active, low-toxic. Drugs of the second row are less active, more toxic and more often cause side effects. The division of anti-tuberculosis drugs into the first and second rows is rather conditional, but allows a more balanced approach to the choice of drug combinations.

Tuberculosis is a serious medical, biological and social problem that has recently been of great concern in Ukraine. At the end of 2019, the number of patients under supervision in anti-tuberculosis institutions was 515 thousand people, including 99 thousand patients with active forms of tuberculosis. As of 2020, the mortality rate from tuberculosis in Ukraine reached 22.1 cases per 100 thousand population.

In connection with the above, the therapeutic and preventive measures used in the fight against the disease require timely and active use of the most effective and safe medicines (MZ).

According to the recommendations of international medical organizations and world experience, the most acceptable among the drugs in terms of effectiveness and relative safety are isonicotinic acid hydrazide derivatives (isoniazid, prothionamide, ethionamide), rifamycins (rifabutin, rifampicin), quinolones and fluoroquinolones (lomefloxacin, moxifloxacin, ofloxacin), drugs of different groups (aminosalicylic acid (ASA), capreomycin, pyrazinamide, thioacetazone, ethambutol, cycloserine) and combined drugs. It should be emphasized that isoniazid and rifampicin have the highest activity against mycobacteria tuberculosis. For a comprehensive effect on the causative agent of tuberculosis, combination therapy is actively used today, which allows achieving a rapid bactericidal effect by acting on different chains of the mycobacterial life cycle, and also slows down the development of drug resistance of the pathogen.

Rational pharmacotherapy of tuberculosis is a complex and not always optimistic process in terms of its consequences. In addition, almost all of the above-mentioned drugs are characterized by adverse reactions (ARs), the development of which is accelerated and intensified for various reasons and can lead, due to lack of vigilance, to serious consequences.

With the medical use of anti-tuberculosis drugs, ARs develop in 10% of patients. The most typical ARs include:

- for aminoglycosides - nephrotoxicity, ototoxicity;
- for fluoroquinolones - damage to the gastrointestinal tract (GI), neurotoxicity;
- for rifampicin - hepatotoxicity;
- for isoniazid - neurotoxicity, hepatotoxicity;
- for ASA - damage to the GI tract;
- for pyrazinamide - increased transaminase levels, hyperuricemia;

• for ethambutol – damage to the organ of vision;
• for ethionamide, prothionamide – neurotoxicity, damage to the gastrointestinal tract;
• for cycloserine – neurotoxicity.

According to the data of the Center for Monitoring Adverse Drug Reactions of the World Health Organization, among monodrugs of antituberculosis drugs, the drugs isoniazid (29.2%), rifampicin (26.7%), capreomycin (17.1%), ethambutol (10.2%) dominate in the world in terms of the frequency of adverse reactions. Less than 10% of adverse reactions were registered when prescribing pyrazinamide (9.8%), ASA (2.2%), rifabutin (2.1%) and combined drugs.

Isoniazid led to disorders of the gastrointestinal tract and liver, various types of rashes, and changes in the cellular composition of the blood. More than 100 deaths due to its use have been recorded.

Among the systemic disorders caused by rifampicin, pathological manifestations of the liver, skin rashes, changes in the cellular composition of the blood, disorders of the gastrointestinal tract prevailed. Ethambutol caused changes in the skin and its derivatives, significant impairment of visual function. In addition, about 90 cases of death of patients during the medical use of this drug have been registered.

One of the conditions for the rational use of anti-tuberculosis drugs is to take into account risk factors.

Risk situations and features of drug use:

1. Pregnancy. Ethionamide and prothionamide are contraindicated in pregnant women. Aminoglycosides can only be prescribed for vital indications due to nephrotoxic and ototoxic effects on the fetus. The use of fluoroquinolones is also not recommended (according to experimental data on their chondrotoxicity). Caution should be exercised when prescribing isoniazid (there is a risk of psychomotor retardation, myelomeningocele and hypospadias, hemorrhages [due to hypovitaminosis K]). Rifampicin is not recommended due to its teratogenic effect, which was detected in experimental animals. The safety of rifabutin, cycloserine, ASA, thioacetazone, and capreomycin during pregnancy has not been proven.

2. Breastfeeding. Rifampicin, which penetrates into breast milk, is contraindicated in infants. The use of fluoroquinolones should be significantly limited due to experimental data on the development of arthropathies in immature animals. Cycloserine, ASA, thioacetazone, capreomycin, rifabutin should not be prescribed due to the lack of adequate data on their safety. Isoniazid should be used with caution (the concentrations of this drug in the milk of a nursing mother are similar to those in blood plasma). There is also information about the development of hepatitis and peripheral neuritis in children as a result of its administration. There is no data on the penetration of ethionamide, prothionamide and ethambutol into breast milk. Pyrazinamide penetrates into breast milk in small quantities (relatively safe).

3. Children's age. Based on experimental data, fluoroquinolones are contraindicated in children. In newborns, the half-life of isoniazid may be increased due to immaturity of liver enzymes. Rifampicin is prescribed to newborns and premature infants only for vital indications. Due to the lack of adequate data on the safety of capreomycin, its administration to children is not recommended. Ethambutol is not recommended for children under 2-3 years of age due to the impossibility of adequate control of visual function. No data on the danger of using rifabutin, ethionamide, prothionamide in children under 14 years of age have been found. Caution should be exercised when prescribing aminoglycosides to premature infants and newborns, since stupor, lethargy, coma, and severe respiratory depression have been described when using them in high doses. Particular vigilance should be exercised when using cycloserine due to its high toxicity to the child's body.

4. Elderly age. Rifamycins should be prescribed with caution due to possible age-related changes in liver function. Elderly people need to reduce the doses of ethambutol, capreomycin, cycloserine and fluoroquinolones. When using fluoroquinolones in this age category of patients, the risk of ligament and tendon ruptures increases. In the case of using aminoglycosides, it is necessary to monitor the function of the hearing organ (its impairment in elderly people is

possible even with the initial normal function), as well as the kidneys.

5. Impaired renal function. In renal failure, the use of drugs that are characterized by nephrotoxic effects (streptomycin, kanamycin, amikacin, reomycin and other drugs of the aminoglycoside group) should be avoided. In patients with renal failure, the half-life of antibiotics of this group is significantly increased, so their doses should be calculated based on the determination of creatinine clearance. In renal failure, dose correction of fluoroquinolones, ethambutol, capreomycin may also be required. The risk of isoniazid toxicity increases with creatinine clearance less than 10 ml/min. Pyrazinamide, ASA are contraindicated in severe kidney disease.

