

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 10: «ADRENERGIC AGENTS»

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

Drugs that excite different types of adrenoreceptors are widely used in medical practice as emergency therapy drugs (anaphylactic shock, Quincke's edema, cardiac arrest, collapse of any etiology, bronchial asthma, etc.) to increase the tone of sympathetic innervation. The study of pharmacological characteristics of these drugs, features of their action, indications for use, side effects will contribute to the formation of skills on scientifically justified and rational use of means of this group in the practice of doctors of many specialties.

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 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 follow academic and work discipline, standards of medical ethics and deontology.

Tasks:

As a result of the study lesson, the student should

know:

- classification and basic characteristics of the studied drugs, pharmacodynamics and pharmacokinetics, indications and contraindications for their use, side effects;
- features of pharmacokinetics and pharmacodynamics, advantages and disadvantages of different dosage forms of these drugs;
- principles of research and testing of new drugs; information and reference and search systems;

be able to:

- analyze the effect of the studied drugs on the set of their pharmacological properties and the possibility of their use in medical practice; to write them in prescriptions;
- use different dosage forms of these drugs, based on the peculiarities of their pharmacodynamics and pharmacokinetics;
- work with scientific literature, search for information about the use and action of the studied drugs;

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. Adrenergic signal transmission. Structure of adrenergic synapses and mechanism of nerve impulse transmission. Regulation of mediator release and their metabolism.
2. Heterogeneity of adrenoreceptors (α and β -adrenoreceptors): localization, effects of physiological and pharmacological stimulation.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Adrenergic agonists (adrenomimetics). Classification. α -Adrenomimetics: α 1-adrenomimetics - phenylephrine; α 2-adrenomimetics - clonidine; α 1, α 2-adrenomimetics (relatively selective α 2-adrenomimetics) - xylometazoline, naphazoline. β -Adrenomimetics: β 1-adrenomimetics - dobutamine; β 2-adrenomimetics - salbutamol, salmeterol, terbutaline; β 1, β 2, β 3-adrenomimetics (non-selective) - isoprenaline. α - and β -Adrenomimetics: epinephrine, norepinephrine, dopamine. Pharmacological effects of adrenomimetics of different groups, indications and contraindications for use, side and toxic effects.

2. Adrenoblocking agents, definition. α -Adrenoblockers: α 1-adrenoblockers - doxazosin, prazosin, tamsulosin; α 2-adrenoblockers - yohimbine; α 1, α 2-adrenoblockers (non-selective) - phentolamine, dihydroergotamine. β -Adrenoblockers: β 1, β 2,-adrenoblockers (non-selective) - propranolol, nadolol, sotalol, pindolol, timolol; β 1-adrenoblockers (cardioselective) - metoprolol, betaxolol, atenolol, nebivolol. α - and β -Adrenoblockers: carvedilol, labetalol. Pharmacodynamics and pharmacokinetics of adrenoblockers of different groups, indications and contraindications for use, side and toxic effects.

3. Criteria for the selection of β -adrenoblockers: selectivity, intrinsic sympathomimetic activity, additional vasodilatory activity, duration of action, effect on lipid and carbohydrate metabolism.

4. Presynaptic agents. Sympathomimetics (ephedrine) and sympatholytics (guanethidine, reserpine); pharmacological effects, use, side effects, contraindications.

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 use of new generation α -adrenoblockers in the treatment of benign prostatic hyperplasia.
2. New β -Adrenoblockers in the treatment of bronchoobstructive syndrome.

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

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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.
4. Rang and Dale's Pharmacology / J.M. Ritter [et al.]. - 9th ed. - Edinburg [et al.]: Elsevier, 2020. - xvi, 789 p.: ill., tab. + Student consult online.

α - agonists – medicinal substances that directly or indirectly stimulate (stimulating) α -adrenergic receptors.

