

CLINICAL PHARMACOLOGY OF ANTITUBERCULOSIS, ANTIFUNGAL, ANTIVIRAL AND ANTIPROTOZOAL DRUGS

A. Actuality

Tuberculosis is an infectious socio-economic disease, which presents an important problem in contemporary medicine. The dramatic increase in the incidence of tuberculosis and the resistance of mycobacteria to specific chemotherapeutic remedies requires major social and financial efforts. Patients need long-term treatment with the creation of appropriate social conditions. The development of effective and harmless anti-tuberculosis preparations is also a difficult problem, determined by the particularities of the pathogen and the pathology.

Fungi represent a specific class of microorganisms that require the elaboration of drugs with targeted and selective action through the influence of key stages in their multiplication and development. Antimycotic treatment presents difficulties, determined by the type of mycosis (local or systemic) and the lack of drugs, able to concentrate in the target organs and tissues, without negatively affecting the macroorganism. These problems become even more important in the case of long-term treatment, when the body faces secondary immunodeficiency states.

Viruses, as pathogens, are a specific class of microorganisms that require the development of targeted and selective drugs on different stages of their multiplication and development. At the same time, antiviral treatment presents some difficulties due to the structural particularities of the viruses and the viral infections evolution. This requires the use of drugs that can concentrate on the affected organs and tissues, influence the key enzymes of viral multiplication, but without exerting a negative influence on the macroorganism. These problems become even more important when treatment has a variable efficacy and is long-lasting. Viruses develop relatively fast resistance and the body is confronted with some secondary immunodeficiency states. Protozoa are capable of causing a range of diseases with a specific clinical picture depending on the causal parasite, and antiprotozoal drugs are represented by various groups of substances with specific action on the parasite depending on the location and form of the disease caused by it.

B. Training aim

Acquiring clinical and pharmacological principles to justify the prescription, use, dosing regimen of drug preparations in the given groups, and to assess their efficacy and harmlessness.

C. Teaching objectives

The student should be able to:

- a) use the principles of the mechanism of action and the particularities of the antibacterial effect of antimycotic, antiviral and antiprotozoal anti-tuberculosis preparations for their rational selection,
- b) analyze and evaluate the results of microbiological, laboratory and instrumental methods for determining the effectiveness and correction of the specific antibacterial treatment;
- c) predict the possible complications and adverse reactions of the antituberculosis, antimycotic, antiviral and antiprotozoic preparations;
- d) predict the dependence of the adverse phenomena on the dosage regime and the functional state of the organs and body systems;
- e) draw up the form of personal medicines, (P-medicines).

D. Knowledge from previously studied disciplines and related subjects

Histology, morphopathology, pathophysiology and microbiology

The structure, particularities of development, multiplication and toxicity of mycobacteria and fungi. Microbiological and serological methods for diagnosing mycobacterial and fungal infection. Determining the sensitivity of pathogens to specific chemotherapies. Structure, particularities of development, multiplication and toxicity of viruses. Microbiological and serological methods for diagnosing viral and parasitic infections.

Phthisiopneumology. Classification of tuberculosis. Pathogenesis, clinical picture and microbiological criteria, serological diagnosis of tuberculosis. Principles of treatment.

Tuberculosis prophylaxis.

Dermatovenereology. Classification of mycoses. Pathogenesis, clinical picture and diagnostic criteria for candidiasis, dermatomycoses, onychomycosis and systemic mycoses. Principles of treatment. Mycoses prophylaxis.

Infectious diseases. Pathogenesis, clinical picture and biochemical and serological criteria for diagnosing viral (hepatitis, AIDS, herpes, influenza, etc.) and protozoal infections. Principles of prophylaxis and treatment.

Pharmacology. Classification of drugs according to chemical structure, mechanism of action and developed effect, spectrum of action. Characterization of the drugs groups according to the spectrum of action, generations. Side effects of drugs of the given groups.

