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 8: « DRUGS AFFECTING THE EFFERENT INNERVATION. CHOLINERGIC DRUGS. MUSCARINIC AGONISTS. ANTICHOLINESTERASE DRUGS. MUSCARINIC ANTAGONISTS»

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 acting on the parasympathetic nervous system are widely used in many areas of medical practice (ophthalmology, neurology, therapy, surgery) and play an important role in the complex therapy of emergency conditions. For this reason, knowledge of the pharmacology of these substances is necessary for the future doctor regardless of the chosen specialty.

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.General scheme of structure, neurotransmitters and receptors of peripheral (somatic and autonomic) nervous system. Cholinergic signaling.

2. Structure of cholinergic synapses and mechanism of nerve impulse transmission. Mechanism of acetylcholine release and its regulation. 3.

3. Molecular structure and heterogeneity of choline receptors: muscarinic (M1-M4) and nicotinic (Nm, Hn) choline receptors. Localization and effects of physiological and pharmacological stimulation.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Cholinergic agonists (cholinomimetic agents). Definition and classification Features of pharmacodynamics and pharmacokinetics of cholinomimetic agents.

2.M-cholinomimetics (pilocarpine, betanechol): effect on eye, smooth muscles of internal organs, gland secretion, cardiovascular and central nervous system; use, side effects, contraindications.

3.M, H-cholinomimetics (acetylcholine chloride); pharmacological effects.

4.Anticholinesterase agents. Reversible cholinesterase inhibitors: neostigmine, pyridostigmine bromide, physostigmine, donepezil, rivastigmine, galantamine. Irreversible cholinesterase inhibitors (organophosphorus compounds: ethyl nitrophenylethyl phosphonate (Armin), insecticides (Malathion), chemical warfare agents). Pharmacological effects, side and toxic effects of anticholinesterase agents; treatment of poisoning: cholinesterase reactivators (pralidoxime mesylate, trimedoxime bromide), choline blockers (atropine sulfate). Acetylcholine release stimulants (itoprid).

5.Pharmacodynamic differences between direct-acting and indirect-acting cholinomimetics.

6. Main indications and contraindications for the use of cholinomimetic agents

7. Choline blocking agents. Definition and classification.

8. Drugs that inhibit the release of acetylcholine (botulinum toxin A); use, side effects.

9. M-cholinoblockers: atropine, hyoscine hydrobromide, ipratropium bromide, propantelline bromide, dicycloverine, tropicamide, pirenzepine, tolterodine, darifenacin. Ef-

fect of M-cholinoblockers on the eye, smooth muscles of internal organs, glandular secretion, cardiovascular and central nervous system.

10. Comparative characteristics of M-cholinoblockers, use, side effects, contraindications. The main signs of poisoning with M-cholinoblockers. Measures of pre-hospital and medical assistance. Prevention of poisoning.

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. Drugs that cause accommodation paralysis and are used in eyeglass fitting.
2. Drugs used to reduce bronchial smooth muscle tone.
3. Drugs used in gastroenterology.
4. Drugs used for controlled hypotension and hypertensive crises.
5. The possibility of using curare-like drugs in 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.
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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.

Muscarinic and nicotinic agonists are drugs directly or indirectly stimulating muscarinic and/or cholinergic receptors.

Classification	**Muscarinic agonists**	**Muscarinic and nicotinic agonists**	
		Direct acting	**Indirect acting (=*anticholinesterase agents*)**
Drugs	**1. Pilocarpine hydrochloride** **2. Aceclylidine**	**3. Acetylcholine** **4. Carbachole**	*Reversible:* **5. Physostigmine** **6. Neostigmine (Proserin)** **7. Galantamine** *Irreversible:* **8. Armin** **9. Organophosphorus_compounds (Chlorophos, Dichlorvos)**
Mechanism of action	Direct stimulation of muscarinic receptors of endings of postganglionic parasympathetic nerve fibers.	Direct stimulation of muscarinic and nicotinic receptors	Inhibit the activity of the acetylcholinesterase enzyme (reversibly/ irreversibly) → prevent the hydrolysis of acetylcholine → increase the effect of acetylcholine on muscarinic and nicotinic receptors.
Pharmacological effects	**1. Myos, ↓ IOP, spasm of accommodation** **2. ↑ secretion of exocrine glands** **3. ↓ AD, heart rate, conduction, contractility** **4. ↑ tone of bronchi, bladder, motility of the gastrointestinal tract** 5. Stimulation of neuromuscular conduction in small doses (3-9)		
Indications for use	1. Glaucoma 2. Atrophy of the optic nerve (1) 2. Atony of the intestine, bladder (2) 3. Rg-diagnostics of diseases of the stomach, intestines (2)	1. Experimental pharmacology (3) 2. Glaucoma (4)	1. Glaucoma (5.8) 2. Atony of the intestine, bladder (6,7) 3. Myasthenia gravis, paresis, paralysis (5-7) 4. Antidotes for non-depolarizing neuromuscular blockers and muscarinic antagonists intoxication (5-7)
Side effects	1. Myisis, accommodation spasm, pain in the eyes 2. Lacrimation 3. Twilight vision disturbance (1)	1. Bronchospasm 2. Hypersalivation, nausea, vomiting, ↑ intestinal peristalsis 3. Arrhythmia 4. Miosis 5. Twitching of the muscles of the tongue and skeletal musculature	
Contraindications	1. Iritis, iridocyclitis, uveitis 2. Bronchial asthma 3. Angina pectoris	1. Bronchial asthma 2. Angina pectoris 3. Epilepsy, hyperkinesis	

