

**Ministry of Public Health of Ukraine
Higher State Educational Institution
"Ukrainian Medical Stomatological Academy"**

"Approved"

at a meeting of the Department of
Experimental and Clinical Pharmacology
with Clinical Immunology and Allergology

Head of the department

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" _____ " _____ 2017 Pr. № _____

**METHODICAL GUIDANCE FOR STUDENTS' SELF-DIRECTED
WORK WHEN PREPARING FOR PRACTICAL SESSION**

Academic discipline	Clinical Pharmacology
Topic 3	The clinico-pharmacological characteristic of the medicines, which influence bronchial capacity. Clinico-pharmacological characteristic of antipyretic means.
Year of study	5
Faculty	Foreign students training (Medical)

Poltava 2017

1. Relevance of theme:

To the number of diseases, which are accompanied by bronchial obstructive syndrome, belong chronic obstructive disease of the lungs (CODL) and bronchial asthma (BA), which need the frequent, and sometimes constant use of broncholytic means. In our country an increase in the bronchopulmonary diseases was noted. Each year a quantity of patients with the unspecific diseases of lungs grows by 5%, and the prevalence of bronchial asthma among the population is of about 8%. About 30% of patients with bronchial asthma rarely use broncholytic means, 30% more are used their 20-25% regularly, suffer the severe form of disease and are forced to use several against the asthmatic means. Frequently with the heavy course of bronchial asthma patients become invalids. Among sick with chronic bronchitis in 25% cases is revealed the unfavorable course of this disease, which is characterized by the progressive bronchial obstruction. It is necessary to combine the bronchial expanding means and the means, which correct inflammatory process, such as non steroid and steroid antipyretic preparations, membrane stabilizing and antihistaminic preparations by the sick chronic obstructive disease of lungs. Frequently, after the application of all these means appear side effects. The timely averting of the development of side effects makes possible long time to carry out therapy and increase the effectiveness of treatment.

2. Learning objectives:

Master habits by effective and safe pharmacotherapy of bronchial asthma, chronic obstructive disease of lungs.

Master the skill of the individual selection of medicines in the patients with CODL.

Know how to conduct if necessary the correction of pharmacotherapy in the case of the appearance of overdosing broncholytic medicines.

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Discipline	To know
Anatomy	Structure and the function of respiratory, cardiovascular systems, gastro intestinal tract, central nervous system
Pharmacology	Pharmacokinetics, pharmacodynamics, the method of application, indication, contra-evidence, side-line of the action of the broncholytic and antipyretic medicines
Pathophysiology	Stages of pathologic process in systems and in tissues of organism with the bronchial obstructive diseases of the lungs
Internal diseases	Symptomatology of the bronchial obstructive diseases of the lungs
Nervous diseases	Pathogenesis and treatment in the clinical picture of the nervous diseases, which are accompanied by the bronchial obstructive syndrome
Infectious diseases	Pathogenesis and treatment in the clinical picture of the infectious diseases, which are accompanied by the bronchial obstructive syndrome
Anesthesiology	Pathogenesis and the treatment of the pressing states

4.1. The list of key terms, parameters, characteristics which the student forits-yity while preparing for the class:

Term	Definition
Asthmatic status	of acute progressive respiratory insufficiency, which develops in armor-hialniy asthma due to obstruction of breathing-lnyh ways and accompanied rezys-tentnistyuu patient to therapy bronholity-chnymy means

4.2. Theoretical questions for the class:

1. Determine the classification of drugs that affect bronchial patency, their mechanisms of action, pharmacodynamics, pharmacokinetics, side effects.

2. Identify the basic principles of pharmacotherapy and bronchodilators vidharku-thick drugs in patients with different degrees of severity of COPD and asthma.

3. Name the drugs used in asthma status.

4. Make a plan pharmacotherapy in patients with different degrees of severity of asthma

5. Make a plan pharmacotherapy in various degrees of severity under-respiratory adequacy.

6. Develop a plan for pharmacotherapy in patients with neurological diseases that are accompanied bronchoobstructive syndrome.

7. Make a plan pharmacotherapy in patients with allergic diseases that sous-provodzhuyutsya bronchoobstructive syndrome.

8. Make a plan for pharmacotherapy in patients with different stages of asthma;

9. Make a plan of therapy, which is used to relieve Astatic first state Class.

10. Make a plan of therapy, which is used to relieve astmatych state-ment of II degree.

11. Make a plan of therapy, which is used to relieve astmatych tion state III degree.

12. Make a plan pharmacotherapy bronchodilators in COPD patients with different degrees of respiratory failure

13. Master the skills of efficacy and safety of bronchodilators and corticosteroids.
14. Master the skills of pharmacotherapy correction in case of side-effects after using bronchodilators and corticosteroids.

Content topics

CODL and BA are developed into the consequence of the persisting inflammation of bronchi, and they are accompanied by the reversible or irreversible bronchial obstruction. The treatment of these illnesses compulsorily must include the pathogenetic basic therapy (antipyretic that broncholytic with the aid of the glucocorticosteroids, the broncholithics of short and long-term effect, cholinolytics, membrane stabilizers and nonsteroid antipyretic medicines). With the infectious aggravations are included antibacterial means, and under the conditions of the excessive production of phlegm - expectorants (mucolytics, mucokinetics). For treating the patients with the bronchial obstructive diseases of the respiratory tract adapt such ways of the introduction of medicines as inhalation, per os, parenteral. If there are an inhalation form of medicines, advantage returns to the inhalation way of introduction (through the dosed inhalation inhalers, the inhalers of dry powder, with the aggravations CODL) and BA - application of nebulizer). Priority is inhalation way - as the most physiological way with the diseases of the respiratory tract, which makes it possible to create locally the high concentration of medicines in the bronchial tree, increases effectiveness, decreases a quantity and the gravity of system effects, decreases the authenticity of interaction of different medicines.

