PHARMACOKINETIC AND PHARMACODYNAMIC PRINCIPLES OF RATIONAL USAGE OF CHEMOTHERAPEUTIC DRUGS

A. Actuality

Today, because the number of patients with serious evolution of infections increases and it appears that microbial populations became more and more resistant to antibacterial therapy, that is why antimicrobial therapy problem is very actual. The rational use of existing antibiotics, as well as the development of new generations or groups of antibiotics is an absolute priority. Synthetic chemotherapeutics - sulfamides, naphthyridine and quinolone derivatives, nitroimidazole, 8-oxyquinoline, nitrofuran, quinoxaline and thiosemicarbazone have antibacterial, antifungal and antiprotozoal properties and are widely used to treat pathogenic infections caused by microorganisms. Knowledge of their pharmacokinetics and pharmacodynamics will allow their rational selection, association with other preparations and establishing the optimal dosage regimen in the treatment of infectious diseases.

B. Training aim

To study clinic-pharmacological principles of prescription, usage, dosage regimen and argumentation of antimicrobial drugs administration. To estimate therapeutic efficiency of antibiotics from different groups.

C. Learning objectives

The students should be able to:

a) Select a minimum complex of investigational methods in order to estimate the pharmacodynamic effect of antimicrobial drugs.

b) Analyze the antimicrobials pharmacodynamic study results, obtained through instrumental and laboratory methods.

c) Prognose possible complications and side-effects of antimicrobial drugs from different groups.

d) Prognose the dependence of side-effects development on dosing regimen and functional state of organs and body systems.

D. Knowledge from other studied tangent subjects

Histology, morphopathology, physiopathology, microbiology. Structure of pathogenic agents. Classification of pathogenic microorganisms. Septic state pathogenesis.

Clinical subjects. Etiology, pathogenesis and clinical evolution of the main forms of infections. Laboratory and functional tests applied in stomatological and other infectious diseases (pulmonology, septic surgery etc). Clinical manifestations of infectious diseases.

Pharmacology. Antibiotic, synthetic chemotherapeutic drugs (quinolones, folate antagonists) classification according to origins, chemical structure, mechanism of action, indications, contraindications, adverse reactions.

E. Questions for self training

I. Pharmacokinetic and pharmacodynamic characteristics of the main groups of synthetic antibiotics and chemotherapeutics

1. Antibiotic's classification according to spectrum of antimicrobian action, mechanism and character of action. Clinical usage.
2. The basic principles of rational use of antibiotics and chemotherapeutics with diverse chemical structure.
3. Pharmacokinetics of antibiotics (absorption from the gastrointestinal tract, ability to bind antibiotics to blood proteins, plasma half-life, elimination pathways). Dependence of the therapeutic effect of antibiotics on the routes of administration.

4. General characteristics of the main groups of antibiotics (curative indications, treatment tactics, rules and principles of association of antibiotics from different groups).
5. Routes of administration of antibiotics, correct selection of doses, indications for administration depending on the severity of the disease (infection) and the type of pathogen, functional status of the liver and kidneys.
6. Peculiarities of antibiotic therapy in the elderly.
7. Antibiotico-prophylaxis. Principles and indications.
8. Rational selection of chemotherapeutic combinations depending on the mechanism and spectrum of action. Routes of antibiotic drugs administration. Indications, dosage regimen, depending on the disease severity and liver and kidney function.
9. Peculiarities of antibioticotherapy according to the age of patients. Usage of antibiotics in pregnant women and children.
10. Classification of adverse reactions and complications of antibiotic therapy. Their prophylaxis and treatment.
11. Natural and acquired resistance to chemotherapeutics; the mechanism of resistance formation. Measures to prevent and eliminate microbial resistance.Pharmacokinetics and spectrum of antimicrobial action of the main antibiotics' groups. Clinical usage and dosing principles, side-effects and their prophylaxis.
12. Sulfamides - classification, antimicrobial spectrum, mechanism of action, causes of development of resistance, pharmacokinetics, indications, contraindications, dosage principles and choice depending on the pathology. Adverse reactions; their prophylaxis and control.Antibiotic prophylaxis. Rational association of chemotherapeutic drugs depending on the mechanism and spectrum of antimicrobial action. Side-effect reactions.
13. Naphthyridine and quinolone derivatives. Classification, antimicrobial spectrum, mechanism of action, pharmacokinetics. Indications, contraindications. Adverse reactions, their prophylaxis and control. Drug interactions.
14. Nitroimidazole derivatives. Antimicrobial spectrum, mechanism of action, indications, adverse reactions, prophylaxis and control.Application of quinolone derivatives in case of microbial resistance to antibiotics and sulfonamides, for treating, stomatological affections. Antimicrobial spectrum and mechanisms of action.
15. 8-oxiquinolone derivatives and nitrofurans. Spectrum and mechanism of action. Pharmacokinetic and pharmacodynamic peculiarities, clinical uses, contraindications, side-effects, their prophylaxis and treatment. Drugs interaction.
16. Fluoroquinolones. Antimicrobial spectrum, mechanism of action, peculiarities of pharmacokinetics, indications. Side effects, prophylaxis and control.
17. Thiosemicarbazone derivatives and similar preparations. Particularities of action, use and dosage. Adverse reactions, their prophylaxis and control.
18. Oxazolidinediones. Peculiarities of the spectrum and mechanism of action, pharmacokinetic aspects. Guidelines and principles for selection and use. Contraindications. Side effects.
19. Pharmacokinetic and pharmacodynamic features of synthetic chemotherapeutics in children. Peculiarities of administration during pregnancy and lactation.
20. Antibiotics indications in stomatological infection of maxilla-facial region of odontogenic inflammatory processes and infection complications after stomatological interventions, ulcerous, combustion surfaces; for antiseptic processing of advanced, complicated profound caries of the teeth, and alveolar canals.
21. Peculiarities of the application of antibiotics (choice of preparations, doses, etc.) in the treatment of osteomyelitis, in the prophylaxis and treatment of septic complications after dental surgery.

