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 20: **« ANTIANGINAL AGENTS. LIPID-LOWERING DRUGS»**

Time: 3 hours

Approved at the meeting of the department of general and clinical pharmacology

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

The high prevalence of coronary heart disease and the severe complications to which it leads require not only early detection and prophylaxis of the disease, but also timely and adequate drug therapy. For this reasons future physicians need deep and conscious studying of antianginal and hypolipidemic medicines, critical perception of information, logical synthesis and analysis of available information.

Learning objective:

- Formation of scientific knowledge, abilities and skills on the issues of antianginal and hypolipidemic drugs, as well as the possibilities of their use in clinical practice. To be able to prescribe medicines of these groups in prescriptions, based on their pharmacokinetic and pharmacodynamic features, indications and contraindications for use, age and concomitant diseases of the patient, for use in medical and preventive activity.

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 importance 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:

- know the classification and main characteristics of the studied drugs, pharma-dynamics and pharmacokinetics, indications and contraindications for their use, side effects;

be able to:

- Analyze the effect of drugs on the topic of the class according to the totality of their pharmacological properties and the possibility of their use in medical practice;
- justify the choice of a drug, taking into account its pharmacological characteristics and individual characteristics of the patient;
- correctly calculate the dose and route of administration of the drug, taking into account the nature of the pathological process;
- Write out in the form of medical prescriptions the medicines on the topic of the class.

possess:

– skills in selecting medications on the topic of the class for therapeutic measures for the most common diseases and conditions;

– skills to calculate an individual dosing regimen for medications on the topic of the class based on pharmacokinetic data and individual characteristics of the patient depending on age;

– skills to correct the dosing regimen when there are pathological changes in the functions of organs or systems responsible for biotransformation and elimination of drugs or when different drugs are used together;

– skills to search, analyze and summarize information about the use and effects of major drugs on the topic of the class.

Motivation for learning the topic:

Specificity of preparation of doctors on this specialty defines the necessity of purposeful studying of basic pharmacological effects, providing therapeutic and prophylactic action of antianginal and hypolipidemic medicines, indications and contra-indications to their use, questions of interaction of medicines, their combined application.

MATERIAL EQUIPMENT

Reference and informational literature, charts, tables, presentations, drug collections.

CONTROL QUESTIONS FROM RELATED DISCIPLINES

- anatomy and physiology of the cardiovascular system;
- mechanism of atherosclerotic plaque formation;
- pathogenesis of local blood flow disorders.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Main groups of antianginal drugs, classification: β-adrenoblockers: propranolol, atenolol, metoprolol; calcium channel blockers: diltiazem, verapamil, nifedipine and its prolonged forms, amlodipine; organic nitrates and nitrate-like agents: nitroglycerin, isosorbide mononitrate, isosorbide dinitrate, molsidomine; other antianginal agents: ni-conradil, mildronate, ivabradine.

2. Mechanisms of action of different groups of antianginal drugs; correlation between coronary blood flow disorders, myocardial oxygen demand and delivery and coronary heart disease development; application points of action mechanisms of different groups of antianginal drugs.

3. Features of pharmacokinetics of various groups of antianginal drugs.

4. Indications for use of antianginal drugs.

5. Side effects of various groups of antianginal drugs, interrelation of side effects with the mechanism of action. Drug incompatibility of separate groups of drugs.

6. Comparative description of basic medicines - representatives of antianginal remedies according to pharmacological properties, indications and side effects.

7. Phenomenon of "stealing" of myocardium. Withdrawal syndrome. Tolerance to nitrates.

8. Modern strategy of pharmacotherapy for coronary heart disease, comparative characteristics of antianginal agents for their influence on the course and prognosis of coronary heart disease, choice of drugs for relieving and preventing angina attacks.

9. Hypolipidemic agents: statins (atorvastatin), fibrates (gemfibrozil), bile acid sequestrants (colestyramine), nicotinic acid. Principles of action, clinical application, comparative characteristics of hypolipidemic agents in terms of efficacy.

PROCESS OF THE STUDY

Theoretical part

The prevalence of CHD conditions has led to the creation of a large number of drugs, allowing effective control of the patient's condition. Knowledge of basic pharmacological

effects, providing therapeutic and preventive action of antianginal and hypolipidemic drugs, indications and contraindications for their use, questions of interaction of drugs, their combined application will allow to master successfully the methods of pharmacotherapy of CHD, to use the knowledge obtained in the treatment of future patients.

Pharmacological characteristics of antianginal and hypolipidemic drugs are presented in appendix to methodical recommendations.

Practical part

1) Take notes on the theoretical material demonstrated by the teacher;

2) To master the technique of solving problems and writing prescriptions on the topic: "Drugs for the treatment of cardiac insufficiency. Cardiotonic drugs. Anti-arrhythmic agents".