The classification of the medicines, which are adapt with the obstructive diseases of the respiratory tract.

1. Bronchodilators.
 - 1.1. Adrenostimulators.
 - A. Selective β_2 -adrenomimetics
 - a) β_2 -adrenomimetics the short action: salbutamol, fenoterol
 - b) β_2 -adrenomimetics the long-term effect: salmeterol, formoterol.
 - B. Nonselective β - adrenomimetics: orciprenaline (Alupent, Astmopen), isadrin.
 - 1.2. M-cholinolytics.
 - a) M-cholinoblocking agents of the short action: Ipratropium bromide (Atrovent)
 - b) M-cholinoblocking agents of the long-term effect: Tiotropium bromide (Spiriva)
 - c) combined preparations (Selective β_2 -adrenomimetics of the short action + M- cholinoblocking agents of the short action): Berodual, Combivent
 - 1.3. Xantines.
 - a) Euphyllinum, theophyllinum
 - b) Doxophyllinum, Aminophyllinum
 - c) the combined preparations.
2. Steroid antipyretic: glucocorticosteroids
 - 2.1 Inhalation glucocorticosteroids: beclomethasone, flunisolide, fluticasone, triamcinolone.
 - 2.2 System glucocorticosteroids: prednisolone, dexamethasone, cortisone, hydrocortisone.
 - 2.3 Combined preparations (Inhalation glucocorticosteroids + the long-term effect β_2 -adrenomimetics): Seretide, Simbicort
3. Membrane stabilizers.
 - 3.1 Stabilizers of the membranes of the fat cells
 - a) Ketotifen
 - b) Cromons: cromolyn-sodium (Intal), nedochromyl-sodium.
 - c) combined preparations (selective β_2 -adrenomimetics the short action + cromons) Intal-plus.
4. Antagonists of the leukotriene receptors: zafirlucast, montelukast.
5. Nonsteroid antipyretic means: fenpropion (erespalum)
6. Stimulators of respiration.
 - 6.1 Respiratory analeptics: caffeine, aethimizol, camphor, sulfocamphocaine, bemegride, cordiamine.
7. Mucolytic means.
 - 7.1 Mucolytics of the direct action.
 - a) Nonenzyme: acetylcysteine, carbocysteine.
 - b) Fermentation: Sert, trypsin, chymotrypsin.
 - 7.2 Mucolytics of the indirect action.
 - a) Bronchosecretor drugs.
 - b) Mycoregulators: fenpropion (erespalum).
 - c) Synthetic mucolytics that increase synthesis of surfactant: bromhexine, ambroxol.
 - 7.3 Drugs of surfactant which change surfactant content in alveoli: alveofast, exosurf.
 - 7.4 Expectorants.
 - a) Expectorants the reflector action: herbae Thermopsis, radix Althaeae.
 - b) Synthetic mucolytics: acetylcysteine, carbocysteine.
 - c) Resorptive action: mucaltin, sodium iodide, potassium iodide, sodium hydrocarbonate.
 - d) Stimulators of the bronchial glands.

- 7.5 Combined preparations
8. Antitussive preparations.
 - 8.1 Narcotic antitussive means: codeini phosphas.
 - 8.2 Non-narcotic antitussive means: glaucini, oxeladini.
 - 8.3 Combined antitussive means: pertusinum.

Bronchodilators adapt in the treatment of bronchial obstructive diseases both for the symptomatic treatment (removal or the decrease of sharp symptoms) and for the purpose of reaching and maintaining prolonged bronchodilatats in the basic therapy as the controlling drugs. The selection between the inhalation broncholithics depends on the clinical form of obstructive disease, degree of gravity, motion of disease, individual answer to them, the decrease of symptoms, associated pathology, appearance of side effects.

If there are no contra-evidence as the symptomatic therapy advantage they have the selective β_2 - agonists of short action, they possess the rapid beginning of the broncholytic effect (after 5-7 minutes), which is dose-dependent and it lasts for the elongation of 4-6 hours. The application of a nonselective β - agonist of [ortisprelnalina], as far as possible, it is better to avoid, because of the presence of the expressed side-line manifestations. Adrenaline is used exclusively for the pressing therapy of immediate type allergic reaction. Inhalation M-cholinolytic of short action cause less expressed bronchodilatats, are characterized by the dose-dependent effect with the slower beginning and the somewhat larger duration of action, than the β_2 - agonists of short action.

Combination of the broncholytic means of short action with the different mechanisms of action (β_2 - agonists and cholinolytics) gives the possibility to increase the degree of bronchodilatats, to obtain the more expressed even more prolonged improvement in the volume of the forced expiration and decrease of hyperventilation of lungs, than during the application of each of the broncholithics separately. In this case decreases the probability of the development of side effects, tahifilaxi during the lasting treatment of β_2 - agonists. The broncholithics of long-term effect adapt in the basic therapy CODL (possibly in the mono-therapy), in BA - only in the complex with the inhalation corticosteroids. The β_2 - agonists of long-term effect produce stronger and more steadfast broncholytic effect, have a certain antipyretic action, a duration of their action of 10-12 hours.

M-cholinolytics prolongedly they act, it is more for the elongation of 24 hours, they produce the stable, considerably stronger effect than of Ipratropium, have antipyretic action, are characterized by high safety and grow prettier by transference by patients.

Theophyllinum, doxophyllinum, aminophyllinum are bronhodilatators of the second line of selection. They have the less expressed broncholytic action, it is potentially toxic, they are characterized by variable metabolism with the specific states, the associated diseases and the simultaneous designation together with other medicines. For the purpose of an increase in the effectiveness in the treatment they can be assigned after the preliminary designation of the broncholithics of the first line of selection (β_2 - agonists and/or cholinolytics) with the heavy flow CODL and BA, or be assigned as the alternative with the impossibility of conducting the inhalation broncholytic therapy.