6. Liver dysfunction. Severe liver dysfunction increases the risk of isoniazid hepatotoxicity, and the use of pyrazinamide, isonicotinic acid hydrazide derivatives, rifamycins, thioacetazone, and ASA is also contraindicated.

On the Ukrainian pharmaceutical market, anti-tuberculosis drugs are represented by 20 companies - 12 foreign (60%) and 8 domestic. Over many years of medical use, these drugs have proven themselves to be highly effective and quite safe, but the expected adverse reactions inherent in them require constant monitoring by doctors. As of 24.01.2008, 533 cases of adverse reactions during the medical use of anti-tuberculosis drugs were registered in Ukraine, information about which came from all regions. Among the received reports, data on adverse reactions that occurred when prescribing pyrazinamide (monodrug - 33.1% and combined form - 0.18%), rifampicin (monodrug - 24.9% and combined form - 0.75%) dominate. Also, adverse reactions were observed when prescribing isoniazid (monodrug - 13.5% and combined form - 0.75%), prothionamide (6.5%), ethambutol (5.8%), ethionamide (2.6%). In 73.5% of cases, these were drugs of domestic production. Among patients in whom adverse reactions were registered, men predominated (60.3%; aged 31 to 60 years - 71.3%). The number of women was 39.7% (in terms of the frequency of adverse reactions, persons aged 19 to 45 years dominated [59.3%]), children - 5.1%. By type, the registered adverse reactions were non-serious, provided for in the instructions for medical use (90.2%), serious foreseen (9.3%), serious unforeseen (not specified in the instructions for medical use) (0.37%). Among systemic lesions, allergic reactions prevailed (46.7%), in particular skin changes and their derivatives (70.6%), general allergic reaction (24.4%), fever and hyperthermic syndrome (5.6%), Quincke's edema (0.2%), anaphylactic shock (0.12%), anaphylactic reaction (0.04%), etc. There were also violations of the gastrointestinal tract (30.39%), central and peripheral nervous system (8.8%), liver and biliary tract (5.06%), general cardiovascular disorders (2.4%). It should be emphasized that the allergic history was burdened only in 5.8% of patients. In 98.68% of patients, the allergic reactions passed without consequences, in 0.11% - with consequences, in 1 case (0.02%) the patient's death was recorded.

As our analysis shows, the withdrawal of the indicated drugs was necessary in 192 cases (35.3%), withdrawal and use of additional pharmacotherapy – in 196 (37.1%), withdrawal of the main and concomitant drugs – in 4 (0.7%), withdrawal of the main, concomitant drugs and additional pharmacotherapy – in 13 (2.4%), dose reduction and additional pharmacotherapy – in 64 (11.7%), dose reduction – in 66 (12.1%); 8 patients (1.5%) remained without correction.

It should be noted that as a result of the above measures, drug withdrawal in 35.3% of patients deprived the patient of specific treatment of the underlying disease for some time. Additional therapy in 48.8% of patients required increased costs. Dose reduction and lack of correction of the dosage regimen in 13.6% of patients did not affect the course of PR.

Thus, the data presented indicate a significant percentage of medical and biological consequences of PR when using anti-TB drugs, which leads to an increase in the costs of treatment or measures to eliminate PR. The latter must be taken into account (pharmacoeconomic approach) when creating treatment standards and implementing measures to regulate the pharmaceutical market.

Questions for self-control on the topic:

1. Tuberculosis: definition, classification.
2. Etiology of tuberculosis, morpho-physiological features of the tuberculosis pathogen.
3. Clinical picture of pulmonary tuberculosis.
4. Features of the clinical course of extrapulmonary tuberculosis.
5. Modern methods of laboratory and instrumental diagnostics of tuberculosis.
6. Clinical pharmacology of 1st-line antituberculosis drugs.
7. Clinical pharmacology of 2nd-line antituberculosis drugs.
8. Safety issues of the use of antituberculosis drugs.
9. Methods of monitoring the effectiveness of antituberculosis therapy.
10. Methods of monitoring the safety of antituberculosis therapy.

List of sources on the topic:

1. Clinical pharmacology / Edited by Prof. M.I. Yabluchansky, Prof. V.M.Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Ed. O.M.Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A.Zupanets, V.P.Chernykh, T.S.Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical pharmacy: textbook for students of pharmaceutical faculties / Ed. V.P.Chernykh, I.A.Zupanets, I.G.Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

LECTURE 18. TOPIC
"The role of the pharmacist in conducting preclinical and clinical trials of new drugs"

Relevance of the topic: The pharmacist plays an important role in conducting drug trials (Drugs), in particular, in ensuring the quality, safety and efficacy of drugs. He controls the production and circulation of drugs, participates in clinical trials, provides advice on the use of drugs and pharmaceutical care to patients.

The main roles of the pharmacist in drug trials:

• Quality control: The pharmacist ensures that drugs meet established quality standards at all stages: from production to storage and sale.

• Participation in clinical trials: The pharmacist can participate in planning, conducting and analyzing the results of clinical trials of drugs, in particular, in ensuring the proper use of drugs and monitoring side effects.

• Pharmaceutical care: The pharmacist provides patients with advice on the correct use of drugs, their interactions with other drugs and food products, as well as on possible side effects.

• Pharmacovigilance: The pharmacist participates in the pharmacovigilance system, which includes the collection, analysis and evaluation of information on adverse drug reactions, in order to ensure the safety of their use.

• Drug circulation control: The pharmacist controls the circulation of drugs, ensuring their storage in appropriate conditions, correct dispensing and accounting.

• Consultations of doctors and patients: The pharmacist provides advice to doctors on the rational use of drugs, as well as to patients on the correct use, dosage and possible side effects.

• Training and advanced training: The pharmacist participates in the training and advanced training of pharmaceutical workers, in particular, in the field of clinical pharmacy and pharmacovigilance.

It is important to note that the pharmacist has in-depth knowledge in the field of pharmacy, chemistry, pharmacology and clinical pharmacy, which allows him to effectively perform his duties in the field of drug testing.

