CARDIOTONIC AND CARDIOSTIMULATOR DRUGS

A. Actuality. Decompensation of chronic heart failure and chronic heart failure is a frequent cause of emergencies and the death of patients with cardiovascular, pulmonary, neurological diseases. The pathogenesis of heart failure is complex, which requires the use of a wide range of inotrope-positive drugs, vasodilators, diuretics, etc.

B. Purpose of training: to familiarize students with the groups of inotropic-positive drugs, which reduce pre- and afterload used in the treatment of heart failure.

C. Didactic purposes.
1) The student **must know**: classification, mechanism of action, effects, indications, contraindications and adverse reactions of inotropic-positive drugs.
2) The student **must be able to**: prescribe cardiotonic and cardiostimulating preparations in all medicinal forms and indicate the groups and preparations in diseases and pathological conditions.

D. Knowledge of previous and related disciplines necessary for interdisciplinary integration.
Physiology. The physiological properties of the myocardium (automaticity, excitability, contractility, conductivity). The excito-conductive system of the heart. Characterization of inotropic-positive, chronotropic-negative, bathmotropic-positive, dromotropic-negative and tonotropic-positive actions. The influence of the sympathetic and parasympathetic autonomic nervous system on the activity of the heart.
Pathophysiology. Heart failure indexes. Tonogenic and myogenic dilation of the heart. Dysregulation of heart rhythm (automaticity, excitability, contractility and conductivity). Myocardial hypertrophy, types and mechanism of evolution.

E. Questions for self-training:
1. Classification of drugs used in heart failure.
2. Classification of inotrope-positive drugs.
3. Cardiac glycosides. The sources of obtaining. Classification of cardiac glycosides according to solubility and duration of action.
4. Mechanism of cardiotonic action of cardiac glycosides. The influence of cardiac glycosides on heart parameters (positive inotropic action, positive bathmotropic action, negative -dromotropic, negative chronotropic, positive tonotropic action) and the mechanisms of these phenomena. Changes on the electrocardiography (ECG) when using cardiac glycosides in therapeutic doses.
5. Influence of cardiac glycosides on systemic and regional hemodynamics, CNS, kidneys, respiratory system and gastrointestinal tract.
6. Pharmacokinetic features of cardiac glycosides (digitoxin, digoxin and strophanthin(ouabain)).
7. Indications, adverse effects and contraindications of cardiac glycosides.
8. Principles of cardiac glycoside dosing, saturation and maintenance phase. Digitalization methods. The concept of elimination ratio.
9. Intoxication with cardiac glycosides. Clinical picture and treatment.
10. Non-glycosidic (synthetic, non-steroidal) cardiotonics. Classification, mechanisms of action, effects, indications, contraindications and adverse reactions.
11. Cardiostimulators (α, β,- and β-adrenomimetics, dopaminomimetics). Classification, mechanisms of action, effects, indications, contraindications and adverse reactions.
12 Comparative characterization of steroidal, non-steroidal cardiotonics and cardiostimulators
13. Drugs that increase the sensitivity of contractile proteins to calcium ions. Mechanisms of action, effects, indications, contraindications and adverse reactions.
14. Drugs that reduce pre- and after-load in heart failure. Classification. The principle of action.

F. Individual works for the student's self-training (points 1, 2, 3 and 4 are obligatory and are made in writing during the training process)

1) To prescribe the following drugs in all medicinal forms:

1. Strophanthin. 2. Digitoxin. 3. Digoxin. 4. Corglycon. 5. Amrinone. 6. Levosimendan. 7. Dopamine. 8. Dobutamine. 9. Epinephrine.

Nr.	***Drug's name***	***Medicinal forms, dosage***
1.	**Strophanthin**	Sol. 0,025% and 0,05% - 1 ml in amp. (i/v)
2.	**Amrinone**	Sol. 0,5% - 20 ml in amp. (i/v)
3.	**Corglycon**	Sol. 0,06% - 1 ml in amp. (i/v)
4.	**Digitoxin**	Tabl. 0,0001 Rectal supp. 0,00015
5.	**Digoxin**	Tablets 0,000125 and 0,00025 Sol. (for internal use) 0,75% - 10 ml in vials Sol. 0,025% - 1 ml and 2 ml in amp. (i/v)
6.	**Levosimendan**	Concentrate for infusion 2,5 mg/ml (0,25%)– 5 and 10 ml in vials
7.	**Dopamine**	Sol.0,5% and 4% - 5 ml in amp. (i/v)
8.	**Dobutamine**	Sol. 0,5%-50 ml in amp.(i/v) lyophilized powder in vials 0,25 (i/v)
9.	**Epinephrine**	Sol. 0,1%-1 ml in amp. (i/v; s/c; i/m)

2) List the groups and drugs used in (for): decompensated chronic heart failure; chronic congestive heart failure; paroxysmal supraventricular tachycardia; tachysystolic atrial fibrillation; poisoning with cardiac glycosides; cardiostimulants in acute myocardial infarction; cardiogenic shock; cardiac arrest; groups of vasodilators used in heart failure; diuretics in chronic heart failure.

3) Tables (knowledge consolidation)

Table 1

Characteristic of the groups of positive inotropic drugs used in heart failure

Pharmacological groups	Drugs	Pozitive inotrop-Mecanism of action	Effects on the heart
Cardiac glycosides			
Non-glycosides cardiotonics			
Alfa-beta-adrenomimetics			
Dopaminomimetics			
Beta-1-adrenomimetics			

Drugs that increase the sensitivity of contractile proteins to calcium ions			

Table 2

Pharmacological effects of cardiac glycosides

Effects	Mecanism of effects	Characteristic modification on ECG
Pozitive Inotrop		
Negative Chronotrop		
Negative Dromotrop		
Pozitiv Bathmotrop		

Table 3

Pharmacokinetics of cardiac glycosides

Drugs	Rout of administration	Fat-soluble (F) Hydrosoluble (H)	Bioavailability (%)	Binding with plasma proteins (%)	Half-life (hours)	Elimination ratio
Digitoxin						
Digoxin						
Strophanthin						

Table 4

The principles of treatment of cardiac glycoside poisoning

Group of medicines	Drugs	Principles of action
Anti-digoxin antibodies		
Adsorbents		
Chelate-forming compounds		
K^+ preparations		
Antiarrhythmic drugs		
M-cholinoblockers		
β-adrenomimetics		
Hydrogen sulphide group donors		

4) Situational problems:

Problem 1

For the treatment of experimental heart failure, preparation A was administered. After its use, the following changes were observed on the ECG: increase in the PQ interval, increase in the amplitude of the R wave, decrease in the QRS complex, increase in the R-R interval**.**

a) Determine the group of preparations and list the drugs.

b) List the cardiac effects observed on the ECG induced by preparation A and the mechanisms of these effects.

Problem 2

In the modeling of experimental chronic heart failure, the following cardiac and hemodynamic parameters were recorded: decrease in systolic volume and minute volume, increase in heart size, tachycardia, increase in pulmonary artery pressure and venous pressure.

a) Which group of positive inotropic preparations can be used for treatment?

b) How will the preparations of this group influence cardiac and hemodynamic parameters?

5) Tests for self-training (Guide for laboratory work in pharmacology. Chisinau 2016, page 165-169).

G. Interactive activity

1. Experimental and virtual didactic film (conclusions)

2. Clinical cases (Guide for laboratory works in pharmacology. Chisinau 2016, page 170).

3. Virtual situations (Guide for laboratory work in pharmacology. Chisinau 2016, page 171-172).