Prolongedly acting theophyllinum at the low doses, is assigned together with the low doses of inhalation corticosteroids (with the average gravity persisting BA), or with the high doses of inhalation corticosteroids (with heavy by persisting BA), which can improve control over the disease.

Treatment of bronchial asthma

Degree of gravity of flow BA	Preventive means of the lasting designation	Means of the special aid
1 degree Intermitisting	They are not necessary	If necessary (to 1 time in the week) the inhalation β_2 - agonists of the short action
2 degree light persisting	Each day inhalation corticosteroids 200-500mkg; cromons or theophyllinum long action.	If necessary (but not more frequent than 3-4 times in a 24 hour period) the inhalation β_2 - agonists of the short action
3 degree Average heavy persisting	Each day inhalation corticosteroids 500-800mkg, long β_2 -agonists	If necessary (but not more frequent than 3-4 times in a 24 hour period) the inhalation β_2 - agonists of the short action
4 degree heavy persisting	Each day inhalation corticosteroids 800-2000mkg, long β_2 -agonists, corticosteroids preformed or in the form the syrup	If necessary (but not more frequent than 6 times in a 24 hour period) the inhalation β_2 - agonists of the short action

The side effects, which are developed with conducting of system glucocorticoid therapy (cortisonum, hydrocortisonum, prednisolonum, triamcinolonum, dexamethasonum): the suppression of the function of the adrenal glands. As a result treatment by glucocorticoids appears such side effects. During the treatment of more than the 2nd months Icencko- Cushing syndrome can develop. The redistribution of adipose tissue from the extremities to the body and face occurs. Appetite rises, insomnia can develop. A constant metabolism of proteins and amino acids leads to an increase in the need for insulin. The mass of body subsequently rises. Consequently, characteristic is the accumulation of adipose tissue, the decrease of muscular mass, thinning the skin, hyperglycemia and, as a result, diabetes. Sick with diabetes frequently resistance to the treatment with insulin, but in them rarely appears ketoacidosis. Osteoporosis frequently is developed. The patients, by whom is carried out the treatment by glucocorticosteroids, it follows to adhere to diet with the high content of proteins and potassium, and also they should assign. One of the complications is peptice stomach ulcer and duodenum. Different bacterial or fungus

infections can not be diagnosed during the treatment by glucocorticoids. Sometimes are developed the psychopathic states, especially in patients, which the large doses of corticosteroids were assigned. The prolonged introduction of data of preparations leads to the development of rear the post of capsular cataract. Glaucoma can develop. Intracranial pressure rises. The delay of increase in children is noted. If are assigned the high doses of hydrocortisone and cortisone it can arise also mineralocorticoid effect - is observed the delay of sodium and water, and also the loss of potassium. In patients with the normal function of kidneys and cardiovascular system this leads to the development of hypokalemia, hypochloremia alkalosis and an increase in the arterial pressure. With hypoproteinemia, diseases of kidneys or liver appear edemas.

The preparations, which are used for the local (inhalation) glucocorticoid therapy of beclomethasonum (beclomet, becotid), budesonidum (goracort), flunisolid (ingacort), flyutikasona propionate (flicsotid). Side-line action of the inhalation glucocorticoid therapy: A) the development of pharyngitis, dystonia as a result of the atrophy of muscles of larynx, candidomikosis of the mucous cavity of mouth;

b) system side effects.

The development of system side effects caused by the partial suction of glucocorticoids, with the inhalation, by the mucous membrane of bronchopulmonary system and gastrointestinal tract (part of the preparation it swallows by patient) and enters system blood circulation. Most frequently side effects are developed after the application of inhalation corticosteroids - beclomethasonum (becotid) at the high daily doses - to 2000 H. System side effects during the application of inhalation glucocorticoids (ingakort, gorakort they are encountered very rarely in comparison with beclomethasonum).

1. Preparations for the system glucocorticoid therapy (cortisonum, hydrocortisonum, prednisolonum, triamcinolonum, dexamethasonum).

2. Preparations for the local (inhalation) glucocorticoid therapy: beclomethasonum (beclomet, becotid) and budesonid (goracort), flunisolid (ingacort), flyuticasonum propionate (flicsotid).

The start in the complex of the therapy of sick with bronchial asthma inhalation glucocorticoids considerably decreases the number of assaults of bronchial asthma and the need for the sympathomimetics. For this purpose use budesonid (goracort), funisolid (ingacort) and flyuticasonum (flicsotid). With the light and moderately heavy forms of bronchial asthma one of these preparations use in the form inhalations at the doses of 400-800 H/days. With the heavier course of bronchial asthma use the higher doses of inhalation glucocorticoids - 1500-2000 H/days. The pharmacological effect of these preparations is connected with the action on the biological membranes and with the decrease of the permeability of capillaries. Inhalation corticosteroids participate in the metabolism of arachidonic acid and the synthesis of leucotrienes and prostaglandins, they inhibit production and secretion of cytokinins, they prevent direct migration and activation, the cells of inflammation. Given preparations suppress the proliferation of fibroblasts and decrease the synthesis of collagen and immune complexes, they decrease the sensitivity of effector cloths to the allergic reactions, they contribute to bronchial celiogenesis, and is decreased the inflammatory defeat of the epithelium of bronchi, they decrease unspecific bronchial hyperreactivity.

