

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

Department of general and clinical pharmacology

Authors:

M.N.Mirge, assistant

A.V.Sennikava, senior lecturer

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

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 16: «DRUGS AFFECTING RESPIRATORY SYSTEM»

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

This topic opens the section of drugs that regulate the functions of the executive organs and systems. Respiratory organ pathology occupies a significant place in the therapeutic practice. The ability to prescribe a drug that affects the main links in the pathogenesis of bronchopulmonary disease is an important part of the activity of the therapist or any other profile.

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 objective:

- To develop their value-personal, spiritual potential, to form the qualities of a patriot and citizen, ready for active participation in the economic, pro-industrial, socio-cultural and public life of the country; to realize the social importance of their future professional activity, learn to comply with academic and labor 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. Anatomical and physiological features of the respiratory system;
2. Mechanisms of the main pathological conditions of the respiratory organs (bronchitis, bronchial asthma, COPD, pulmonary edema, etc.);
3. Pharmacological characteristics of H-cholinomimetics, H-cholinoblockers, M-cholinoblockers and adrenomimetics.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Drugs to treat bronchial asthma and relieve bronchospasm: β -adrenomimetics (salbutamol, salmeterol, formoterol), glucocorticosteroids (beclomethasone, budesonide), inhibitors of allergy mediators release (cromoglic acid, ketotifen), M-cholinoblockers (ipratropium bromide), Leukotriene receptor antagonists (zafirlukast, montelukast), phosphodiesterase inhibitors (aminophylline, theophylline and its prolonged forms), allergy mediator inhibitors (fenspiride), immunoglobulin E inhibitors (omalizumab). Choice of pharmacotherapy drugs for bronchial asthma, cessation and prevention of asthmatic attacks.

2. Stimulants of the respiratory center: almitrin, doxapram, bemgrid, etimi-zol, nikethamide. Mechanisms of stimulating effect of drugs on the function of external respiration. Comparative characteristics of respiratory stimulants from groups of analeptics and H-cholinomimetics. Pharmacodynamics of etimizole.

3. Surfactants (colfosceryl palmitate, poractant alfa) and stimulants of their synthesis (ambroxol), ways of administration.

4. Expectorants and mucolytic agents: preparations of thermopsis, potassium iodide, guaifenesin, ambroxol, acetylcysteine, dornase alfa.

5. Cough suppressants: dextromethorphan, prenexdiazine, codeine phosphate and other codeine-containing drugs.

6. Principles of action of different groups of drugs affecting respiratory functions, use, side effects.

7. Drugs used in treatment of pulmonary edema: morphine, furosemide, mannitol, sodium nitroprusside, hexamethonium benzosulfonate, aminophylline, ethyl alcohol. Principles of pharmacotherapy of pulmonary edema.

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. Phytotherapy of diseases of the respiratory organs.
2. Systemic glucocorticosteroids: principles of therapy of bronchospastic syndrome and possible complications.

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. Харкевич, Д. А. Фармакология : учебник для использования в учеб. процессе образоват. организаций, реализующих программы высш. образования по специальностям 33.05.01 "Фармация", 31.05.01 "Лечеб. дело", 31.05.02 "Педиатрия", 32.05.02 "Мед.-профилакт. дело", 31.05.03 "Стоматология" / Д. А. Харкевич. - 12 изд., испр. и доп. - Москва : ГЭОТАР-Медиа, 2017. - 754 с. : ил., табл., фот. - Рек. ФГАУ "ФИРО".

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 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 1. – 56 с.

5. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 2. – 84 с.

Respiratory stimulants (analeptics) are drugs stimulating respiratory and vasomotor centers in the medulla oblongata.

