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HYPOLIPIDEMIC THERAPY IN THE COMPLEXITY OF IBS AND TYPE 2 DIABETES: MODERN OPPORTUNITIES AND PROSPECTS

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Abstract
The combination of coronary heart disease (CHD) and type 2 diabetes mellitus (DM2) is associated with an extremely high cardiovascular risk and accelerated progression of atherosclerosis. Dislipidemia in type 2 diabetes has a specific aterogenic profile characterized by increased triglyceride levels, decreased cholesterol, high-density lipoproteins, and the presence of small dense particles of low-density lipoproteins. The article presents modern approaches to hypolipidemic therapy in this category of patients, including the use of statins, ezetimibe, PCSK9 inhibitors, and small interfering RNAs (inclysiran). Particular attention is paid to combined treatment strategies, their effectiveness and safety, as well as promising areas of therapy.
Keywords: Coronary heart disease, type 2 diabetes mellitus, dyslipidemia, statins, PCSK9 inhibitors, inclisiran, ezethimib

Introduction

Cardiovascular diseases remain the leading cause of morbidity and mortality worldwide, with coronary heart disease (CHD) occupying a central place in the structure of cardiovascular pathology. The combination of coronary artery disease with type 2 diabetes mellitus (DM2) is of particular clinical importance, which is considered equivalent to a very high cardiovascular risk. According to the International Diabetes Federation, the number of patients with type 2 diabetes exceeds 530 million, and more than half of them die from complications of atherosclerotic origin [1]. The presence of diabetes increases the risk of developing coronary artery disease by 2-4 times, as well as significantly worsens the prognosis, increasing the likelihood of recurrent myocardial infarctions and cardiovascular mortality [2].

One of the key pathogenetic factors in the development and progression of atherosclerosis in patients with type 2 diabetes is dyslipidemia, which has a specific aterogenic nature. It manifests as a combination of hypertriglyceridemia, a decrease in high-density lipoprotein cholesterol levels, and an increase in the concentration of small, dense, low-density lipoprotein particles with high penetration capacity and pronounced atherogenicity [3,4]. Under conditions of insulin resistance, the synthesis of very low-density lipoproteins in the liver increases and their catabolism is disrupted, which further contributes to the progression of vascular damage [5].

Despite significant achievements in the field of hypolipidemic therapy, including the widespread use of statins, the problem of achieving target levels of low-density lipoprotein (LDL) in patients with CHD and type 2 diabetes remains relevant. According to clinical studies, up to 40-50% of patients do not achieve the recommended target LDL values even with high-intensity statin therapy [6]. In this regard, modern recommendations from the European Society of Cardiology and the European Society of Atherosclerosis emphasize the need for a more

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aggressive reduction in LDL levels (<1.4 mmol/l, and in some cases <1.0 mmol/l) and the extensive use of combined approaches [7].

In recent years, the arsenal of hypolipidemic agents has expanded significantly, including cholesterol absorption inhibitors (ezethimib), monoclonal antibodies to PCSK9, and small interfering RNA-based drugs such as Inclisiran. These drugs allow for a more pronounced and stable reduction in LDL levels, as well as contribute to an additional reduction in the risk of cardiovascular events [8-10]. Combined therapy aimed at various links of lipid metabolism is of particular interest, which is particularly relevant in patients with type 2 diabetes who are characterized by multifactorial metabolic disorders.

Thus, improving hypolipidemic therapy in patients with coronary artery disease and type 2 diabetes mellitus is one of the priority tasks of modern cardiology and endocrinology. This review is dedicated to analyzing the modern capabilities and prospects of lipid-lowering therapy in this category of patients, taking into account the latest clinical recommendations and the results of large randomized studies.

Features of dyslipidemia in type 2 diabetes

Dyslipidemia in type 2 diabetes mellitus (DM2) has a specific aterogenic nature and is one of the key factors in the accelerated development and progression of atherosclerosis. Unlike classical hypercholesterolemia, DM2 is characterized by so-called "diabetic" or atherogenic dyslipidemia, characterized by complex quantitative and qualitative changes in lipoproteins [1].

The main components of dyslipidemia in type 2 diabetes are a moderate increase in triglyceride levels (by 30-50% compared to the population norm), a 10-20% decrease in the concentration of high-density lipoprotein cholesterol (HDL-C), and an increase in the proportion of small dense lipoprotein particles (small dense LDL) possessing high aterogenicity [2,3]. At the same time, total cholesterol and LDL-C levels may remain within reference values, creating a false impression of lipid profile well-being [4].

