

**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 2	The clinico-pharmacological characteristic the antianginal and antiischemic medicines. The clinico-pharmacological characteristic the antihypertensive medicines.
Year of study	5
Faculty	Foreign students training (Medical)

Poltava 2017

1. Relevance of theme:

Cardiovascular mortality occupies key place among the reasons for mortality in the entire world. In the Ukraine this index compose about 63%. The decrease of the frequency of stenocardic assaults on minimum and increase in the tolerance to the physical load is the basic task to antianginal therapy. Antianginal means - preparations, which decrease the need of myocardium for oxygen, they improve coronary blood circulation, increase the supply of cardiomyocytes by oxygen, they optimize energy exchange in the cells of myocardium. Operational provisions of heart with the ischemic disease of heart (IDH) is one of the most important tasks. Antianginal preparations create the more favorable hemodynamic conditions for the work of heart because of the dilation of veins and arteries, the decrease of general peripheral resistance and before and after load. In the contemporary medical practice a large quantity of the antianginal means is used: nitrates, molsidominum, the antagonists of calcium, the activators of potassium channels, anabolic means and others.

2. Learning objectives:

1. To master the habits of effective and safe pharmacotherapy by antianginal means.
2. To master the skill of the individual selection of antianginal preparations in patients with the ischemic disease of heart.
3. To know how to conduct, after the need, the correction of pharmacotherapy in the case of the appearance of overdosing antianginal means.

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

Discipline	To know
Anatomy	Structure and the function of cardiovascular, respiratory system, gastro intestinal tract, CNS
Pharmacology	Pharmacodynamics, pharmacokinetics, the method of application, contra-evidence, the side- actions of the antianginal preparations
Pathophysiology	Classification, pharmacokinetics, pharmacodynamics, the side- actions of the antianginal preparations
Internal diseases	Pathogenesis and treatment pressing of states in the clinical picture of the internal diseases
Nervous diseases	Pathogenesis and treatment with pressing states in the clinical picture of the nervous diseases
The infectious diseases	Pathogenesis and treatment with the pressing states in the clinical picture of the infectious diseases
Surgical diseases	Pathogenesis and treatment with the pressing states in the clinical picture of the surgical diseases

4. Tasks for work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for the class:

Term	Definition
Hemorrhagic shock	severe form of hemostasis disorders, which developed as a result of significant blood loss.
Atherosclerosis	is the most common disease among residents of developed countries. With this disease (both main and concomitant) are physicians of any specialty.
Antioxidants	are substances that inhibit non-enzymatic reaction of free radical oxidation of lipids and biopolymers - proteins, nucleic acids and mucopolysaccharides.

4.2. Theoretical questions for the class:

1. What phase of blood coagulation.
2. Describe the basic properties of heparin.
3. What are the anticoagulants low.
4. Share prokoahulyantiv indications for use.
5. Share the indications for use of antiplatelet agents.
6. What are the main complication in the treatment of anticoagulant direct action.
7. Clinical and pharmacological characterization of lipid-lowering drugs.

Content topics

Theses of maintenance of theme.

Antianginal means - preparations, which decrease the need of myocardium for oxygen, they improve coronary blood circulation, increase the supply of cardiomyocytes by oxygen, they optimize energy exchange in the

cells of myocardium. Operational provisions of heart with the ischemic disease of heart (IDH) - stenocardia and the myocardial infarction depends, first of all, on the state of coronary blood flow. Therefore the object of pharmacological action with IDH is, in the first place, the mechanism of the regulation of the tone of the large and small vessels of heart (especially arterioles), reduction in the need of myocardium for oxygen, the normalization of metabolism in the myocardium, the level of fibrinogen, prothrombin in the plasma of blood and intravascular aggregation of thrombocytes. Basic antianginal means are nitrates, molsidominum, the antagonists of calcium, β -adrenoblockers, preductalum, trimethazideinum, mildronatum.

Classification of antianginal means.

