

CLINICAL PHARMACOLOGY OF CARDIOTONIC AND CARDIOSTIMULATORY MEDICINES

A. Actuality

The pathology of the cardiovascular system has held stable the first place for the last decades according to the indicators of morbidity, mortality and invalidation. The evolution of cardiovascular disease is complicated in most cases with acute or chronic heart failure. The multitude of pathogenic links responsible for the development of heart failure require the use of a wide range of medications with influence on the parameters of the heart which are welcome in the concrete clinical situations.

The beneficial effect of cardiac glycosides (digitalis) in the treatment of heart failure has been demonstrated for 200 years and remains the basic medication for this serious condition. The pharmacodynamics of the digitalis, their influence on the function of the heart and the hemodynamics, as well as on other organs and systems, the low therapeutic index, require the careful study of these drugs. At the same time, vasodilator, diuretic and cardiostimulator medications will be used depending on the pathogenetic link involved in the development of insufficiency of the heart work.

B. Purpose of training :

Assimilation and application of pharmacokinetic and pharmacodynamic principles in the individualization and optimization of the administration of cardiac glycosides, non-glycosidic cardiotonics, adrenergic cardiostimulators, vasodilators and diuretics.

C. Teaching purposes :

The student must have the ability to:

- a) choose methods of clinical and laboratory examination in order to assess the effectiveness of cardiac glycosides;
- b) analyze and evaluate the examination results of the pharmacodynamics of digitalis, non-glycosidic cardiotonic and adrenergic cardiostimulators;
- c) predict the occurrence of adverse reactions and possible complications, in the use of cardiotonic and cardiostimulatory medications;
- d) determine the dependence of the adverse reactions on the dosage regimen and the functional state of the organs and systems;
- e) apply the methods of prevention and treatment of adverse reactions of the medications used in the treatment of heart failure;
- f) predict the interaction of the medications used in the treatment of heart failure between them and with other drugs.

D. Knowledge from the subjects studied previously and those of tangency

Histology. Structure of the contractile muscle fiber. Histophysiology of excito-conductive tissue. The cellular and molecular bases of muscle contraction.

Pathophysiology. Homeostasis of Ca²⁺ ions in cardiac muscle fiber. Coupling excitation with myocardial contraction. Functional features of the myocardium. Mechanisms for regulating hemodynamics.

Clinical disciplines. The pathophysiological basis of heart failure. Functional classification (NYHA) and clinical picture of heart failure. Paraclinical exploration in heart failure.

Pharmacology. Classification of cardiotonic remedies: cardiac glycosides, non-glycosidic cardiotonics and adrenergic cardiostimulators; mechanism of action, adverse reactions, contraindications.

