

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 23: «DRUGS AFFECTING BLOOD»

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

Blood diseases, both hereditary and acquired, are considered among the most life-threatening and account for about 8% of the total number of diseases. In the mechanism of thrombosis, acute and chronic bleeding from internal organs, an important role is played by changes in the vessel wall, platelet aggregation properties, hemodynamic parameters, activity of blood coagulation factors, fibrinolysis. Since blood is a liquid connective tissue that supplies organs with oxygen and essential nutrients, a violation of hematopoiesis inevitably leads to disturbances in all body systems. Knowledge of the pharmacokinetics and pharmacodynamics of drugs that affect the blood system will enable the future doctor to learn how to navigate in the selection of adequate therapy for patients with these diseases.

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. Hematopoiesis. Mechanisms of blood coagulation. Metabolism of iron in the body.
2. Classification of anemia. Etiology and pathogenesis of iron deficiency anemia.
3. Etiology and pathogenesis of leukemia.

CONTROL QUESTIONS ON THE TOPIC OF THE LESSON

1. Medicines used for anemia. Pharmacological characteristics of the group.
2. Medicines that stimulate leukopoiesis. Features of pharmacodynamics and pharmacokinetics.
3. Antihemorrhagic and hemostatic agents. Their place in modern pharmacology.
4. Antiaggregants and anticoagulants. Thrombolytics. Pharmacological characteristics.

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. Coagulants of plant origin. Their role in modern medicine (filling in workbooks).
2. Therapeutic nutrition for anemia.

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.

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Agents **increasing** blood coagulation

Classification	Hemostatic agents		Inhibitors of fibrinolysis
Drugs	Topical	Resorptive	
Mechanism of action	The natural components of the coagulation system – provide the formation of blood clot (1-4, 6), ↑ formation of thromboplastin (5).		Inhibition of activation of the plasminogen → plasmin formation inhibition. Brakekinin systems and the activity of fibrinolysis (7-9). Inhibit fibrinolysin (plasmin), heparin → inhibit fibrinolysis and ↑ activity of the coagulation system blood (10).
Pharmacological effects	1. Hemostatic 2. Anti allergic effect, ↑ liver detoxification (7) 3. Inhibition of proteolytic enzymes (trypsin, chymotrypsin, kallikrein, plasmin) (10)		
Indications	1. Bleeding: capillary (1, 2, 5) and parenchyma (1, 2, 5). 2. Hypofibrinogenemia: postpartum hemorrhage. DIC-syndrome(3) 3. Bleeding against liver diseases and vitamin K absorption disorders (4) 4. Congenital/acquired coagulation factors deficiency (6)		1. Local (nasal bleeding, tonsillectomy, extraction of teeth, etc.) and generalized (in thoracic and abdominal surgery) 2. Acute pancreatitis (contrycal), ↑ risk of bleeding (gordox) 3. Bleeding during an overdose of fibrinolytic agents
Side effects	1. Allergic reactions, nausea, headache(5)		1. Intra vascular thromboses 2. Hypotension, arrhythmia 3. Impairment of color vision (8) 4. Allergic reactions (8, 10)
Contraindications	1. Increased blood clotting 2. Thrombo embolism		1. DIC-Syndrome 2. Bleeding from the kidneys and ureters 3. Propensity for thrombosis and embolism 4. Pregnancy
NB!	Not for i/m or i/v use → thrombosis	Hemophilia A (VIII factor), haemophilia B (IX)	Aprotinin is useful for extra corporeal circulation of blood during heart operations and liver transplantation.
	Vegetable coagulant: Leaves of nettle, yarrow, corn bark, arnica flowers		