1. Nitrates: nitroglycerinum, trinitrolong, nitrobid, nitrostat, 1% solution of nitroglycerinum for the injections, perlinganit, sustak, nitrong, nitrosorbid, izosorbid-5-mononitrat, nitromack, dinitrosorbitollong, nitro-oointment, nitroderm TTS-10;
2. Vasodilator of the nitrato-like action: molsidomin, bickamalin;
3. Calcium channel - blocking: verapamilum (izoptin), nifedipinum (corinfar), diltiazemum (cardil), nicaidipinum, nisoldipinum, amlodipinum (stamlo), lacidipinum (lacipil);
4. β -adrenoblockers: anaprilinum, obzidanum, trazikor, atenololum, talinololum (cordanum), nadololum ([corgard), secktral (atsebutalolum), pindololum (viscken), esmololum;
5. "Hybrid" ($\alpha+\beta$) - the adrenoblockers: labetalolum (trandat);
6. Activators of the potassium channels: pinacidilum, nicorandilum;
7. Preparations of metabolic action on the myocardium (gliosiz, milrinon, trimetazidinum (preductal), ranolazinum, ATP, fosfaden, coenzim of q10, riboxinum, retabolilum).
8. The means, which have the β -adrenoblocking activity and prolong action potential: amiodaronum and sotololum.
9. Anticoagulant means: heparinum, warfarinum, phenylinum.

Besides these means, which compose the basis of contemporary therapy, widely are employed psycho-sedative preparations, anticoagulants, trombolitics, vitamins, anti-sclerous means, which increase resistance of myocardium to hypoxia and ischemias (antioxidants, anabolic means, ATF, ascorbic acid).

Mechanism of the action of nitrates

Nitrovazodilators are connected with the SH- groups of endogenous nitrate receptors inside the smooth-muscle cells, they are metabolized into oxide of nitrogen (NO) and S -nitrozotiol, which causes the activation of adenylate cyclase and the accumulation of the intracellular of cGMF, which impedes the ion flow of calcium inside the cells and simultaneously accelerates the output from them of these ions (nitroglycerine, the nitroglycerine retard, glycerol trinitrate, isolitterbiyes dinitrate, isolitterbiyes mono-nitrate, pentaeritritila tetranitrate).

Nitroglycerine also stimulates the formation of vasodilator prostacyclins in the wall of vessels, reflector stimulates the isolation of catecholamines, which increase the flow of retarding impulses to the vasomotor to center (clofelin-like mechanism).

The antianginal mechanism of molsidomin is similar of nitroglycerine, but for the realization of the antianginal effect it is unnecessary of interaction with the SH- groups of proteins. It belongs to the pro- means: in the organism it is converted on NO, that also predetermines antianginal effect.

The blockers of slow calcium channels decrease the transmembrane calcium flow inside the cardiomyocytes, the cells of the smooth musculature of vessels and peysmeyer cells as a result of the decrease of a quantity of functioning channels and shortening of the period of a stay of calcium channel in the open state. The mechanism of the action of the antagonists of calcium is considerably wider than the blockade of the calcium channels: direct influence on calmodulin, oppression of the activity of phosphodiesteraz, liberation of calcium from the intracellular depot and aggregations of thrombocytes.

Amiodaronum (cordaron) noncompetitively blocks β -adrenoreceptors, calcium and sodium channels.

β -adrenoblockers block the β -adrenoreceptors of myocardium, this removes sympatho-adrenal influence on the myocardium, which predetermines the decrease of the work of the heart: reduction in force and frequency of the reductions of heart and the decrease of the need of myocardium for oxygen.

Dipyridamolum suppresses ferment adenosinedeaminase, it contributes to the accumulation of adenosin in the myocardium, which leads to the expansion of small coronary vessels.

Trimetazidinum ensures the transmembrane transfer of sodium, potassium, is supported homeostasis in the cardiomyocytes.

Pharmacodynamics. All enumerated preparations have antianginal effect. But each group of antianginal means has its special features of pharmacodynamics. Nitrovazodilator cause the expansion of veins and arteries; the decrease before and afterward the load to the myocardium; the decrease of the pressure, diastole, and the stress of the wall of ventricle, an improvement in the perfusion of myocardium (especially the zones of ischemia). Nitrovazodilator improve blood circulation in the sub-eneocardial divisions and collateral blood circulation, the decrease of central vasospastic reflexes. Nitrovazodilator decrease BP, the aggregation of thrombocytes, causes reflector tachycardia.