Classification	α, β – agonists	α_1 - agonists	α_1, α_2 - agonists	α_2 - agonists
Drugs	<u>Direct-acting</u> 1. Epinephrine (Adrenaline) 2. Norepinephrine (Norepinephrine) <u>Indirect-acting</u> 3. Ephedrine hydrochloride	4. Phenylephrine hydrochloride (Mezaton) 5. Midodrin (Gutron)	6. Naphazoline (Naphthysine, Sanorin) 7. Xylometazoline (Galazolin) 8. Oxymetazoline (Nazivin, Nazol)	9. Clonidine (Clopheheline) 10. Methyldopa (Dopanol)
Mechanism of action	1. Stimulates the β_1 , β_2 -adrenoceptors, at high doses α_1 too (1) 2. Stimulates α_1 -adrenergic receptors, as well as β_1 (2) 3. Stimulates the release of noradrenaline and inhibits its re-uptake by presynaptic membrane (3)	1. Stimulate α_1 -adrenoceptors	1. Stimulate α_1 and α_2 -adrenergic receptors (predominantly α_1)	1. Stimulate presynaptic α_2 -adrenoreceptors of the CNS (predominantly in the solitary nucleus in the medulla oblongata) \rightarrow \downarrow sympathetic impulse to the vessels and heart \rightarrow \downarrow cardiac output and peripheral vascular resistance (9) 2. Stimulate presynaptic α_2 -adrenoreceptors neurons of the vasomotor center of the medulla oblongata \rightarrow \downarrow sympathetic impulse to vessels \rightarrow \downarrow peripheral vascular resistance (10)
Pharmacological effects	1. \uparrow BP, cardiostimulating (positive ino-, chrono-, dromo- and batmotropic action) 2. Bronchodilating (1,3) 3. \uparrow glycogenolysis and lipolysis (1,3)	1. Narrowing of arterioles \rightarrow \uparrow BP 2. Narrowing of the vessels of the nasal mucosa and conjunctiva (4)	1. Narrowing of the vessels of the nasal mucosa and conjunctiva \rightarrow anti-inflammatory action	1. Hypotensive 2. Sedative (9) 3. \downarrow IOP (9)
Indications for use	1. Anaphylactic shock, treatment of an attack of asthma (1) 2. Hypoglycemic coma (1,3) 3. Prolongation of the action of local anesthetics (1,2) 4. Hypotension 5. Drug poisoning (3)	1. Arterial hypotension 2. Rhinitis (4) 3. Conjunctivitis (4)	1. Acute rhinitis, sinusitis, sinusitis 2. Nasal bleeding 3. Conjunctivitis	1. Hypertensive crisis, AH (9) 2. Alcohol and opiate withdrawal (9) 3. AH in pregnant women (10) 4. Glaucoma (9)
Side effects	1. Arrhythmias, \uparrow BP 2. Ischemia of the myocardium (1) 3. Tremor 4. Hyperglycemia (1,3) 5. Tachyphylaxis (3)	1. Headache 2. Bradycardia, arrhythmia 3. Tremor	1. In long administration – desensitisation of α -adrenergic receptors 2. Mucosa irritation and damage 3. \uparrow BP, tachycardia	1. The withdrawal syndrome (9) 2. Dry mouth (9,10) 3. Constipation (9) 4. Peripheral edema (10) 5. Depression, anxiety condition (10)
Contraindications	1. Arterial hypertension (AH) 2. Diabetes mellitus (1,3) 3. Anesthesia with fluorotane (1,2) 4. Complete AV blockade (2)	1. AH, bradycardia 2. Pheochromocytoma (5) 3. Prostatic hypertrophy	1. AH 2. Tachycardia 3. Severe atherosclerosis	1. Arterial hypotension 2. AV blockade II-III degree (9) 3. Hepatitis, cirrhosis (10) 4. Depression (10)

α -antagonists – medicinal substances directly blocking α -adrenergic receptors.