Blood thinners

Anti platelets are drugs decreasing platelet aggregation

Classification	Cyclooxygenase (COX) inhibitors	Phosphodiesterase inhibitors	ADP receptor blockers	Glycoprotein IIb / IIIa receptors Blockers
Drugs	1. Acetyl salicylic acid (aspirin) <i>in small doses</i>	2. Dipyridamole	3. Ticlopidine 4. Clopidogrel	5. Abciximab 6. Tirofiban
Mechanism of action	Their reversible blockade of COX of thrombocytes (an enzyme involved in the formation of thromboxane A2 and prostacyclin from arachidonic acid).	It blocks phosphodiesterase and adenosine uptake → ↑ cAMP level ↓ intracellular content of Ca ²⁺ → ↓ platelet aggregation and has a vasodilating effect.	Block ADP receptors on the platelet membrane → interfere with the interaction of platelet receptors with fibrinogen.	Eliminate the activation of glycol protein receptors GP IIb / IIIa → disrupt platelet aggregation.
Pharmacological effects	1. Antiplatelet 2. Improve myocardial and cerebral microcirculation 3. Coronary vasodilatation (2)			
Indications	1. Angina pectoris 2. Prevention of MI (in the presence of risk factors) 3. Prevention of thrombosis and embolism after operations on the heart and vessels	1. Prophylaxis of ischemic chronic cerebrovascular insufficiency 2. Prevention of thromboembolic complications after operations on peripheral vessels	1. Prophylaxis of thrombosis in patients with ischemic heart disease (after MI) 2. Atherosclerosis of cerebral and peripheral vessels 3. Intolerance to acetylsalicylic acid	1. Acute coronary syndrome 2. Atherectomy and angioplasty operations (in combination with aspirin and heparin).
Side effects	1. Dyspepsia 2. Risk of bleeding 3. Allergic reactions	1. Coronary steal when IHD. 2. Dyspepsia 3. ↓ AP, headache	1. Dyspeptic disorders 2. Thrombocytopenic purpura 3. Neutropenia, agranulocytosis (3)	1. Bleeding, thrombocytopenia 2. Allergic reactions
Contraindications	1. Exacerbation of erosion-ulcerative lesions of the gastrointestinal tract 2. Pregnancy 3. as an anti pyretic for viral infection in children	1. Acute myocardial infarction, unstable angina	1. Increased risk of bleeding 2. The gastro duodenal ulcer 3. Liver disease	1. Thrombocytopenia 2. Hemorrhagic diathesis 3. Aneurysm
NB!	The COX of the vascular wall restores its activity for several hours in contrast to the COX of platelets → anti thromboxane effect of prostacyclin. For ↓ irritating effect on the stomach → enteric-coated forms	Effective only in combination with aspirin or in direct anticoagulants	Antiplatelet effect → in 24-48 h. Peak action → in 3-10 days, and for acetylsalicylic acid in 1 h.	In the congenital absence of this receptor complex, blood loss develops - Glanzmann's thrombasthenia

Blood thinners (continued)
Anticoagulants– drugs reducing blood coagulation and prolonging coagulation time.