Nitroglycerinum (nitroglycerin-retard) decreases the tone of predominantly venous vessels myocardium, the brain, internal organs, retina, bronchi.

The blockers of calcium channels decrease the force and the frequency of the reductions of heart; enlarge peripheral vessels and coronary arteries, decrease afterward the load by the myocardium; they have anti-

hypertensive and antiarrhythmic effects. Have cardio protector action and ability to prevent necrosis a myocardium. They contribute to the rational division of oxygen in combination with the prolonged expansion of coronary arteries.

Amiodaronum (cordaron) has antianginal effect, decreases pulse. As a result the action of amiodaronum decreases the need myocardium for oxygen. Preparation also decreases the resistance of coronary arteries, which predetermines an improvement in the blood flow in the coronary vessels. Besides this, amiodaron it contributes to an increase in the energy reserves of myocardium.

β -adrenoblockers decrease the force and the frequency of the heart contractions (antianginal effect), slow down conducting pulse in the autonomous system of heart (antiarrhythmic effect), decrease the heart emission, the adrenergic stimulation of peripheral vessels and the liberation of renin by kidneys (anti-hypertensive effect).

Furthermore, propranololum has sedative, bronchospastic, hypoglycaemic effects.

Dipyridamolum increases collateral blood circulation and entering of oxygen to the myocardium.

Trimetazidinum (preductal) normalizes metabolic processes in the zone of ischemia of myocardium, decreases the damage of the membranes of cells (caused by free radicals), has antithrombocytic action. By the fundamental special feature of the action of preparation the optimization of the use of oxygen, such as it enters myocardium with the development of its ischemia, trimetazidinum is the first means of metabolic action. The effectiveness of the therapy by this preparation can be compared with the antianginal action of β -adrenoblockers, antagonists of calcium and nitrates.

Indications to the application and the interchangeability of nitrates

1. Stopping (sublingually - nitroglycerine, isolitterbiyes dinitrat, molsidominum) and the preventive maintenance of the assaults of stable and unstable stenocardia (nitrovazodilatator, amiodaronum).

2. Sharp myocardial infarction (intravenous introduction – nitroglycerinum, glycerylum trinitrat, izosorbidum dinitrat), reducing treatment after sharp myocardial infarction (glicerol trinitrat, izosorbidum dinitrat, izosorbidum mono-nitrat).

3. Complex therapy of sharp and chronic heart insufficiency (all nitrovazodilatators).

4. The Ischemic heart disease (β -adrenoblockers, the blockers slow calcium channels, nifedipinum – only prolonged forms).

5. Hypertonic disease (nifedipinum, amlodipinum (norvask), atenololum, isradipinum, nicardipinum), hypertonic crisis (nifedipinum).

6. Above (supra) ventricular tachyarrhythmias (atenololum, verapamilum, galopamilum, diltiazemum), chronic heart insufficiency (without the tachycardia) and the disturbance of peripheral blood circulation (nifedipinum, amlodipinum (norvask), isradipinum, nicardipinum).

7. Vascular defeats of brain (isradipinum, nicardipinum).

8. Stenocardia of stress and tachyarrhythmia, hypertonic disease, myocardial infarction in the reducing period β - adrenoblockers, trimetazidinum, riboxinum). 9. Preventive maintenance of the headache of vascular genesis - atenololum, metoprololum, propranololum.

10. Preventive maintenance of the assaults of the stenocardia of stress (nitroglycerinum retard, atenololum, carbocromenum, dipyridamolum).