Insulin resistance plays a key role in the formation of this dyslipidemia, leading to increased lipolysis in adipose tissue and increased intake of free fatty acids into the liver. This, in turn, stimulates the synthesis of very low-density lipoproteins (VLDL) and increases the concentration of triglycerides in plasma [5]. Simultaneously, the activity of lipoprotein lipase is impaired, which slows down the catabolism of triglyceride-containing lipoproteins and contributes to their accumulation [6].

An important pathogenetic link is also the change in the qualitative characteristics of LDL. Small, dense LDL particles penetrate the vascular endothelium more easily, have an increased tendency to oxidize, and circulate in the blood for longer, which significantly increases their aterogenic potential [7]. An increase in oxidized LDL levels contributes to the activation of inflammatory processes in the vascular wall and accelerates the formation of atherosclerotic plaques [8].

An additional factor is the decrease in HDL functional activity, including the impairment of their antioxidant and anti-inflammatory properties. Even with normal HDL-C levels, their protective role in patients with type 2 diabetes may be significantly reduced [9].

It should be noted that patients with type 2 diabetes often exhibit an increase in apolipoprotein B (ApoB), which reflects the total number of atherogenic lipoproteins, as well as an increase in the non-HDL-C indicator, which is considered a more accurate marker of cardiovascular risk in this population [10]. According to several studies, it is specifically ApoB and non-HDL-

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C that correlate better with the risk of cardiovascular events than the traditional LDL-C indicator [11].

Thus, dyslipidemia in type 2 diabetes mellitus is characterized by a complex multifactorial pathogenesis and requires a comprehensive approach to diagnosis and treatment. Assessing the level of LDL-C alone is insufficient, which justifies the need for an expanded lipid profile and the application of modern therapeutic strategies aimed at correcting all components of atherogenic dyslipidemia.

Target lipid levels (with recommendations)

In patients with coronary heart disease (CHD) and type 2 diabetes mellitus (DM2), the correction of lipid profile is considered one of the key directions for the secondary prevention of cardiovascular complications. Modern European recommendations classify such patients as having a very high cardiovascular risk, which requires a more intensive reduction in the level of atherogenic lipoproteins. According to ESC recommendations, for very high-risk patients, the target level of low-density lipoprotein (LDL) cholesterol is <1.4 mmol/L (<55 mg/dL), while simultaneously reducing LDL by at least 50% of the baseline level is recommended. In the event of a recurrent vascular event within 2 years, an even stricter target of <1.0 mmol/L (<40 mg/dL) can be considered against the background of maximum tolerable therapy. The 2025 focused update ESC/EAS separately notes that LDL targets themselves have not changed compared to the 2019 version.

In the ESC recommendations on cardiovascular diseases in patients with diabetes, it is also emphasized that the choice of hypolipidemic strategy should be based on the total cardiovascular risk, and in patients with established atherosclerotic cardiovascular disease, maximum active achievement of target LDL levels is required. This is especially important in cases of combined coronary artery disease and type 2 diabetes, as diabetes is associated with a faster progression of atherosclerosis, a higher frequency of multifocal vascular involvement, and an increased risk of recurrent ischemic events.

According to ADA Standards of Care, target LDL levels of <55 mg/dl (about <1.4 mmol/l) are recommended for patients with diabetes as part of secondary prevention. For primary prevention in adults aged 40–75 with diabetes, LDL <70 mg/dl (about <1.8 mmol/l) is considered a target. The ADA also recommends monitoring the lipid profile during diagnosis, then at least once a year, and after the start or intensification of lipid-lowering therapy, repeatedly after 4-12 weeks to assess response to treatment and adherence.

In addition to LDL, other indicators of lipid metabolism should be taken into account in clinical practice. In patients with diabetes and hypertriglyceridemia, non-HDL cholesterol and triglyceride levels are of additional importance. Although the primary therapeutic goal remains specifically related to LDL, an expanded assessment of the lipid profile allows for a more accurate determination of residual atherogenic risk, especially in patients with atherogenic diabetic dyslipidemia.

Thus, in patients with coronary artery disease with type 2 diabetes, the primary target for hypolipidemic therapy is achieving a LDL level of <1.4 mmol/l with a reduction of at least 50% from the baseline, and in cases of extremely high risk and recurrence, striving for a level of <1.0 mmol/l. This approach aligns with the modern concept of "the lower the LDL level, the better the prognosis," which forms the basis of modern European and American recommendations.

