

Ministry of health of the Republic of Belarus
Educational institution
«Gomel State Medical University»

Department of general and clinical pharmacology

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METHODOLOGICAL RECOMMENDATIONS

for a practical lesson on the discipline "Pharmacology"
for the third-year students of the Faculty of Foreign Students,
studying at the specialty 1-79 01 01 "General medicine"

**TOPIC 19: «DRUGS FOR THE TREATMENT OF HEART FAILURE.
CARDIOTONICS. ANTIARRHYTHMIC DRUGS »**

Time: 3 hours

Approved at the meeting of the department of general and clinical pharmacology
the protocol № 18 of 30.06.2022

LEARNING AND EDUCATIONAL GOALS, OBJECTIVES, MOTIVATION FOR LEARNING THE TOPIC

Heart failure accompanies many acute and chronic heart diseases: CHD, myocarditis, valve defects, myocardiodystrophy. The prognosis of this pathological condition is extremely serious, since the average life expectancy after the appearance of the first symptoms of chronic CH is on average 5 years, regardless of treatment. In patients with severe CH, mortality reaches 50% per year, which is significantly higher than in most malignant neoplasms.

Arrhythmia develops in 1 of 25 persons over 60 years of age and in 1 of 10 persons over 80 years of age. The number of patients is predicted to increase 3-fold in 30 to 35 years, affecting younger patients, particularly after age 40. Arrhythmias, as a rule, are not independent diseases, but occur as a symptom of cardiac dysfunction in CHD, myocarditis, pneumonia, endocrine diseases, hormonal disorders, etc. They, in turn, can cause severe complications, often determining a serious prognosis for the work and life of patients.

Therefore, knowledge of the pharmacokinetics and pharmacodynamics of cardiotonic and antiarrhythmic agents is necessary for doctors of many specialties, which will allow them to competently conduct pharmacotherapy of cardiovascular diseases, reducing mortality and improving the quality of life of patients.

Learning objective:

formation of scientific knowledge of the main pharmacological effects, providing therapeutic and preventive effect of cardiotonic and antiarrhythmic drugs, indications and contraindications for their use, the interaction of drugs, their combined use for use in medical and preventive activities.

Educational purpose:

- to develop their value-personal, spiritual potential, to form the qualities of a patriot and citizen, ready for active participation in the economic, industrial, socio-cultural and public life of the country; to realize the social significance of their future professional activities, to learn to comply with academic and labor discipline, standards of medical ethics and deontology.

Tasks:

As a result of the study lesson, the student should

know:

- Fundamentals of pathogenesis, clinic and principles of therapy of heart failure and arrhythmias;
- Pharmacodynamics and pharmacokinetics of cardiotonic and antiarrhythmic drugs;
- indications and contraindications for the use of cardiotonic and antiarrhythmic drugs;
- benefit/risk ratio in the use of cardiotonic and antiarrhythmic drugs;
- algorithm of care for patients with intoxication by cardiac glycosides, the principle of action of antidotes;
- the dependence of the action of cardiotonic and antiarrhythmic drugs on the specific pharmacokinetics in patients of different ages, the presence of concomitant diseases and their therapy;

- side effects of cardiotonic and antiarrhythmic drugs and ways to prevent them. **be able to:**

- assess the possibility of practical use of cardiotonic and antiarrhythmic drugs for the treatment of various forms of heart failure and normalization of heart rhythm in various types of arrhythmias;

- write prescriptions for cardiotonic and antiarrhythmic drugs and conduct pharmacotherapeutic analysis of prescribed drugs.

possess:

- skills to calculate an individual dosing regimen of drugs based on pharmacokinetic data and individual characteristics of the patient, depending on age;

- skills to correct the dosing regimen in case of pathological changes in the functions of organs or systems responsible for biotransformation and elimination of drugs or in the joint use of different drugs.

Motivation for learning the topic:

The specifics of training doctors in this specialty determines the need for focused study of the main pharmacological effects, providing therapeutic and preventive effect of cardiotonic and antiarrhythmic drugs, indications and contraindications for their use, the interaction of drugs and their combined use, which will allow students to successfully master the course of specialized disciplines in this specialty.

MATERIAL EQUIPMENT

Reference and informational literature, charts, tables, presentations.

CONTROL QUESTIONS FROM RELATED DISCIPLINES

- mechanism of cardiac contraction and electrical activity of the heart;
- the concept of heart failure, pathogenetic mechanisms of formation, causes of development and types, clinical manifestations and main approaches to treatment;
- Classification of arrhythmias, mechanisms of their development and correction principles;
- prescription rules.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. The concept of heart failure, pathogenetic mechanisms of formation, types and clinical manifestations, principles of pharmacotherapy.