Classification	Central action	Reflex action	Mixed action
Drugs	1. Bemegride 2. Etymisol 3. Caffeine	4. Dopraxam 5. Cytiton 6. Lobeline hydrochloride	7. Cordiamine (niketamide) 8. Carbogen (O₂ + 1,5-90% CO₂)
Mechanism of action	Activate respiratory and vasomotor centers directly	Stimulation of the nicotinic receptors of the sino-carotid zone → ↑ activity of the respiratory center	Central effect + stimulation of chemoreceptors of the carotid glomerulus
Pharmacological effects	1. Stimulation of the respiratory center → ↑ <u>respiratory rate and</u> ↑ <u>breathing depth</u> 2. Stimulation of the vasomotor center → ↑ AP 3. Psychostimulating (3)	1. Stimulation of the respiratory center → ↑ <u>respiratory rate and</u> ↑ <u>breathing depth</u>	1. Stimulation of the respiratory center → ↑ <u>respiratory rate and</u> ↑ <u>breathing depth</u> 2. Stimulation of the vasomotor center → ↑ AP
Indications	1. Recovering from anesthesia 2. Poisoning with sleeping pills and barbiturates (1) 3. Asphyxia of newborns (2,3) 4. Poisoning with carbon monoxide, analgesics (2) 5. Shock, collapse, increase of working capacity, migraine (3)	1. Respiratory failure, respiratory depression in opioid overdose, shivering after surgery (4) 4. Smoking cessation (5, 6)	1. Apnea of newborns 2. Collapse, shock states (7) 2. Decrease in vascular tone and weakening of respiration in patients with infectious diseases (7) 3. Poisoning with sleeping pills, barbiturates (7)
Side effects	1. Seizures (1,3,6), 2. Nausea, vomiting (1,2,4,5), 3. Sleep disorder (2,3), 4. Arterial hypertension (3), 5. Allergic reactions (7)		
Contraindications	1. Psychomotor agitation 2. Hypertension 3. Organic heart and vessels diseases (atherosclerosis)	1. Severe organic diseases of the heart and blood vessels, arterial hypertension 2. Gastric and duodenal ulcers	1. Predisposition to convulsive reactions
NB!	Caffeine increases the effect of non-narcotic analgesics (eg, caffeine + paracetamol + acetylsalicylic acid)		

Antitussives are cough suppressants.

Classification	Centrally acting		Perypherally acting
	Addicting	Non-addicting	
Drugs	Less addicting: <ol style="list-style-type: none"> 1. Codeine 2. Dihydrocodeine Potent addicting: <ol style="list-style-type: none"> 3. Morphine 4. Hydromorphone 	Opioid <ol style="list-style-type: none"> 4. Dextrometorphan Non-opioid <ol style="list-style-type: none"> 5. Glauicine 6. Oxeladine 7. Butamirate 	Mixed-action drugs: <ol style="list-style-type: none"> 8. Prenoxdiazine 9. Bithiodine Local anesthetics: <ol style="list-style-type: none"> 10. Lidocaine
Mechanism of action	Directly suppress the cough and respiratory centers.		Block sensitive receptors of the bronchial mucosa. 8-9 + block cough center
Pharmacological effects	1. Antitussive 2. Analgesic (1-3, 10) 3. Locally anesthetic (8-10) 4. Antiinflammatory (5, 6) 5. Bronchodilating (6,7)		
Indications	<ol style="list-style-type: none"> 1. Non-productive cough (rhinopharyngitis, laryngitis, tracheitis or tumor of the bronchi) 2. Dry pleurisy 3. Postoperative period 4. Cough of central origin (pathologic irritation of the cough center) 5. Tuberculosis 		
Side effects	<ol style="list-style-type: none"> 1. Tolerance+dependence 2. Constipation 3. Arterial hypotension 4. Inhibition of respiration. 	<ol style="list-style-type: none"> 1. Dizziness 2. Nausea 3. Allergic reactions 	<ol style="list-style-type: none"> 1. Dry mouth and throat mucosa 2. Nausea 3. Diarrhea 4. Allergy
Contraindications	<ol style="list-style-type: none"> 1. Respiratory failure 2. Alcohol intoxication 3. Craniocerebral trauma 4. Arterial hypotension 5. Pregnancy 6. Impaired liver and kidney function 	<ol style="list-style-type: none"> 1. Productive cough 2. Hypersensitivity to the drug components 	<ol style="list-style-type: none"> 1. Intensive secretion in the respiratory tract (in the postoperative period after inhalation anesthesia) 2. Hypersensitivity to the components of the drug
NB!		<u>Do not affect the respiratory center, do not cause drug dependence.</u> Combined drug: broncholitín (Glaucin + ephedrine + sage oil + citric acid)	

Expectorants and mucolytics are drugs which aid in the clearance of mucus from the airways and are used for productive cough.