Statin as the basis of therapy

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Statin is a first-line drug in the treatment of dyslipidemia in patients with coronary heart disease (CHD) and type 2 diabetes mellitus (DM2), due to its proven effectiveness in reducing cardiovascular disease and mortality. The main mechanism of action for statins is related to the inhibition of the enzyme GMG-CoA-reductase, which leads to a decrease in cholesterol synthesis in the liver and an increase in the expression of low-density lipoprotein (LDL) receptors, ensuring enhanced clearance of atherogenic lipoprotein from the bloodstream [1].

The largest meta-analysis by the Cholesterol Treatment Trialists' Collaboration, which included more than 170,000 patients, showed that a decrease in LDL levels by every 1 mmol/l is accompanied by a 21% reduction in the risk of major cardiovascular events, including myocardial infarction, stroke, and cardiovascular death [2]. This effect is proportional to the degree of LDL reduction and is observed regardless of the initial cholesterol level.

In patients with diabetes mellitus, the effectiveness of statins has also been confirmed in several large randomized studies. In the CARDS study (Collaborative Atorvastatin Diabetes Study), the use of atervastatin in patients with type 2 diabetes without established coronary artery disease led to a 36% reduction in the risk of acute coronary events and a 48% reduction in the risk of stroke [3]. In the HPS (Heart Protection Study) study, a 13% decrease in general mortality and a 17% decrease in vascular mortality was noted in patients with diabetes [4].

Despite its high efficacy, statin monotherapy does not always achieve target LDL levels in very high-risk patients. According to modern registries, up to 40-50% of patients with coronary artery disease and type 2 diabetes do not reach a LDL level of <1.4 mmol/l even when using high-intensity doses of statins [5]. This is due to both the severity of metabolic disorders and dosage restrictions due to side effects.

High-intensity statin therapy (atorvastatin 40–80 mg, rosuvastatin 20–40 mg) allows for a 50% or more reduction in LDL levels compared to the baseline [6]. However, increasing the dose is accompanied by an increased risk of adverse events, including myalgia, increased liver enzyme activity, and, in rare cases, the development of rhabdomyolysis. The frequency of statin-associated muscle symptoms ranges from 1 to 5% in clinical studies, but in real practice, it can reach 10-15% [7].

Special attention is paid to the issue of the influence of statins on carbohydrate metabolism. It is known that the use of statins can slightly increase the risk of developing type 2 diabetes (by approximately 9-12%), but this risk is significantly lower than their cardioprotective effect and does not constitute a basis for refusing therapy [8]. In patients with pre-existing type 2 diabetes, statin therapy does not worsen clinically significant glycemic control.

Modern recommendations from the European Society of Cardiology and the American Diabetes Association emphasize the necessity of prescribing statins to all patients with coronary artery disease and type 2 diabetes, regardless of the initial LDL level. In cases of insufficient monotherapy efficacy, the early addition of other hypolipidemic drugs, such as ezetimib or PCSK9 inhibitors, is recommended [9].

Thus, statins remain the foundation of hypolipidemic therapy in patients with CHD and type 2 diabetes mellitus. Their use ensures a significant reduction in cardiovascular risk, but achieving target LDL levels in very high-risk patients often requires a combined approach.

Ezetimib in combined therapy

Ezetimib occupies an important place in modern hypolipidemic therapy as a second-line drug used in combination with statins in patients who have not reached target levels of low-density lipoproteins (LDL), as well as in cases of intolerance to high doses of statins. The action mechanism of ezetimib differs fundamentally from that of statins and is associated with the

