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DISLIPIDEMIA: DEFINITION, DIAGNOSTICS AND TREATMENT

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The review article presents the pathogenetic role of atherosclerotic vascular lesions in the development of cardiovascular diseases. The relationship between atherosclerosis and inflammation, which is characterized by the identical mechanism in the early phases, which includes the enhancement of the interaction between the vascular endothelium and circulating leukocytes is shown. The definition of such concepts as dyslipidemia, hyperlipoproteinemia and hyperlipidemia is given. The classification of hyperlipoproteinemia by Fredrickson, the clinical classification of dyslipidemia, proposed by the u krainian Scientific Society of Cardiologists, 2011 is considered. The correction of dyslipidemia, by both non-medicamentous measures, and drug treatment according to different variants of dyslipidemia is shown. The main groups of lipid-lowering drugs are listed. Their main mechanisms of action to reduce blood lipid levels are noted, and their side effects are listed. General recommendations are given on the monitoring of lipids and liver enzymes in patients taking lipid-lowering therapy.

Key words: dyslipidemia, hyperlipoproteinemia, cholesterol, triglycerides, very low density lipoproteins, low density lipoproteins, high density lipoproteins, statins, fibrates.

Cardiovascular diseases (CVD) remain the leading cause of mortality and morbidity in Western countries and other regions of the world, they continue to occupy the main place (65.2 %) in the mortality structure of Ukrainian citizens. In the overwhelming majority of cases, the basis of their pathogenesis is atherosclerosis (AS) and atherothrombosis of blood vessels, causing the development of coronary heart disease (CHD) in 67.5 %, and cerebrovascular diseases in 21.8 % [4].

Recent clinical and fundamental scientific studies have confirmed what Rudolf Ludwig Karl Virchow described as early as in 1845: atherosclerosis is an inflammatory lesion of the vascular wall (intima and the middle coat) and the response to damage due to the action of numerous factors. Activation and dysfunction of the endothelium trigger an atherosclerotic process after structural and functional changes in the endothelial wall [1].

Atherosclerosis develops gradually over the course of decades, manifesting as a mild form of endothelial damage with functional changes. Foamy cells (macrophages containing oxidized low-density lipoprotein cholesterol (LDL-C)) are the first sign of endothelial dysfunction. Foamy cells infiltrate the vessel, forming fat bands, then transitional lesions are formed with the presence of small extracellular lipid aggregations in the layers of smooth muscles; formed loci destroy the intimate lining. The formation of fat bands takes place at the earliest stage of plaque formation and is reversible. It is found in autopsy in 50 % of 10–14-year – old children [1]. The zones of the primary AS in the branches of the arteries, zones of springing the branches, the convex sides of the vessels contribute to the passive transport of blood components through the vascular wall. Progression to an apparent atheroma is observed in case when accumulated lipids, cells and other components of the plaque destroy the vascular wall [2].

Dyslipidemia is dysfunction and/or composition of blood lipids and lipoproteins, due to many reasons, which is capable, alone or in conjunction with other risk factors to cause the manifestation of an atherosclerotic process. Among disorders of the lipid of the blood, hyperlipoproteinemia (HLP) and hyperlipidemia are distinguished. Hyperlipoproteinemia (HLP) is any increase in the level of lipids and lipoproteins in the plasma above the optimal level. Hyperlipidemia is increase of blood lipids (cholesterol) and triglycerides (TG) levels above the optimal level [4].

The increase in total cholesterol and LDL cholesterol is important because it is precisely these disorders that are associated with an increase of cardiovascular risk (CVR). Their correction is possible by modifying the lifestyle and taking therapy.

Along with these disorders, the most significant is the so-called atherogenic lipid triad, which is characterized by an increase of the very low density lipoproteins (VLDL), and the associated increase of the level (TG) and the level of «small dense particles» of LDL cholesterol and the decrease of the level of high-density lipoprotein cholesterol (cholesterol HDL) [4].

In experimental and clinical studies it was shown that the disorder of endothelial function in hyperlipidemia occurs earlier than the development of intimal lesions. It has now been established that hypercholesterolemia causes endothelial dysfunction in the coronary circulation and resistive vessels of a person, preceding the angiographically detected atherosclerotic lesions in large coronary arteries. In human coronary arteries, the ratio of LDL to HDL is more essential than the absolute value of LDL for defining the degree of endothelial dysfunction, which indicates the influence of the protective properties of HDL cholesterol on the functional state of the endothelium.