22. Peculiarities of topical application of antibiotics and sulfamides for the treatment of deep tooth decay, its complications and other infectious processes in the oral cavity. Biological method of treatment of pulpitis and periodontitis. Complications of topical use of antibiotics (patient sensitization, oral candidiasis and development of microbial resistance).
23. Topical application of nitrofuran derivatives in case of microbial resistance to antibiotics and sulfamides, for toileting, treatment, processing of suppurative processes in the oral cavity.
24. Administration of combined antibacterial preparations in dentistry and maxillofacial surgery.Sulfonamides utilization for local and systemic administration to treat stomatological infections. Pharmacotherapeutic stomatological side-effects and complications.

II. Selection and clinical-pharmacological use of medicinal preparations in some clinical conditions and conditions:
Principles of selection and use of antimicrobial preparations:
rational use of antibiotics.
Rational use of preparations of synthetic chemotherapeutics.

F. Individual work

1. Brief characterization of the main preparations
vertical - International Common Name (INN) of the preparation (in Romanian),
horizontal - synonyms, forms of delivery, mode of administration, doses (therapeutic, maximum), mechanisms of action, indications, contraindications, adverse reactions: meropenem, amikacin, oxacillin, carbenicillin, cephalexin, tobramycin, ceftobiprol, co-trimoxazole, clindamycin
2. Medical prescription exercises (see Methodological guidelines for pharmacology):
amoxicillin, ampicillin,benzilpenicillin, doxycycline, clarithromycin, spiramycin, gentamicin, erythromycin oxacillin, carbenicillin, cephalexin, tobramycin, cefazolin, lincomycin, cefaperazone, cefoxitin chloramphenazole, sulfamadoxine, sulfamethoxaz, trimoxazole, ciprofloxacin, ofloxacine, pipemidic acid, nalidixic acid, nitrophurantoine, nitrofural, furagine.
3. **Indicate the preparations used in (for):** Streptococcal infections; infections caused by B. fragilis; infections caused by the pyocyanic bacillus; osteomyelitis; trichomonadoză; treatment of odontogenic infectious processes; antimicrobial medication for dental caries and its complications; antimicrobial treatment of infectious diseases of the oral mucosa; treatment of ulcers, canker sores, burning surfaces, erosions with chemotherapeutics; abscesses, phlegmons of soft tissues in the maxillofacial region.
4. Tests (Clinical Pharmacology (self-assessment tests), Chisinau-2000, pp. 345, 375.
5. Clinical Pharmacology (self-assessment tests), Chisinau-2014. стр. 123, 131.
6. Clinical cases (Clinical case guide), Chisinau-2017, page 113.
7. Virtual situations (movies). Guide for laboratory works on pharmacology Chisinau-2016.
8. Selection of P-personal drugs and P-personal treatment according to the criteria of efficacy, harmlessness, acceptability and cost for inclusion in the personal form (P drugs).