At the inhalation way of the introduction of glucocorticosteroids rapidly is reached the high concentration of medicine directly in the tracheobronchial tree, which makes it possible to avoid the development of system side effects. One should consider that during the inhalation application of glucocorticoids can appear such local complications, as candidiasis, and disphonia. An increase in the yeastlike caps of the kind of Candida in the cavity of mouth and in the throat is the result of the inhibiting action of inhalation corticosteroids on the shielding functions of neutrophils, macrophages and T-lymphocytes on the surface of the mucous membrane of the cavity of mouth and throat. Recently adapts the inhalation of the dry powder (powder) of glucocorticosteroids in the form of disks for the mouth form with haler for the mouth. The preparations of medicinal form of new generation are given. The inhalers, in which medicinal substance is represented in the form powder, do not contain Freon, are more ecologically safe, lighter in the application, since there is no need for coordinating the work of inhaler and respiration. The inhalation application of powder of glucocorticoids makes it possible to combine powerful local and minimum system action. This makes it possible to use such preparations long time and leads to the decrease of antipyretic processes. Are used haler-flicsotid, (in one pocket it is contained 1 dose, which is equal to 50, 125 and 500 mH to preparation), haler-beclomethasonum (200 doses), or another form - turbohaler-beclomethasonum (200 doses). Budosonid-ciclohale (benacort) of 300 doses). Using ciclohale, it is possible to inhale and the preparation of salben (salbutamol). The absence of irritation of the mucic shell of bronchi is the advantage of aerosol forms with the powder, since in the disk systems is not used gas Freon. Furthermore, with the use of such systems is removed the problem of the synchronization of inhalation and pressure on the small balloon. The construction of ciclohale is sufficiently simple and is convenient for the use.

Treatment of asthmatic status

Asthmatic status - syndrome of the sharp progressive respiratory insufficiency, which is developed with bronchial asthma as a result of the obstruction of the respiratory tract and is accompanied by the resistance of patient to the therapy by broncholytic means.

Two clinical forms of asthmatic status are distinguished: anaphylactic and metabolic. The first is characterized by the progressive (even complete total) bronchial obstruction, predominantly as a result bronchospasm and by sharp respiratory insufficiency. The anaphylactic form of asthmatic status they estimate as anaphylactic shock. This form of asthmatic status appears as a result sensitization to the nonsteroid antipyretic means, in particular to aspirin, to antibiotics, to sulfanilamide preparations, to the proteolytic enzymes, and also to

the sera and the vaccines.

The metabolic form of asthmatic status can be observed. This form is developed gradually for a period of several days and even weeks and appears as a result progressive hyperreactivity of bronchi. Characteristically gradual increase in edema of the mucous membrane of bronchi and an increase in the quantity of thick (viscous) phlegm. The reason for the appearance of the metabolic form of asthmatic status are bacterial and virus inflammation, prolonged and uncontrolled application of β - agonists, antihistaminic and sedative means.

I stage.

For asthmatic status is characteristic the formation of steadfast bronchoobstructiv syndrome. The development of the obstruction of bronchi is caused by accumulation and delay of the phlegm against the background of diffusion edema of mucous membrane and expiratory collapse of small bronchi. Furthermore, the obstruction of bronchi can arise with the sharp decrease of dose or the cancellation of glucocorticoids. I the stage of asthmatic status is the stage of compensation, can be formed resistance to the adrenomimetics.

With I of the stage of asthmatic status are conducted these measures:

1. The application of glucocorticoids is required during the treatment of asthmatic status.

Glucocorticoid preparations are assigned intravenously jet or drop every 3-4 hours at the large doses. The one-time dose of prednisolone can reach 10 g/kg of the mass of the body of patient. If effect from the preparation is absent prednisolone it is introduced intravenously drop on 90 mg every 4 hours or on 90-120 mg. Hydrocortisone hemisuccinate or hydrocortisone phosphate is assigned at the one-time dose of 200-250 mg intravenously drop together with 200-250 ml of physiological the solution of sodium of chloride. Large effectiveness has the combined application of hydrocortisone 200-250 mg intravenously drop and prednisolonum 60 mg inward. Furthermore, it is possible to appoint intravenously drop introduction of hydrocortisone of succinate of sodium - it is intravenously drop at the dose of 200-300 mg together with 200-250 ml of physiological solution of sodium of chloride or 5% of solution of glucose.

Large effectiveness, than prednisolonum, has intravenously drop introduction 125 mg of metilprednizolonum together with 150-200 ml of physiological solution of sodium of chloride. The action of metilprednizolonum is developed more rapidly, it more rapidly and more deeply penetrates the wall of bronchi. Every 3-4 hours repeat conducting preparation at the dose of 62,5-125 mg. Uses intravenously the introduction of metilprednizolonum during 2-4 days.

Hydrocortisonum is introduced intravenously drop on 200-250 mg of 4-5 times in the day. The speed of the injection of preparation is 4 mg/the short circuit of 1 hours. In the case of the absence of positive result after the introduction of hydrocortisone, the dose of preparation increases to 2000-4000 mg/day. However, the duration of the introduction of hydrocortisone must not exceed 2-3 days. An appearance of an effective cough and an increase in the index the volume of the forced expiration is considered as the positive result of the therapy by the data by preparation.

Not is less effective the therapy - parenteral introduction of prednisolonum and the designation of preparation inward. After the removal of patient from asthmatic status the dose of prednisolonum they daily decrease on 30-40 mg/day.

In some patients, who earlier assumed prednisolonum inward, the application of this preparation 20-40 mg of every 6 hours orally have larger effect than intravenously the introduction of hydrocortisonum or metilprednizolonum.

1. It is achieved the inhalation of the aerosol β - agonists: salbutamol on 100-200 g (1-2 inhalations), terbutalinum on 250 g (1 inhalation), -formterol (berotek) on 200 g (1 inhalation), gexoprenalinum (ipradol) on 200 g (1 inhalation).