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selective inhibition of the NPC1L1 protein in small intestinal enterocytes, which leads to a decrease in cholesterol absorption and a decrease in its entry into the liver [1].
Adding ezetimib to statin therapy ensures an additional reduction in LDL levels by an average of 20-25%, which significantly increases the proportion of patients achieving target lipid values [2]. The combination of statin and ezetimib affects two key links in cholesterol metabolism: synthesis and absorption, providing a synergistic effect.
The key study confirming the clinical efficacy of ezetimibe is IMPROVE-IT, which evaluated the effect of combining simvastatin with ezetimibe compared to statin monotherapy in patients with acute coronary syndrome. The study showed that the addition of ezetimib led to a decrease in LDL levels to 1.4 mmol/L, and was also accompanied by an additional 6.4% reduction in the risk of major cardiovascular events [3].
IMPROVE-IT results are of particular importance for patients with type 2 diabetes mellitus. The sub-analysis demonstrated that in patients with type 2 diabetes, combined therapy ensured a more pronounced reduction in the risk of cardiovascular complications - up to 14% compared to monotherapy with statins [4]. This is explained by a higher initial risk and pronounced atherogenic dyslipidemia in this category of patients.
Ezetimib is characterized by a favorable safety profile and good tolerance. The frequency of side effects is comparable to that of a placebo, and the risk of developing myopathies remains low with combined therapy [5]. This makes the drug an optimal choice for enhancing hypolipidemic therapy in patients with limited tolerance for high doses of statins.
Modern recommendations from the European Society of Cardiology and the American Diabetes Association recommend adding ezetimib in the early stages of treatment for very high-risk patients, including patients with CHD and type 2 diabetes, if LDL levels are insufficiently reduced against the backdrop of the maximum tolerated dose of statin [6]. This approach allows for faster achievement of target levels and reduces residual cardiovascular risk.
Thus, ezetimib is an effective and safe component of combined hypolipidemic therapy. Its use in combination with statins significantly increases treatment efficacy, especially in patients with type 2 diabetes, for whom a high residual risk is characteristic even with adequate basic therapy.

PCSK9 inhibitors

PCSK9 inhibitors represent one of the most significant breakthroughs in modern hypolipidemic therapy, especially in patients with very high cardiovascular risk, including patients with coronary heart disease (CHD) and type 2 diabetes mellitus (DM2). The PCSK9 protein (proprotein convertase subtilisin/kexin type 9) regulates the degradation of low-density lipoprotein (LDL) receptors in the liver. Increased activity of PCSK9 leads to a decrease in the number of LDL receptors and, accordingly, an increase in plasma LDL levels [1].
Monoclonal antibodies to PCSK9, such as Evolocumab and Alirocumab, block the interaction of PCSK9 with LDL receptors, preventing their degradation and promoting enhanced clearance of atherogenic lipoproteins. This leads to a pronounced decrease in LDL levels - by an average of 50-60% in addition to statin therapy [2].
The clinical efficacy of PCSK9 inhibitors has been confirmed in a number of large randomized studies. In the FOURIER trial (27 564 patients with atherosclerotic cardiovascular diseases), the use of evolocumab reduced LDL levels to 0.78 mmol/l and was accompanied by a 15% reduction in the risk of a primary combined endpoint (cardiovascular death, myocardial

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infarction, stroke). At the same time, the risk of myocardial infarction decreased by 27%, and stroke by 21% [3].
Similar results were obtained in the ODYSSEY OUTCOMES study, which included patients with acute coronary syndrome. The use of alirocumab led to a reduction in LDL levels to ≈1.0 mmol/l and a 15% reduction in the risk of major cardiovascular events, as well as a reduction in overall mortality in patients with the highest initial LDL levels [4].
The effectiveness of PCSK9 inhibitors in patients with type 2 diabetes is of particular interest. Sub-analysis of FOURIER and ODYSSEY studies showed that the reduction in cardiovascular risk in patients with type 2 diabetes is comparable or even more pronounced than in patients without diabetes, while the drugs do not have a negative impact on glycemic control and do not increase the risk of developing diabetes [5].
PCSK9 inhibitors are characterized by a favorable safety profile. The most frequent side effects are local reactions at the injection site (up to 2-5%), while systemic undesirable phenomena are rare. Unlike statins, these drugs are not associated with an increased risk of myopathy or hepatotoxicity [6].
According to the recommendations of the European Society of Cardiology, PCSK9 inhibitors are indicated for very high-risk patients, including patients with coronary heart disease and diabetes mellitus type 2, if target LDL levels are not achieved against the backdrop of maximum tolerance for statin therapy in combination with ezethimib [7]. Their application allows for achieving extremely low LDL values (<1.0 mmol/l), which aligns with the modern concept of "the lower the better."
Despite their high efficiency, the widespread use of PCSK9 inhibitors is limited by their high cost and accessibility, which is particularly relevant for developing countries. Nevertheless, given the significant reduction in cardiovascular risk, their use is justified in patients with the highest risk and insufficient effect of standard therapy.
Thus, PCSK9 inhibitors are a highly effective tool for intensifying hypolipidemic therapy in patients with CHF and type 2 diabetes mellitus. Their inclusion in combined treatment regimens significantly improves lipid profile control and reduces the frequency of adverse cardiovascular outcomes.