11. Preventive maintenance of syndrome, hypercoagulation (dipyridamolum).

12. Myocardial dystrophy (riboxinum, ATP).

Side-action of nitrates. After only 9 years after the discovery of the antianginal effect of nitroglycerine D.D. Stewart for the first time described the phenomenon, which is subsequently named “**tolerance to nitrates**”. The author discovered reduction in the anti-hypertensive effect of nitroglycerine with his constant method for a period of 6 months, which is not restored even with an increase in the dose of preparation 160 times. Today are separated real tolerance, pseudo-tolerance, tahifilaxy and cross tolerance to nitrates. By real tolerance is understood reduction in the effectiveness of medicine during its prolonged application, which requires an increase in the primary dose of preparation for the support of the initial level of its antianginal, anti-ischemic, hemodynamic, antiagregation action. Real tolerance - specific for the therapy by nitrates state, for the realization of mechanisms of which it is necessary not less than two-three days, whereas pseudo-tolerance - unspecific reaction of organism, which can be developed to the method of any preparation by the mechanism of feedback in first 24 hours of treatment. By tahifilaxy it is customary to assume the tolerance, which is developed with lightning speed after the application of one or several doses of nitrates. Cross tolerance - this is tolerance to the different medicinal forms of the preparation of one group. It is necessary to note that the time of the development of tolerance to nitrates, and also the degree of its manifestation depend on many factors, including the initial structural-functional state of heart and vessels of patient, the specific features of metabolism, dose and the methods of the injection of these preparations. Thus, a number of the authors they showed that the prolonged application of trans-dermal nitrates (from the week to three months) does not lead to reduction in their effectiveness in 20-26% of patients. The different versions of primary reaction to nitrates are known. Thus, in patients with IHD are described four types of the reaction of microcirculatory river bed to the sublingual the intake of nitroglycerine.

Normal type. It is characterized by the expansion of venules and arterioles, by an increase in the arteriole-venular relationship, quantity of functioning capillaries and by the decrease of the degree of the aggregation of erythrocytes.

The paradoxical type, with which in response to the method of preparation is developed the spasm of micro-vessels, arteriole -venular relationship and quantity of functioning capillaries decreases, the degree of the

aggregation of erythrocytes increases.

The areactive type, with which the reaction of microcirculatory river bed to the nitroglycerine is absent.

Diatonic type - with the signs of vascular dystonia (symptom "of rosary") without changes in the arteriole-venous relationship, quantity of functioning capillaries and the degree of the aggregation of erythrocytes.

In patients with the unstable stenocardia primary unresponsiveness of microcirculatory river bed to the sublingual nitroglycerine it was noticeable in 5,9%, and paradoxical reaction - in 23,5% of cases, i.e., practically in 30% of patients with the unstable stenocardia (in each third!) the effect of nitrates can differ from that expected already with their first method. The clinical signs of developed tolerance is: an increase in the single and daily need for high speed and prolonged nitrates, the decrease of the manifestations of side effects (headache and so on), the recovery of arterial pressure (AP) and frequency of the heart contractions (pulse) to the initial indices, reduction in the tolerance to the physical load, the restoration of positive effect with an increase in the dose. The development of tolerance to nitrates can be confirmed on the basis the dynamics: data of echocardiography (tolerance to the hemodynamic action of preparation);

the results of testing load according to the data of bicycle ergometry and treadmill- test (tolerance to the hemodynamic and anti-ischemic action of preparation); the indices of the aggregative ability of thrombocytes (tolerance to the antiaggregation action of nitrates).

Most frequently for overcoming the tolerance to nitrates is used the so-called "pragmatic" method, which provides for either an increase in the dose or the cancellation of preparation on 3-5 days (concentric diagram), either the guarantee of an 10-12- hour "non" period, or the sporadic method of preparation if necessary (eccentric diagram). But it is necessary to consider, that with the observance of the eccentric diagrams of the treatment of reduction in nitrate concentration in the blood against the background of physical activity, that it continues, it is possible to lead to the development of the assault of the angine pain (the so-called "syndrome of early negative aftereffect") or the relapse of the angine pain in "non" period, it is more frequent at night. Therefore for overcoming the reduction in the effectiveness of nitrates is recommended also their alternation with blockers of slow calcium channels and sydnoneimines. Orthostatic hypotonia is possible with the intake of nitroglycerinum, with the method of the latter in the vertical position - tachycardia, headache as a result of an increase in the intracranial pressure. At the large doses (are more than therapeutic) rises intraocular pressure and appears methemoglobinemia.

Important side effect of nitrates - syndrome "of cancellation". It to be manifested by worsening in the clinical course of stenocardia and even death of patients 1-2 days after the sharp curtailment of the method of preparations. During the application of ointment or mat are possible allergic reactions, the irritation of the skin. During the application of molsidominum is possible the headache and a small decrease in arterial pressure.