Theme learning control

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

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.Therapeutic nutrition for atherosclerosis.

2.Modern approaches to the prevention and treatment of coronary heart disease.

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.

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Antianginal drugs are substances used for angina pectoris.

Classification	Nitrates and *sydnonimine derivatives	ß-adrenoblockers	Calcium channel blockers
Drugs	**1. Nitroglycerine** ***Short-acting (***tablets Nitrolingual, Nitrostat; spray Nitromist) ***Long-acting*** (buccal form Nitrogard; patch Minitran) **2. Isosorbide dinitrate (Isordil)** **3. Isosorbide-5-mononitrate (Imdur, Ismo)** ***4. Molsidomine**	*Non-selective ß-blockers:* **5. Propranolol** *Selective ß1-blockers:* **6. Atenolol, Metoprolol, Bisoprolol** *ß1, α1-blockers:* **7. Carvedilol, Labetalol** *With ISA (intrinsic sympathomimetic activity)* **8. Acebutalol, Talinolol**	*Dihydropyridine:* **9. Nifedipine** **10. Amlodipine** *Phenylalkylamine:* **11. Verapamil** *Benzothiazepine:* **12. Diltiazem**
Mechanism of action	SH-groups → are metabolized into S-nitrosothiols with NO release → activate guanylate cyclase, intracellular cGMP is accumulated → ↓ flow into the cells and accelerates the release of Ca^{2+}, relaxes the smooth muscles of the veins and arterioles (including the coronary vessels) (1-3). *Is converted to NO, does not form S-nitrosothiols (4).	Blockage of ß-adrenergic receptors → ↓ cAMP → ↓ Ca^{2+}entry and ↓ intracellular concentration of Ca^{2+}→ ↓ force of the heart contractions.	Blockade of slow calcium channels ↓ entry of Ca^{2+}ions into the cell → ↓ conversion of phosphate energy into mechanical work → muscle fiber does not develop sufficient mechanical stress.
Pharmacological Effects	**1. Antianginal** (↓pre- and afterload) **2. Antiplatelet**	1**. Antianginal** **2. Hypotensive** **3. Antiarrhythmic**	1**. Antianginal** **2. Hypotensive** 3. Antiarrhythmic (11,12)
Indications	1. Angina pectoris (all kinds) 2. Acute myocardial infarction (i/v 1, 2) 3. Chronic heart failure (2-4) 4. Pulmonary edema (1)	1. Angina pectoris 2. Arterial hypertension 3. CHF 4. Tachyarrhythmia 5. Migraines	1. Angina pectoris, vasospastic angina 2. Arterial hypertension 3. Supraventricular tachyarrhythmias (11, 12)
Side effects	1. Headache, tinnitus, reflex tachycardia 2. Hypotension, orthostatic collapse 3. Nausea, vomiting 4. Tolerance (1-3) 5. ↑ intraocular and intracranial pressure	1. Bronchospasm 2. Hypotonia 3. Bradycardia, AV blockade	1. Headache, dizziness, skin hyperemia, tachycardia, legs edema (9, 10) 2. Bradycardia, AV blockage (11) 3. Tachy-, bradycardia (12)
Contraindications	1. Allergy 2. Arterial hypotension 3. ↑ intraocular pressure 4. Closed-angle glaucoma	1. Bronchial asthma 2. Bradycardia, AV blockade 3. Arterial hypotension, severe CHF 4. Pregnancy	1. Severe hypotension 2. Acute MI, progressive HF 3. Sick sinus syndrome
NB!	**Angina attack treatment: nitroglycerine** sublingually.	**New drugs: ivabradine** (funny channel blocker. ↓HR. doesn't affect BP conductivity)	**Metabolic therapy:** trimetazidine (preductal), nicorandil, meldonium (mildronate).

Lipid-lowering drugs – agents decreasing lipid plasma level.

