

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

Department of general and clinical pharmacology

Authors:

A.V.Sennikava, senior lecturer

E.I. Mikhailova, head of department, DMS, prof.

A.Y. Braga, assistant

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 21: «ANTIHYPERTENSIVE AGENTS. ANTIHYPOTENSIVE AGENTS»

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

The high prevalence of hyper- and hypotensive vessels, as well as pulling complications that lead to consequences, require not only early detection and prevention of diseases, but mandatory and adequate drug therapy. For this reason, future physicians need a deep and informative study of antihypertensive and antihypotensive drugs, critical perception of information, logical synthesis and analysis of available information.

Learning objective:

– formation of scientific knowledge about the main pharmacological effects, providing therapeutic and preventive effect of drugs on the topic of the class, 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 a 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 observe educational and labor discipline, the norms of medical ethics and deontology.

Tasks:

As a result of the training session, the student should:

know:

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

be able to:

- analyze the effect of drugs on the topic of the lesson in terms of the totality of their pharmacological properties and the possibility of their use in medical practice;

- justify the choice of the drug, taking into account its pharmacological characteristics and the 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 medicines in the form of medical prescriptions on the topic of the lesson.

possess:

– skills in choice of drugs on the topic of the lesson;

– the rules of prescribing the studied drugs in the treatment of various diseases and pathological conditions, taking into account the indications;

– skills of dosage regime correction in case of pathological changes in functions of organs or systems responsible for biotransformation and elimination of drugs or in case of joint use of different drugs;

– skills to search, analyze and summarize information about the use and effects of the studied drugs.

Motivation for learning the topic:

– the specifics of training doctors in this specialty determines the need for students to purposefully study the main pharmacological effects, providing therapeutic and preventive effects of drugs on the topic of the class, indications and contraindications for their use, the interaction of drugs, their combined use, which will successfully complete the specialized disciplines of the specialty.

MATERIAL EQUIPMENT

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

CONTROL QUESTIONS FROM RELATED DISCIPLINES

1. Influence of the CNS, peripheral nervous system and vascular smooth muscle tone on the support of systemic pressure.
2. Biochemistry of the adrenergic impulse, the role of catecholamines in the transmission of the nerve impulse and their biochemical transformations.
3. The concept of essential and secondary arterial hypertension. Etiopathogenesis and clinic of essential arterial hypertension. Hypertensive crises and their complications.
4. Definition, basics of pathogenesis and clinic of arterial hypotension.
5. Rules for writing prescriptions and Latin terminology on the topic of the lesson.

CONTROL QUESTIONS ON THE TOPIC OF THE LESSON

1. The main groups of antihypertensive drugs: diuretics (hydrochlorothiazide, indapamide, furosemide, spironolactone, triamterene); inhibitors of the renin-angiotensin-aldosterone system (RAAS) (aliskiren, captopril, enalapril, lisinopril, losartan, valsartan); β -blockers (propranolol, metoprolol, atenolol, bisoprolol, nebivolol) and mixed α - and β -blockers (labetalol, carvedilol); calcium channel blockers (nifedipine and its prolonged forms, amlodipine, verapamil, diltiazem); additional means: central action (clonidine, methyldopa, moxonidine, rilmenidine), α_1 -blockers (doxazosin), vasodilators (diazoxide, sodium nitroprusside, magnesium sulfate, bendazole), sympatholytics (guanethidine, reserpine).
2. Mechanisms of action, pharmacokinetics, side effects of antihypertensive drugs, principles of their combination.
3. Principles of pharmacotherapy of arterial hypertension and criteria for choosing antihypertensive drugs.
4. Differences in pharmacotherapeutic approaches to the treatment of arterial hypertension and relief of hypertensive crises.
5. Antihypertensive drugs.

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. The role of neurotropic drugs (sedatives, anxiolytics, antidepressants) in the treatment of arterial hypertension.
2. The place of herbal antihypertensive drugs in modern medicine.

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. Kharkevitch, D.A. Pharmacology: textbook for med. students: transl. of 12th ed. of Russ. textbook "Pharmacology" (2017) / D.A. Kharkevitch. - 2nd ed. - Москва: ГЭОТАР-Медиа, 2019. - 676 с.: ил., табл. - Рек. ФГАУ "ФИРО". – Режим доступа: <http://www.studmedlib.ru/book/ISBN5970402648.html> – Дата доступа: 23.05.2022.

2. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts / Е.И. Михайлова [и др.]. – Ч. 1. – Гомель: ГомГМУ, 2020. – 56с. – Режим доступа: <http://elib.gsmu.by/xmlui/handle/GomSMU/7128> – Дата доступа: 23.05.2022.

3. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts / Е.И. Михайлова [и др.]. – Ч. 2. – Гомель: ГомГМУ, 2020. – 76с. – Режим доступа: <http://elib.gsmu.by/xmlui/handle/GomSMU/7129> – Дата доступа: 23.05.2022.

Antihypertensives are medicines used for the treatment of hypertension

Ist line drugs are used in the first complaints of the patient.

Classification	Drug saffecting the RAAS		Diuretics	β-blockers	Calcium channel blockers (calcium antagonists, CCB)
	Angiotensin converting enzyme inhibitors (ACE inhibitors)	Angiotensin II receptor antago- nists (sartans)			
Drugs	<i>Sulphydryl-containing agents:</i> 1. Captopril (Capoten) <i>Dicarboxylate-containing agents:</i> 2. Enalapril (Enap) 3. Lisinopril (Diroton) 4. Ramipril (Tritace) <i>Phosphonate-containing agents:</i> 5. Fosinopril (Monopril) <i>Hydroxame-containing agents:</i> 6. Idrapril	7. Losartan (Cozaar) 8. Valsartan (Diovan) 9. Irbesartan (Aprovel) 10. Candesartan (Atacand) 11. Eprosartan (Teveten) 12. Telmisartan (Micardis)	See lesson №22 "Diuretics. Drugs affecting the tone and contraction activity of the myometrium »	See lesson №10 «Adrenergic drugs»	See lesson №20 «Anti- anginal and hypoli- pidemic agents»
Mechanism of action	1. Inhibition of ACE → violation of the conversion of angiotensin I to angiotensin II → vasodilation, ↓ retension of Na and H ₂ O, ↓ stimulating effect on the sympathetic innervation → ↓ BP. 2. Inhibition of ACE → ↓ in activation of brady- kinin→ vasodilation.	1. Antagonists of the angiotensin re- ceptors → eliminate all the effects of angiotensin II (vasopressor action, ↑ production of aldosterone, stimula- tion of adrenergic innervation)			
Pharmacological effects	1. Hypotensive 2. Protection of organs (cardio, angio - and nephroprotective action)				
Indications	1. Arterial hypertension 2. Diabetic nephropathy 3. CHF 4. Postinfarction condition 5. Intoleranceto ACE inhibitors				
Side effects	1. Dry cough, bronchospasm 2. Hyperkalemia 3. Deterioration of renal function in chronic renal failure. Hypotension	<i>Rarely:</i> 1. Hypotension 2. Dyspepsia 3. Hyperkalemia			
Contraindications	1. Pregnancy and lactation 2. Stenosis of the renal arteries 3. Severe and chronic renal failure or hyperkalemia	1. Pregnancyandlactation 2. Hyperkalemia			
NB!	Classification of ACEinhibitors by duration of action: short-acting (captopril), intermediate-acting (enalapril), long-acting (ramipril, lisinopril). The majority of ACE inhibitors (except captopril and lisinopril) are prodrugs.				

AH- arterial hypertension, CHF - chronic heart failure, ACE angiotensin-converting enzyme, RAAS - renin-angiotensin-aldosterone system.

Antihypertensives (continued)

IInd line drugs are used when the Ist line drugs are non-effective.