Classification	α_1, α_2 -antagonists	α_1 - antagonists	α_2 - antagonists
Drugs	<ol style="list-style-type: none"> 1. Fentolamine (Regitin) 2. Dihydroergotamine (Redergin) 3. Pyrroxane 4. Nicergoline (Sermion) 	<ol style="list-style-type: none"> 5. Prazosin (Minipress) 6. Terazosin (Kornam) 7. Doxazosin (Cardura) 8. Tamsulosin (Omnice) 	<ol style="list-style-type: none"> 9. Yohimbine
Mechanism of action	<ol style="list-style-type: none"> 1. Block the α_1 and α_2-adrenergic receptors and inhibit the transmission of excitation in the adrenergic synapses \rightarrow \downarrow peripheral resistance of blood vessels and blood pressure, \uparrow norepinephrine release into the synaptic cleft 2. They \downarrow pressor effect of adrenaline, because after the blockade of α-adrenergic receptors the vasodilating action of adrenaline is manifested due to activation of β_2-adrenergic receptors 	<ol style="list-style-type: none"> 1. Block postsynaptic α_1-adrenoreceptors \rightarrow arterio- and vein-dilating effect \rightarrow \downarrow venous return of blood to the heart \rightarrow \downarrow peripheral resistance \rightarrow \downarrow pre- and post-load on the myocardium 2. Blockade of α_{1A}-adrenergic receptors \rightarrow \downarrow tonus of smooth muscles of the prostatic part of the urethra and the neck of the bladder 	<ol style="list-style-type: none"> 1. Block the α_2-adrenergic receptors
Pharmacological effects	<ol style="list-style-type: none"> 1. Dilation of peripheral vessels (1,3,4) and cerebral vessels (4) 2. Hypotensive 3. Narrowing of intracerebral vessels (2) 	<ol style="list-style-type: none"> 1. Hypotensive (5-7) 2. \downarrow tonus of smooth musculature of the prostatic part of the urethra (5,7,8) 	<ol style="list-style-type: none"> 1. Improves blood circulation of the pelvic organs, increases the potency
Indications for use	<ol style="list-style-type: none"> 1. Pheochromocytoma (1) 2. Violations of peripheral circulation: Raynaud's disease, endarteritis (1,2,4) 3. Disturbance of cerebral circulation (4) 4. Trophic ulcers of limbs, pressure sores (1) 5. Hypertensive crisis (1,2,3) 6. Migraine (2,4) 	<ol style="list-style-type: none"> 1. AH (5-7) 2. Hyperplasia of the prostate (5,7,8) 3. Violations of peripheral blood circulation: Raynaud's syndrome (5) 	<ol style="list-style-type: none"> 1. Psychogenic impotence
Side effects	<ol style="list-style-type: none"> 1. Arterial hypotension 2. Tachycardia 3. Dyspepsia 	<ol style="list-style-type: none"> 1. Dizziness, insomnia 2. Dyspepsia 	<ol style="list-style-type: none"> 1. Tremor 2. Tachycardia, arterial hypotension
Contraindications	<ol style="list-style-type: none"> 1. Organic changes in the heart and vessels 2. Arterial hypotension 	<ol style="list-style-type: none"> 1. Pregnancy and lactation (5) 	<ol style="list-style-type: none"> 1. Arterial hypotension

β -agonists – medicinal substances directly stimulating β -adrenergic receptors.