WHO experts in 1970 recommended for clinical use the classification of HLP, proposed by Fredrickson et al. [5] in 1967, according to which the following five types of HLP are distinguished, they are presented in Table 1.

Chylomicrons (CM) are large globular and light formations that contain mainly TG (more than 90 %) and to a lesser extent cholesterol esters. CM are synthesized in the small intestine and serve to carry the TG in the first hours after food intake. CM transports edible fats and cholesterol from the intestine to the liver and peripheral tissues. The level of CM in the blood increases sharply after eating fatty foods.

Table 1. **Classification of hyperlipoproteinemia by Fredrickson**

Phenotype	Plasma cholesterol	TG	LP Excess	Atherogenicity
I	Increased	Increased or normal	Chylomicrons (CM)	Non-atherogenic phenotype
IIa	Increased	Normal	LDL	High
IIb	Increased	Increased	LDL and VLDL	High
III	Increased	Increased	HDL	High
IV	More often normal	Increased	VLDL	Moderate
V	Increased	Increased	CM and VLDL	Low

Very low density lipoproteins (VLDL) contain cholesterol 10–15 %, triglycerides 55 %, phospholipids 10–20 % and are the main transport form of endogenous triglycerides, formed predominantly in the liver. VLDL transport from 25 to 50 grams of liver-synthesized triglycerides during the day. VLDL are synthesized in the liver. After VLDL enter the blood, they are exposed to lipoprotein lipase, under the influence of which the triglycerides split [6].

Low-density lipoproteins (LDLs) are the main carriers of cholesterol in the form of its esters from the site of synthesis to "organs and tissues-consumers" (adrenal glands, genital glands, to the liver itself). LDL are the richest cholesterol lipoproteins (cholesterol 55 %, triglycerides 5–15 %, phospholipids 20–25 %). Lipoproteins rich in triglycerides (with the exception of chylomicrons) and cholesterol are atherogenic, i.e. they participate in the development of atherosclerosis [6].

High-density lipoproteins (HDL) are lipid-protein complexes that contain the greatest amount of phospholipids and protein and have an anti-atherogenic effect. The share of HDL is about 20–30 % of total blood cholesterol. The synthesis of HDL is carried out in two main ways:

1) formation in hepatocytes, small intestine cells (enterocytes) of HDL precursors with their subsequent conversion into "mature" HDL in the bloodstream;
2) in blood flow during catabolism of triglyceride-rich lipoproteins (chylomicron, VLDL). The most important function of HDL is the reverse transport of cholesterol from peripheral tissues to the liver, where it undergoes further catabolism. HDL cholesterol actively takes cholesterol from smooth muscle cells, fibroblasts, macrophages, endothelial cells and other cells, and in the form of esterified cholesterol it is transferred to the residues of lipoproteins that are absorbed by hepatocytes. Further, cholesterol is excreted by the liver in the bile, both in the form of free cholesterol, and in the form of bile acids, for the synthesis of which cholesterol is used. Thus, HDL has an anti-atherogenic effect and interferes with the development of coronary heart disease (CHD) [6].

Ukrainian Scientific Society of Cardiologists, 2007 suggested clinical classification of dyslipidemia:

1. Hypercholesterolemia (corresponds to IIa type of hyperlipoproteinemia according to Fredrickson);
2. Combined dyslipidemia (corresponds to IIb and III types of hyperlipoproteinemia by Fredrickson);
3. Hypertriglyceridemia (corresponds to the IV type of hyperlipoproteinemia according to Fredrickson) [4].

Target levels in the treatment of dyslipidemia are primarily based on the results of clinical studies. Recently, all studies of lipid lowering have used LDL cholesterol as an indicator of response to therapy. Therefore, the level of LDL cholesterol remains the primary goal in most strategies for the treatment of dyslipidemia. In patients with very high cardiovascular risk (established cardiovascular disease (CVD), type 2 diabetes mellitus (DM), type 1 diabetes with target organ damage, moderate or severe chronic kidney disease (CKD), or SCORE risk ≥ 10 %) the target level of LDL cholesterol is < 1.8 mmol/l. In patients with a high cardiovascular risk (a significant increase in a single risk factor, a SCORE risk of ≥ 5 to < 10 %), a target LDL cholesterol level of

< 2.5 mmol/l should be achieved. Patients with moderate cardiovascular risk (SCORE risk ≥ 1 to < 5 %) should achieve a target LDL-C level < 3.0 mmol/l [4].