Purpose: To familiarize the HES with the basic principles of conducting pre-clinical and clinical trials of medicinal products, to explain the importance of the pharmacist, clinical pharmacist in conducting trials of new medicines, in monitoring the effectiveness and safety of the use of medicines in a given specific patient.

Basic concepts (list of questions):

Preclinical drug testing is a stage of drug development, which includes a set of research procedures and operations to determine the safety and specific activity in order to obtain permission for their clinical trials with the subsequent introduction of the drug into industrial production and medical practice.

Clinical drug testing is a scientific and research work, the purpose of which is any study involving a person as a research subject, designed to identify or confirm the clinical, pharmacological and/or other pharmacodynamic effects of one or more study drugs.

Phase I clinical trials - Includes the first tests of a new drug on humans, usually with the participation of 20-80 healthy volunteers, during which researchers establish a range of doses within which the drug is well tolerated with a single or repeated administration.

Phase II clinical trials - Provides for obtaining the first experience of using the study drug in patients with the disease for which it will be prescribed. Early studies in this phase are often called pilot studies, as the results obtained provide optimal planning for more expensive and extensive studies.

Phase III clinical trials - testing of a drug to confirm therapeutic efficacy, safety and establish long-term effects, including adverse reactions.

Phase IV clinical trials - testing of a drug, which is carried out after the drug is registered and enters the market, in order to determine the therapeutic significance of the drug, the strategy for its further use, as well as to obtain additional information about the spectrum and frequency of possible side effects.

A clinical pharmacist is a pharmaceutical specialist who works in a medical institution, working closely with doctors and other members of the medical team, in order to optimize pharmacotherapy and improve patient treatment outcomes.

The main tasks of a clinical pharmacist:

• Participation in the development and implementation of a local drug formulary: This includes the selection of drugs, consideration of proposals for their inclusion/exclusion, as well as updating and distributing the formulary among doctors.

• Optimizing drug prescribing: The clinical pharmacist assesses the effectiveness and safety of prescribed drugs and provides recommendations for their rational use.

• Monitoring pharmacotherapy: He analyzes complications and errors associated with the use of drugs and develops measures to avoid them.

• Providing doctors with information on rational pharmacotherapy: The clinical pharmacist acts as an expert on the use of drugs, providing relevant and reliable information to doctors.

• Interaction with patients: Providing information about drugs, their use, side effects and interactions with other drugs.

• Participation in clinical trials: The clinical pharmacist may participate in the development and conduct of clinical trials of new drugs.
• Estimating the needs of health care institutions for drugs: This helps to avoid shortages or surpluses of drugs and ensure efficient use of resources.

The difference between a clinical pharmacist and a pharmacist:
A clinical pharmacist is a specialization within the profession of a pharmacist. A pharmacist is a general name for a specialist with a pharmaceutical education who can work in a pharmacy, in production, in research institutions or engage in clinical pharmacy. A clinical pharmacist has more in-depth knowledge in the field of pharmacotherapy and clinical medicine, which allows him to work more effectively in a medical institution and take an active part in the treatment process.

Lecture content (lecture text)

PRE-CLINICAL RESEARCH OF DRUGS - a stage of drug development, which includes a set of research procedures and operations to determine the safety and specific activity in order to obtain permission for their clinical trials with the subsequent introduction of the drug into industrial production and medical practice.

One of the most important tasks on the way to developing effective, safe competitive drugs in Ukraine is to create an effective system of pre-clinical trials that meet international standards. The system of rules of Good Laboratory Practice (GLP) is aimed at ensuring the quality and reliability of the results obtained during research. The principles of GLP are an administrative concept that covers the organizational process and conditions under which laboratory tests are planned, performed, monitored, recorded and stored, and a report on the test results is provided. In order to unify the testing schemes of new drugs in different countries, which is a necessary condition for international trade, the member countries of the Organization for Economic Cooperation and Development have declared the need for international unification of test methods and the introduction of the principles of the GLP system. The use of the GLP principles is extremely important for national authorities and departments responsible for evaluating test results and determining the level of toxicity of chemical compounds. The GLP principles provide for the use of recommended standards for conducting a wide range of tests and are aimed at regulating them at a high level. The GLP principles apply to a wide range of commercial chemicals, including pharmaceuticals, cosmetics, industrial chemicals, and pesticides. To date, the greatest experience in complying with GLP requirements has been accumulated in areas related to preclinical testing, which is considered extremely important from the point of view of health protection. Compliance with GLP rules in the process of preclinical studies contributes to obtaining high-quality, substantiated, guaranteed data that are recognized by other countries, which helps to avoid duplication of preclinical trials, thus saving time and costs for their conduct. The application of GLP principles contributes to the promotion of tested products on international markets, the protection of human health and the protection of the environment. GLP rules require the implementation of a number of standard conditions in everyday practice that cover all stages of preclinical studies of toxicity and safety of medicinal substances. Each EU country has a laboratory that is certified in accordance with GLP requirements. Both internal (national) and external (by authorized bodies of international organizations) certification according to GLP requirements is allowed. In this case, the state must ensure the presence of a National GLP Control Body, a National GLP Program, and a National GLP Regulatory Body. Control over compliance with GLP rules in Ukraine is carried out by the group of certification and inspection of bases of preclinical study of drugs at the State Pharmaceutical Research Center and the Committee on Hygienic Regulation of the Ministry of Health of Ukraine.

The purpose of the preclinical study is to obtain scientific methods of assessments and evidence of their effectiveness and safety. Preclinical studies are conducted by developing organizations according to the rules of laboratory practice approved by the national drug quality control body, an approved plan with maintaining a protocol and drawing up a report on the results of the studies. After the completion of the studies, the drug developer organization gives conclusions on the possibility of further clinical studies of the drug with the aim of introducing it into production and medical practice. The preclinical study is preceded by the stage of searching for new drugs through pharmacological screening of some BAS of synthetic or natural origin, which includes studying specific activity and acute toxicity. The potential active substance is determined as a result of pharmacological and pharmacoeconomic analysis of the results of pharmacological screening and chemical synthesis. The division of the complex of D.d.l., which includes pharmacological and toxicological studies, is conditional, since these studies are interconnected. Thus, the results of the study of acute toxicity of a drug provide information for further pharmacological studies, which determine the degree and duration of the study of its chronic toxicity.

