

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 22: « DIURETICS. DRUGS AFFECTING THE TONE AND
CONTRACTIVE ACTIVITY OF UTERUS»**

Time: 3 hours

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

2022

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

Diuretics and drugs that affect the myometrium are widely used in the clinic of internal diseases, surgery, obstetrics and gynecology. For this reason, every doctor should be able to prescribe drugs of these groups, taking into account the peculiarities of their pharmacokinetics and pharmacodynamics, to know, prevent and promptly identify possible complications of such therapy.

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 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. The main functions of the kidneys and their role in maintaining homeostasis.
2. Nephron as a structural and functional unit of the kidney.
3. Renin-angiotensin-aldosterone system and its role in the pathology of the cardiovascular system.
4. The concept of acute and chronic renal failure.
5. Features of the anatomy and physiology of the myometrium.

CONTROL QUESTIONS ON THE TOPIC OF THE LESSON

1. Diuretics, classification: thiazide and thiazide-like: hydrochlorothiazide, chlorthalidone, indapamide; loop (furosemide); potassium-sparing (triamterene, spironolactone, eplerenone); osmotic (mannitol); carbonic anhydrase inhibitors (acetazolamide); watercolors (demeclocycline).
2. Mechanisms of diuretic action, speed of onset and duration of effect. Effect of diuretics on ionic balance.
3. Criteria for choosing diuretics, use, side effects. Principles of combining diuretics.
4. Medicines that affect the tone and contractile function of the myometrium. Classification.
5. Tocomimetics. Medicines to enhance labor activity (oxytocin, dinoprost); agents for stopping uterine bleeding (ergot preparations, oxytocin), tocolytic agents (hexoprenaline, etc.): mechanisms of action, pharmacological effects, use, features of the pharmacological group.

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. Medicinal plants as a means of increasing diuresis.
2. Drugs that promote the excretion of urinary calculi.
3. Renal colic, clinical manifestations and methods of relief.

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. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 1 : для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической фармакологии с курсом

ФПКИПК. - Витебск: ВГМУ, 2019. - 294 с.: ил., табл. - Рек. УМО по высш. мед., фармацевт. образованию.

3. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 2 : для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической фармакологии с курсом ФПКИПК. - Витебск: ВГМУ, 2019. - 165 с.: ил. - Рек. УМО по высш. мед., фармацевт. образованию.

4. 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.

5. 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.

DIURETICS

Diuretics are medicinal substances that increase diuresis

Classification	Loop	Thiazide	Thiazide-like	Osmotic	Inhibitors of carbonic anhydrase
Drugs	1. Furosemide 2. Torasemide 3. Ectric acid	4. Hydrochlorothiazide	5. Chlorthalidone 6. Indapamide 7. Clopamide	8. Mannitol	9. Acetazolamide
Mechanism of action	Inhibit active transport of chloride ions in the ascending part of the loop Henle → reduce reabsorption Na ⁺ , K ⁺ , Mg ²⁺ and Ca ²⁺	Inhibit the active transport of chloride ions in the distal tubules → reduce reabsorption Na ⁺ , K ⁺ and Mg ²⁺ , but Ca ²⁺ retention		Increase osmolarity of urine in the proximal renal tubules and, to a lesser extent, in the descending part of the Henle loop → reduce water reabsorption	Inhibits carbonic anhydrase enzyme in the proximal tubules → reduces reabsorption of bicarbonate Na ⁺ , promotes K ⁺ , Ca ²⁺ elimination and acidosis
Pharmacological effects	1. Diuretic (1-9). 2. Hypotensive (1-7). 3. Dehydration (8). 4. Decrease in intraocular and intracranial pressure (1-3, 8, 9).				
Indications	1. Hypertensive crisis (1,3). 2. Arterial hypertension (1-7). 3. Forced diuresis (1,3-5) 4. Heart failure, cirrhosis, toxicosis of pregnant women, nephrosis, nephritis (1-7). 5. Diabetes insipidus, glaucoma (4-7). 6. Edema of the brain and lungs, acute and chronic renal failure (1,3).			1. Cerebral and pulmonary edema (8), glaucoma (8,9). 2. Forced diuresis (in poisoning with water-soluble poisons) (8). 3. Edema associated with chronic heart failure, craniocerebral trauma, epilepsy, pulmonary emphysema, salicylate poisoning, severe hyperphosphatemia, metabolic alkalosis (9).	
Side effects	- Hypokalemia (1-7,9), - hypocalcemia (1-3), - hypochloremic alkalosis (1-7), - hyponatremia (1-8), - hypervolemia (8), - metabolic acidosis (9), - hypercalcemia (4-7), - hyperuricemia, hyperglycemia (1-4), - ototoxicity, (1-3).				
Contraindications	- Allergy to sulfonamide-containing drugs - anuria - hypovolemia	- Allergy to sulfonamide-containing drugs - Severe renal failure - gout - hyperuricemia, hypokalemia		- heart failure - severe renal insufficiency - anuria	- severe forms of COPD - acute renal failure - liver failure - acidosis - pregnancy
NB!	Incompatible with aminoglycosides - risk of hearing loss. Eliminate K ⁺ and increases sensitivity to cardiac glycosides → exclude combination	Delay uric acid → danger of gout attack		Has local irritating effect → isn't administered subcutaneously and intramuscularly	Do not take more than 5 days → metabolic acidosis.
Alcohol intensifies the cardiotoxic effect of diuretics. To be taken before meal: 1, 5, 6. To be taken after meal: 2, 3, 4, 7.					