If the LDL cholesterol level can not be determined, the following target cholesterol levels should be used according to the European Recommendations (2007): less than 5 mmol/l for the general population, less than 4.5 mmol/l for patients with high cardiovascular risk and less than 4.0 mmol/l for patients with very high cardiovascular risk [4].

Dyslipidemia (DLP) can be both primary (consequence of genetic disorders) and secondary (and / or consequence of concomitant diseases).

Treatment of dyslipidemia includes:

1. Non-medicamentous measures – diet, reduction of excess body weight, increase in physical activity, complete refusal to smoke;
2. Drug treatment according to different options of dyslipidemia.

DLP pharmacotherapy is constantly combined with a special anti-sclerotic diet, which is characterized by a lower (by 10 %) fat content and a predominance of unsaturated (vegetable) fatty acids among them; preservation of the amount of proteins that are recommended to replace with plant (soybeans, beans, kidney beans); prevalence of unrefined carbohydrates, the amount of which should ensure the calorie content of food and maintain a stable weight of the patient [7].

In asymptomatic patients, if by modifying the mode of life for 8–12 weeks it is not possible to achieve the optimal lipid profile, it is necessary to start drug-induced lipid-lowering treatment according to the variant of dyslipidemia [4].

Medicamentous treatment includes the following groups of drugs: statins, fibrates, nicotinic acid (niacin), omega-3 polyunsaturated fatty acids, bile acid sequestrants, polysponin.

Drugs of choice for the treatment of hypercholesterolemia is the group of statins [4]. Statins are largely able to reduce the level of both total cholesterol and the level of LDL cholesterol, as well as cardiovascular morbidity and mortality in primary and secondary prevention. The possibility of secondary hypercholesterolemia should be taken into account before starting treatment. Secondary hypercholesterolemia can be caused by such pathological conditions as: hypothyroidism, nephrotic syndrome, Cushing's syndrome. The manifestation of secondary hypercholesterolemia is possible in pregnant women, in persons taking immunosuppressants or corticosteroids, with anorexia nervosa. The group of statins or inhibitors of reductase 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) is represented by: lovastatin (a natural metabolite excreted from the fungus Aspergillus terreus); simvastatin, pravastatin, fluvastatin, (semisynthetic prodrugs); atorvastatin, cerivastatin (semi-synthetic active compounds). The mechanism of their action is in the competitive inhibition of HMG-CoA reductase, which catalyzes the formation of cholesterol in the liver at the stage of mevalonic acid. Since the process of mevalonate formation with HMG-CoA occurs at an early stage of cholesterol biosynthesis, treatment with simvastatin is not accompanied by the accumulation of potentially harmful, toxic sterols in the body. HMG-CoA quickly turns into an acetyl-CoA substance, which actively participates in many biological synthesis processes of the body [3, 7].

According to data from multicenter randomized clinical trials, more than two dozens of pleiotropic (pleiwn (Greek) – more, tropos-directed) effects of statins have been identified. In studies of MAAS (Multicentre Anti Atheroma Study) (simvastatin) [18], LCAS (Lipoproteins and Coronary Atherosclerosis Study) [12] and RECIFE (Reduction of cholesterol in ischemia and function of the endothelium) (fluvastatin) [9], REVERSAL (Reversal of Atherosclerosis with Aggressive Lipid Lowering) (atorvastatin) [14] there has been found that with prolonged administration of statins, the vasodilating function of the endothelium is improved, by increasing the level of nitric oxide (NO).