Classification	Statins	Bile acid sequestrants	Fibrates	Derivatives of nicotinic acid	Inhibitors of sterol intestinal absorption	Other
Drugs	**1. Atorvastatin** **2. Lovastatin** **3. Pravastatin** **4. Simvastatin**	**5. Cholestyramine** **6. Colestypol**	**7. Fenofibrate** **8. Gemfibrozil** **9. Ciprofibrate**	**10. Nicotinic acid (niacin)**	**11. Ezetimibe**	**12. Probucol**
Mechanism of action	1. ↓ synthesis of cholesterol in the liver due to competitive inhibition of the enzyme HMG-CoA reductase → ↑ number of receptors for LDL → ↑ capture of cholesterol from the plasma 2. The LDL particles also contain triglycerides (TG) → ↓ TG	↑catabolism and excretion of bile acids and cholesterol	1. Violate lipid metabolism → stimulated lipoprotein lipase and ↑ catabolism of VLDL 2. Inhibit acetyl-CoA carboxylase, inhibition of lipolysis → ↓ synthesis of TG 3. ↑ intake of cholesterol and TG by HDL	1. Directly inhibits hepaticVLDL → ↓ synthesis of TG 2. ↓ plasma cholesterol level	Selectively inhibits the absorption of phytosterol and cholesterol in the small intestine	Inhibits the synthesis of lipids, ↓ absorption of cholesterol and atherogenic properties of lipoproteins
Pharmacological effects	**1. ↓ total cholesterol plasma level** 2. ↓ triglycerides plasma level (1-4, 7-10) 3. ↑ HDLP level (1-4, 7-9, 12) 4. Antiplatelet (1-4)					
Indications	1. **Atherosclerosis,** **2. Hyperlipoproteinemia IIa;** IIb (1-4, 7-12); III and IV (1-4, 7-9, 10), 3. Hypercholesterolemia (1-6, 10, 11) 4. Hypertriglyceridemia (1-4, 7-10)					
Side effects	1. Dyspepsia 2. Liver function impairment 3. Myalgia, myosite	1. Constipation, вздутие живота 2. Malabsorbtion	1. Nausea, vomiting, diarrhea 2. ↑ bile cholesterol level → ↑ cholelithiasis risk 3. ↑ ALT, AST	1. Skin hyperemia 2. Hepatotoxicity 3. Hyperuricemia	1. Liver function impairment	1. Diarrhea, bloating, nausea 2. QT widening
Contraindications	1. ↑ ALT, AST 2. ↑ creatinkynase 3. Pregnancy, lactation, age before 18	1. Severe Hypertriglyceridemia	1. Hepatitis 2. Cholelithiasis	1. Gastroduodenal ulcers 2. Liver function impairment 3. Gout	1. Hepatic diseases 2. Hyper sensibility	1. QT widening, ventricular tachyarrhythmia 2. Pregnancy, lactation
NB!	**1. The basic treatment of cholesterol is the DIET!** 2. Bile acid sequestrants should be taken during meal. 3. Statins are taken in the evening before going to bed cause cholesterol is synthesized in the night. 4. Omega-3 polyunsaturated fatty acids have lipid-lowering (↓ TG, VLDL) antiplatelet, anti-inflammatory effects. Can be used as a supplement for lipid-lowering therapy.					

Myocardial infarction management (MI is ischemic necrosis of heart muscle because of prolonged lack of oxygen supply – ischemia)

Aim	Group	Drugs
1. Pain management	1.1***Opioid analgesics***	Morphine, Promedol, Fentanyl
	1.2 Neuroleptanalgesia	Fentanyl + droperidol
	1.3 Inhalation anesthesia	Nitrous oxide (80 vol% N2O and 20 vol% O2)
2.Restoration of coronary blood flow(trombolysis) and thrombi formation prevention	2.1 ***Fibrinolytics***	Alteplase, Tenteplase (no antigenicity); Streptokinase
	2.2 ***Anticoagulants***	Heparin, Enoxaparin, Fondaparinux
	2.3 ***Antiplatelets***	Acetylsalicylic acid (250-500 mg to be chewed), Clopidogrel 300 mg
3. Necrosis zone restriction	3.1 ***Nitrates (в/в)***	Nitroglycerin, isosorbide dinitrate
4. Acute cardiac uploading	4.1 ***β-blockers***	Metoprolol, Bisoprolol, Carvedilol, Atenolol
	4.2 ***ACE inhibitors***	Captopril, Enalapril, Lisinopril, Perindopril
5. Atherosclerotic plaque stabilization	5.1 ***Statins***	Atorvastatin, Rosuvastatin

Migraine treatment (migraine is a disease with biphasic change in cerebral vessels tone: short constriction is followed by dilatation)

Acute attack treatment	
Group	Drug
1. Ergot alkaloids and its derivatives **NB!** Vasoconstriction→↓ pulsation of meningeal vessels	Ergotamine, dihydroergotamine
2. Triptans **NB!** The agonists of serotonin (5-HT1) receptors → narrow the cerebral vessels	Sumatriptan, Zolmitriptan, Riza-tryptan
3.The methylxanthine derivative **NB!**Cerebral vasoconstriction	Caffeine
4.NSAIDs **NB!**Analgesic action	Paracetamol, Acetylsalicylic acid, Naproxen, Indomethacin
5. Adjuvant agents: Antiemetic	Metoclopramide
Attacks preventionе (cerebral vessels spasm prevention)	
1. β-blockers	Propranolol, Metoprolol, Timolol
2. Antiepileptic drugs	Carbamazepine, Valproic Acid
3. Calcium channel blockers	Cinnarizine, Nimodipine
4. Tricyclic antidepressants	Amitriptyline
5. 5-HT2 receptor antagonists	Metisergid
6. Caffeine, NSAIDs, magnesium sulphate	