CLINICAL PHARMACOLOGY OF ANTIHYPERTENSIVE, ANTIHYPOTENSIVE AND DIURETIC DRUGS

A. Actuality

The pathology of the cardio-vascular system in the last decades maintains the first place according to the indicators of morbidity, mortality and invalidity. The evolution of cardiovascular diseases is complicated in most cases with acute or chronic cardiac insufficiency, cardiogenic shock and sudden death.

Arterial hypertension is a pathology with high frequency in the general population, affecting about one-third of all adults in developed economic countries with serious disabling consequences for patients. Hypertensive emergencies are associated with significant increases in disability and mortality, remaining actually a problem of antihypertensive therapy.

Acute arterial hypotension accompanies some states of emergency, being a manifestation of some hemodynamic disorders, which endanger the patient's life.

Antihypertensive and antihypotensive treatment must correspond to the clinical variations of these diseases.

B. Training aim

To apply the principles of clinical pharmacology (pharmacokinetic and pharmacodynamic) to the individualization and optimization of the drug administration with influence on the cardiovascular system (antihypertensives and antihypotensives, diuretics) and the appreciation of their efficiency.

C. Teaching objectives

The student must have the ability:

a) to choose the complex of minimum investigations for determination of the pharmacodynamic effect of antihypotensive and antihypertensive drugs, diuretics;
b) to analyze and evaluate the results of studying the pharmacodynamics of antihypertensives, antihypotensives, and diuretics;
c) to predict the possible complications and adverse reactions of the drugs;
d) to predict the dependence of adverse reactions on the dosage regime and the functional state of the organs and systems;
e) to apply contemporary methods of pharmacological correction of adverse reactions, caused by antihypertensive, antihypotensive and diuretic drugs;
f) to select the personal drug (P-drug) and personal treatment (P-treatment) in hypertension and hypotension states.
g) to predict the drug interaction of antihypertensives, antihypotensives and diuretics.

D. Knowledge of the medico-biological and clinical disciplines necessary for interdisciplinary integration:

Medical-biological subjects. Anatomy and physiology of the cardiovascular system. The role of the sympathetic and parasympathetic systems in the regulation of hemodynamics. The main factors that determine blood pressure. The main mechanisms of blood pressure regulation. Homeostasis of Ca2+ ions in the vessels smooth muscle.

Clinical subjects. Etiopathogenic and clinical peculiarities of blood pressure disorders in different diseases. The clinical manifestation of arterial hypertension, classification, complications. Classification of hypertensive emergencies, principles of treatment. Etiopathogenic peculiarities of essential and symptomatic hypertension (caused by pheochromocytoma, coarctation of the aorta, etc.). Etiopathogenic peculiarities of arterial hypotension in different types of shock.

Pharmacology. Antihypertensive drugs: classification by mechanism of action, mechanism of antihypertensive action, indications, contraindications, adverse reactions of centrally acting drugs, alpha-adrenoblockers, beta-adrenoblockers, sympatholytics, musculotropic vasodilators,

angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists, diuretics. Antihypotensive drugs: classification by mechanism of action, indications, adverse reactions of centrally acting drugs, adrenomimetics, vasoactive peptides, isothioureic derivatives, positive inotropic agents, plasma volume expanders and plasma substitutes.

E. Questions for self-training:

1. Classification of antihypertensive drugs.
2. Clinical pharmacology of centrally acting antihypertensives: particularities of the antihypertensive effect, indications and principles of use, adverse reactions and their prophylaxis, pharmacokinetics.
3. Ganglioplegics and sympatholytics, particularities of the antihypertensive effect, indications and principles of use, adverse reactions and their prophylaxis, pharmacokinetics.
4. Alpha-adrenoblockers, classification, particularities of the antihypertensive effect, indications and principles of use, adverse reactions and their prophylaxis, pharmacokinetics.
5. Clinical pharmacology of beta-adrenoblockers, particularities of the antihypertensive effect, indications, contraindications, adverse reactions, pharmacokinetics and interactions with other drugs.
6. Clinical pharmacology of Ca channel blockers, particularities of the antihypertensive effect, indications, contraindications, adverse reactions, pharmacokinetics and interactions with other drugs.
7. Clinical pharmacology of drugs acting on the renin-angiotensin-aldosterone system (SRAA). Direct renin inhibitors: the particularities of the antihypertensive effect, indications, contraindications, side effects, pharmacokinetics and interactions with other drugs.
8. Clinical pharmacology of angiotensin-converting enzyme (ACE) inhibitors: particularities of the antihypertensive effect, indications, contraindications, adverse reactions, pharmacokinetics, principles of use and interactions with other drug groups.
9. Clinical pharmacology of angiotensin II receptor antagonists: particularities of the antihypertensive effect, indications, contraindications, side effects, pharmacokinetics and interactions with other drug groups.
10. Musculotropic vasodilator drugs (arteriodilators, venodilators, arterio-venodilators): the particularities of the mechanism of action and of the pharmacological effect, indications and principles of use, adverse reactions and their prophylaxis, the pharmacokinetics of drugs and drug interactions.
11. Sympathetic inhibitors with mixed action: particularities of the antihypertensive effect, indications, contraindications, adverse reactions, pharmacokinetics.
12. Diuretics: classification (by latency, duration and potency of the effect), particularities of the antihypertensive effect. Influence on ion exchange (K, Mg, Ca, uric acid):
a) Loop diuretics: mechanism of action, particularities of action, indications and principles of use, adverse reactions, pharmacokinetics.
b) Thiazide and thiazide-like diuretics: mechanism of action, particularities of action, indications and principles of use, side effects, pharmacokinetics.
c) Competitive antagonists of aldosterone: mechanism of action, particularities of action, indications and principles of use, adverse reactions, pharmacokinetics.
d) Non-competitive aldosterone antagonists: mechanism of action, particularities of action, indications and principles of use, adverse reactions, pharmacokinetics.
13. Classification of antihypotensives according to mechanism and duration of action, pathogenesis, character and selectivity of action on vessels.
14. Alpha-beta-adrenomimetics as antihypotensives: the particularities of the hypertensive effect, the influence on central and regional hemodynamics, the heart, indications and principles of use, adverse reactions, pharmacokinetics.
15. Alpha-adrenomimetics, used as antihypotensives: the particularities of the hypertensive effect, the influence on central, regional and heart hemodynamics, indications and principles of