Studies of HPS (Heart Protection Stady) (simvastatin) [13], FLARE (Fluvastatin-Angioplasty-Restenosis) (fluvastatin) [10] and MIRACL (Myocardial Ischemia Redaction with Aggressive Cholesterol Lowering Substud) (atorvastatin) [17] have shown

the role of statins in stabilization of unstable atherosclerotic plaques. These drugs have a positive effect on the migration and functional state of macrophages, reducing the synthesis of metalloproteases and pro-inflammatory cytokines in them, which loosen the atherosclerotic plaque. The latter, thus influencing the migration and proliferation of smooth muscle cells in the vascular wall, improve its biochemical and histochemical characteristics. As a result, the risk of plaque rupture and intravascular thrombus formation is reduced. Reduced proliferation of smooth muscle cells leads to a decrease in the potential volume of atheroma.

In the FACT study (Fair Access to Clinical Trials) (fluvastatin) it was noted that fibrinolysis was improved by lowering the plasma fibrinogen level, normalizing the lipid composition of blood cell membranes, inhibiting ADP-dependent platelet aggregation, suppressing thromboxane production, and decreasing the concentration of the 1st tissue plasminogen activator .

The anti-inflammatory effect of statins was established in AFCAPS/TexCAPS (Air Force/Texas Coronary Atherosclerosis Prevention Study) (lovastatin) [11] and CARE (Cholesterol and Recurrent Events trial) (pravastatin) trials [16]. In particular, pravastatin decreasing the level of C-reactive protein, reduces the manifestations of cardiovascular diseases associated with this marker of inflammation. Atorvastatin reduces the secretion of interleukin-6 and tumor necrosis factor . In monocytes, in cultures of human smooth muscle and endothelial cells, atorvastatin reduces the activity of the nuclear factor of transcription of NF-Kappa B, which is important for suppressing the inflammatory process in the vessels.

In recent years, a new drug from the group of statins – rosuvastatin, which has pronounced hypolipidemic properties and high pleiotropic activity is increasingly used [3]. In addition to the above-listed anti-atherosclerotic effects, rosuvastatin has the ability to inhibit the development of tolerance to nitrates. Randomized studies of ASTEROID (A Study To evaluate the Effect of Rosuvastatin On Intravascular ultrasound – Derived coronary atheroma burden), METEOR (Measuring Effects on Intima-Media Thickness: an Evaluation of Rosuvastatin) using the intravascular ultrasound showed the effect of 40 mg of rosuvastatin over the course of 24 months on the possibility of reverse development of the thickness of intima-media complex of carotid arteries and thus on the regression of coronary atheroma [8, 15].

Table 2 shows the initial and maximum daily doses of statins.

Table 2. **Therapeutic doses of the statin group**

Preparation	Initial dose, mg per day	Maximum dose, mg per day
Simvastatin	10	40
Atorvastatin	10	80
Pravastatin	20	40
Fluvastatin	40	80
Rosuvastatin	5	40

In the absence of effect, the daily dose is gradually increased with an interval of 4 weeks – maximum up to 80 mg/day. Single reception in the evening is more effective than in the morning reception (synthesis of cholesterol is carried out mainly at night). It is recommended to take directly before eating, which contributes to a better absorption of the drug into the bloodstream.

Drugs are usually applied for a long time (for several months), are tolerated relatively well. Side effects are: dyspeptic disorders, insomnia, headache, skin erythema, rash. A dose-dependent side effect, hepatotoxicity (with an increase in the level of transaminases – ALAT ASAT or without it) , can be caused by all drugs of the statin group.

The characteristic and most severe side effect for all drugs is myopathy. In some patients, there may be the appearance of myalgia, muscle soreness, muscle weakness, rhabdomyolysis, an increase in the content of creatinine phosphokinase in blood [3, 5, 7].

For the treatment of combined dyslipidemia, both statins and statins in combination with fibrates are administered. Fibrates are derivatives of fibroic acid. Among this group of drugs are: clofibrate (1st generation), bezafibrate, gemfibrozil (II generation), fenofibrate, ciprofibrate (III generation). The mechanism of their hypolipidemic action is due to the blockade of the enzyme of the biosynthesis of cholesterol in the liver at the stage of conversion of acetylcoenzyme A into mevalonic acid, the difficulty of absorption of food fats in the intestine and the acceleration of the metabolism of cholesterol and TG with the participation of thyroid hormone thyroxin. The hypolipidemic effect is manifested in the form of a decrease in blood plasma of the levels of TG, LDL, a slight decrease in cholesterol and a significant increase in the content of HDL. This pharmacological group is able to reduce blood clotting, platelet aggregation and enhance fibrinolytic blood activity due to the direct action of fibrates on the synthesis of the plasminogen activator inhibitor. Clofibrate is also able to reduce the level of uric acid in the blood plasma.