Large effectiveness, than the application of the aerosol β - agonists has nebulirovanie of β -adrenostimulators. Salbutamol (ventolin) is introduced by inhalation in nebulayzere for a period of 10-15 minutes on 5 mg in 2,5 ml of physiological solution of sodium of chloride. Then is achieved the introduction of salbutamol into that to dose itself for the elongation of several hours. Instead of salbutamol is possible to achieve nebulirovanie of terbutalinum at the dose of 10 mg or proterenolaum at the dose of 15 mg (0,3 ml 5% solution). In the case of an improvement in the state of patient to the β - agonists is added by 0,5 mg of ipratropium bromidi (atrovent). This leads to the prolongation of broncholytic action. It is more than 3- X of the doses of this mixture cannot be nebulirovat before obtaining of the positive clinical result: the decrease of shortness of breath and improvement in the exponential function of the external respiration: the vital capacity of lungs (VCL), volume of the forced expiration in first second (VFE1) and index Tifno (relationship VFE1 to VCL). The most explicit broncholytic effect is observed after the application of β - agonists of intravenously drop, in particular salbutamol on 100-300 mg together with 100 ml of physiological solution of sodium of chloride for a period of 20 minutes. Instead of salbutamol is possible to use terbutalin. In the comparison with salbutamol of terbutalin has the advantage. After the application of this preparation more rarely appear such side effects, as tachycardia, disturbance of cardiac rhythm, increase BP. Terbutalin is introduced intravenously jet with a velocity of 5 mg/s. The speed of introduction can be increased or reduced in the dependence on the frequency of the heart contractions. One should consider that the age is more than 40 years and the presence of cardiovascular diseases, in particular hypertonic disease and the ischemic disease of the heart are contra-evidence for the designation of β - agonists. Intravenously introduction of β - agonists most frequently use with the insufficient effectiveness of the therapy by the aerosols of β -agonists and glucocorticosteroids.

3. Euphyllinum (aminophyllinum) adapts intravenously at the initial dose of 5-6 mg/kg. The injection of this preparation is achieved intravenously drop at a rate of 0,9 mg/kg for hour (approximately 2,5 ml 2,4% an hour)

before to better of state, and then it adapts the same dose for the elongation of 6-8 hours. The maximum daily dose of preparation is 1,5-2 g of euphyllinum (aminophyllinum) in a 24 hour period (62-83 ml 2,4% solution).

4. Adapts also the hypodermic introduction of adrenaline of hydrochloride on 0,3 ml every 20 minutes (3 times in the hour). It should be noted that adrenaline hydrochloride one ought not to assign by sick bronchial asthma and hypertonic disease. Adrenaline does not have advantages over β -agonists that those times as long as sick it can independently breathe. But in certain cases, when β -agonists are ineffective (with their overdose), adrenaline can have a sufficient bronchodilators effect.

One should remember, adrenaline has rapid, but short-term broncholytic effect. During the prolonged application of adrenaline the possible development of inverse effect - development of bronchospasm. In the case of the development of progressive asthmatic status and with the ineffectiveness of the therapy of intravenously by the glucocorticoids, inhalation by β -adrenostimulators and intravenously of euphyllinum (aminophyllinum) use intravenously the introduction of neopinephrinum (isobeatenLA). The therapy by neopinephrinum, intravenously introduction, must be achieved only in the persons of young age and in the absence cardiovascular diseases. This therapy is necessary to accomplish and only if treatment by glucocorticoids, by cholinolitics means, by euphyllinum (aminophyllinum) are ineffective. First the speed of the introduction of neopinephrine is 0,1 g/kg per minute. In the absence sufficient expressed effect the dose of preparation increases by 0,1 g/kg of every 15 minutes.

Safer is the application of selective β_2 -adrenostimulators. The partially selective β_2 -agonist is assigned: orciprenalinum sulfate (astmopent) of intravenously drop on 0,5 ml 0,05% of solution together with 250-300 ml of physiological solution of sodium of chloride. It is possible to introduce preparation also intramuscular on 0,5 ml 0,05% of solution of 2 times in the day. Are used also the β_2 -agonists, which have high selectivity - 0,05% solution of terbutalinum (bricanil) on 0,5 ml intramuscular of 2-3 times in the day or in 1% solution of ipradol on 2 ml of intravenously drop are together with 300-400 ml 5% solution of glucose. Most effective are intravenously introduction of the selective β_2 -agonist of tronkvinol hydrochloridum (inolina) intramuscular or intravenously at one-time dose 25, 50 or 100 mg. With intravenously introduction the preparation is introduced together with 20 ml 5% of solution of glucose or better than intravenously drop is at the same one-time dose together with 100-150 ml 5% of solution of glucose.

5. Infusion therapy for the purpose of hydration and improvement in microcirculation is achieved. This therapy compensates the scarcity of the volume of the circulating blood and extracellular liquid and contributes to an improvement in the dilution of phlegm. For intravenously of infusion therapy adapt 5% solution of glucose, solution of Ringer, isotonic solution of sodium of chloride. In the case of expressed hypovolemia, low arterial pressure the introduction of reopoliglukinum is expedient. The total volume of infusion therapy is about 3 liters in the first twenty-four hours, during the subsequent days the dose composes 1,6 l/m² of body surface, f.e., about 2,3-2,5 l in a day. 2 500 Units of heparin are added to every 500 ml of solution for the infusions.

6. For an improvement in the isolation of phlegm mucolytics adapt: intravenously the introduction of lazolvanum (ambroksolum) on 30-45 mg (2-3 ampules) of 3 times in the day or nebulirovanie 2 ml 20% of solution of acetylcysteinum. Simultaneously Is assigned ambroksolum inward on 30 mg of 3-4 times in a 24 hour period. However, it is necessary to consider that the application of these means is insufficiently effective with the therapy of asthmatic status. Furthermore, for the purpose of an improvement in the isolation of phlegm are assigned 10% solution of sodium of iodide in the dose from 10 to 30 ml for a period of twenty-four hours. It is possible to simultaneously assume 3% solution of sodium of iodide inward on 1 table spoon of 5-6 times in the day.