2. Cardiac glycosides: definition, sources of production; mechanism of action, the main pharmacological effects. Features of the pharmacokinetics of strophanthine, digoxin and digitoxin. Intoxication by cardiac glycosides: predisposing factors, symptoms, treatment. Effect of cardiac glycosides on mortality in patients with chronic heart failure.

3. Nonglycoside inotropic agents: peculiarities of action, place in modern therapy of heart failure.

4. The concept of arrhythmias, pathogenetic mechanisms of formation, types and principles of pharmacotherapy.

5. Classification of means for treatment of tachyarrhythmias (according to Vaughan-Williams, with the name of the main drugs). Other drugs for tachyarrhythmia treatment. Comparative effectiveness of antiarrhythmic agents in different types of tachyarrhythmias.

6. Bradyarrhythmia treatment agents: pharmacological characteristics and selection principles.

PROCESS OF THE STUDY

Theoretical part

Theoretical questions are described in the appendix to the methodological recommendations.

Practical part

1. Take notes on theoretical material demonstrated by the teacher.
2. Master the methods of solving the tasks and writing out prescriptions on the topic of the class.

Theme learning control

Conducted in the form of independent written work (solution of practical problems and prescriptions for individual task).

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF STUDENTS' INDEPENDENT WORK (SIW)

The time given for independent work can be used by students for:

- preparing for the practical classes;
- completing the tasks on the topic of the class in the workbook;
- preparing thematic reports, essays and presentations;
- taking notes from academic literature.

The main methods of organizing independent work:

- completing tests and practical tasks of the electronic educational-methodical complex (EEMC) for self-monitoring and self-assessment.

The list of tasks of the SIW:

- solving practical problems in the EEMC;
- completing the test tasks of the EEMC.

Control of the SIW is carried out in the form of:

- assessment of an oral answer to a question, report, report, or solution of a task in a practical class;
- individual conversation.

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF CONTROLLED INDEPENDENT WORK OF STUDENTS (CIWS)

Recommended forms of CIWS organization:

- doing exercises on the topic of the class in the workbook;
- writing an essay on a given topic;
- preparing a report and a multimedia presentation on a given topic.

The list of tasks of the CIWS:

Topics of essays / multimedia presentations:

1. Pharmacotherapy of chronic heart failure in elderly patients.
2. Principles of treatment and prevention of life-threatening arrhythmias.
3. Pharmacotherapy of heart rhythm disorders in children.

Forms of control of CIWS realization:

- checking and grading an essay on a given topic;
- checking and grading a multimedia presentation on a given topic.

LIST OF REFERENCES

1. Харкевич, Д. А. Фармакология : учебник для использования в учеб. процессе образоват. организаций, реализующих программы высш. образования по специальностям 33.05.01 "Фармация", 31.05.01 "Лечеб. дело", 31.05.02 "Педиатрия", 32.05.02 "Мед.-профилакт. дело", 31.05.03 "Стоматология" / Д. А. Харкевич. - 12 изд., испр. и доп. - Москва : ГЭОТАР-Медиа, 2017. - 754 с. : ил., табл., фот. - Рек. ФГАУ "ФИРО".

2. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 1. – 56 с.

3. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 2. – 84 с.

Inotropic agents

Inotropics are drugs that affect the strength of contraction of [heart](#) muscle