Classification	Direct anticoagulants		Indirect anticoagulants	Direct oral factor Xa inhibitors
	Indirect thrombin inhibitors	Direct thrombin inhibitors		
Drugs	1. Heparin <i>Low molecular weight heparins (LMWHs):</i> 2. Nadroparin (Fraxiparine) 3. Enoxaparin (Clexane) 4. Dalteparin (Fragmin) <i>Synthetic LMWH:</i> 5. Fondaparinux	6. Lepirudin, 7. Bivalirudin 8. Argatroban	9. Warfarin 10. Fenindione, 11. Acenocoumarol (syncumar) 12. Ethyldicoumarol (Neodicum Marine)	13. Rivaroxaban 14. Apixaban
Mechanism of action	<p>1. <i>Heparin</i> + Antithrombin III → blockage of thrombin active center → <i>inactivation of thrombin</i> (factor IIa); <i>inhibition</i> of a number of activated <i>coagulation factors</i> (XIIa, XIa, IXa and especially Xa (prothrombinase)).</p> <p>2. <i>LMWH</i> practically do not effect thrombin, mostly <i>affect X coagulation factor</i> (increase the effect of anti thrombin III on factor Xa).</p>	Independently attach to the active center of thrombin and do not require binding to anti thrombin III.	Vitamin K antagonists: block the synthesis of vitamin K-dependent coagulation factors (II - prothrombin, VII, IX, X) in the liver.	Selectively inhibit pro thrombinase (factor Xa) → the rein conversion of prothrombin to thrombin.
Pharmacological effects	1. Anticoagulant 4. Hypoglycemic, diuretic, anti-inflammatory, antiallergic, vasodilating (1) 2. Anti platelet 5. Choleragogue, relax the smooth musculature of the vessels, analgesic and sedative action (9-12) 3. ↓ plasma lipid level (1,6-8)			
Indications	Prevention and therapy of thromboembolic diseases and their complications (prevention of thrombosis during surgery, unstable angina, acute myocardial infarction, thrombosis and embolism of peripheral arteries and deep veins)			
Side effects	1. Bleeding of various localization, thrombosis-mourning 2. Paradoxical thrombosis (antibodies to heparin) 3. Allergic reactions	1. Bleeding	1. Bleeding 2. Alopecia 3. ↑ level of liver enzymes	1. Bleeding 2. ↑ level of hepatic enzymes 3. Nausea
Contraindications	1. Hemophilia, thrombocytopenia, hemorrhagic diathesis, bleeding 2. Malignant neoplasm and ulcerative lesions of the digestive tract 3. Dysfunction of the liver and kidneys			
NB!	Heparin is given to increase PPT (activated partial thromboplastin time) twice (30-35 sec) – this is optimal dose. Antidote for overdose - protamine sulfate.	For the treatment or prevention of thromboses associated with heparin-induced thrombocytopenia.	INR (international normalized ratio) should be controlled (INR < 2-3). Antidote is vitamin K (phytonadione).	Do not require a regular study of blood clotting.

Fibrinolytics– drugs that breakdown blood clots.

Classification	I generation	II generation
Drugs	1. Streptokinase 2. Urokinase 3. Antistreptase	1. The tissue activator of plasminogen (alteplase) 2. Recombinant plasminogen activator (reteplase) 3. Tenecteplase
Mechanism of action	Equally activate both plasminogen on the surface of the thrombus and plasminogen in the plasma → plasmin (fibrinolysin)	Activate predominantly plasminogen on the surface of the thrombus
Pharmacological effects	1. Fibrinolytic (dissolve the filaments of fibrin, destroy fresh thrombi in the arteries, veins and cavities)	
Indications	1. Thrombosis of veins and arteries 2. Acute myocardial infarction (1-2 days) 3. Pulmonary thrombo embolism	
Side effects	1. Bleeding 2. Allergic reactions(1-3)	
Contraindications	1. Acute bleeding 2. Recent (up to 10 days) surgery and trauma 3. Violations of the blood coagulation system 4. Recent hemorrhagic stroke 5. Dissecting aortic aneurysm	
NB!	1. Apart from streptokinase, all thrombolytic drugs are administered together with heparin (unfractionated or LMWHs), usually for 24 to 48 hours. 2. Thrombolysis shouldn't be done in patients with acute coronary syndrome but without ST-segment elevation.	

Anemia drugs (*erythropoiesis-stimulating agents*)

Anemia is a medical condition in which the red blood cell count or hemoglobin is less than normal.

Pathology	Drugs
Iron deficiency anemia (hypo chromic) NB! Ferrous iron (Fe^{2+}) combination with vitamin C is absorbed better. An exception is preparations of iron (III)-hydroxyl poly maltose complex (IPC, Maltofer)	Iron supplements: 1. Ferrous fumarate (Ferrocite) 2. Ferrous gluconate (Fergon, Ferralet) 3. Ferrous sulfate (Ferrousal, Ferosul) 4. Maltofer Cobalt supplements: 5. Ionic cobalt Human recombinant erythropoietin: 6. Epoetin alfa – i/v, s/c
Megaloblastic anemia	Cyanocobalamin (B12), folic acid (B9)