The side effects of the blockers of slow calcium channels (besides amlodipinum (norvasc) are expressed by sharp arterial hypotension, bradycardia, weakness. During the prolonged application the bolts of atonic nature can appear. With the prolonged method of the large doses of amiodaronum is possible the appearance of ataxia, tremor, muscular weakness, nausea, bolt, hepatitis, sine bradycardia resistance to the cholinolytics, hypotension, heart insufficiency, is possible the development of the hypo- and of hyper-thyroidism, photo-sensitization, allergic reactions and reduction in the sexual activity. In the cases of the prolonged application of amiodaronum in patients are observed postponement in the epithelium the corneas of the eyes of lipofuscin, the disturbance of the function of the thyroid gland appears.

During the application of β -adrenoblockers - in the case of the method of nonselective preparations - sine bradycardia, arterial hypotension, heart insufficiency, bronchospasm, the development of angiospasm. After the rapid cancellation of β - adrenoblockers for a period of several days can be developed the syndrome "of cancellation". During the application of dipyridamolum are possible allergic reactions, the hypotonia, the syndrome "of robbing" (it decreases the blood supply of ischemic sections).

Contra-evidence to the designation of nitroglycerine.

Nitroglycerinum and other organic nitrates is forbidden to take by the patient with glaucoma, epilepsy, cerebral forms of hypertonic disease, during the hemorrhage into the brain. The application of molsidominum is contraindicated with cardiogenic shock and heavy hypotension.

Absolute contra-evidence to the application of blockers of calcium channels is cardiogenic shock, heavy stagnant heart insufficiency, turn arterial hypotension, hepatic and kidney deficiencies, pregnancy and lactation. Contra-evidence before the adoption of amiodaronum, is the weakness of sine unit, hypokalemia, pregnancy and lactation.

β - adrenoblockers cannot be used with the stagnant heart insufficiency, the bronchospasm, the heavy depressions, during insulin therapy. Dipyridamolum cannot be assumed with extended atherosclerosis of coronary arteries. The preparations of nitrates must not be assigned simultaneously with the vasos-dilatator, the blockers of calcium channels, the tricyclic antidepressants.

During the application of nitroglycerine and other organic nitrates one should consider that their continuous prolonged application leads to the tolerance, when for achievement effect is necessary an increase in the dose, and sometimes also the frequency of method. This is caused by the scarcity of sulfhydryl groups, by reduction in the activity of the ferments, which participate in the transformation of nitrates. It is expedient to assign nitrates with the donors of sulfhydryl groups, the antioxidants, to combine with the β -adrenoblockers. It is necessary to assign nitroglycerine in patients with severe atherosclerosis of the vessels of brain with the caution. Side-line phenomena can be decreased by the combining of nitroglycerine with menthol, by acetylsalicylic acid, β -adrenoblockers.

Amlodipinum (norvask) and filodipinum are the antagonists of the calcium channels, such as must be safely used with the associated expressed heart insufficiency (study PRAISE). Verapamilum, galopamilum are not recommended to combine with β -adrenoblockers, by antiarrhythmic means, by inhalation anesthetics, by heart glycosides. Contra-evidence it is to carry out the combined therapy diltiazemum and by the medicines, which cause bradycardia, for example, with the β -adrenoblockers. All antagonists of calcium are connected with the proteins of the plasma of the blood; therefore in the case of their designation with the quinidinum, heart glycosides, anticoagulants, which are capable of being displaced from the complexes with the protein, an increase in their concentration is possible.

Atenololum-lact more long-term effect in comparison with other β -adrenoblockers. Talinololum does not cause the development of orthostatic hypotension. Propranololum, oxprenololum, pindololum cause bronchospasm and disturbance of peripheral blood circulation. β -adrenoblockers are not connected with the narcotic analgesics, the inhibitors holinesteraze, the tricyclic antidepressants. Interaction of β -adrenoblockers with the medicines, which have negative inotropic and chronotropic action, can lead to the heavy side-line phenomena. On an empty stomach assumes amiodaronum (cordaron). After food assume metoprololum, galopamilum.