Clofibrate is prescribed inside by 0.25 g in capsules after eating. The daily dose (0.5–0.75 g) is divided into 2–3 doses. Treatment is usually conducted in courses of 20–30 days with the same interruptions (4–6 courses). Gemfibrozil is usually administered at 1200 mg per day in two divided doses 30 minutes before the morning and evening meals. The dose for patients with V type of DLP can be increased to 1500 mg/day. Fenofibrate is taken by adults at 0.1 g (100 mg) twice a day before or during meals: 0.02 g (2 capsules) at breakfast and 0.01 g (1 capsule) at dinner.

Among the side effects when taking fibrates are: increased hepatic enzymes; cholelithiasis; disorders of the gastrointestinal tract (nausea, vomiting, diarrhea); muscle damage (myalgia, myositis, rhabdomyolysis); influence on the central nervous system (dizziness, headache, visual impairment, fatigue); influence on blood (leukopenia, reduction of hemoglobin and hematocrit, anemia, thrombocytopenia, bone marrow hypoplasia); allergic reactions (skin rash); impotence; decrease in body weight [3, 7].

Control of blood lipids is performed before taking lipid lowering therapy, at least two measurements, with an interval of 1–12 weeks, with the exception of conditions where immediate administration is necessary, for example, in acute coronary syndrome. The level of lipids should be determined in patients after starting lipid-lowering therapy: 8 ± 4 weeks after the start of treatment; (8 ± 4) weeks after correction of therapy to achieve the target level. The level of cholesterol or lipids after the patient has achieved a target or optimal level of cholesterol should be determined annually. Control of hepatic and muscle enzymes should be performed before the start of treatment, 8 weeks after the start of treatment or after increasing the dose of the drug, then annually, if the level of hepatic enzymes did not increase more than 3-fold.

With an increase in the level of liver enzymes in people taking lipid-lowering therapy, it is noted lower than 3-fold, continue this therapy and repeat tests for liver enzymes after 4–6 weeks. If the hepatic enzyme is increased more than 3 times, it is necessary to stop taking statins or reduce the dose of this drug and repeat the analysis for hepatic enzymes in 4–6 weeks. A cautious recovery of therapy is considered after the normalization of ALT levels.

The level of creatinine phosphokinase (CK) in patients taking lipid-lowering therapy should be determined before treatment before prescribing therapy. With a five-fold increase in the baseline of the CK, statin therapy is not started. Monitoring: routine determination of the level of CK is not necessary; to determine the level of CK, if the patient is concerned with myalgia.

If the level of CK is increased fivefold or higher in patients taking statins or fibrates, it is necessary to stop this therapy, check the kidney function and determine the level of CK every two weeks. It is necessary to consider the possibility of transient elevation of CK for another reason, for example muscle exercises (loads), to consider secondary causes of myopathy if the level of CK remains elevated.

With an increase in the level of CK less than five times in the absence of muscle symptoms, it is recommended to continue therapy with statins (patients should be warned about adverse symptoms, to consider questions about further determination

of CK level). If the patient has muscular symptoms, it is necessary to control the symptoms and regularly determine the level of CK [5].

Hypertriglyceridemia is a risk factor for cardiovascular disease, however, prior to initiating drug therapy, it is necessary to take into account possible secondary causes of its development. The latter are: genetic predisposition, obesity, type 2 diabetes, alcohol abuse, a diet with a high content of easily digestible carbohydrates, hypothyroidism, kidney disease, pregnancy (physiological elevation of the TG level twice during the third trimester of pregnancy), autoimmune disorders (paraproteinemia, systemic lupus erythematosus). Admission of medications, namely corticosteroids, estrogen, tamoxifen, β-adrenoblockers (except carvediol), thiazides, isotretinoin, resins that bind bile acids, cyclosporine, antiretroviral drugs (protease inhibitors), and psychotropic drugs can also cause hypertriglyceridemia.

In patients with high risk and TG levels > 2.3 mmol/l, the following regimens of medications are used: fibrates, niacin, omega-3 fatty acids, statins in combination with nicotinic acid, statins in combination with fibrates, a combination with omega-3 fatty acids [4].