The purpose of D.d.l. is to determine their therapeutic efficacy, as well as the effect on the main anatomical and physiological systems of the body. In the process of studying the pharmacodynamics of a new drug, not only its specific pharmacological effect is determined, but also possible side effects associated with the mechanism of its action. The effect of a drug on a healthy and sick body can be different, therefore pharmacological studies are conducted on healthy animals and animals with simulated pathology. In toxicological studies, the nature and severity of the possible harmful effect of a drug on the body of experimental animals are determined by studying acute toxicity with a single administration, toxicity with repeated administration (subacute, subchronic and chronic) and specific types of toxicity: embryotoxicity, teratogenicity, gonadotoxicity, immunotoxicity, allergenicity, mutagenicity, ulcerogenicity, local irritant effect, pyrogenicity. Thus, according to the results of the D.d.l. stage can largely guarantee the safety of their clinical trials and subsequent medical use.

CLINICAL TRIALS — a mandatory stage of research of a new or already known drug, which is registered for use. This stage is carried out in clinical conditions, that is, under the supervision of doctors in equipped hospitals. To conduct a clinical trial, it is necessary to obtain official permission from the competent authorities for its medical use (registration certificate or trade license), which in turn is based on carefully verified positive data from preclinical trials (see Preclinical study of drugs). Clinical trials, in which new conditions for the use of registered drugs are studied (new indications, new route of administration or new dosage forms), are considered as tests of a new drug. Clinical trials are carried out in four phases:

Phase I. Includes the first human trials of a new drug, usually involving 20–80 healthy volunteers, during which researchers establish a range of doses within which the drug is reasonably well tolerated with single or repeated administration. Data obtained in animal studies during preclinical trials are used to calculate the starting dose. The importance of conducting phase I studies is to obtain data on the tolerability and safety of the drug to make a decision about its further development. Studies in this phase are often called clinical pharmacology or biomedical trials, since their goal is to compile an initial characterization of the pharmacodynamic and pharmacokinetic properties of the drug in humans, and sometimes to determine the initial efficacy indicators in human trials. At this stage, the dose-dependent effect is studied and the selection of the dose range that will be studied later. Information on pharmacokinetics and pharmacodynamics should be obtained for each dose, each dosage form of the study drug, and its route of administration. The average duration of this phase is from 6 months to 1 year.

Phase II. It involves obtaining the first experience of using the study drug in patients with the disease for which it will be prescribed. Early studies in this phase are often called pilot studies, since the results obtained provide optimal planning of more expensive and extensive studies. The main goal is to prove the clinical efficacy of the drug when tested on a certain group of patients. Additionally, the tasks of this phase may include determining the therapeutic dose level of the drug, its dosage regimen, etc. In Phase II clinical trials, as a rule, from 200 to 600 people participate. Sometimes it is divided into phases IIa and IIb. Phase IIa are pilot clinical trials, which are planned mainly to determine the level of safety of the drug. During this phase of clinical trials, it is necessary to verify the activity of the study substance, assess short-term safety, establish a contingent of patients, dosage regimen, find out the dependence of the effect on dose, determine criteria for assessing effectiveness, etc. Phase IIb — larger clinical trials (pivotal trials), which are planned to determine both the efficacy and safety of the drug. The main task is to determine the optimal dose level of the drug in order to continue the Phase III study of the clinical trial. Many consider the Phase II study to be the most important stage of the clinical trial, necessary for making a decision to continue the development of the drug, which significantly affects the decision to register it. As a rule, Phase II trials are carefully controlled studies in which the effects of the study drug are compared with the effects of a placebo or standard treatment, where the control group is a group of patients who did not receive treatment at all. During the trials, positive effects and side effects of the study drug are monitored. The minimum concentration of the drug in the systemic circulation at which it exhibits a therapeutic effect (minimum effective concentration) and the minimum concentration at which it can cause a toxic effect (minimum toxic concentration) are specified.

Phase III. It is planned to determine the safety and effectiveness of the drug in conditions close to those in which it will be used if it is approved for medical use. The trials usually involve thousands of patients (over 2000). The studies are conducted using large and diverse groups of patients. Recently, in phase III of the C.v. so-called mega-trials are sometimes conducted, which involve more than 10,000 patients. The new drug is prescribed to patients with concomitant diseases who are simultaneously receiving other drugs. This helps to identify significant drug interactions. In this phase, patients of different ages, patients with impaired blood circulation, liver and kidney function, etc. can be included in the study. In Phase III clinical trials, adverse reactions that occur relatively rarely can be detected. For drugs intended for the treatment of chronic diseases, safety is studied during their long-term use. Sometimes phases IIIa and IIIb are distinguished. Phase IIIa - tests are carried out after the effectiveness of the drug has been proven, but before submitting an application for registration to regulatory authorities. Phase IIIb - Clinical trials are carried out after submitting an application for registration, but before receiving approval for the drug and a decision on its introduction into production.

Phase IV. Clinical trials of this phase are often called post-marketing trials, thereby emphasizing that they are conducted after the licensing (registration) of the drug. This phase of testing includes studies conducted to obtain more detailed information about the safety and efficacy of the drug. It can be used to evaluate data on improving drug dosing regimens, different treatment terms, interactions with food and/or other drugs, comparative analysis with other standard courses of treatment, use of the drug in other age groups or in patients of other categories, the effects of long-term effects of the drug, and the results of long-term use in patients of different groups. In practice, phase IV clinical trials are often confused with pharmacological surveillance, the functions of which are significantly different.

Questions for self-control on the topic:

1. Preclinical studies of drugs: essence, tasks.

2. Phase I clinical trials of drugs: essence, meaning, tasks.
3. Phase II of clinical trials of drugs: essence, significance, tasks.
4. Phase III of clinical trials of drugs: essence, significance, tasks.
5. Phase IV of clinical trials of drugs: essence, significance, tasks.
6. Clinical pharmacist, role in conducting drug trials.
7. Methods and methods of monitoring the effectiveness of new drugs.
8. Methods and methods of monitoring the safety of new drugs.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M. Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical schools. (pharmac.) scholastic. sklad. / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: a textbook for students of pharmaceutical faculties / Ed. V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.

LECTURE 19. TOPIC
"Drug Interaction. Drug-Food Interaction"

Relevance of the topic: Drug interactions are a pressing problem in medicine, as they can significantly affect the effectiveness of treatment and patient safety. Understanding these interactions helps doctors optimize drug prescriptions, reduce the risk of side effects, and achieve better treatment outcomes.