| Classification | Cardiac glycosides | | Non-glycoside agents | |
|-------------------------|--|--|--|---|
| Drugs | | | Adrenergic drugs | Phosphodiesterase inhibitors |
| | <u>Drugs of digitalis:</u> 1. Digoxin (Lanicore, Dilacor) 2. Digitoxine (Cardiotoxin) 3. Lanatoside (Celanide, Isolanide) 4. Methylldigoxine (Bemecor, Digi-cor) | <u>Drugs of strophant:</u> 5. Strofantin to 6. StrofantinG <u>Drugs of lily of the valleysha:</u> 7. Korglikon <u>Drugs of Adonis:</u> 8. Adonisid | 9. Dobutamine (Dobutrex) 10. Dopamine | 11. Amrinon (Vincoram, Inocor) 12. Milrinon (Primacor, Corothrop) |
| Mechanism of action | Block of SH-group of Na ⁺ /K ⁺ -ATPase → violation of Na ⁺ and K ⁺ flow inside the cell ↓ K ⁺ and ↑ Na ⁺ → ↓ difference between intra- and extra cellular concentration of Na ⁺ → ↓ transmembrane Na ⁺ /Ca ²⁺ metabolism → ↓ elimination of Ca ²⁺ from the celland ↑ its intracellular concentration; Ions of Ca ²⁺ interact with the troponin complex and eliminate its inhibitory effect on contractile proteins of the myocardium → there is an interaction of actin with myosin → rapid and severe myocardial contraction. | | 1. See lesson 10 "Adrenergic drugs " (9) 2. Stimulation of peripheral D-receptors, β1-, α-adrenergic receptors (10) | Inhibition of phosphodiesterase (III) → ↑ cAMP → ↑ intake of Ca ²⁺ into myocardial cell sand stimulation of the function of contractile proteins |
| Pharmacological effects | <u>Cardiac:</u> 1. Positive inotropic effect (strengthening and shortening of the systole, ↑ minute and stroke volume of the heart); 2. Positive bathmotropic effect (↑ excitability of the myocardium); 3. Negative chronotropic effect (bradycardia → elongation of the diastole); 4. Negative dromotropic effect (↓ conduction of the myocardium). <u>Extra-cardiac:</u> 5. ↑ <i>diuresis</i> (inhibition of Na ⁺ /K ⁺ -ATPase in the cells of the epithelium of the renal tubules and ↓ reabsorption of Na ⁺), 6. ↑ <i>glomerular filtration</i> (improvement of renal circulation by increasing the impact and minute volume of the heart), 7. ↓ <i>edema</i> (↑glomerular filtration and diuresis); 8. <i>Vasodilating effect and ↓ activity of RAAS</i> (due to the depression of the sympathoadrenal system), 9. ↑ <i>smooth muscle tone</i> (Inhibition of Na ⁺ /K ⁺ -ATPase of smooth muscle cells). | | 1. Positive inotropic effect 2. Positive chronotropic effect 3. ↑ blood flowin internal organs (10) | 1. Positive inotropic effect 2. Vasodilating effect |
| Indications | 1. Acute heart failure (3.5-7) 2. Chronic heart failure (1-4,8) 3. Supraventricular tachyarrhythmias (1,2,7) | | 1. Acute heart failure 2. Chronic heart failure (CHF), exacerbation According to some data, the use of PDE inhibitorsinchronicheartfailureleadstoanincreaseinthedeathrateofpatients. | |
| Side effects | 1. Extrasystole, bradycardia, AV blockade 2. Nausea, vomiting, diarrhea 3. Visualimpairment (↓ acuity, impaired perception of the spectrum, ↓ visualfields) | | 1. Tachyarrhythmias, headache 2. Exacerbation of existing myocardial ischemia | 1. Tachyarrhythmia, ↓ BP 2. Thrombocytopenia, hepatotoxicity 3. Nausea, vomiting |

| | | | |
|--------------------------|--|--|---|
| Contraindications | 1. Digital intoxication 2. Severe bradycardia, WPW syndrome and sick sinus syndrome 3. Acute myocarditis, endocarditis, unstable angina 4. Hypertrophic and restrictive cardiomyopathy 5. Paroxysmal ventricular tachycardia | 1. Cardiac tamponade, pericarditis, severe aortic stenosis 2. Ventricular arrhythmias | 1. Obstructive cardiomyopathy 2. Acute hypovolemia |
| NB! | Physico-chemical structure of cardiac glycosides: polar glycosides (strophanthin, korglikon), relatively polar (digoxin, Celanide), nonpolar (digitoxin). Polar are administered parenterally, act briefly, have a predominantly systolic effect; Non-polar act for a longtime, are administered orally, have a predominantly diastolic effect. Disadvantages of cardiac glycosides: narrow therapeutic range → possibility of intoxication; Refractory in hyperthyroidism, mitral stenosis, chronic pulmonary heart. | | |
| | In decompensation of CHF and acute heart failure, levosimendan can be used. This substance is a sensitizer of contractile proteins to calcium ions. Currently, levosimendan has not yet become wide spread in the clinic. | | |

Glycoside intoxication

| Clinics: | Management: |
|---|---|
| 1. CVS: heart rhythm disturbances (AV blockade, ventricular extrasystoles, etc.) 2. Digestive tract: anorexia, nausea, vomiting and diarrhea 3. Central nervous system: dizziness, headache, hallucinations, etc. 4. Visual function: xantopsy (visual impairment, in which all objects appear yellow-colored), photophobia, loss of visual fields, mydriasis. | 1. The withdrawal of the drug, 2. Antidotes of cardiac glycosides: digitalis-antidote (antibodies to cardiac glycosides), unitiol (donor of SH-groups binding cardiac glycosides) and EDTA (binds calcium ions), 3. Preparations of K ⁺ - potassium chloride (1-1.5 g per 100 ml of 5% glucose and 4 units of insulin, up to 8 g of potassium chloride per day) into the vein, or tablets "Asparcam", "Panangin", 4. Antiarrhythmics: lidocaine, phenytoin (difenin), β-adrenoblockers, in AV blockade - M-holinoblokatory. |