Comparative characteristic of preparations the vasodilator

Nitro-compounds, are the esters of nitric acid. Nitroglycerine is the standard preparation of nitrates and antianginal means. Nitroglycerine causes myotropic action on the muscles of vessels, predominantly enlarges vessels, including large coronary arteries, and also veins with the following increase in them of the volume of the deposited blood. The venous recovery of the blood to the heart decreases due to this and decreases pressure in the vessels of small circle. The hemodynamic unloading of myocardium appears.

Nitroglycerine through the system of prostaglandins A, E contributes to the release of prostacyclin (causing vasodilation) from the vascular wall it suppresses the production of thromboxane (factor of aggregation); therefore under the action of nitroglycerine disappears the syndrome of the intravascular coagulation, characteristic for IHD. With the sublingual way of the introduction of nitroglycerine the effect begins after 30 seconds and remain 15-30 minutes. The forms of the nitroglycerineum of prolonge action (sustac, nitro-poppy, nitrong) are obtained via the micro-encapsulation of nitroglycerine on the sorbents. Nitroderm - mat, is transdermal system and supports the prolonged operation of nitroglycerine (about 24 hours). The prolonged action has a nitroglycerinum retard, which is used for warning the assaults of stenocardia with IDH and the chronic heart insufficiency.

Glicerolum trinitrat consists of the fractions of nitroglycerine, which are sucked rapidly and slowly. The action of the first begins in 10-15 minutes, and 8-10 hours last by the second. They use for the preventive maintenance of the assaults of stenocardia. Izosorbidum dinitrat is one of the basic antianginal preparations for the oral application. The general duration of the action of the preparation of 4-5 hours is more. Izosorbidum mono-nitrat after the nature of action is close to izosorbidum dinitrat, has highest bio-accessibility and the more continuance of half-life.

Pentaeritritilum tetranitrat with the method per os slowly is sucked in the bowels, causing the soft and prolonged (5 hours) antianginal action.

The derivatives of sydnoniminum

Molsidominum increases the capacity of venous system, decreases the impact volume, improves collateral blood circulation, decreases the aggregation of thrombocytes. They use for the preventive maintenance of the assaults of stenocardia. The antianginal effect in 2-10 min is revealed, the duration of its action compose about 5 hours. Much less is developed tolerance after the method of molsidominum.

Blockers of the calcium channels

The antagonists of calcium share into the following preparations: First generation: verapamilum, nifedipinum, diltiazemum. Second generation: with the slow liberation of the acting substance. Third generation: the preparations of the new chemical structure: amlodipinum (norvask), felodipinum, lacidipinm.

The antagonists of calcium have cardio protector action and are capable of preventing the development of the necrosis of myocardium; therefore they have an advantage over other vasodilator means with IHD. Verapamilum contributes to the optimum division of oxygen in combination with the prolonged expansion of coronary arteries. Nifedipinum in contrast to verapamilum has the more expressed vasodilator action and does not have the suppressing influence on the leading system of heart (weak antiarrhythmic activity).

Antianginal effect mainly is ensured due to the expansion of coronary vessels. Preparation assumes per os and sublingually for the preventive maintenance of the assaults of stenocardia. Its action begins after 30-60 min, last 4-6 hours, sometimes to 24 hours.

Amlodipinum (norvask) – is the preparation of long-term effect. The effect of preparation is observed to 50 hours. Norvask enlarges peripheral arterioles and thus is reduced outlying resistance (after load), decreasing the work of heart. Since [CHSS] in this case practically does not change, reduction in afterward the load on the heart, leads to the decrease of the use of energy and need of myocardium for oxygen. Preparation does not cause reflector tachycardia, which makes it more effective during the treatment of ischemia of myocardium. It can be used both independently and in the combination [s], by other antianginal means in patients from by the stenocardia, resistance to the treatment with nitrates, and with the adequate doses of β -adrenoblockers. In connection with the slow development of effect the preparation better is transferred than the dihydropyridine derivatives of short action.

Isradipinum does not have the suppressing influence on the reductibility myocardium, it causes less than the side effects, connected with the vasodilation. Nicardipinum uses with the stenocardia of stress and rest.