Classification	β_1, β_2 -agonists	β_1 -agonists	β_2 -agonists
Drugs	1. Isoprenaline (Izadrin) 2. Orciprenaline sulfate (Astomopent, Alupent)	3. Dobutamine (Dobutrex)	<u>Intermediate-acting (up to 3-4 h.):</u> 4. Salbutamol (Ventolin, Salgim) 5. Fenoterol (Berotek) <u>Long-acting (~ 12 h):</u> 6. Salmeterol (Serevent) 7. Clenbuterol (Spiropent) 8. Formoterol (Foradyl)
Mechanism of action	Stimulate the β_1 - and β_2 -adrenergic receptors 1. Stimulation of β_1 -adrenergic receptors \rightarrow \uparrow Heart rate and contraction, excitability, conduction (cardio-stimulating effect) 2. Stimulation of β_2 -adrenergic receptors \rightarrow bronchodilating and tocolytic action, dilation of vessels of the brain, heart, skeletal muscles and liver	Stimulation of β_1 -adrenergic receptors \rightarrow positive inotropic action, weak chronotropic action	Stimulation of β_2 -adrenoreceptors \rightarrow bronchodilating action, \downarrow tonus of the pregnant uterus (tocolytic action), dilation of vessels of the brain, heart, skeletal muscles and liver
Pharmacological effects	1. Cardiostimulating 2. Bronchodilating 3. \downarrow PVR \rightarrow \downarrow BP 4. Tocolytic (2)	1. Cardiostimulating (positive ino- and weak chronotropic action)	1. Bronchodilating 2. Improvement of mucociliary clearance 3. Tocolytic
Indications for use	1. Treatment and preventing of attacks of bronchial asthma (inhalation) 2. Violation of AV conductivity (sublingually) 3. The threat of premature birth (2)	1. Cardiogenic shock 2. Heart surgery 3. Chronic heart failure in the acute stage	1. Causing an attack of asthma (4,5) 2. Prevention of asthma attacks (6-8) 3. Asthmatic status (4,5) 4. The threat of premature birth
Side effects	1. Tachycardia 2. Nausea, dry mouth 3. Arm tremors	1. Tachycardia, arrhythmias, pain in the heart, headache 2. Nausea, vomiting	1. Tachycardia 2. Tremor, headache
Contraindications	1. Acute myocardial infarction 2. Angina pectoris 3. Thyrotoxicosis	1. Idiopathic hypertrophic subaortic stenosis	1. Structural heart defects, IHD 2. Thyrotoxicosis 3. Arrhythmias

HR - heart rate, PVR – peripheral vascular resistance, AV-conductivity – atrioventricular conductivity, IHD – ischemic heart disease

β-antagonists (β- blockers) – drugs directly blocking β-adrenergic receptors.

Classification	β ₁ , β ₂ - blockers	β ₁ - blockers	Mixed-action β- blockers	β- blockers with ISA
Drugs	1. Propranolol 2. Pindolol 3. Sotalol 4. Timolol 5. Nadolol	6. Atenolol 7. Metoprolol 8. Bisoprolol 9. Talinolol 10. Betaxolol 11. Nebivolol	12. Labetalol 13. Carvedilol	14. Пиндолол 15. Ацебуталол 16. Целипролол
Mechanism of action	1. Block β ₁ and β ₂ -adrenergic receptors	1. Block β ₁ -adrenergic receptors (6-10) 2. Affects the release of NO in vessels → vasodilation (11)	1. Block α- and β-adrenergic receptors	1. Slightly stimulate β ₁ or β ₂ -adrenoreceptors. NB! With an excess of catecholamines, such a weak stimulation is equal to the blockade of these receptors.
Pharmacological effects	1. Hypotensive (Block of β ₁ -adrenoreceptors of renal juxtaglomerular apparatus → ↓ renin secretion → ↓ tonus of peripheral vessels; Block of β ₁ -adrenergic receptors of the heart → ↓ systolic blood pressure; Depression of the central links of the sympathetic nervous system → ↓ of the tone of the peripheral vessels) 2. Antianginal (Blockage of β ₁ -adrenergic receptors of the heart and suppression of the central links of the sympathetic nervous system → ↓ heart rate → ↓ stroke and minute output → ↓ myocardial oxygen demand) 3. Antiarrhythmic (Block β ₁ -adrenoreceptors of the conduction system of the heart → ↓ automatism, conduction and excitability of the myocardium) 4. ↓ IOP (1, 4, 10)			
Indications for use	1. AH, 2. IHD, 3. Tachyarrhythmias, 4. Thyrotoxicosis, 5. Glaucoma (1,4,10), 6. Acute myocardial infarction (6-9), 7. CHF (7,8,13)			
Side effects	1. Bronchospasm 2. Bradycardia, AV blockade 3. The withdrawal syndrome 4. Dyspepsia			
Contraindications	1. Bronchial asthma 2. Bradycardia, AV-blockade, SA-blockade II-III degree, sick sinus syndrome 3. Arterial hypotension 4. Severe heart failure 5. Pregnancy (relative contraindication)			

ISA – intrinsic sympathomimetic activity, IOP - intraocular pressure, CHF - chronic heart failure, CHD - ischemic heart disease