Relevance of drug interactions:

• Change in efficacy: When several drugs are taken at the same time, their effects may be enhanced or weakened, which affects the achievement of the desired therapeutic effect.
• Occurrence of adverse reactions: Drug interactions can lead to unwanted side effects that can be dangerous to the patient's health.

• Decrease in treatment efficacy: Interactions can reduce the concentration of the active substance in the blood, which makes treatment less effective.
• Increase in toxicity: Some interactions can increase the toxicity of one or both drugs, which can lead to serious complications.
• Need for monitoring: Due to the possibility of drug interactions, it is important to monitor the patient's condition, especially when taking multiple drugs for a long time.
• Importance of information: Patients should be informed about possible drug interactions and the consequences of non-adherence.
• Food effects: Food can also affect the action of drugs, so it is important to consider this factor when prescribing treatment.
Examples of drug interactions:
• Mixing alcohol with some drugs can increase their sedative effect and lead to dangerous consequences.
• Taking some antibiotics with dairy products can reduce their effectiveness.
• Some drugs used to treat cardiovascular diseases can interact with certain painkillers.

Therefore, understanding and considering possible drug interactions is critical to ensuring the safety and effectiveness of treatment.

Purpose: To familiarize the student with the basic principles of drug combinations, drug interactions with each other and with food, to explain the importance of monitoring the effectiveness and safety of combined drug use in a given patient.

Basic concepts (list of questions):

Drug interaction - simultaneous use in medical practice of several drugs. At the same time, they, interacting, change the manifestations and nature of the main effect, its duration, enhance or reduce side and toxic effects

Types of drug interaction - the following types of drug interactions are distinguished: pharmaceutical, pharmacokinetic, pharmacodynamic.

Pharmaceutical drug interaction - a type of interaction that occurs outside the body. At the stages of preparation and storage of combined drugs, as well as when mixing drugs in one syringe, changes may occur that make the drug unnatural for use. In this case, the activity of the components of the mixture decreases or disappears or new properties appear, sometimes toxic.

Pharmacokinetic drug interaction - is associated with a change in pharmacokinetic characteristics.

Pharmacodynamic interaction of drugs - associated with a change in the effects of drugs.

Synergism - a combination of drugs that mutually enhance the effect of each of them.

Synergism - the interaction of two drugs, which is characterized by the fact that at some doses it has the form of synergism, and at others - antagonism.

Antagonism - a type of interaction of substances in the body, which is characterized by the fact that one of them weakens or completely prevents the action of the other.

Potentiation - the strengthening of the biological or pharmacological action of one factor (substance) by others, which as a result is more significant than the sum of the individual effects of these factors.

Lecture content (lecture text)

DRUG INTERACTION (DI)as a term is used in situations when, when two or more drugs are taken simultaneously, the specific effect on the body of at least one of them changes significantly. Later, this concept was significantly expanded and is now used in cases where drugs show inadequate effects when interacting with food, change the results of clinical and laboratory studies, or in the presence of concomitant diseases in patients. One of the possible

consequences of drug interactions may be an excessive reaction of the body to one of the components of the drug, which can lead to serious complications or noticeable changes (increase, decrease or complete loss) of its effectiveness. This concept also includes the unpredictability of the specific action of the drug, when the pharmacokinetic or pharmacodynamic properties of the active substance are not sufficiently studied.

In medical practice, it is customary to distinguish four classes of drug interactions. Class A - when the interaction of drugs is not clinically significant, e.g. ranitidine with phenobarbital; class B - when V.l. is not described; class C - when DI changes the therapeutic effect and requires adjustment of drug dosage regimens, e.g. cimetidine with theophylline; class D - when simultaneous administration of drugs is impossible due to the development of dangerous reactions or therapeutic inefficiency, e.g. indomethacin with triamterene. The unpredictability of DI causes the problem of the need for careful control and supervision of combined pharmacotherapy in order to prevent dangerous cases of DI, which are increasingly found in medical practice. Despite the complexity of the problem of V.l. in general, combined pharmacotherapy is generally recognized when another drug is prescribed together with the main drug in order to modify the effects of the previous one (enhance the effectiveness or reduce the side effect). There are numerous cases when DI is used in clinical practice for a specific purpose, e.g. in antidote therapy. Factors that cause DI include: the ability of medicinal substances to affect several physiological systems simultaneously (when pharmacotherapy takes into account the primary effect and ignores the weaker secondary one, which may be significantly manifested when taking two or more drugs simultaneously); prescribing drugs with different trade names or simultaneous use of prescription and non-prescription drugs that have the same drug substances; simultaneous use of drugs and dietary supplements and other cases. DI can also be caused by patients' incompetence or their violation of the recommendations of specialists (doctor, pharmacist), or inattention to the recommendation (instructions) on the method of using drugs, especially several at the same time. Detection and elimination of many of the above cases of V.l. becomes possible if the patient receives drugs in one pharmacy, in which information and accounting of patient service are well organized using computer programs. In the area of prevention of numerous undesirable, and sometimes extremely dangerous cases of DI the pharmacist can significantly influence the quality of drug therapy.

Numerous cases of DI necessitate their classification. Given the practical significance, cases of DI are conveniently divided into pharmaceutical and pharmacological. Pharmaceutical interactions should be understood as processes occurring between components of the drug system, based on their physicochemical laws and determining the properties of the drug during development, production, storage, transportation and use. Most pharmaceutical interactions are predictable and can be avoided by knowing the properties of the components of the drug or by adhering to a separate dosing regimen.