use, adverse reactions, pharmacokinetics.
16. Beta-1-adrenomimetics as antihypotensives: the particularities of the hypertensive effect, indications and principles of use, adverse reactions, pharmacokinetics.
17. Dopaminomimetics as antihypotensive agents: the particularities of the hypertensive effect, the influence on central, regional and heart hemodynamics; indications and principles of use, adverse reactions, pharmacokinetics.
18. Antihypotensives from the group of isothioureic derivatives: the particularities of the hypertensive effect, the influence on central and regional hemodynamics, of the heart, indications and principles of use, adverse reactions, pharmacokinetics.
19. Clinical pharmacology of central acting antihypotensive drugs (analeptics, CNS stimulants, tonics, adaptogens), mechanism of action, indications, contraindications, side effects, pharmacokinetics, interactions with other drug groups.
20. Clinical pharmacology of antihypotensive drugs with permissive and complex action, mechanism of action, indications, contraindications, adverse reactions, pharmacokinetics, interactions with other drug groups.
21. Antihypotensives that increase the volume of circulating blood (plasma): classification, particularities of the hypertensive effect, influence on central, regional and heart hemodynamics, indications and principles of use, adverse reactions, pharmacokinetics
22. The particularities of using antihypertensives and antihypotensives during pregnancy, in pediatric and geriatric patients.

F. Individual work (the **1.1 and 1.2 sequences are to be done in writing form):**

1.1. Indicate the pharmacological groups and drugs used in (for):

cardiogenic shock, essential arterial hypertension grade I, essential arterial hypertension grade III, renovascular hypertension, diagnosis of pheochromocytoma, treatment of pheochromocytoma, arterial hypertension with hypercholesterolemia (atherosclerosis), hypertensive crises, hypertensive emergencies in eclampsia, hypertensive emergencies in encephalopathy, arterial hypertension with heart failure, arterial hypertension in young patients, arterial hypertension in elderly patients, arterial hypertension in diabetics, arterial hypertension after acute myocardial infarction, arterial hypertension in patients with obstructive pulmonary diseases, controlled hypotension, arterial hypotension resistant to alpha-adrenomimetics, orthostatic hypotension induced by alpha-adrenoblockers, chronic arterial hypotension, hypotonic arterial hypotension (collapse, etc.), hypertonic arterial hypotension (cardiac).

1.2. Prescribe the following medications in their respective pharmaceutical forms, indicating the dosage regimen according to the respective pathology.

No.	Drug Name	Pharmaceutical Form; Dosage
1	Methyldopa	Tablets 0.25
2	Moxonidine	Tablets 0.0002; 0.0003; 0.0004
3	Propranolol	Tablets 0.1
4	Metoprolol	Tablets 0.025; 0.05; 0.1
5	Bisoprolol	Tablets 0.0025; 0.005; 0.01
6	Nebivolol	Tablets 0.005
7	Carvedilol	Tablets 0.00625; 0.0125; 0.025
8	Nifedipine	Tablets 0.01; 0.02
9	Lercanidipine	Tablets 0.01; 0.02
10	Captopril	Tablets 0.05; 0.025; 0.0125
11	Enalapril	Tablets 0.005; 0.01; 0.02
12	Losartan	Tablets 0.025; 0.05; 0.1
13	Epinephrine	Solution 0.18% - 1 ml ampoules
14	Norepinephrine	Solution 0.1% - 1 ml; 2 ml; 4 ml; 5 ml; 8 ml; 10 ml
15	Phenylephrine	Solution 1% - 1 ml ampoules
16	Dopamine	Solution 0.5% - 5 ml; 4% - 5 ml ampoules
17	Sodium caffeine benzoate	Infusion/oral solution 2% - 1 ml; 3 ml ampoules
18	Sacubitril + Valsartan	Tablets 0.024/0.026; 0.049/0.051; 0.097/0.103
19	Furosemide	Tablets 0.04; Solution 1% - 2 ml

20	Spironolactone	Tablets 0.025; 0.05; 0.1; Capsules 0.05
21	Indapamide	Tablets 0.0015; 0.0025; Capsules 0.0025

2. Tests. ***Tests on clinical pharmacology*** **(for faculty of medicine).** Chisinau, 2014.

G. Interactive activity

1. The didactic instructional work and the patient's discussion.

2. Clinical-pharmacological selection and use of drugs in cardio-vascular system disorders:

- Combined antihypertensive drugs: the principles of combination and use;
- Principles of treatment of various types of hypertensive emergencies;
- The principles of selection and use of drugs in hypotonic arterial hypotension;
- The principles of selection and use of drugs in hypertonic arterial hypotension;
- The principles of selection and use of drugs in hypovolemic arterial hypotension.

3. Clinical cases. ***Clinical cases in clinical pharmacology***. Chisinau, 2017.

4. Personal Drug (P-Drug) selection according to the criteria of efficacy, safety, acceptability and cost.