Inclisiran - a new paradigm for hypolipidemic therapy

Inclisiran is an innovative drug for reducing low-density lipoprotein (LDL) levels, belonging to the class of small interfering RNAs (siRNAs). Unlike monoclonal antibodies to PCSK9, inclisiran affects the synthesis of this protein at the hepatocyte level, inhibiting the expression of the PCSK9 gene and thereby reducing its production [1].
The mechanism of inclisiran's action is based on RNA interference technology: the drug penetrates liver cells and binds to the PCSK9 matrix RNA, causing its degradation. This leads to a decrease in PCSK9 synthesis, an increase in the number of LDL receptors on the surface of hepatocytes, and increased LDL clearance from blood plasma [2]. Thus, inclisiran ensures a prolonged and stable decrease in the level of aterogenic lipoproteins.
The clinical efficacy of inclisiran was demonstrated in a series of large randomized studies conducted under the ORION program. In the ORION-10 and ORION-11 studies, which included patients with atherosclerotic cardiovascular diseases and high risk, adding inclisiran to standard therapy allowed for a 52-55% reduction in LDL levels compared to placebo [3].
A feature of the drug is its dosage regimen: after initial injection and repeated administration after 3 months, subsequent doses are administered once every 6 months, which significantly increases treatment adherence [3]. In conditions of chronic diseases such as type 2 diabetes,

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where patients receive multiple drug therapies, this advantage is of particular clinical importance.

Additional data from the long-term ORION-8 study showed that the effect of LDL reduction persists for more than 4 years, with no decrease in therapy efficacy over time [4]. This confirms the stability and reproducibility of inklisiran's lipid-lowering effect.

In patients with type 2 diabetes mellitus, inclisiran demonstrates comparable efficacy with the general population, ensuring a significant reduction in LDL levels without affecting glycemic control. It is important to note that the drug is not associated with an increased risk of developing new cases of diabetes, unlike some other hypolipidemic agents [5].

Inclisiran's safety profile is favorable. The most frequent side effects are local reactions at the injection site (about 5-8%), which are usually mild in severity. The frequency of systemic adverse events is comparable to a placebo [3].

According to modern recommendations of the European Society of Cardiology, inclisiran can be considered an alternative or supplement to PCSK9 inhibitors in very high-risk patients, including patients with CHD and DM2, if target LDL levels are not sufficiently achieved against the background of standard therapy [6].

Although there is currently no definitive data on reducing "rigid" endpoints (cardiovascular mortality, myocardial infarction), it is expected that ongoing studies (specifically ORION-4) will confirm the clinical benefits of inclisiran in the long term [7].

Thus, inclisiran represents a promising direction in hypolipidemic therapy, ensuring an effective, long-term, and convenient reduction in LDL levels. Its application is particularly relevant in patients with high and very high cardiovascular risk, including patients with type 2 diabetes mellitus, where achieving strict target lipid levels and high adherence to treatment is required.

Combined hypolipidemic therapy

In patients with coronary heart disease (CHD) and type 2 diabetes mellitus (DM2), combined hypolipidemic therapy is a necessary element of modern treatment strategy, as statin monotherapy often fails to achieve the target levels of low-density lipoproteins (LDL). According to clinical practice, up to 40-50% of very high-risk patients do not reach a LDL level of <1.4 mmol/l even during high-intensity statin therapy [1].

The combined approach is based on influencing various links in lipid metabolism:

• suppression of cholesterol synthesis (statins),
• decrease in its absorption in the intestines (ezethimib),
• enhancing LDL clearance through receptors (PCSK9 inhibitors, inclysiran).

This mechanism provides an additive and synergistic effect, allowing for a more pronounced decrease in LDL levels and a reduction in residual cardiovascular risk [2].

Modern recommendations from the European Society of Cardiology offer a step-by-step strategy:

1. High-intensity statin
2. Adding ezetimib if the goal is not achieved
3. Addition of PCSK9 inhibitor or inclisiran if high LDL levels persist.