7. For the blockade of the action of the mediators of allergy, decrease of the intensity of inflammation in the mucous membrane of bronchi uses the inhibitor of the proteolytic enzymes of aprotininum (gordoks, contrikal, trasylol). Treatment by this preparation contributes also to the decrease of inflammation in the mucous membrane of bronchi. The daily dose of preparation is 1000 Units on 1 kg of the mass of body. Aprotininum for a period of twenty-four hours is introduced 4 times at the one-time dose of 250 Units on 1 kg of the mass of body. The injection of preparation is achieved intravenously drop together with 250-300 ml 5% of solution of glucose.

8. During the combination of bronchial asthma with arterial hypertension is assigned the neuroleptic droperidol of intravenously jet 0,25% solutions on 1 ml together with 10-20 ml of the physiological solution of sodium of chloride. This preparation decreases the bronchospasm, the toxic phenomena after the application of adrenomimetics. Furthermore, droperidol decreases arterial pressure and excitation, which frequently is observed with asthmatic status. Smaller effectiveness has intramuscular the introduction of droperidolum on 1-2 ml 0,25% of solution. Intravenously or intramuscular the injection of preparation is possible to repeat 3 times/day at such doses themselves.

9. With asthmatic status there is a threat of the development of tromboembolic complications. This is connected with dehydration and increase in the coagulability of the blood in the patients with bronchial asthma during the development of asthmatic status. This causes the application of heparin (anticoagulant), which decreases edema of the mucous membrane of bronchi. Heparin is assigned hypodermically in the region of stomach on 5 000 Units intramuscular of 4 times in a 24 hour period.

10. For the purpose of fight with hypoxemia is assigned the inhalation oxygen-air mixture with the oxygen content 35-40%. The inhalation of moistened oxygen is accomplished at a rate of 2-6 l in one minute.

11. The correction of metabolic acidosis is achieved. Although with I of the stage of asthmatic status rarely is observed expressed metabolic acidosis, if pH of the blood of less than 7,2 is expedient to introduce 200-250 ml 4% of solution of sodium of bicarbonate. After introduction of which is determined pH of the blood and scarcity of

buffer bases. The introduction of sodium bicarbonate if necessary is repeated.

12. If after the application of means enumerated above asthmatic status is not diluted, then the possible application of halothane narcosis. The application of this narcosis is caused by the fact that Fluothane has broncholytic action. In many patients afterward the end of halothane narcosis the bronchospasm is not developed.

However, asthmatic status again is developed in the part of the patients after the termination of the action of Fluothane. One should consider that the application of halothane narcosis can lead to the development of the disturbances of the rhythm of heart, even to the development of the fibrillation of ventricles. Therefore this narcosis is undesirably used in the patients with bronchial asthma and by cardiovascular diseases (the ischemic disease of the heart, myocardites, myocardiopathies and by others) and in the patients of old and senile age.

II stage of asthmatic status - these are the stage of decompensation or the stage "silent lung". For II stage is characteristic the development of the progressive ventilation disorders. The state of patient is heavy. The high degree of respiratory insufficiency is characteristic. For the clinical picture II stage of asthmatic status is also characteristic pale gray skins, frequent and shallow breathing, listening the sibilant remote wheezes, during the auscultation above the pulmonary fields the wheezes are not audible "silent lung". It is determined frequent pulse - 120-140 into 1 minute, in the arterial blood is observed hypoxemia of PaO₂ is equal to 50-60 mm Hg and hypercapnia of PaSO₂ is equal to 50-70 mm Hg. The consciousness of patient is preserved. The principles of the treatment of this stage are similar as during stopping I of the stage of asthmatic status. However, the doses of glucocorticoids increase 1,5-3. Decreases the interval between the introductions of glucocorticoids to 1,5 hours. Prednisolone is introduced at the one-time dose of 90-120 mg every 1,5 hours. In the case of the absence of effect the one-time dose of prednisolone increases to 150 mg. Simultaneously with the interval of 4-6 hours uses intravenously the drop introduction of hydrocortisone of succinate of sodium (I salt - kortefa) - intravenously drop at the dose of 300-400 mg or hydrocortisone of hemisuccinate - intravenously drop at the dose of 200-300 mg together with 200-250 ml of phys. solution of sodium chloride or 5% of solution of glucose. Instead of hydrocortisone of hemisuccinate is possible to use intravenously the drop introduction of hydrocortisone of phosphate at the same dose. Instead of prednisolone is possible to use methylprednisolone to sodium succinate - intravenously jet on 125-250 mg together with 10-20 ml of phys. solution of sodium chloride with the interval of 1,5 hours.

Adapts also intravenously introduction to 2,4% of solution of euphyllinum (aminophyllinum) on 10-20 ml together with 10-20 ml of phys. solution of sodium chloride. The dose of preparation is determined from the calculation 5-6 mg/kg. The inhalations of moistened 25-60% of oxygen through the mask or the nose catheter are accomplished. In the case of worsening in the clinical state of patient and ineffectiveness of the therapy achieved the necessary conducting of endotracheal intubation and the transfer of the patient with mechanical ventilation of lungs (MVL). Indications for the conducting MVL are also:

- 1) the progressive warmly- pulmonary insufficiency;
- 2) decrease and absence of respiratory sounds on the inhalation on the strength of the fact that decreases respiratory volume, which is accompanied by decrease and/or or by the disappearance of expiratory wheezes;
- 3) the expressed tension of auxiliary muscles and retraction of between edge spaces, the expressed fatigue and the danger of the exhaustion of patient;
- 4) the increasing increase in the level CO₂ in the arterial blood;
- 5) worsening in mental status of patient with the development of apprehension, irritability, tangled nature of consciousness, and finally, the comatose state.