E. Questions for self-training

I. Clinical and pharmacological characteristics of antituberculosis, antifungal, antiviral and antiprotozoal drugs

1. Classification of anti-tuberculosis (WHO) preparations. Mechanisms of action of anti-tuberculosis preparations. New groups of tuberculosis drugs. of antibiotics according to spectrum and mechanism of action, antibacterial effect.
2. Clinical pharmacology of ansamycins: particularities of the spectrum and mechanism of action, indications and principles of selection, contraindications and precautions for administration, typical adverse reactions and their prophylaxis, pharmacokinetics.
3. Clinical pharmacology of hydrazide derivatives: particularities of the spectrum and mechanism of action, indications and principles of selection, contraindications and precautions, typical adverse reactions and their prophylaxis, pharmacokinetics.
4. Clinical pharmacology of antibiotics as anti-tuberculosis drugs: particularities of the spectrum and mechanism of action, indications and principles of selection, typical adverse reactions and their prophylaxis, pharmacokinetics.
5. Clinical pharmacology of synthetic preparations used as anti-tuberculosis drugs: particularities of the spectrum and mechanism of action, indications and principles of selection, typical adverse reactions and their prophylaxis, pharmacokinetics.
6. Particularities of the mechanisms of action, indications and principles of use of fluorquinolones, oxazolidinediones, delamanide, bedacvilin, clofazimine.
7. Principles of tuberculosis treatment. Resistance to anti-tuberculosis preparations: mechanisms and pathways to combat them.
8. Particularities of the administration of anti-tuberculosis drugs during pregnancy and the period of lactation.
9. Classification of antifungal preparations. Mechanisms of action of antifungal preparations. New groups of antifungal preparations.
10. Clinical pharmacology of antimycotic antibiotics: particularities of the spectrum and mechanism of action, indications and principles of selection, typical adverse reactions and their prophylaxis, pharmacokinetics.
11. Clinical pharmacology of azoles as antifungal agents: particularities of the spectrum and mechanism of action, indications and principles of selection, typical adverse reactions and their prophylaxis, pharmacokinetics.
12. Clinical pharmacology of echinocandins and synthetic preparations as antifungal agents: particularities of the spectrum and mechanism of action, indications.
13. Classification of antiviral drugs according to clinical use.
14. Anti-influenza drugs: classification, spectrum peculiarities and mechanism of action. Indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
15. Anti-herpes virus drugs: classification, spectrum peculiarities and mechanism of action. Indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
16. Antiretroviral drugs (AIDS): classification, spectrum peculiarities and mechanism of action. Indications and principles of selection, typical side effects and their prophylaxis,

pharmacokinetics.

17. Clinical pharmacology of drugs used in treatment of viral hepatitis: spectrum peculiarities and mechanism of action, indications and principles of selection, side effects and their prophylaxis.
18. Clinical pharmacology of drugs used in the treatment of cytomegalovirus, papillomavirus and coronavirus infection: spectrum features and mechanism of action, indications.
19. Peculiarities of antiviral drugs administration in pregnancy and lactation period.
20. Classification of antiprotozoal preparations. Particularities of the spectrum and mechanism of action, indications and principles of use of the preparations used in the treatment of malaria, amoebiasis, trichomoniasis, lambylosis and pneumocystosis.

II. Clinical and pharmacological selection and use of drugs in some pathological conditions and diseases:

Principles of selection and use of anti-tuberculosis preparations in the treatment of sensitive and resistant tuberculosis.

Principles of selection and use of antifungal preparations in the treatment of systemic and local mycoses.

Principles of selection and use of antiviral preparations in the treatment of influenza, cytomegalovirus and papillomavirus infections.

Principles of selection and use of antiprotozoal preparations in the treatment of trichomonadosis, pneumocystosis.

F. Individual work

1. Brief characterization of main drugs

vertically – **International Nonproprietary Name (INN) of drug,**

horizontally – **synonyms, forms of delivery, mode of administration, (therapeutic, maximal) doses, mechanisms of action, indications, contraindications, side effects:**

moxifloxacin, levofloxacin, capreomycin, kanamycin, linezolid, rifampicin, ganciclovir, oseltamivir, lamivudine, stavudine, hydroxychloroquine, co-trimoxazole, bedacvilin, delamanide.

2. Exercises on medical prescription (see methodological instructions for practical works on pharmacology for the 3rd year):

isoniazid, ethambutol, pyrazinamide, streptomycin, amphotericin B, nystatin, clotrimazole, ketoconazole, fluconazole, terbinafin, mycheptin, interferon alfa, rimantadine, acyclovir, foscarnet, ribavirin, vidarabine, zidovudine, zidovudine, zidovudine metronidazole, furazolidone, solusurmin, pyrimethamine, tetracycline.

3. Indicate the drugs used in (for):

sensitive pulmonary tuberculosis; pulmonary tuberculosis with polyresistance; tuberculosis prophylaxis; tuberculous meningitis; systemic candidiasis; systemic mycoses (aspergillosis, histoplasmosis, etc.); vaginal candidiasis, cutaneous candidiasis; intestinal candidiasis; onychomycosis; dermatomycosis (epidermophia, trichophygia, microspore); skin herpes infections; ophthalmic herpes infections; systemic herpes infections; seasonal influenza prophylaxis; influenza treatment in patients at high risk; treatment of HIV infection; treatment of viral hepatitis B; treatment of viral hepatitis C; treatment of chronic granulocytic leukemia; treatment of Kaposi's syndrome in HIV patients; treatment of pneumonia with respiratory syncytial virus, lambliosis, toxoplasmosis, trichomonadosis, amoebic dysentery, access to malaria, individual malaria prophylaxis, pneumocystosis, papillomavirus infection, cytomegalovirus infection.

4. Tests on Clinical Pharmacology (for faculty of medicine), Chisinau-2004, page 103.

5. Clinical cases in Clinical Pharmacology (Clinical Cases Guide), Chisinau-2017, page 141.

6. Virtual situations.

7. Personal Drug (P-Drug) Selection and P-Treatment (Personal Treatment) according to the criteria of effectacy, safety, acceptability and cost for inclusion in the personal form (P drugs).