Nicotinic acid (niacin) and its prolonged form (enduracin) exert hypolipidemic action by reducing the mobilization of free fatty acids from fat stores and entering the liver, which leads to a decrease in the biosynthesis of TG in the liver, and the formation of VLDL and the suppression of secretion by the VLDLP. The level of plasma VLDL, HDL and LDL is reduced, and the level of anti-atherogenic HDL is increased. Nicotinic acid can be used for hyperlipoproteinemia of IIa, IIb, III, IV and V types. The biggest problem with the use of nicotinic acid is the need to apply large doses of the drug (3 grams a day or more), which provide positive effects on lipid metabolism, but often have side effects. Among side effects should be noted: skin manifestations (itching and redness of the skin, rash, increased secretion of sebaceous glands of the skin, hyperpigmentation); from the side of the central nervous system (headache, dizziness, blurred vision); toxic effect on the liver (increased liver enzymes, jaundice); from the gastrointestinal tract (pain in the epigastric region, nausea, vomiting, diarrhea); metabolic disorders (hyperglycemia, hyperuricemia); from the cardiovascular system (tachycardia, palpitations, arrhythmias, hypotension) [3, 7].

Omega-3 polyunsaturated fatty acids reduce the level of TG, cholesterol by increasing their catabolism and reducing VLDL, reduce the content of arachidonic acid and, accordingly, thromboxane A2. Epadol is a mixture with a high content (not less than 43 %) of esters of omega-3-polyunsaturated fatty acids (0.5 g). The course of treatment is for at least four weeks at 1g twice a day [3].

Low level of HDL cholesterol is a strong and independent predictor of early development of atherosclerosis and cardiovascular diseases (CVD), therefore, a desirable secondary goal in the treatment of patients with dyslipidaemia is an increase in the level of HDL cholesterol. At the present time, the niacin drug most effectively increases the level of HDL cholesterol. A statin group as well as a group of fibrates can also be used, which equally increase the level of HDL cholesterol. The efficacy of fibrates to increase HDL cholesterol may be weakened by long-term admission in patients with type 2 diabetes mellitus (DM).

In the treatment of combined DLP, the level of HDL cholesterol should increase and the level of TG and LDL cholesterol levels decrease, which can be achieved with the administration of statins. Therefore, it is possible to prescribe statins in combination with nicotinic acid, but the side effect in the form of redness of the face can reduce the patient's adherence to treatment. It is good to prescribe a combination of statins and fibrates, controlling the indicators that show the possible development of myopathies, but it is necessary to avoid the prescription of a combination with gemfibrozil. If there is no possibility to control the level of TG with statins and fibrates, it is possible to prescribe omega-3-polyunsaturated fatty acids for further reduction of TG level, because this combination is safe and well tolerated by patients.

Levels of lipids in blood plasma are significantly determined by the genetic factor. In the worst case, there is family hyperlipidemia. If genetically determined dyslipidemia is

suspected, the patient should be sent to a specialized department dealing with lipid metabolism disorders. The most serious form of dyslipidemia is family dyslipidemia. Treatment of family dyslipidemia includes not only recommendations for the modification of the way of life, but also the administering lipid-lowering therapy. The patient should also remember the need to be examined for the presence of severe atherothrombosis [4].

Familial hypercholesterolemia (FH) may be suspected in patients with CVD in men under the age of fifty years old and in women under the age of sixty years old, in patients with early development of CVD or known FH in relatives. It is recommended to confirm the diagnosis according to clinical criteria or, if possible, according to DNA analysis. Screening of the whole family is recommended in the identification of a patient with FH; if possible, cascade screening can be performed. Patients with FH can be prescribed statins in high doses, and if necessary in combination with cholesterol absorption inhibitors in the intestine and / or bile acid sequestrants [4].

Bile acid sequestrants – cholestyramine, cholestide are anion-exchange resins. The formation of hardly soluble complexes with bile acids leads to an increased excretion of them from the body through the gastrointestinal tract and impaired absorption of cholesterol.

Preparations of this group are used for hyperlipoproteinemia IIa type inwards, but can increase the level of triglycerides. Cholestyramine: 5–30 mg in one or two doses. Side effects of sequestrants of bile acids are dyspeptic disorders, unpleasant taste, impaired absorption of other drugs, especially fat-soluble.