DIURETICS (continued)

Classification	Potassium-sparing	Different groups with a diuretic effect	Vegetable agents: Monopreparations and combined *
Drugs	<ol style="list-style-type: none"> 1. Spironolactone 2. Triamterene 3. Amyloride 	<ol style="list-style-type: none"> 4. Aminophylline 5. Cardiac glycosides (Digoxin, Digitoxin, Strophanthine, etc.) 	<ol style="list-style-type: none"> 6. Leaves of cranberries 7. Bearberry Leaves 8. Grass horsetail field 9. Artichoke extract (hofitol) 10. Kanefron * 11. Phytolysin * 12. Cyston *
Mechanism of action	<ol style="list-style-type: none"> 1. Blocks aldosterone receptors in collective and distal tubules → reduces reabsorption Na^+, Cl^- and water, detain K^+, Mg^{2+} (1). 2. Reduces the permeability of epithelial membranes of collecting tubules for ions Na^+ (2,3) 	<ol style="list-style-type: none"> 1. Improve renal circulation and filtration processes in the glomeruli 	Contain biologically active substances that improve kidney circulation and filtration processes, partially affect tubular reabsorption
Pharmacological effects	<ol style="list-style-type: none"> 1. Diuretic (1-12). 2. Hypoazotemic (9-12). 3. Anti-inflammatory, antimicrobial, spasmolytic (6,7, 10-12). 4. Choleric (6,7). 5. The vasodilator (4,5). 6. Hypotensive (1-4). 		
Indication	<ol style="list-style-type: none"> 1. Hyperaldehydonism, liver cirrhosis (1). 2. Together with saluretic, cardiac glycosides for prophylaxis of hypokalemia, chronic heart failure, arterial hypertension, nephritis (1-3) 	<ol style="list-style-type: none"> 1. Complex therapy of edema in cardiac and renal insufficiency (4,5). 2. Disorders of cerebral circulation, broncho-obstructive processes (4). 	<ol style="list-style-type: none"> 1. Prevention of edema in cardiovascular and renal pathology (6-12). 2. Inflammatory processes of the urinary bladder and urinary tract, nephritis (6,7,10-12). 3. urolithiasis disease (6). 4. Cholecystitis, chronic hepatitis (9).
Side effects	<ul style="list-style-type: none"> - Hyperkalemia, hyponatremia (1-3), - gynecomastia, thrombosis (1), - hyperglycemia, hyperuricemia (2), - nausea, vomiting, headache, lowering blood pressure (1-4,10). 		
Contraindications	<ul style="list-style-type: none"> - Hyperkalemia, - acute renal failure, - liver cirrhosis, - macrocytic anemia (3). 	<ul style="list-style-type: none"> - acute myocardial infarction, - epilepsy, stomach and duodenal ulcer (4), -intoxication with glycosides, unstable angina, pronounced bradycardia, AV blockade (5). 	<ul style="list-style-type: none"> - Hypersensitivity - glomerulonephritis, phosphate nephrolithiasis (11).
NB!	<ul style="list-style-type: none"> - do not combine with ACE inhibitors (риск развития гиперкалиемии). - усиливают действие тиазидных диуретиков. 	Aminophylline is forbidden to be take simultaneously with the xanthines-containing products, glucose solution. Cardiac glycosides can easily provoke glycoside intoxication!	During the storage of Kanefron's solution, slight turbidity or precipitation of a slight precipitate is possible, it does not affect the effectiveness of the drug.
Diuretics are recommended to be taken in the morning to avoid nocturia. Also development of tolerance is possible. After meal: 2,6, 11,12. During meal: 7.			