Galopamilum - new preparation of the prolonged action (it is let out in tablets and tablets - retard). Duration of the action of preparation – is 6 hours. Diltiazemum on the actions to be close to verapamilum, but something it more strongly influences the smooth muscles of vessels and the conducting system of heart.

Blockers of the β - adrenoreceptors

Atenololum is not allotted by internal sympathomimetic activity. In comparison with metoprololum has more long-term effect. Atenololum does not disrupt sleep, emotional sphere. It is effective with the second preventive maintenance in the patients, who transferred myocardial infarction, and the patients with stenocardia. Myocardium in patients with the injuries of chairman decreases the progress of necrosis. Metoprololum - selective β_1 -adrenoblocker, suppresses the stimulating effect of catecholamines with the physical and psychoemotional load, especially in patients with bronchial asthma and diabetes mellitus.

Talinololum- selective (β_1 - adrenoblocker). The application of preparation in the patients with myocardial infarction contributes to the limitation of the zone of infarction and decreases the risk of the development of arrhythmias. It acts anti-hypertensively without orthostatic hypotension. Acebutylum butyrateol has also antiarrhythmic action. Propranololum is sucked well by mucous membrane of the gastro intestinal tract, penetrates through the placental barrier. It use with the ineffectiveness of other preparations, for treating the stenocardia of rest, but especially stenocardias stress, with the presence of associating IHD arrhythmias and arterial hypertonia. They cease application to preparation with IHD gradually.

Oxoprenololum in comparison with propranololum has a less expressed influence on the force and a frequency of the heart contractions; therefore it has internal sympathomimetic activity. Myocardium suppresses the reducing activity. Pindololum on the hypotensive action to be less active than propranololum.

The means, which increase the entering of oxygen to the myocardium

Dipyridamolum to be the derivative of pyrimidine. Dipyridamolum reduces the resistance of small coronary arteries, it contributes to the formation of the collaterals of the vessels of myocardium, increases the blood supply of myocardium, has antiagregation action due to strengthening of the synthesis of prostacyclin and oppression of thromboxane, improves microcirculation myocardium. Papaverinum causes the moderate expansion of coronary vessels, suppresses phosphodiesterase, increases the level of cAMP, is reduced the content of calcium in the cardiomyocytes. Drotaverinum (no-spa) after to chemical structure is close to the papaverinum, but the action of drotaverinum to be more expressed and more prolonged. Validolum is the solution of menthol in menthol ether of isovaleric acid, reflector causes the expansion of coronary vessels.

The means, which increase the resistance of myocardium to hypoxia Trimetazidinum normalizes energy exchange and electrolytic balance with ischemia. Against the background treatment by preparation considerably decreases the use of nitrates. Riboxinum increases the energy balance of myocardium, positively it acts on the processes of exchange in the myocardium. Coronary blood circulation improves. Adenosinum triphosphoric acid participates in many processes of exchange of substances. Cerebral and coronary blood circulation strengthens.

Materials for students' self-directed work.

A. Tasks for students' self-directed work.

1. Determine the classification of antianginal preparations, their mechanisms of action, pharmacodynamics, pharmacokinetics, side effects.
2. Determine the basic principles of pharmacotherapy by antianginal preparations in sick IHD.
3. Name the preparations, which are used during stopping of the assault of stenocardia.
4. Lay out the classification of antianginal preparations, their mechanisms of action, pharmacodynamics, pharmacokinetics, side effects.
5. Compile the plan of pharmacotherapy the patients have with the different classes of the stenocardia of stress in sick IHD
6. Compile the plan of pharmacotherapy in the patients with sharp myocardial infarction
7. Develop the plan of pharmacotherapy with the unstable stenocardia.
8. Compile the plan of pharmacotherapy the patients have with the diagnosis the spontaneous stenocardia

B. Tests for the self-control.

1. Preparations from the group of nitrates of the long-term effect.
2. Selective (β - adrenoblocker) has the internal sympathomimetic activity.
3. The antagonist of calcium, which has a tropism to the peripheral of the vessels.
4. The antagonist of calcium, which has predominantly antiarrhythmic effect.
5. The antagonists of calcium of the long-term effect, which are assigned only one time in a 24 hour period.
6. The medicines, which decrease the sensitivity of myocardium to hypoxia
7. The preparation, which has the β - adrenoblocking activity and lengthens action potential myocardium.
8. The preparation, such as suppresses adrenergic influence on the myocardium, effective with the stenocardia of stress.
9. β - adrenoblocker of the long-term action.
10. Name antianginal preparations for the treatment IHD: Stenocardias of stress in the patients of the elderly and senile age
11. Which of the antianginal means can be included in the complex of the therapy of patients with the

obstructive diseases of lungs?