Table 1. Main schemes for combined hypolipidemic therapy

Treatment Scheme	Mechanism of Action	LDL-C Reduction	Clinical Benefits	Limitations

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Statin (monotherapy)	↓cholesterol synthesis	30–50%	Basic therapy, proven to reduce mortality	Insufficient for very high risk
Statin + ezetimib	↓ synthesis + ↓ cholesterol absorption	50–65%	Availability, good tolerance	Limited efficacy in some patients
Statin + PCSK9 inhibitor	↑ LDL receptors (through PCSK9 blockade)	65–75%	Rapid and significant reduction in cardiovascular risk	High cost
Statin + Inclisiran	↓ PCSK9 (siRNA) synthesis	50–60%	Long-term effect, 2 times a year	Limited availability
Triple therapy (statin + ezetimib +PCSK9 (inclisiran)	Comprehensive effect	up to 80%	Maximum risk reduction	Cost, need for control

Combined therapy allows for achieving target LDL levels in more than 80-85% of patients, which significantly exceeds the effectiveness of monotherapy [3]. Early intensification of treatment is particularly important in patients with type 2 diabetes, who exhibit a pronounced residual risk even with a moderate decrease in LDL.

It should be noted that combined therapy not only improves the lipid profile but also has a positive impact on clinical outcomes. Meta-analyses have shown that a more intensive decrease in LDL is accompanied by an additional 20-30% reduction in the risk of cardiovascular events compared to standard therapy [4].

The choice of combination must be individualized, taking into account:

- level of cardiovascular risk
- initial LDL level
- drug tolerance
- presence of comorbidities (including CBP)
- economic factors

In patients with coronary artery disease and type 2 diabetes, the optimal strategy is the early application of combined therapy to quickly achieve target LDL levels and reduce the risk of recurrent cardiovascular events.

Conclusion

The combination of coronary heart disease (CHD) and type 2 diabetes mellitus (DM2) forms a category of patients with extremely high cardiovascular risk, requiring the most aggressive and simultaneously individualized strategy of hypolipidemic therapy. Aterogenic dyslipidemia, characteristic of type 2 diabetes, causes not only quantitative but also qualitative changes in lipoproteins, which intensifies the progression of atherosclerosis even with relatively moderate levels of cholesterol and low-density lipoprotein (LDL).

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Modern clinical studies convincingly demonstrate that achieving low and very low LDL levels (<1.4 mmol/l, and in some cases <1.0 mmol/l) is accompanied by a significant reduction in the risk of cardiovascular complications. At the same time, the concept of "the lower the better" remains relevant and is confirmed by the results of large-scale randomized studies.

Statin remains the foundation of therapy, but in most very high-risk patients, early intensification of treatment using combined regimens is required. The addition of ezethimib, PCSK9 inhibitors, or Inclisiran allows for a more pronounced and stable reduction in LDL levels, as well as a reduction in residual cardiovascular risk. Innovative approaches, including siRNA therapy, open up new perspectives in the treatment of dyslipidemia, ensuring high efficacy and improved adherence to therapy.

Thus, modern hypolipidemic therapy in patients with coronary heart disease and type 2 diabetes must be multi-level, personalized, and aimed at achieving the lowest possible target LDL levels, taking into account the patient's individual characteristics.

Practical recommendations

1. Risk stratification

All patients with coronary artery disease and type 2 diabetes should be considered individuals with very high cardiovascular risk and a target LDL level of <1.4 mmol/L.

2. Early initiation of therapy

Prescribing high-intensity statins should be done as early as possible, regardless of the initial LDL level.

3. Assessment of treatment effectiveness

Monitoring of the lipid profile is recommended 4-12 weeks after starting or changing therapy, followed by regular monitoring.

4. Early intensification of therapy

If target LDL levels are not achieved, it is necessary to add the second drug (ezethimib) in a timely manner, without delaying treatment correction.

5. Use of modern drugs

If high LDL levels persist during double therapy, it is indicated to prescribe PCSK9 or Inclisiran inhibitors.

6. Individualization of treatment

The choice of therapy regimen should take into account:

- patient's age
- presence of comorbidities (including chronic kidney disease)
- drug tolerance
- risk of drug interactions

7. Safety control

It is necessary to monitor liver enzyme levels, myopathy symptoms, and other possible side effects.

8. Increasing adherence to therapy

Consideration should be given to the convenience of the treatment regimen (e.g., infrequent administration of drugs such as inclisiran) to improve compliance.

9. Comprehensive approach

Hypolipidemic therapy should be combined with the correction of other risk factors:

- arterial hypertension
- hyperglycemia
- obesity

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