Classification	Expectorants (mucokinetics)		Mucolytics	
	Directly acting	Reflex acting	A) Synthetic mucolytics	B) proteolytic enzymes
Drugs	<u>Vegetable:</u> 1. Terpine hydrate 2. Fruits of anise 3. Eucalyptus oil 4. Pine buds <u>Synthetic:</u> 5. Potassium and sodium iodides 6. Guaiphenesin 7. Potassium and sodium citrates 8. Guaifenesin	<u>Vegetable:</u> 8. Grass of thermopsis, Ledum bog- berry, Viola tricolor 9. Leaves of coltsfoot 10. Root of Althea and Glycyrrhiza glabra <u>Synthetic:</u> 11. Sodium benzoate	12. Acetylcysteine 14. Carbocysteine 14. Bromhexine 15. Ambroxol	16. Trypsin 17. Chymotrypsin 18. Ribonuclease 19. Deoxyribonuclease (dor- nase-alpha)
Mechanism of action	Are absorbed in the gastrointestinal tract → are sectered by bronchial mu- cosa → stimulate the secretion of bron- chial glands, dilute sputum and pro- mote drainage of mucus	Irritant gastric mucosal receptors → form the initial stage of excitation of the vo- meting center → ↑ (through the vagus nerve) separation of mucus in the gastro- intestinal tract and liquid secretion in the respiratory tract → ↑ peristalsis of the bronchi and flicker of the cilia → ↑ spu- tum discharge.	Cause depolymerization of protein and other sputum molecules (fibrin, muco- polysaccharides, DNA, RNA, etc.) → reduce its viscosity. Increase the formation of surfactant in the lungs – a substance that prevents alveoli collapse and im- proves gas exchange in the lungs.	
Pharmacological effects	1. Expectorant, 2. Mucolytic, 3. Surfactant-like (14,15)			
Indications	1. Cough with sputum during bronchitis, tracheitis, tracheobronchitis, and pneumonia 2. Bronchoectatic disease, bronchial asthma exacerbation 3. Infant respiratory distress syndrome (14,15), cystic fibrosis 4. Preventive maintenance of complications after operations on respiratory organs			
Side effects	1. Allergy	1. Nausea, vomiting (high doses) 2. Allergy	1. Dyspeptic disorders 2. Allergy (rarely)	1. Bronchospasm, allergy 2. Pulmonary haemorrhage
Contraindications	1. Open pulmonary tuberculosis 2. Diseases with a tendency to pulmo- nary hemorrhage	1. Gastroduodenal ulcer 2. Open pulmonary tuberculosis 3. Diseases of the nervous system with violation of the reflex mechanism of ex- pectoration	1. Gastroduodenal ulcer 2. Pregnancy, lactation 3. Childhood 4. Open pulmonary tuberculosis	1. Open pulmonary tuberculosis 2. Pulmonaty emphysema with respiratory insufficiency

Pharmacotherapy of bronchial asthma

Bronchial asthma is a disease marked by recurrent attacks of dyspnea, with airway inflammation and wheezing due to spasmodic constriction of the bronchi. Can be allergic (atopic) and intrinsic (secondary to chronic or recurrent infections of the bronchi, sinuses, or tonsils and adenoids).

Bronchodilators and anti-inflammatory agents are used.