Chemical DI is a type of pharmaceutical interaction and can be observed in the formation of insoluble complexes of tetracyclines with a number of ions Ca++, Al+++, Fe++, Mg++, etc., e.g. in interaction with food components. Since when taking drugs, the interaction of components occurs with the participation of not only physicochemical, but also biochemical laws (with the participation of components of the biosystem or directly in the body), biopharmaceuticals should be distinguished from the group of pharmaceutical (i.e. physicochemical) interactions. This is convenient for practical reasons, since physicochemical interactions are, as a rule, undesirable, while biopharmaceuticals are usually useful and are used in clinical practice. Pharmacological DI, which are implemented with the participation of various functional systems of the body, are divided into pharmacokinetic and pharmacodynamic. Pharmacokinetic DI can be noted, first of all, at the stage of absorption in the gastrointestinal tract. So, sorbents, when taken simultaneously with other drugs, reduce their absorption and bioavailability. Ion-exchange resins, e.g. cholestyramine, give their ions to digoxin, butadione, indirect anticoagulants, which

become insoluble and are excreted through the intestines. Under the influence of cholestyramine, the absorption of thyroid hormones can be significantly inhibited, which leads to the development of hypothyroidism in patients receiving hormone replacement therapy. The completeness of drug absorption and their bioavailability can be significantly affected by the pH of gastric juice. So, when interacting with weak acids, the absorption of antacids, proton process inhibitors, H2-histamine receptor blockers decreases, and when interacting with weak alkalis, their absorption increases. DI can change intestinal motility and affect its biocenosis. If medicinal substances have a high degree of binding to blood proteins, then their interaction is also likely at the stage of distribution. Examples of DI associated with competition for the binding site with blood transport systems are observed with the simultaneous use of bilirubin with sulfonamides or vitamin K (jaundice), tolbutamide with salicylates or phenylbutazone (hypoglycemia), methotrexate with salicylates or sulfonamides (agranulocytosis) and in other cases. DI at the stage of metabolism is possible in the case when medicinal substances act as inducers or inhibitors of metabolic enzymes, which leads to a change in their T½ and requires certain monitoring during pharmacotherapy (regulation of the concentration of the substance in the blood plasma). DI at the elimination stage is often detected due to changes in urine pH (sodium bicarbonate increases the rate of excretion of barbiturates and salicylates) and competition of drugs for the transport systems of the renal tubules (probenecid reduces the excretion of penicillins, furosemide slows down the excretion of β-lactam antibiotics). DI at the elimination stage can cause side effects. Thus, phenylbutazone, inhibiting the excretion of oxyacetohexamedine, leads to the development of hypoglycemia; ammonium chloride - to the formation of a sulfadimezine derivative, which damages the renal epithelium.

Unlike pharmacokinetic interactions observed at the stages of absorption, distribution, metabolism and elimination, pharmacodynamic interactions are associated with such mechanisms as competition of medicinal substances for receptors, change in kinetics at the site of their action, influence on synaptic transmission, interaction of effects, etc. There are a large number of the most diverse mechanisms of interactions, including those dangerous to the patient's life. Not all interactions have been studied and can be explained; in addition, they can develop not only with a single dose of drugs, but also during a certain time in the body. Therefore, to prevent interactions, in some cases, preference should be given to monotherapy.

Questions for self-control on the topic:

1. Content, basic concepts of the topic "Interaction of drugs" in modern medical practice and pharmacy. Types of drug interactions, main classes by clinical significance (A, B, C, D), their practical clinical significance for safe use in patients. Antagonism and synergism as a consequence of drug interactions. Types of synergism. Concept of pharmaceutical, pharmacodynamic, pharmacokinetic drug interactions.
2. Pharmaceutical drug interactions: causes of development, main mechanisms and possible consequences of interaction. Practical clinical significance of drug interaction results.
3. Pharmacodynamic drug interactions: causes of development, main mechanisms and possible consequences of interaction. Practical clinical significance of drug interaction results.
4. Pharmacokinetic drug interactions: causes of development, main mechanisms and possible consequences of drug interactions.
5. The role of the doctor and pharmacist in modern medical practice in reducing the risk of side effects of drugs due to irrational drug interactions, their educational work in reducing the number of cases of irrational use of drugs by patients (polypharmacy) in order to optimize pharmacotherapy for each patient.

6. Interaction between drugs as a risk factor for medical errors and side effects when using drugs. Combined use of drugs: undesirable effects and methods of early detection to prevent their development in patients.
7. Study of the main mechanisms and features of drug interactions due to polymorbidity of the patient's morbidity. Assessment of risks associated with the potential likelihood of developing a side effect due to undesirable drug interactions among drugs of the main groups of drugs.
8. The effect of food on the absorption and pharmacokinetics of drugs, features of the safe use of drugs of different pharmacological groups. The influence of liquids and drinks on the absorption and pharmacokinetics of drugs, features of the safe use of drugs of different pharmacological groups.
9. Features of drug interactions and issues of effectiveness and safety of the use of drugs together with herbal medicines, food additives, features of the safe use of drugs of different pharmacological groups.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M. Bilovola. – Vinnytsia: Nova Kniga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others. – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical Pharmacy: a textbook for students of pharmaceutical faculties / Edited by V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Protocols of a pharmacist / Edited by V.P. Chernykh, I.A. Zupanets, O.M. Lischyshyna. – Kharkiv: Golden Pages, 2013. – 192 p.

LECTURE 20. TOPIC
"Pharmacoeconomics: definition, basic principles and concepts. Evidence-based medicine and pharmacology. Formulary system"

Relevance of the topic: Pharmacoeconomics is a relevant science that deals with the assessment of the cost and effectiveness of medicines and medical technologies. Its relevance is due to the need for rational use of resources in healthcare and ensuring maximum clinical effect at minimal costs.

Relevance of pharmacoeconomics:

• Cost optimization: Pharmacoeconomics helps to compare different drugs and medical technologies, identifying the most effective and cost-effective options.

• Rational use of resources: In conditions of limited financial resources, pharmacoeconomics allows you to make informed decisions on the allocation of funds for medicines, ensuring maximum benefit for patients.

• Improving the quality of medical care: By analyzing costs and results, pharmacoeconomics contributes to the choice of optimal treatment methods, which improves the quality of life of patients and overall health.

• Evidence-based medicine: Pharmacoeconomics is an integral part of evidence-based medicine, as it provides scientific justification for the choice of drugs and treatment methods.

• Pharmacoepidemiological studies: Pharmacoeconomics is closely related to pharmacoepidemiology, which studies the use of drugs in large populations. Pharmacoeconomic analysis helps to assess the impact of drugs on the health of the population and the effectiveness of their use.

• Pharmacy development: Pharmacoeconomics contributes to the development of the pharmaceutical industry, stimulating the creation of new, more effective and economically beneficial drugs.

Pharmacoeconomic methods:

• Cost analysis: Estimating the cost of drugs, medical procedures and other costs associated with treatment.

• Effectiveness analysis: Studying the impact of drugs on patient health and assessing clinical outcomes.