IOP – intraocular pressure

Muscarinic antagonists are drugs directly blocking muscarinic receptors.

Classification	**Muscarinic antagonists**	
	Non-selective	**Selective**
Drugs	**1. Atropine sulfate** **2. Tropicamide** **3. Scopolamine hydrobromide** **4. Platifillin hydrotartrate**	**5. Pirenzepine (Gastrotsepin)** **6. Ipratropium bromide (Atrovent)** **7. Tiotropium bromide (Spiriva)** **8. Butylskopolamine bromide (Buscopan)**
Mechanism of action	Block muscarinic receptors → Interfere the interaction of acetylcholine mediator with them → parasympathetic innervation of organs is blocked	
Pharmacological effects	1. Mydriasis, ↑ IOP, accommodation paralysis 2. ↑ heart rate and myocardial contractility 3. ↓ secretion of exocrine glands 4. ↓ bronchus tone (bronchial dilatation) 5. ↓ smooth muscle tone, gastrointestinal motility	
Indications for use	1. Bradycardia, AV blockade (1,3,4) 2. Spasm of the intestines and urinary tract (1,3,4) 3. Gastric and duodenal ulcer (1, 3, 4) 4. Premedication (1, 3) 5. Poisoning with M-cholinomimetics and AChE (1) 6. Investigation of the fundus (1-4) 7. Irit, iridocyclitis (1, 2) 7. Marine and air sickness (3)	1. Gastric and duodenal ulcer (5, 8) 2. Bronchial asthma, chronic obstructive bronchitis (6, 7) 3. Spasm of the intestines and urinary tract (5, 8) 4. Irritable bowel syndrome (8)
Side effects	1. Dry mouth 2. Middriasis, ↑ IOP, paralysis of accommodation 3. Tachycardia 4. Paresis of the intestine 5. Stimulation of urination	1. Dry mouth 2. Violation of accommodation 3. Retention of urination, constipation 4. Increase in sputum viscosity (6, 7)
Contraindications	1. Glaucoma 2. Obstructive diseases of the intestines and urinary tract.	1. Glaucoma 2. Hypertrophy of the prostate

AChE – anticholinesterase agents

Muscarinic and nicotinic agent's intoxication

Muscarinic agonists	Anticholinesterase agents	Muscarinic antagonists
Myos, ↓ IOP, spasm of accommodation		Mydriasis, ↑ IOP, paralysis of accommodation
Salivation, sweating		Dry hyperemic skin, hyperthermia
Bradycardia, AV blockade		Tachycardia
Bronchospasm		Dry mouth
Vomiting, diarrhea, tenderness in the abdomen, involuntary urination		Urination retention
↓ BP	BP first ↓, then ↑	–
Minor twitching of muscles, agitation, convulsions	Excitation is more pronounced (organophosphorus compounds penetrate into the the CNS), convulsions	Mental excitement, delirium, hallucinations, acute psychosis

Intoxication treatment

General (non-specific) therapy		
1. Gastric lavage; 2. The use of laxatives and adsorptive agents to prevent further absorption; 3. Catheterization of the bladder, forced diuresis; 4. Hemosorption, hemodialysis.		
Specific (antidote) therapy		
Muscarinic antagonist (atropine)	Muscarinic antagonist (atropine) + Cholinesterase reactivators (dipyroxime, isonitrosine) in the first hours	Anticholinesterase drugs (physostigmine)
Symptomatic therapy		
1. Correction of respiratory and cardiovascular disturbances		1. Drugs depressing the CNS (diazepam)
2. Diazepam for psychomotor agitation		2. ß-blockers