Classification	Bronchodilators of neurotropic action			Bronchodilators of myotropic action
	Non-selective adrenergic agonists	Selective β_2 -agonists	Muscarinic antagonists	Methylxanthines
Drugs	<u>Universal adrenergic agonists:</u> 1. Epinephrine 2. Ephedrine <u>Non-selective β-agonists:</u> 3. Isoprenaline 4. Orciprenaline	<u>Short-acting (do 3-4 ч.):</u> 5. Salbutamol 6. Terbutaline 7. Fenoterol <u>Long-acting (~ 12 h.):</u> 8. Salmeterol 9. Clenbuterol 10. Formoterol	<u>Non-selective:</u> 11. Atropine 12. Metacin 13. Platifillin <u>Selective:</u> 14. Ipratropium bromide (atrovent) 15. Tiotropium bromide (spiriva)	<u>Short-acting:</u> 16. Aminophylline 17. Theophylline <u>Long-acting:</u> 18. Euphyllong 19. Theotard
Mechanism of action	1. Stimulates α - and β -adrenoceptors (1, 2) 2. Increase release of norepinephrine (2) 3. Stimulate β_1 - and β_2 -adrenoceptors (3, 4)	Stimulation of β_2 -adrenoceptors \rightarrow activation of adenylate cyclase \rightarrow \uparrow cAMP \rightarrow stimulation of protein kinase \rightarrow cleavage of kinase catalyzing phosphorylation of myosin kinase, its activity \downarrow \rightarrow no myosin phosphorylation \rightarrow relaxation of smooth muscles.	Blockage of the transmission in the postganglionic muscarinic receptors \rightarrow the tone of the smooth muscles of the bronchi decreases, the reflex bronchoconstriction is prevented, and the secretion of bronchial glands is suppressed.	1. Blockage of adenosine receptors involved in bronchospasm \rightarrow \uparrow release of catecholamines into the synaptic cleft \rightarrow relaxation of the bronchi. 2. Inhibition of PDE \rightarrow \uparrow cAMP, \downarrow intracellular concentration of Ca^{2+} ions and stabilization of mast cells \rightarrow dilatation of bronchi.
Pharmacological effects	1. Bronchodilating 2. Cardiostimulating	1. Bronchodilating 2. Improve mucociliary clearance 3. Tocolytic	1. Bronchodilating 2. \downarrow gland secretion (11-13)	1. Bronchodilating 2. Vasodilating 3. Antiplatelet
Indications	1. Acute attack treatment 2. Asthmatic status (1,2) 3. Anaphylactic shock (1,2)	1. Acute attack treatment (5-7) 2. Prevention of an attack of asthma (8-10) 3. Asthmatic status (5-7) 4. Emphysema of the lungs (9) 5. Threat of premature birth (5.7)	1. Bronchial asthma 2. Chronic obstructive pulmonary disease (15) 3. Bronchoobstruction induced by physical exertion, cold, inhalation of dust	1. Bronchospasm 2. Violation of cerebral circulation 3. Pulmonary hypertension 4. Hypertensive crisis (16)
Side effects	1. Tachycardia, arrhythmia 2. \uparrow blood pressure 3. Nausea	1. Tachycardia 2. Tremor, headache	1. Dry mouth, \uparrow Sputum viscosity 2. Tachycardia, mydriasis, \uparrow IOP	1. Dyspeptic disorders 2. Arrhythmia, tachycardia 3. Headache, insomnia
Contraindications	1. AH, IHD (1-2) 2. DM, pregnancy (1-2) 3. Tachyarrhythmias (3-4)	1. Individual intolerance 2. Diabetes mellitus 3. Arrhythmias	1. Closed-angle glaucoma 2. Pregnancy	1. Pregnancy and lactation 2. Paroxysmal tachycardia, myocardial infarction

Pharmacotherapy of bronchial asthma

Anti-inflammatory agents

Classification	Glucocorticoids		Mast cells stabilizers	Leukotriene receptor antagonists	Monoclonal anti-IgE antibodies
	Inhalational	Systemic			
Drugs	1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Flunisolide	5. Prednisolone 6. Methylprednisolone	7. Cromolyn 8. Nedocromil 9. Ketotifen	10. Montelukast 11. Zafirlukast	12. Omalizumab
Mechanism of action	1. Inhibit phospholipase A2 → violate the formation of leukotrienes, serotonin, and prostaglandins. 2. Stabilize the membranes of lysosomes. 3. ↓ release of histamine by basophils.		1. Inhibition of PDE → ↑ cAMP → ↓ contractility of myofibrils of protein and stabilization of mast cells. 2. Blockage of Ca ²⁺ ions entry into the mast cell → prevention of mediator release.	Block leukotriene receptors	Inhibits binding of IgE to mast cells
Pharmacological effects	1. Anti-asthmatic 2. Anti-allergic 3. Anti-inflammatory (1-6, 10,11) 4. Immunodepressive (1-6)				
Indications	1. Bronchial asthma 2. Prevention of attacks of atopic bronchial asthma (7-9) 3. Asthmatic status (5,6) 4. Aspirin-, cold- and exercise induced asthma (7-11)				
Side effects	1. Candidiasis of the mouth 2. Dysphonia <u>Prophylaxis: rinsing the mouth after inhalation, using a spacer</u>	1. Osteoporosis, myopathy 2. Puffiness, hypertension 3. Cushing's syndrome 4. Peptic ulcers 5. The withdrawal syndrome	1. Cough 2. Dry mouth 3. Bronchospasm	1. Hepatotoxicity 2. Nausea, vomiting 3. Allergic reactions	1. Local reactions in the site of administration 2. Dispeptic disorders 3. Headache
Contraindications	1. Acute bronchospasm 2. Infectious diseases	1. Osteoporosis 2. Peptic ulcers 3. Severe hypertension 4. Diabetes mellitus	1. Hypersensitivity 2. Pregnancy, lactation	1. Hypersensitivity 2. Lactation 3. Childhood (up to 5 years)	1. Hypersensitivity 2. Lactation 3. Childhood (up to 5 years)
NB!	Combined preparations containing a beta-2-agonist and inhaled glucocorticoid (prevention of asthma attacks) Salmeterol + Fluticasone = Seretide Formoterol + Beclomethasone = Foster Formoterol + Budesonide = Symbicort Combined preparations containing a beta-2-agonist and a stabilizer of mast cell membranes Aerocrom = Cromolyn+ Salbutamol Duotec = Cromolyn + Fenoterol				

