**CARDIAC GLYCOSIDES AND CARDIOSTIMULATORY AGENTS (CARDIOTONICS)**

**A. Actuality.** Acute and chronic heart failure are common causes of the emergency and lethal conditions of patients with cardiovascular, pulmonary, neurological diseases, etc. The pathogenesis of heart failure is complex, requiring the use of a variety of positive inotropic drugs, vasodilators, diuretics, etc.

**B. The purpose of the training is** to familiarize students with the groups of positive inotropic drugs, vasodilators and diuretics, used to treat heart failure.

**C. Learning objectives:**

1) The student must **know:** classification, mechanisms of action, effects, indications, contraindications and adverse reactions of positive inotropic drugs.

2) The student must **be able to:** make out prescriptions of mandatory drugs in various forms and indicate them in various diseases and pathological conditions.

**D. Initial level of knowledge required for interdisciplinary integration:**

**Human physiology.** Physiological properties of the myocardium (automatism, excitability, conductivity, contractility and refractivity). The electrical conduction system of the heart. Characterization of positive inotropic, negative chronotropic, positive batmotropic, negative dromotropic and positive tonotropic actions. Influence of sympathetic and parasympathetic autonomic nervous system on heart activity.

**Pathophysiology.** Indices of heart failure. Systolic and diastolic types of the heart failure. Disturbances of the heart rate (automatism, excitability, contractility and conductivity). Myocardial hypertrophy, types and evolutionary mechanisms.

**E. Self-training questions:**

1. Classification of drugs used in heart failure.
2. Cardic glycosides. Sources of obtaining. Classification of cardiac glycosides by solubility and duration of action.
3. Cardiotonic mechanism of action of cardiac glycosides. Influence of cardiac glycosides on the main functional indexes of the heart (positive inotropic, positive batmotropic, negative dromotropic, negative chronotropic, positive tonotropic and mechanisms of these phenomena). Systolic and diastolic effects. ECG changes caused by cardiac glycosides.
4. The metabolic changes in myocardium, caused by cardiac glycosides. Comparison with the cardiostimulant action of α,β- and β-adrenomimetics.
5. Influence on systemic and regional hemodynamics, CNS, kidney, respiratory system and gastrointestinal tract.
6. Pharmacokinetics of digitoxin, digoxin and strophanthine.
7. Changes of the pharmacodynamics of cardiac glycosides in case of combined administration with other medicines.
8. Principles of dosing of cardiac glycosides, saturation (digitalization) and maintenance phases. Methods of digitalization. The meaning of elimination coefficient.
9. Indications, side effects, and contraindicartions of cardiac glycosides.
10. Specific features of cardiac glycosides in children.
11. Intoxication with cardiac glycosides. Clinical picture and treatment.
12. Cardiostimulators (α,β- and β-adrenomimetics, dopamine). Classification, mechanisms of action, effects, indications, contraindications and adverse reactions.
13. Nonglycosidic cardiotonics (synthetic, non-steroidal). Classification, mechanisms of action, effects, indications, contraindications and adverse reactions.
14. Comparative feature of steroid cardiotonics, non-steroid cardiotonics, and cardiostimulatory medicines.
15. Medicines that increase the sensitivity of contractile proteins (troponin C) to calcium ions. Mechanisms of action, effects, indications, contraindications and adverse reactions.
16. Indirect cardiotonics (vasodilators and diuretics used in heart failure). Classification. Principles of action.

**F. Independent work** (is done in written form while preparing for the lesson)

**1.) Brief characteristics of compulsory drugs:**

**Down:** Drug name. 1. Strophanthin. 2. Digitoxin. 3. Digoxin. 4. Corglycon. 5. Amrinone. 6. Levosimendan. 7. Dopamine. 8. Dobutamine. 9. Epinephrine.

**Across:** 1. Medicinal form. 2. Way of administration. 3. Doses (therapeutic, maximal for one intake and for 24 hours). 4. Spectrum of action 5. Mechanism of action. 6. Indications and contraindications. 7. Side effects.

# 2.) Questions on medical prescriptions.

**To prescribe** the following drugs in all the possible medicinal forms: 1. Strophanthin. 2. Digitoxin. 3. Digoxin. 4. Corglycon. 5. Amrinone. 6. Levosimendan. 7. Dopamine. 8. Dobutamine. 9. Epinephrine.

**Drugs used in (for):** acute heart failure, chronic heart failure, decompensated heart failure, atrial fibrillation, cardiac glycoside intoxication, acute myocardial infarction, cardiac arrest, supraventricular paroxysmal tachycardia, cardiogenic shock.

**3.) Tests** (Guidelines for Laboratory Work in Pharmacology).

**4.) Clinical case** (Guidelines for Laboratory Work in Pharmacology).

**5.) Virtual situations** (Guidelines for Laboratory Work in Pharmacology).

**6.) Virtual didactic movie.**

**7.) Tables**

Table 1

**Cardiac glycosides action on cardiomyocytes**

|  |  |  |
| --- | --- | --- |
| Parameters | | Changes caused by cardiac glycosides |
| Activity of Na+/K+-ATP-ase | |  |
| Quantity in cardiomyocytes | Na+ ions |  |
| K+ ions |  |
| Ca2+ ions |  |
| Actin-myosin interaction | |  |

Table 2

**Pharmacological effects of cardiac glycosides**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Effects | Mechanism of development of the effect | Consequences of effect (change in hemodynamic indices) | Clinical significance of the effect | |
| Positive | Negative |
| Positive inotropic |  |  |  |  |
| Negative Chronotropic |  |  |  |  |
| Negative dromotropic |  |  |  |  |
| Positive batmotropic |  |  |  |  |
| Positive tonotropic |  |  |  |  |
| Diuretic |  |  |  |  |

Table 3

**Comparative feature of cardiac glycosides**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Parameters | Liposolubility (L) and Hydrosolubility (H) | Protein binding  (%) | Route of administration | Latency of action (min, hours) | Maximum action (hours, days) | Postaction (duration) | Elimination pathways |
| Digitoxin |  |  |  |  |  |  |  |
| Digoxin |  |  |  |  |  |  |  |
| Strophanthin K |  |  |  |  |  |  |  |

Table 4

**Drug therapy of intoxication with cardiac glycosides**

|  |  |  |
| --- | --- | --- |
| Grupa de medicamente | Medicamentele | Principii de acţiune |
| Anti-digoxin antibodies |  |  |
| Adsorbent drugs |  |  |
| Chelating agents |  |  |
| K+ containing medicines |  |  |
| Antiarrhythmic drugs |  |  |
| M-cholinoblockers |  |  |
| β-adrenomimetics |  |  |
| Sulfhydryl group donors |  |  |

**8.) Solve the case:**

A patient with chronic heart failure and pronounced edema was treated with drugs from the group of digitalis. In order to speedup removal of the edema the patient has been given hydrochlorothiazide (a diuretic medicine). On this background symptoms of overdose of cardiac glycosides have occurred.

Explain the cause of the overdose. Name the measures for prophylaxis of overdose.