Classification	Central-acting drugs	Ganglionic blockers	α -adrenoblockers	Sympatholytics	Potassiumchannels openers
Drugs	1. Clonidine hydrochloride (Clopheline) 2. Moxonidine 3. Methyldopha (Dopegit, Aldomet)	<i>Quaternary ammonium compounds:</i> 4. Hygronium 5. Azamethonium bromide 6. Hexamethonium <i>Amines:</i> 7. Pempidine	<i>Selective $\alpha 1$-adrenergic blockers:</i> 8. Prazosin (Minipress) 9. Doxazosin (Cardura) 10. Terazosin (Kornam)	11. Reserpine (Serpasil) 12. Octavin	13. Minoxidil 14. Diazoxide
Mechanism of action	1. Effect on $\alpha 2$ -adrenoreceptors (1,3) and imidazolineI1 receptors (1,2) of solitary tract nuclei \rightarrow oppression of VMC and \uparrow tonus of the vagus nerve \rightarrow \downarrow cardiac workput, \downarrow release of renin and \downarrow TPR \rightarrow \downarrow AD (1-3) 2. Stimulation of peripheral pre-synaptic $\alpha 2$ -adrenergic receptors \rightarrow \downarrow of norepinephrine release in synaptic cleft (1)	See lesson № 9 «Cholinergic drugs. Nicotinic receptor agonicts. Nicotinic receptor antagonists (ganglionic blockers, neuromuscular blockers)»	See lesson №10 «Adrenergic drugs»	Violate noradrenalin storing in the vesicles \rightarrow \downarrow amount of the mediator released in response to nerve impulses	Open potassium channels in the smooth muscle vessels \rightarrow vasodilation and \downarrow BP.
Pharmacological effects	1. Hypotensive 2. Sedative(1,3) 3. \downarrow IOP			1. Hypotensive 2. \downarrow IOP (12) 3. Sedative, antipsyhotic (11)	1. Hypotensive
Indications	1. Resistant AH 2. Hypertensive crisis 3. Glaucoma (1) 4. AH in pregnant women (3) 5. Abstinence syndrome (1)			1. Resistant AH	1. Resistant AH 2. Hypertensivecrisis
Side effects	1. Arterial hypotension 2. The withdrawal syndrome (1,3) 3. Drymouth (1,3) 4. Drowsiness			1. Peripheraledema 2. Pain in the chest 3. Bradycardia 4. Dyspepsia	1. Peripheraledema 2.Tachycardia, arrhythmia
Contraindications	1. Arterial hypotension 2. Depression 3. Sick sinus syndrome, AV-blockade			1. Acute stroke, MI 2. Arterial hypotension	1. Pheochromocytoma
NB!	Other drugs with antihypertensive action: nitrates, dibazol, magnesium sulfate.				

VMC - vasomotor center, TPR – total peripheral resistance, IOP – intraocular pressure, MI – myocardial infarction, AH – arterial hypertension.

Antihypotensive drugs – drugs increasing BP

Group	Drug
1. α-adrenomimetics	Phenylephrine (Mezaton), Midodrine
2. β_1-adrenomimetics	Dobutamine
3. Dopaminomimetics	Dopamine
4. Analeptics	Nikethamide (Coramine), Caffeine
5. Non-selective α- and β-adrenomimetics	Epinephrine, Ethylphrine
6. Plant stimulants	Extracts and tinctures of ginseng and eleutherococcus

Hypertensive crisis management

Hypertensive crisis –an umbrella term for hypertensive urgency and hypertensive emergency. These two conditions occur when blood pressure becomes very high, possibly causing organ damage.

<i>Hypertensive urgency</i> (no impairment of <u>organ systems</u>)	
Captopril	12,5-50 mg orally or sublingually
Nifedipine	5-20 mg sublingually
Metoprolol	25-50mg orally
Propranolol	10-40 mg orally
Clonidine (clonidine)	0,075-0,15 mg orally
Moxonidine	0,4 mg orally
<i>Hypertensive emergency</i> (acute life-threatening impairment of <u>organ systems</u> , especially the central nervous, cardiovascular systems or the kidneys. Management depends on complications)	
Sodium nitroprusside (For pulmonary edema, aortic dissection)	0,25-10 mkg/kg/mini/v slowly
Nitroglycerine (For pulmonary edema, aortic dissection)	50-200 mkg/mini/v slowly
Enalapril (For pulmonary edema, ischemic stroke, subarachnoid hemorrhage)	1,25-5 mgi/v quickly
Labetalol (For aortic dissection, ischemic stroke, subarachnoid hemorrhage)	20-80 mg quickly, 1-2 mg/min quickly
Furosemide (For pulmonary edema)	40-200 mgi/v
Magnesium sulfate (For convulsions, eclampsia)	5-20 ml 20% solution i/v quickly
Clonidine	i/v 0,5-1,0 ml 0,01% solution or i/m 0,5-2,0 ml 0,01% solution