DRUGS AFFECTING TONE OF UTERUS. Tocomimetics are drugs increasing tone of uterus

Classification	Labor inducing drugs (drugs increasing the rhythmic contraction of the myometrium)			Drugs for hypotonic uterine bleeding (agents increasing tonic contraction of the myometrium)		
	Hormonal drugs of the pituitary gland	Estrogenic preparations and antiprogestagens *	Prostaglandins and their synthetic analogues *	Ergot preparations	Ganglionic blockers	Herbal preparations
Drugs	1. Oxytocin 2. Demoxytocin	3. Estrone (Folliculin) 4. Estradiol dipropionate (Femoston) 5. Mifepristone * (Gynepriston)	6. Dinoprost 7. Dinoprostone (Prostin E2) 8. Misoprostol * (Mirolut)	9. Ergometrine maleate (Ergonovin) 10. Ergotamine	11. Pachycarpine	12. Grass of shepherd's purse
Mechanism of action	1. Violation of the transmembrane motion of ions In smooth musculature myometrium → uterine contraction (1-5). 2. Stimulation of cervical ripening due to the increased activity of collagenase and hyaluronidase → the opening of the cervix during normal delivery (3-8).			1. Direct stimulation of the myometrium; Partial agonist / antagonist of α-adrenergic, dopaminergic and serotonergic receptors (9,10) 2. Reduces the excitability of the ganglia of the vegetative nervous system and inhibits conduction of nerve impulses (11). 3/ Contains vitamin K, choline and acetylcholine, tyramine, organic acids and saponins, due to which increases blood coagulability (12).		
Pharmacological effects	1. Increase the tone and enhance rhythmic contractions of the myometrium (1-8, 11). 2. Causes prolonged tonic contractions of the uterus, vasoconstrictor effect, influence on the central nervous system (9,10). 3. Increase the sensitivity of the uterus to oxytocin and prostaglandins (3-5). 4. Strengthens the walls of the vessels of the uterus (12).					
Indication	1. Weak contractions, premature pregnancy (1-8). 2. Hypotonic uterine bleeding, involution of the uterus after childbirth and abortion (1,2, 9-11). 3. Termination of pregnancy for medical reasons (5-8). 4. Climax, infertility, amenorrhea (3,4). 5. Dysfunctional uterine bleeding and bleeding against fibroids (12).					
Side effects	1. Allergic reactions, dyspeptic disorders (1-12). 2. Bradycardia, bronchospasm, water retention (1,2). 3. Depression, weight gain, endometrial hyperplasia, tenderness of the mammary glands, edema, liver damage (3-5). 4. Atony of the intestine and bladder (11). 5. Increase in blood clotting. lowering blood pressure for a long time application (12).					
Contraindications	1. Pregnancy. 2. Hypersensitivity. 3. Wrong fetal position 4. Inflammatory pelvic disease. 5. Presence of factors predisposing to uterine rupture. 6. Severe diseases of the heart, kidneys and liver.					
NB!	Oxytocin to be used cautiously in combination with sympathomimetics; when intravenous injection constant monitoring is needed. Ergometrine maleate strengthens the action of other vasoconstrictors. It is not recommended to take dinoprostone longer than for 2 days.					

Tocolytics and drugs reducing the tone of the uterus

Classification	β_2 - adrenomimetics	Gestagenic agents
Drugs	<ol style="list-style-type: none"> 1. Fenoterol (Partusisten) 2. Ritodrine 3. Hexoprenaline (Ginipralin) 4. Salbutamol 	<ol style="list-style-type: none"> 5. Allylestrenol (Turinal) 6. Dydrogesterone (DUFASTON) 7. Progesterone (Utrogestan)
Mechanism of action	Excitation of β_2 -adrenoreceptors of myometrium → muscular relaxation	Interact with steroid membrane and cytosolic receptors → physiological and morphological changes in target organs
Pharmacological effects	<ol style="list-style-type: none"> 1. Tocolytic (1-7). 2. Bronchodilating(1-4). 	
Indications	<ol style="list-style-type: none"> 1. Prevention and treatment of threatening abortion and premature labor (1-7). 2. Violation of utero-placental circulation, endometriosis, infertility, dysmenorrhea, premenstrual syndrome, breast diseases, postmenopausal replacement therapy (5-7). 	
Side effects	<ol style="list-style-type: none"> 1. Allergic reactions. 2. Tachycardia, pain behind the sternum. 3. Tremor, anxiety, headache, dizziness 4. Dyspeptic disorders. 5. Hyperglycemia, hyperkalemia. 6. Muscle weakness, spasms. 	<ol style="list-style-type: none"> 1. Headache, drowsiness, decreased libido. 2. Hirsutism, acne, weight gain. 3. Depression. 4. Edema
Contraindications	<ol style="list-style-type: none"> 1. Hypersensitivity. 2. Hypertrophic obstructive cardiomyopathy, tachyarrhythmias. 	<ol style="list-style-type: none"> 1. Hypersensitivity. 2. Malignant neoplasms of genital organs and breast. 3. Vaginal and uterine bleeding of unknown etiology. 4. Diseases of the liver.
NB!	<p>When using β_2-adrenomimetics in obstetrics, it is recommended to monitor potassium levels in blood, blood pressure, heart rate in pregnant women, and the heart rate in the fetus. During treatment with progesterone concentration is decreased (care must be taken when driving vehicles and engaging in other potentially dangerous activities requiring rapidity of psychomotor reactions). The use of any progestogen to prevent a habitual miscarriage currently in Western countries is considered unfounded.</p>	