ODESSA NATIONAL MEDICAL UNIVERSITY
DEPARTMENT OF DRUGS TECHNOLOGY

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«27» august 2021 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №6 **«Bioequivalence of drugs - as a criterion for their quality.»**

Methodical recommendations on IWS developed by:
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Methodical recommendations of IWS were discussed at the methodical meeting of the department
«27» august 2021 y.
Protocol № 1

Odessa - 2021

Topic: "Bioequivalence of drugs - as a criterion for their quality" - 4 hours.
Objective: To deepen knowledge in the consideration of bioequivalence of drugs - as a criterion for their quality ..
Basic concepts: Bioequivalence.

Plan

I. Theoretical questions for the lesson:

The concept of bioequivalence is closely related to the concept of bioequivalence. Two drugs are considered bioequivalent if they provide the same bioavailability of the drug substance after administration in the same dose and the same dosage form. According to the WHO regulations (1994, 1996) and the EU (1992), the differences in pharmacokinetic parameters for the bioequivalence of drugs should not exceed 20%.

Currently, the study of bioequivalence is the main type of medical and biological quality control of generic drugs. The introduction of the definition of bioequivalence as a method allows to make a reasonable conclusion about the quality, efficacy and safety of comparable drugs on the basis of less primary information and in a shorter time than in clinical trials.

To date, there are regulations for studying the bioequivalence of the WHO (1996), the EU (1992). They set out the main rationale for the need for bioequivalence studies. These studies must be performed if there is a risk of lack of bioequivalence or a risk of reduced pharmacotherapeutic action and clinical safety of the drug.

For example, drugs for the treatment of conditions that require a guaranteed therapeutic effect must be evaluated; drugs with a small therapeutic breadth; drugs whose pharmacokinetics are complicated by a decrease in absorption of less than 70% or with high elimination (more than 79%); drugs with unsatisfactory physicochemical properties (low solubility, instability, polymorphism); drugs with documented evidence of a bioavailability problem.

Bioequivalence studies (pharmacokinetic equivalence) should in no way be considered as an alternative to pharmaceutical equivalence testing - the equivalence of generic drugs in terms of qualitative and quantitative composition of drugs assessed by pharmacopoeial tests, as pharmaceutical equivalence does not guarantee equivalence. However, bioequivalence studies suggest that the bioequivalence of the original generic drugs provide the same efficacy and safety of pharmacotherapy, ie are therapeutic equivalents.

Assessment of bioequivalence is based on the results of studying the relative bioavailability of the drug in the compared drugs. In essence, the study of bioequivalence is a special type of pharmacokinetic study. First of all, it should be emphasized that the study of bioequivalence is a clinical trial where the subject of the study is a person. Therefore, such studies are subject to all the official requirements and regulations that apply to all other clinical trials. A team of specialists in various fields should plan and conduct research to determine bioequivalence: clinical pharmacologists, clinicians, biochemists, chemists-

analysts. The study of bioequivalence should be conducted in full compliance with the principles of "Good Clinical Practice" (GLP) in order to guarantee the quality of data presented and protect the rights, health and well-being of subjects.

Animal bioequivalence studies have not been widely accepted and are practically not used. They are used only at the stage of preclinical studies or in the case of the study of drugs intended for use in veterinary medicine. Typically, the term "bioequivalence" in this case is replaced by the term "pharmacokinetic equivalence".

In determining the equivalence of antimicrobial drugs, it is possible to use in vitro methods, however, in this case, the term "bioequivalence" is preferred not to use.

Currently in Ukraine there is a sufficient material and technical base, highly effective methods are used to determine pharmacokinetic parameters, specialists are trained in the field of bioequivalence research, which allows to solve the urgent problem of assessing the effectiveness and safety of domestic and foreign generic drugs.

1. Biopharmacy: textbook / edited by: Borisyuk IY, Fizor NS, Akisheva AS Odessa, ONMedU, 2020. - pp. 58-60.

Questions for self-control

1. Generic drugs. Quality control.
2 . Bioequivalence of drugs.
3. The concept of chemical, biological, therapeutic equivalence of drugs.
4. Modern methods for determining the effectiveness of drugs.
5. Methods "in vitro" (direct diffusion through the membrane, "agar plates", chromatographic, solubility test, etc.).
6. Methods "in vivo", which are carried out on laboratory animals, healthy people, volunteers, isolated organs with single and multiple injections.
7. Modern methods for determining the concentration of drugs in biological fluids (blood, urine, excretion).
8. Microbiological and acanthosis tests.
9. Graphic method of calculating the area of the pharmacokinetic curve and the degree of absorption of drugs. Determination of absorption and elimination constants.
10. Radioisotope method.
11. Correlation of methods "in vitro" and "in vivo" in determining the bioavailability of drugs.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic

2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	**The main tasks**	**Instructions**	**Answers**
1.	Which drugs are considered bioequivalent?	Open the question	Drugs are considered bioequivalent if the 90% confidence interval for the geometric mean, calculated for individual relationships of logarithmically converted values of each of these pharmacokinetic parameters (except Stach), for the study drug to those for the comparison drug, is within 0.80 .. .1 , 25. For Stach, the corresponding limits are 0.70 ... 1.43. The limits of the above confidence interval are calculated using two one-way tests (mainly by the method of Schuirmann) after logarithmic conversion of pharmacokinetic parameters. If the specified confidence interval in the case of AUCt or AUC ∝ παραμετερσ□exceeds the established limits, the drugs are considered non-bioequivalent.

II. Practical work (tasks) that will be performed in class:

Task1

To establish the effect of polymorphic modifications of insulin preparations on the rate of its release by the "in vivo" method.

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs technology / Tests Step-2 on the following topics: Industrial production of soft dosage forms. Quality assessment

IV. Individual tasks for students on the topic of the lesson

Therapeutic equivalence.

List of recommended reading

Main:

. . 1. Біофармація : підруч. для студентів закл. вищ. освіти / О. І. Тихонов [та ін.] ; за ред. О. І. Тихонова. – 2-ге вид., перероб. і допов. – Харків : НФаУ: Золоті сторінки, 2019. – 224 с

2. Настанова СТ-Н МОЗУ 4242-7.1:2005 «Лікарські засоби. Настанова з клінічних досліджень. Дослідження біодоступності та біоеквівалентності» - Київ, 2018.

3. Настанова СТ-Н МОЗУ 4242-7.1:2005 «Лікарські засоби. Настанова з клінічних досліджень. Дослідження біодоступності та біоеквівалентності» - Київ, 2018.

4. Настанова СТ-Н МОЗУ 42-7.2:2018 Лікарські засоби дослідження біоеквівалентності. – Київ, 2018. – 77 с.