12. What speed of the infusion of nitroglycerinum?

- A) 50 m kgf/min
- B) 10 m kgf /min
- C) 150-200 m/ kgf min

13. What antianginal means can be assigned for treating the chronic heart insufficiency in the absence of IHD: Stenocardias of stress.

- A) Nitrong of the tablet of 6,5 milligrams
- B) Sustac-fort of the tablet of 6,4 milligrams
- C) Trinitrolong of the plate of 4 milligrams
- D) Isopoppy sprej (aerosol)
- E) Molsidominum (sidnofarm) of the tablet of 2 milligrams
- F) Isolitterbiyes dinitrate (nitrosorbid) of the tablet of 10 milligrams
- G) Propranololum of the tablet of 40 milligrams
- H) Nitroglycerinum 1% alcoholic solution. Ampules on 1 ml

SITUATION TASKS:

1. Sick G. Diagnosis: IHD: Stable stenocardia of the stress of III fc. Atherosclerotic myocardioclerosis with the disturbance of the rhythm in the form of the ventricular of the extra of systolic arrhythmia. Hypertonic disease II st. The chronic insufficiency of the blood circulation I st. Determine the special features of the tactics of antianginal therapy in this situation.

2. Sick S. Diagnosis: IHD: Stenocardia of stress II f. class. Atherosclerotic . myocardioclerosis. Hypertonic disease II st. The chronic insufficiency of the blood circulation I st. To patient were assigned the following therapy: cristepin on 1 lozenge 3 times in the day, nitrosorbidum on 20 milligrams 4 times in day, riboxinum on 0.2 g 3 times in the day, asparkamum of 0,35 milligrams 3 times in the day. Quickening of the assaults of stenocardia was observed 1 week after the beginning of therapy.

3. Sick W. Diagnosis: IHD: Stenocardia of stress II f. class. Atherosclerotic myocardioclerosis with the disturbance of the rhythm in the form of ventricular extrasystole arrhythmia. The chronic insufficiency of the blood circulation I st. In anamnesis diabetes mellitus, hyperthyroidism. Which of the enumerated preparations it is possible to appoint - anaprillinum, verapamilum, cordaronum, nifedipinum.

4. To the patient, who suffers IHD: stenocardia of stress II f. class. Atherosclerotic myocardioclerosis was appointed cordaronum on 200 milligrams 3 times in the day. The angine assaults disappeared 1 week after the beginning of treatment, but appeared head cold, epiphora, hypersalivation. How you explained the medicinal action of amiodaronum (cordaron)? What could be the reason for this complication?

5. Sick M. Diagnosis: IHD: unstable stenocardia. Atherosclerotic myocardioclerosis. The chronic insufficiency of the blood circulation II- A. Was intravenously assigned 1% the alcoholic solution of nitroglycerinum. First the speed of the injection of preparation was 20-30 g/min, and subsequently - 50-75 H/minute. During the injection of preparation arose the hypotonia (AP of 90/55 mm Hg.) and bradycardia (45-60 heart contractions per minute). Your tactics of further therapy?

Literature:

Basic (studing):

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Additional:

- 1. Basic and Clinical Pharmacology by Anthony J. Trevor, Bertram G. Katzung, Susan B. Masters, 2009.
- 2. Medical Pharmacology at a Glance by Michael J. Neal, 2009.
- 3. Introduction to Clinical Pharmacology by Marilyn W. Edmunds, 2009.
- 4. Introduction to Clinical Pharmacology by Marilyn W. Edmunds, 2009.
- 5. Introductory Clinical Pharmacology by Sally S. Roach, Susan M. Ford, 2008.

Web sources:

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- 3. <http://intl-ajrcm.atsjournals.org/>
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<http://www.zheludok.ru/>

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