E. Questions for self-training:

1. Clinico-pharmacological characteristic of the drugs used in the diseases of the cardiovascular system.

1. Classification of the remedies used in heart failure. Classification of cardiac glycosides. Physico-chemical peculiarities. Sources of medicines obtaining.
2. Pharmacokinetics of cardiac glycosides:
 - a. administration ways, absorption of cardiac glycosides, possible interactions at the level of absorption;
 - b. distribution of cardiac glycosides, coupling with plasma proteins, interactions with other drugs;
 - c. metabolization and elimination of cardiac glycosides, drug interactions in metabolism and excretion.
3. Mechanism of action of cardiac glycosides.
4. Pharmacodynamics of cardiac glycosides: inotrop-positive, chronotrop-negative, dromotrop-negative, batmotrop-positive, tonotrop-positive actions and their mechanisms. ECG changes. Effect duration. Influence of cardiac glycosides on systemic hemodynamics indices and of other systems functions : central nervous system, gastrointestinal tract, urinary tract, coagulation system, etc.
5. Indications, contraindications and precautions in the administration of cardiac glycosides.
6. The dosing principles of cardiac glycosides: fast, medium, slow digitization. Attack dose, maintenance dose, individual dose and average dose. The dosage particularities of strophanthin, digoxin and digitoxin. Daily elimination coefficient.
7. Methods and criteria for assessing the effectiveness of cardiac glycosides. Criteria for digitization. Tolerance and resistance to cardiac glycosides, their treatment and prevention.
8. cardiac glycosides Symptoms and mechanisms of the occurrence of toxic action a. Typical changes on ECG in cardiac glycoside poisoning. Prophylaxis and treatment of cardiac glycoside poisoning.
9. Particularities of the association of cardiac glycosides with other groups of drugs.
10. Particularities of the association of cardiac glycosides with other drugs used in heart failure.
11. Clinical pharmacology of non-glycosidic cardiotoxic (phosphodiesterase inhibitors): particularities of mechanism of action and pharmacological effects. Indications and principles of use, adverse reactions and their prevention, pharmacokinetics, drug interactions.
12. The clinical pharmacology of adrenergic cardiostimulators: the particularities of the mechanism of action and the cardiostimulatory effect, the indications and principles of use, the adverse reactions and their prevention. Pharmacokinetics of drugs and drug interactions.
13. Clinical pharmacology of calcium sensitizers used in heart failure: particularities of mechanism of action and pharmacological effect. Indications and principles of use, adverse reactions and prophylaxis. Pharmacokinetics.
14. Particularities of use in heart failure of medications that reduce the preload and postload (vasodilators and diuretics): mechanism of action and pharmacological effect, indications.
15. Particularities of the use of beta-blockers in the treatment of heart failure.
16. Particularities of cardiotoxic and cardiostimulatory use in children.

I. Clinico-pharmacological selection and use of SM in some clinical conditions of the cardiovascular system.

- Principles of drug selection and use in acute and chronic heart failure.
- The principles of selection and use of cardiotoxic and cardiostimulatory drugs in geriatrics, pediatrics.
- The principles of selection and use of cardiotoxic and cardiostimulatory drugs in patients with different comorbidities: renal, hepatic impairment, etc.
- Interactions of cardiotoxic and cardiostimulatory drugs with other groups of drugs: diuretics, IECA, BCC and others.

F. Individual work:

1. Short description of the main drugs :

Vertically: the name of the medications (in Romanian)

Horizontally: synonyms, delivery forms, mode of administration, doses (therapeutic, maximal), indications, contraindications, adverse reactions.

Strophanthin, corglicon, digoxin, digitoxin, amrinone, dopamine, dobutamine, levosimendan, bisoprolol, carvedilol, nebivolol, lisinopril, enalaprilate, perindopril, losartan, furosemid, indapamid, torasemide, hydrochlorothiazide, amlodipine, sodium nitroprusside, spironolactone, eplerenone.

2. Exercises of medical prescription: (see year III)

Strophanthin, amrinone, digoxin, dopamine, enoxymone, losartan, corglicon, dobutamine, digitoxin, bisoprolol, carvedilol, lisinopril, spironolactone.

3. Indicate the preparations used in:

Acute heart failure; heart failure with pulmonary edema; chronic heart failure class I-II (NYHA); chronic heart failure classes III-IV (NYHA); heart failure with hyperaldosteronism; heart failure in hypertrophic cardiomyopathy, chronic atrial fibrillation tachysystolic form; atrial or junctional paroxysmal tachycardia; cardiogenic shock; heart failure in acute myocardial infarction; cardiotoxic glycoside poisoning; cardiotoxic glycoside poisoning and hypokalemia; cardiotoxic glycoside poisoning and hypercalcemia; prevent the absorption of cardiotoxic glycosides in digital intoxication.

4. Tests. "Farmacologia clinică" (self-assessment tests), Chisinau, 2000, pages 116-14

5. Клиническая фармакология (тесты для самоподготовки. Кишинэу 2014, стр. 31 и 51)

6. Clinical cases. Ghid cazuri clinice, Chisinau, 2017, page 66

7. Virtual situations: Îndrumar pentru lucrări de laborator la farmacologie. Chisinau, 2016, page 165

8. Selection of antihypertensive and antihypotensive drugs according to the criteria of effectiveness, harmlessness, acceptability and cost, for inclusion in the personal form (P drugs).