Polisponin – a dry extract from the rhizomes and roots of the disco niphone, inhibits the absorption of exogenous cholesterol in the intestine. The mechanism of its action is based on the formation of sparingly soluble compounds of cholesterol with the saponins contained in the plant (steroidal glycosides), which inhibits its absorption. Polisponin has a moderate hypocholesterolemic effect. The effect develops slowly and is sustained by the long-term administration of the drug: 1 to 2 tablets are taken orally 2 to 3 times a day after meals, 20 to 30 days with 7 to 10-day intervals during 3–4 months. Side effects of polisponin are loss of appetite, a tendency to diarrhea, sweating, itching, disorder of absorption of fat-soluble vitamins and medicinal substances [3, 7].

Children of patients with FH are recommended: early diagnosis, adherence to appropriate diet, medical therapy in older school age or in adulthood. Children with a homozygous FH require special respect from the first year of life. Treatment is aimed at achieving the target level of LDL cholesterol, as in patients with high risk (< 2.5 mmol/l), and in patients with a very high risk (< 1.8 mmol/l). If the target level can not be achieved, it is necessary to achieve the maximum reduction in LDL cholesterol level by using appropriate combinations of drugs and doses that are well tolerated by the patient [4].

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ДИСЛІПІДЕМІЯ: ВИЗНАЧЕННЯ, ДІАГНОСТИКА І ЛІКУВАННЯ

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В оглядовій статті описано патогенетичну роль атеросклеротичного ураження судин у розвитку серцево-судинних захворювань. Показано взаємозв'язок між атеросклерозом і запаленням, які характеризуються тотожним механізмом на ранніх фазах, що включає посилення взаємодії між ендотелієм судин і циркулюючими лейкоцитами. Дано визначення таких понять, як дисліпідемія, гіперліпопротеїнемія і гіперліпідемія. Розглянуто класифікацію гіперліпопротеїнемії за Фредриксоном, клінічну класифікацію дисліпідемії, запропоновану Українським науковим товариством кардіологів, 2011 р. Показана корекція дисліпідемій, як за допомогою немедикаментозних заходів, так і медикаментозне лікування відповідно до різних варіантів дисліпідемії. Перераховані основні групи гіполіпідемічних препаратів. Відмічено їх основні механізми дії щодо зниження рівня ліпідів крові, перераховані їх побічні ефекти. Дано загальні рекомендації згідно з моніторингом рівня ліпідів і ферментів печінки у пацієнтів, які приймають ліпідознижувальну терапію.

Ключові слова: дисліпідемія, гіперліпопротеїнемія, холестерин, тригліцериди, ліпопротеїни дуже низької щільності, ліпопротеїни низької щільності, ліпопротеїни високої щільності, статини, фібрати.

ДИСЛИПИДЕМИЯ: ОПРЕДЕЛЕНИЕ, ДИАГНОСТИКА И ЛЕЧЕНИЕ

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В обзорной статье описана патогенетическая роль атеросклеротического поражения сосудов в развитии сердечно-сосудистых заболеваний. Показана взаимосвязь между атеросклерозом и воспалением, которые характеризуются тождественным механизмом на ранних фазах, что включает усиление взаимодействия между эндотелием сосудов и циркулирующими лейкоцитами. Дано

определение таких понятий, как дислипидемия, гиперлипопротеинемия и гиперлипидемия. Рассмотрена классификация гиперлипопротеинемии по Фредриксону, клиническая классификация дислипидемии, предложенная Украинским научным обществом кардиологов, 2011 г. Показана коррекция дислипидемии, как немедикаментозных мероприятий, так и медикаментозное лечение соответственно разным вариантам дислипидемии. Перечислены основные группы гиполипидемических препаратов. Отмечены их основные механизмы действия по снижению уровня липидов крови, перечислены их побочные эффекты. Даны общие рекомендации согласно мониторинга липидов и ферментов печени у пациентов, принимающих липидоснижающую терапию.

Ключевые слова: дислипидемия, гиперлипопротеинемия, холестерин, триглицериды, липопротеины очень низкой плотности, липопротеины низкой плотности, липопротеины высокой плотности, статины, фибраты.