• Pharmacoeconomic analysis methods:

• ABC analysis: Classification of drugs by cost, which allows you to identify the most expensive and most common drugs.

• VEN analysis: Classification of drugs by vital, important and unimportant, which allows you to optimize their purchase.

• Frequency analysis: Determining the frequency of use of certain drugs and treatment methods.

Pharmacoeconomics is an important science that helps to rationally use resources in healthcare, improve the quality of medical care and ensure maximum benefit for patients. Its relevance is growing due to the need for effective and economical use of medicines and medical technologies.

Purpose: To familiarize HES with the basic principles and provisions of evidence-based medicine, evidence-based pharmacology, the formulary system, the principles and provisions of pharmacoeconomics, and methods of pharmacoeconomic analysis.

Basic concepts (list of questions):

Evidence-based medicine is an approach to medical practice in which decisions on the use of preventive, diagnostic and therapeutic measures are made based on available evidence of their effectiveness and safety, and such evidence is subject to search, comparison, generalization and wide dissemination for use in the interests of the patient.

Pharmacoeconomics is a modern applied science that offers a methodology for comparative assessment of the quality of two or more methods of prevention, diagnosis, drug and non-drug treatment based on a simultaneous complex interrelated analysis of the clinical results of the use of medical intervention and the costs of its implementation.

Pharmacoeconomic analysis allows you to identify treatment methods and drugs that provide the maximum total benefit per unit of cost.

Lecture content (lecture text)

PHARMACOECONOMICS is an applied science that is a methodology for the comparative assessment of medical technologies (methods of prevention, diagnosis and treatment, including the use of drugs), based on a comprehensive comprehensive analysis of the results of their application and economic costs. In essence, pharmacoeconomics is an eclectic integral science that uses terms and concepts that belong to three scientific categories: medical (characterize the clinical results of medical technologies (efficacy, efficiency, safety)), humanistic (reflect the clinical results of medical technologies through their perception by the patient and society (improvement of the patient's quality of life, compliance)), and economic (describe the financial component of medical technologies (costs, economic efficiency)). The above categories are generalized concepts that reflect the phenomena and processes inherent in pharmacoeconomics as a separate scientific direction in the field of medical and biological sciences and are used in pharmacoeconomic research.

Efficacy is the proven effect of a drug established under controlled conditions (phase I and II clinical trials) before its registration. Usually, efficacy is the direct clinical effects of a drug: changes in physiological, biochemical and physical indicators of the patient's body (decrease in blood pressure in hypertension, increase in hemoglobin level in anemia); elimination of symptoms of the disease (reduction in the intensity of pain in the joints, etc.); reduction in the frequency of complications or the number of repeated hospitalizations.

Therapeutic effectiveness is the effectiveness of a drug after its registration and release on the pharmaceutical market, which is established on a large (over 10,000 people) number of patients in real clinical practice when conducting pharmacoepidemiological studies (see Pharmacoepidemiology). Most often, indicators of therapeutic efficacy are those whose determination is reliable and significant in a large number of patients in long-term conditions, namely: reduced mortality (e.g., total or cardiovascular in hypertension), increased survival, increased life expectancy (e.g., after chemotherapy), i.e., indirect clinical effects.

Safety is the frequency, number and severity of side effects when using drugs (e.g., when using diclofenac sodium, gastrointestinal disorders occur in about 30% of patients). Drug safety must be taken into account, since the frequency, number and severity of side effects affect the cost of pharmacotherapy.

Utility is an indicator of the effectiveness of medical technologies, established by improving the quality of life of patients after treatment.

Compliance is the patient's willingness to adhere to the treatment regimen and conditions for the rational use of prescribed drugs.

Economic efficiency (benefit) — an indicator of the efficiency of spending financial resources (profit per invested monetary unit, — “costs–benefit (benefit)”) when using drugs or medical technologies.

Costs (cost) in F. — material and non-material costs associated with the use of medical technologies.

The establishment of F. as a separate science within the framework of health care is due to: first, the general global disproportion between the limited financial resources of states and the constantly growing volumes of financing the health care sector; second, a significant increase in the number of drugs on the world pharmaceutical market and the search for approaches that would contribute to their rational use and allow reducing and optimizing, first of all, budget spending on health care, as well as the costs of insurance companies and patients on the basis of

a reasoned choice. The object of F. as an independent applied science is the assessment of the cost-effectiveness indicator (the ratio of costs and the effectiveness of medical technologies) or the cost of a unit of effectiveness. The subject of F. there are the results (consequences) of medical technologies and the financial costs of their use.

When conducting pharmacoeconomic assessment, various sources of information are used to analyze clinical results (effectiveness of medical technologies): reports on clinical trials of drugs, reports of medical and preventive institutions, scientific publications: articles and reviews that highlight the results of clinical and pharmacoepidemiological studies of drugs, meta-analyses, systematic reviews, statistical data on drug consumption. To analyze financial costs, industry tariffs and price lists for medical services, drug price lists of pharmacies and pharmaceutical companies, valid at the time of the study, are used, based on general economic approaches. The main methodological approaches of pharmacoeconomic analysis are methods of pharmacoeconomic analysis, as well as other pharmaceutical sciences, including ABC, VEN and frequency analyses. The purpose of pharmacoeconomic analysis is to justify the choice of the optimal medical technology based on the cost-effectiveness indicator. Pharmacoeconomic calculations allow predicting the required amount of funding at different levels, starting from specific medical and preventive institutions and ending with the national one. The leading feature of the methodological approach of pharmacoeconomics is the complexity, which consists in choosing drugs based on the analysis of safety, quality, therapeutic and economic efficiency, the level of their consumption and the structure of the population's morbidity.

The main task of pharmacoeconomics as a component that ensures the functioning of evidence-based medicine is to promote the rational use of drugs, that is, to achieve the maximum clinical effect by using cheaper and more effective drugs.

In the context of the introduction of a formulary system and standards of medical care in the health care of all developed countries, the results of pharmacoeconomic analysis are the basis for selecting only those drugs for standards and formulas whose use is economically justified. These are drugs whose therapeutic efficacy and safety, on the one hand, have been proven in pharmacoepidemiological studies, and on the other hand, they are characterized by optimal costs per unit of effectiveness, which corresponds to the capabilities of the State Budget in relation to health care.