Antiarrhythmic agents

Antiarrhythmic agents are drugs used to treat heart rhythm disturbances (arrhythmias).

| Classification | Class I (Na ⁺ -channel blockers) | | | Class II (β-blockers) | Class III (K ⁺ -channel blocker) | Class IV (Ca ²⁺ -channel blockers) |
|-------------------------|--|---|--|---|--|---|
| | IA | IB | IC | | | |
| Drugs | 1. Quinidine 2. Procainamide 3. Dysopyramide | 4. Lidocaine 5. Phenytoin | 6. Propaphenone 7. Ethacizine | 8. Propranolol 9. Atenolol 10. Metoprolol | 11. Amiodarone 12. Bretiliumtosylate | 13. Verapamil |
| Mechanism of action | ↓ Permeability of membranes for Na ⁺ and Ca ²⁺ ions→↓ Depolarization rate; ↓ automaticity and conductivity; ↑ repolarization. | Blockage of Na ⁺ entry in the phase 4 and ↑ permeability of membranes for K ⁺ ions in the phase 3 → ↓ automaticity; ↓ duration of repolarization. <i>Do not affect the conductivity and heart beat strength</i> | Na ⁺ -channel blockage→ ↓ depolarization and automatism. <i>Do not affect repolarization.</i> | See lesson № 10 "Adrenergic drugs» | 1. ↓ permeability of the cardiomyocyte membrane for potassium ions, delay repolarization (11) 2. NA synaptic release blockage and ↓ of the effect of the neurotransmitter on adrenoceptors (12) | The slow transmembrane current of Ca 2+ ions is blocked in the cell → phase 0 inhibition in the cells with "slow response" → ↓ automaticity of SA- and AV-nodes and ectopic foci. |
| Pharmacological effects | 1. Antiarrhythmic 2. Anticonvulsant (5) 3. Local anesthetizing(4) | | | | 1. Antiarrhythmic 2. Antianginal (11) 3. Hypotensive(12) | 1. Antiarrhythmic 2. Antianginal 3. Hypotensive |
| Indications | 1. Atrialfibrillation (1,2) 2. Ventricular tachycardia 3. Supraventricular paroxysmal tachycardia (1-3,7) 4. Atrialfibrillation / flutter (2.6) | | | | 1. Supraventricular and ventricular tachyarrhythmia, including life threatening 2. Refractory arrhythmias | 1. Supraventricular tachyarrhythmia and extrasystoles 2. Angina pectoris 3. Arterial hypertension |
| Sideeffects | 1. Negative inotropic effect 2. Nausea, vomiting 3. Cholinolytic effect 4.α-blocking effect (1) | 1. Headache, dizziness 2. Tremor 3. Gingival enlargement (5) | 1. Negative inotropic effect 2. Proarrhythmogenicaction 3. Headache | | 1. Intestinal pneumonia; 2. Hypo- / hyperthyroidism (11) 3. Hypotension 4. Ataxia, tremor (11) 5. Deposition of lipofuscin in the cornea (11) | 1. Nausea, vomiting 2. Hyperemia of the face 3. Bradycardia, AV blockade 4. Peripheral edema 5. Constipation |
| Contraindications | 1. Intra cardiac blockades 2. Decompensation of heart failure | 1.Sick sinus syndrome 2. Liver diseases | 1. Sick sinus syndrome 2. Severe heart failure | | 1. Sick sinus syndrome (11) 2. Violation of thyroid function (11) 3. Arterial hypotension (12) | 1. Sick sinus syndrome, bradycardia 2. Arterial hypotension 3. Cardiogenic shock, IM |

NB!

- Treatment of bradyarrhythmia: *muscarinic antagonists* (eliminate the influence of the vagus nerve); *β 1-adrenomimetics* (dobutamine, dopamine).
- Additional drugs for the treatment of arrhythmias: *cardiac glycosides* for supraventricular arrhythmias, *potassium* preparations (panangin, asparcam) in arrhythmias to prevent hypokalemia; *dihydropyridine calcium channel blockers* (nifedipine, amlodipine, etc.) in brady-dependent arrhythmias (\uparrow heart rate); inhibitors of angiotensin-converting enzyme (captopril, enalapril, etc.) for ventricular arrhythmias.

NA – noradrenaline,