First for the input narcosis is used predion (viadril), which is introduced intravenously from the calculation 10-12 mg/kg in the form by 5% of solution. Before the endotracheal intubation is achieved intravenously introduction of the myorelaxant of lystenone. Basic narcosis is achieved with the aid of the nitrous oxide. It is used nitrous oxide in the mixture with oxygen in the relationship 1:2. For the basic narcosis it is possible to use also Fluothane.

The sanitation of bronchial tree is accomplished during mechanical ventilation of lungs. For this is accomplished therapeutic bronchoscopy from by posegmental lavage of bronchi. Is accomplished washing bronchial tree with that heated before 30-35 °C 1,4% of solution of sodium bicarbonate with the subsequent sucking of bronchial contents.

For the elongation of realization MVL continues the therapy by the medicines, which are used for stopping asthmatic status. With the interval of 1,5 hours is achieved intravenously the introduction of glucocorticoid means, euphyllinum (aminophyllinum), β -agonists, cholinolytic means, expectorant preparations. Clinically stopping II stage of asthmatic status is determined during the elimination of the picture "silent lung". Further after stopping the II stage of asthmatic status continues the therapy by the bronchodilators means, in particular by glucocorticoids, by β -adrenostimulators, by cholinolytic means, by euphyllinum (aminophyllinum). However, the one-time doses of data of preparations considerably decrease.

III stage is characterized by very grave condition. It is determined diffuse cyanosis, sweating, arrhythmia of respiration, during the auscultation the absence of dry wheezes, a thready pulse, low arterial pressure - stage of decompensation or the stage "silent lung". In the arterial blood of pO₂ it is below 50 mm Hg, and pO₂ is above 70 mm Hg.

Treatment is accomplished only under the conditions of intensive care unit. If an improvement in the state of patient does not begin after 1,5 hours it is not diluted the picture "silent lung" necessary to carry out endotracheal

intubation and to transfer patient to mechanical ventilation of lungs (MVL). For the elongation of conducting mechanical ventilation of lungs every 4 hours are determined pH of the blood, stress of oxygen and carbonic acid dioxide in the blood. The bronchoscopic sanitation of bronchial tree is accomplished. Required is posegmental lavage of bronchi. With the interval 1 hour of intravenously are introduced the glucocorticoids. The doses of data of preparations increase. Prednisolone adapts at the one-time dose of 120-150 mg. Hydrocortisonum hemisuccinati or hydrocortisonum phosphati are introduced intravenously drop at the one-time dose of 250-400 mg together with 200-250 ml of phys. solution of sodium of chloride. The one-time dose of metilprednisolonum can be increased to 250-312,5 mg. Adapts intravenously introduction to 2,4% of solution of euphyllinum (aminophyllinum) in the one-time dose of the calculation 5-6 mg/kg.

Are assigned the β - agonists of intravenously drop, in particular salbutamol on 100-300 mg together with 100 ml of phys. solution of sodium of chloride for the elongation 20 minutes or terbutalin of intravenously drop with a velocity of 5 mg/kg. Instead of salbutamol is possible to use terbutalin. In the comparison with salbutamolum of terbutalin has the advantage. After the application of this preparation more rarely appear such side effects, as tachycardia, disturbance of cardiac rhythm, increase BP. Terbutalin is introduced intravenously jet at a rate of 5 mg/min. The speed of introduction can be increased or reduced in the dependence on the frequency of the heart contractions. One should consider that the age is more than 40 years and the presence of cardiovascular diseases, in particular hypertonic disease and IHD is contra-evidence for the designation of β - agonists. Intravenously drop introduction of β - agonists most frequently use with the insufficient effectiveness of the therapy by the aerosols of β -agonists and by glucocorticosteroids. The inhalations of moistened 25-60% of oxygen through the mask or the nose catheter are accomplished. The correction of metabolic acidosis is required. For this purpose adapts intravenously drop introduction to 4% of solution of sodium of bicarbonate on 200-400 ml. It is necessary to achieve control of pH of blood and determination of the scarcity of buffer bases. The introduction of sodium of bicarbonate if necessary is repeated. Furthermore, intravenously is introduced 2,4% solution of euphyllinum (aminophyllinum) in the one-time dose of 5-6 mg/kg, adapts lazolvan (ambroksol) intramuscular, hypodermic or intravenously on 30-45 mg (2-3 ampules) of 3 times in the day. Are assigned also the inhalations of acetilcistein (mucomista, mucosolvin, flyuimutsil) on 5 ml 20% solution or nebulirovanie of this medicine on

Materials for students' self-directed work.

A. Tests for students' self-directed work.

Test 1.

To patient are established diagnosis "bronchial asthma of the average degree of gravity, persisting flow". What preparation can appoint for the planned treatment?

- A. Intal
- B. Berotec
- C. Becotidum
- D. Budesonidum
- E. Salbutamolum

Standard of the answer: advantage returns Budesonidum

Test 2

It has the greatest selectivity to the adrenoreceptors

- A. Fenoterolum
- B. Salbutamolum
- C. Salmeterolum
- D. Formoterolum
- E. Izadrinum

Standard of the answer: Salmeterolum.

Test 3

To the preparations of the long action can carry

- A. Astmopent
- B. Berotec
- C. Salbutamolum
- D. Serevent
- E. Ventolinum

Standard of the answer: Serevent.

Test 4

The smallest system of bioaccessibility is inherent:

- A. Ingacort
- B. Astmacort
- C. Becotid
- D. Budesonidum
- E. Flixotidum

Standard of the answer: Flixotidum.

Test 5.

To glucocorticosteroids in the high dosages can carry:

- A. Budesonidum
- B. Becotid
- C. Ingacort
- D. Berodualum
- E. Salbutamolum

Standard of the answer: Budesonidum.

Test 6.