Rules for the prescribing of iron supplements:

1. Treatment begins with oral administration of drugs;
2. Iron preparations are prescribed 1 hour before meals or 2 hours after meals;
3. Monitor the effectiveness of therapy (A week later an increase in the number of reticulocytes, a month later - hemoglobin);
4. If oral use has no effect the drugs should be given intravenously;
5. Treatment begins with parenteral administration of drugs (after a tolerance test) In impaired absorption (diseases of the stomach and intestines) and with the aim of achieving rapid effects in severe anemia;
6. Prevent the simultaneous intake of iron preparations by mouth and by injection;
7. The duration of the course is at least 2 months.
8. To avoid darkening of the teeth, you should thoroughly rinse your mouth after taking iron-containing drugs.

Side effects: Metallic taste in the mouth, nausea, vomiting, decreased appetite, constipation, black stool.

Iron poisoning: Necrotizing gastroenteritis, vomiting, abdominal pain, bloody diarrhea, shock, metabolic acidosis, coma and death.

Help with poisoning: gastric lavage, **antidote is deferoxamine**, symptomatic treatment (correction of acidosis, anti-shock measures, gastrointestinal bleeding management).

Drugs effecting erythropoiesis and leucopoiesis (continued): agents stimulating / depressing erythropoiesis and leucopoiesis.

Classification	Leukopoiesis stimulants	Erythropoiesis inhibitors	
Drugs	1. Methyluracil 2. Pentoxyl 3. Leukogen <i>Human colony-stimulating factors:</i> 4. Filgrastim (Neupogen) 5. Lenograstim (granitocyte) 6. Molgramost (leukomax)	7. Phosphorus-32-radio labeled solution of sodium phosphate	8. Methotrexate 9. Mercaptopurine 10. Busulfan (myelosan) 11. Cyclophosphamide
Mechanism of action	1. ↑ synthesis of nucleic acids, proteins, cell division, leucopoiesis, tissue regeneration (1, 2) 2. ↑ leucopoiesis in severe disturbances (3) 3. Bond to the receptors of myeloid cells and ↑ Proliferation and differentiation of cells- Precursors of neutrophils (4,5) and monocytes / macrophage(6)	↓ Red bone marrow	1. Violation of the formation of purine and thymidine → ↓ DNA synthesis (8). 2. Disrupts the bio synthesis of purine nucleotides (9). 3. Inhibits myeloid tissue and granulocytopoiesis (10). 4. Active metabolites are formed in the liver (phosphamide and acrolein) → antitumor effect (11).
Pharmacological effects	1. ↑ Leucopoiesis, accelerate regeneration processes (1-3) 2. Regulate the production of neutrophils and their entry from the bone marrow into the blood (4,5) 3. regulates the production of granulocytes and monocytes / macrophages (6)	↓ erythrocyte formation	↓ leukocyte formation
Indications	1. Leukopenia 2. Patients with burns, long-lasting wounds (1, 2) 3. Aplastic anemia (6) 4. Bone marrow transplantation (4,6)	1. Polycythemia (erythremia)	1. Acute leukemia (8,9,11) 2. Lymphogranulomatosis (8) 3. Chronic myelogenous leukemia(10)
Side effects	1. Allergic reactions (1-3) 2. Skin vasculitides, musculo-articular pain, edema, pericardial and pleural effusion (6) 3. Leukocytosis, thrombocytopenia(4,5)	1. Thrombocytopenia 2. Anemia	1. Leukopenia, anemia 2. Nausea, vomiting, ulcerative stomatitis 3. Headache
Contraindications	1. Lymphogranulomatosis (1-3) 2. Myeloid leukemia(1-6)	1. Anemia, leukopenia, thrombocytopenia, 2. Heart failure, 3. Dysfunction of the liver and kidneys	1. Hypersensitivity 2. Leukopenia, thrombocytopenia 3. Pregnancy (8,10,11) 4. Diseases of the liver and kidneys