Status asthmaticus (acute severe asthma)

An acute exacerbation of asthma that does not respond to basic treatments with bronchodilators (inhalers) and steroids.

Group	Drugs
1. Short-acting β -agonists	<i>Salbutamol</i> 2.5 mg (2.5 ml), fenoterol 1 mg (in 3 ml 0.9% solution of sodium chloride to be inhaled, repeat up to 4 times during 1 hour. NB! Can be given as a constant inhalation
2. α , β -agonists	<i>Adrenalin</i> 0.01 mg/kg s/c as a 1:1000 solution, max 0.3-0.4 mg intravenously 0.1-1 mkg/kg/min as a constant infusion NB! 0.1 % solution (1:1000) – 1 mg in 1 ml; 0.01% solution (1:10000) – 100 mkg in 1 ml
3. Systemic glucocorticoids NB! They are used to ↓ inflammation of bronchial mucosa and restore the sensitivity of β -adrenoceptors.	<i>Prednisolone</i> , methylprednisolone: starting dose is 2 mg/kg, supporting dose - 0.5-1 mg/kg every 6 h i/v NB! Glucocorticoids are given in lack of effect of inhalation of β -agonists.
4. Methylxanthines	<i>Theophylline</i> : 6 mg/kg intravenously during 20 min, maintenance dose – 0.5-0.7 mg/kg/h as a constant infusion

Inhalation of *oxygen*.

Infusion therapy (replenishment of circulating blood volume): intravenously by drop infusion 15% solution of glucose or 0.9% solution of sodium chloride at a infusion rate of 150 ml/h.

Magnesium sulfate 2 g (in children 25 mg/kg) intravenously with 0.9% solution of sodium chloride during 10-20 min.

In severe cases: inhalation anesthetics (isoflurane, sevoflurane)

Drugs for pulmonary edema

When normal blood pressure	<ol style="list-style-type: none"> To sit a patient with legs down <i>Glyceryl trinitrate</i> 0.5 mg sublingually (or aerosol) repeatedly or once <i>Morphine</i> intravenously by 3 mg (0.3 ml 1% solution) until the effect appears or up to total dose 10 mg (1 ml 1% solution) <p>NB! Depress the respiratory center → ↓ unproductive dyspnea → ↓ fear of death</p> <ol style="list-style-type: none"> <i>Furosemide</i> 40-80 mg (4-8 ml 1% solution) intravenously <p>NB! ↓ blood volume → facilitation of cardiac performance</p> <ol style="list-style-type: none"> <i>Glyceryl trinitrate</i> intravenously (up to 10 mg in 100 ml of 0.9% sodium chloride solution by drop infusion, increase the infusion rate from 25 mkg/min until the effect appears under the control of blood pressure) <p>NB! ↓ pre- and postload → facilitation of cardiac performance</p> <ol style="list-style-type: none"> <i>Oxygenotherapy</i> with 100% oxygen and <i>defoamer</i> (ethanol 70%)
When ↑ blood pressure	+ 1 ml 2.5 % solution of <i>hexamethonium benzenesulfonate</i> in 20 ml of a 0.9% solution of sodium chloride intravenously by slow bolus injection under the control of blood pressure after every 2 ml of solution
When ↓ blood pressure	<ol style="list-style-type: none"> Lay the patient lifting the headboard <i>Oxygenotherapy</i> with 100% oxygen and <i>defoamer</i> (ethanol 70%) <i>Dopamine</i> 200-400 mg in 200-400 ml of 0.9% solution of sodium chloride or 5% glucose solution intravenously by drop infusion. Gradually increase the infusion rate from 5 mkg/kg/min until the blood pressure stabilizes <i>Furosemide</i> 40 mg (4 ml of 1% solution) intravenously after stabilization of blood pressure