It possesses the greatest affinity for the glucocorticoid receptors:

- A. Flixotidum
- B. Budesonidum
- C. Ingacort
- D. Becotidum
- E. Beclofortum

Standard of the answer: Flixotidum

Test 7.

With the heavy course of bronchial asthma, the application of glucocorticosteroids at the daily dose is not less:

- A. 400 mkg
- B. 500 mkg
- C. 600 mkg
- D. 700 mkg
- E. 800 mkg

Standard of the answer: 800 mkg

Test 8.

Membranostabilizator are the preparations of selection with:

- A. Syndrome of the hyperreactivity of the bronchi
- B. Intermittent bronchial asthma
- C. Light persisting BA
- D. Persisting BA the average degree of the gravity
- E. Not one disease

Standard of the answer: Not one disease

Test 9.

What preparation with the overdose can strengthen the bronchial obstruction:

- A. Euphyllinum
- B. Astmopent
- C. Beclomethasonum
- D. All
- E. No one

Standard of the answer: Astmopent

Test 10.

Asthmatic status is diagnosed when the assault of asthma lasts:

- A. 8 hours
- B. 12 hours
- C. 18 hours
- D. 24 hours and more
- E. 3 hours

Standard of the answer: 24 hours and more.

SITUATION TASKS:

1. The woman of 37 years for a period of 15 years is ill by bronchial asthma. Recently the assaults of asthma appear 4-5 once a week, night assaults - 2-3 times per month. For stopping the assaults is used salbutamol. Objective: state is relatively satisfactory. Respiratory rate - 20 in 1 minute. Ps - 76/min., BP - 120/80 mm Hg. In the light of respiration vesicular. The tones of heart are muted, rhythm correct. What preparation must be appointed for the preventive maintenance of the assaults of bronchial asthma during the first stage?

- A. Cromolyn - sodium
- B. Corticosteroids injection
- C. Regular adoption salbutamolum
- D. Corticosteroids are inhalation
- E. Corticosteroids preformed (tablets)

Standard of the answer: Cromolyn - sodium

2. Sick 22 years, for the first time it turned to the doctor apropos of the assaults of asthma, expiratory

shortness of breath, weakness. The diagnosis was established: bronchial asthma of the light degree of gravity, the persisting flow. What version of treatment is optimal in this situation?

- A. the introduction intravenously course of 30mg of prednisolonum
- B. begin from the minimally necessary doses of inhalation glucocorticosteroids, in the absence effect to increase the dose
- C. begin from maximally necessary doses of inhalation glucocorticosteroids, with the following decrease to the optimally low dose.

- D. appoint 30mg of prednisolonum in the preformed form
- E. appoint introduction intravenously of prednisolonum with the following transfer into the preformed form with the subsequent reduction in the dosage

Standard of the answer: begin from maximally necessary doses of inhalation glucocorticosteroids, with the following decrease to the optimally low dose.

3. The patient of 49 years complains about the suffocation, the cough. Phlegm is not separated. Repeatedly he used salbutamolum, intal, but without effects. Objective: sits, relying on table. Cyanosis of face, acrocyanosis. There are no peripheral edemas. Respiration superficially, is hindered, by places it does not listen; the scattered wheezes, considerably prolonged breathed out. The tones of heart are muted, tachycardia. Ps - 112/min, BP of - 110/70 mm Hg. Liver is near the edge of edge arc. Preliminary diagnosis?

- A. Aspiration of the foriegn body
- B. Heart asthma
- C. Chronic obstructive bronchitis is the aggravation
- D. Asthmatic status
- E. Bronchial asthma, the average degree of the gravity

Standard of the answer: Asthmatic status

4. The patient of 19 years complains about dry cough, shortness of breath. It is ill for a period of year. The assaults of asthma are short-term - 1-2 times per month. It is objective: child is agitated, the skin pale, the cyanosis of nasolabial triangle, expiratory type shortness of breath. Respiratory rate- 48/min. It is percussion: above the lungs sound with the box nuance; is auscultatory - respiration weakened, the dry sibilant wheezes from both sides. Volume of the forced expiration - 80% of the proper. Which of the preparations is most expedient to appoint to patient?

- A. Suprastinum
- B. Euphyllinum
- C. Prednisolonum
- D. Indometacinum
- E. Salbutamolum

Standard of the answer: Salbutamolum, Berotec, Ventolinum.

5. In sick 35 years the infrequent (2 times per month) assaults of shortness of breath, which are easily removed by the inhalation of β_2 -sympathomimetics of short action, are noted. The dry sibilant wheezes listen in the period of assault in the lungs, in the spaces between the assaults of shortness of breath VFE is more than 80% of that being proper. What most probable diagnosis?

- A. asthma of the average gravity
- B. Severe persisting asthma
- C. Intermitisting bronchial asthma
- D. This information is insufficient for determining the degree of gravity of bronchial asthma
- E. Light persisting asthma

Standard of the answer: Intermitisting bronchial asthma

6. The patient of 56 years complains about shortness of breath with the difficulty of expiration, the isolation of phlegm in the morning for a period of 22 years. Cigarette during the day from the 18- summer age smokes 1 bundle. During conducting of test on VFE the reversibility of obstruction composes 10%. What preparations should be appointed at the beginning of treatment?

- A. Inhalation glucocorticosteroids
- B. Membranostabilizers (intal, tayled)
- C. Antibiotics
- D. Inhalation cholinolytics (atrovent)
- E. Inhalation sympathomimetics (berotec)

Standard of the answer: Inhalation cholinolytics (atrovent)

3. Sick 47- mi of years it is prolongedly observed apropos bronchial asthma of infectious etiology. Recently assaults were increased in frequency, are not diluted by inhalations astmopentum and berotec. From the designation of what preparation it is expedient to begin intensive treatment?

- A. Glucocorticoids
- B. Heart glycosides
- C. Oxygen therapy
- D. Infusion therapy
- E. Bronchodilators

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