The relevance of pharmacoeconomic analysis is confirmed by the possibility of using the results of pharmacoeconomic analysis by various participants in the pharmaceutical market. Health care system managers and formulary committee members use the results of pharmacoeconomic analysis to form an optimal list of drugs, which allows optimizing and reducing state costs for their use. Drug manufacturers use the results of pharmacoeconomic analysis to justify pricing policy, selecting drugs for state lists of drugs and formularies, the costs of which are reimbursed by the state or social assistance institutions; heads of pharmacy institutions, pharmaceutical companies - to form an optimal assortment and promote drugs on the pharmaceutical market; pharmacists, doctors - for a more complete use of the assortment of registered drugs and prescribing them taking into account the predicted result and the patient's economic status; employees of research laboratories - to substantiate the prospects and economic feasibility of developing and introducing new drugs.

Pharmaceutical management is a mechanism of pharmaceutical management and marketing to ensure the effective functioning of healthcare, namely, drug provision on the basis of modern evidence-based medicine.

EVIDENCE-BASED MEDICINE (English: evidence-based medicine; syn.: scientifically based medical practice) is the use in daily medical practice (in diagnostics, treatment and

prevention) of medical technologies and drugs, the effectiveness of which has been proven in pharmacoepidemiological studies using mathematical estimates of the probability of success and risk.

E.M. spread in the late 80s of the twentieth century. as a concept of new clinical thinking in the process of forming a new field of medical knowledge - clinical epidemiology, which uses epidemiology methods in relation to the results of the use of various medical technologies. E.M. can be defined as a new technology for collecting, analyzing, synthesizing and applying scientific medical information, which allows making optimal clinical decisions both in terms of patient care and economic efficiency. In the process of forming E.M., the following areas of medical science were formed: pharmacoepidemiology, new areas of pharmacoinformatics, pharmacoeconomics, formulary system.

Formation of E.M. at the present stage of development of society is connected with development of health care system as a result of rapid scientific and technological progress, increase of health care expenses due to increase of price of medicines, high cost of new medical technologies of diagnostics and treatment of various diseases, expansion of spectrum of medical services and for other reasons. Financial resources allocated by the society for health care are limited even in the most highly developed countries, and need for state expenses for medical care is constantly growing. Therefore the problem of choice of medical technology with proven efficiency from a large number of alternative options nowadays is becoming especially urgent, because it increases efficiency of treatment.

The main principle of E.m. — each clinical decision should be based on scientific facts, proven statistically on a large representative group of patients; no new medical technology (new method of treatment, diagnostics, prevention) can be recognized without obligatory verification in conditions of conducting randomized controlled trials. The mechanism of implementation of the principles of D.m. into widespread clinical practice is the standardization of medical care and the implementation of a formulary system.

The main method of E.m. (gold standard) is randomized controlled trials, when patients are randomly assigned to groups using randomization tools. In practical terms, D.m. sets itself the following tasks: 1) to improve the quality of medical care in terms of effectiveness, safety and cost; 2) to optimize the activities of the national health care system.

To obtain evidence of the effectiveness of medical technologies, E.m. operates with the following basic pharmacoepidemiological concepts: actual (final) clinical outcome (clinical outcome) - a phenomenon that is important for changing health indicators (recovery, disability, mortality, life expectancy) and/or quality of life; indirect (indirect) criterion of effectiveness - a laboratory indicator or symptom, the dynamics of which directly characterizes the patient's condition and is reflected in the final clinical result; absolute risk — the absolute difference between the frequency of development of an undesirable effect when using a drug and the frequency of development of the same effect without using the drug; relative risk — the ratio of the frequency of development of an undesirable effect among persons exposed to the factor being studied (used the drug) to the frequency of development of a similar effect in a group of persons not exposed to this factor (did not use the drug).

In most economically developed countries of the world, E.m. has become widespread today. Symposia on the problems of clinical epidemiology and E.m. are constantly held, monographs, handbooks and international journals are published, in particular "Clinical Evidence", "Evidence Based Medicine", "ACP Journal Club", etc., which inform the medical community of the world on these problems. In accordance with the principles of E.m., the international Regulation of Scientific Research in Medicine — GCP (GCP — GCP) has been created. It guarantees the reliability of the results of various methods of pharmacotherapy and the protection of the rights of subjects of clinical trials - patients. In Ukraine, D.m. has recently been rapidly developing: modern principles of organizing the health care system are based on the most important provisions of E.m., the number of publications on this topic has significantly increased, the public organization “Center for Evidence-Based Medicine” has been created,

teaching the basics of E.m. has begun at the National University of Physics and Technology, medical universities of Kyiv, Ternopil, Dnipropetrovsk, etc.

Questions for self-control on the topic:

1. Evidence-based medicine: concept, methodology, fundamental principles.
2. Basic terms of evidence-based medicine.
3. International experience in the application of evidence-based medicine.
4. Formulary system: concept, methodology, principles.
5. Principles of forming drug formulas and formulas for pharmacists.
6. Formulary implementation algorithm: development of drug formulary lists, publication of formulary guides, implementation of treatment standards, implementation of a program and methods for assessing the effectiveness and safety of drugs.
7. Pharmacoeconomics: terms, concepts, basic principles.
8. Methods of pharmacoeconomic analysis: types, definitions, examples.
9. Cost-benefit analysis: definition, examples.
10. Cost-benefit analysis: definition, examples.
11. Cost minimization analysis: definition, examples.
12. Cost-effectiveness analysis: definition, examples.

List of sources on the topic:

1. Clinical pharmacology / Edited by prof. M.I. Yabluchansky, prof. V.M. Savchenko. – Kharkiv, 2011. – 406 p.
2. Clinical pharmacology: textbook / Edited by O.M. Bilovola. – Vinnytsia: Nova Knyga, 2021. – 544 p.
3. Clinical pharmacy (pharmaceutical care): textbook for students of higher medical (pharmaceutical) schools / I.A. Zupanets, V.P. Chernykh, T.S. Sakharova and others – Kh.: NFAU: Golden Pages, 2011. – 704 p.
4. Clinical pharmacy: textbook for students of pharmaceutical faculties / Edited by V.P. Chernykh, I.A. Zupanets, I.G. Kupnovytska. – Ivano-Frankivsk, 2013. – 1612 p.
5. Pharmacoeconomics: Textbook for university students / Ed. L.V. Yakovleva. – Vinnytsia: Nova kniga, 2009. – 208 p.