



EFFECTIVENESS OF STATINS IN THE PREVENTION OF ISCHEMIC HEART DISEASE

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ABSTRACT

The main cause of the development of ischemic diseases of the cardiovascular system is atherosclerosis. Other less common causes of coronary heart disease include pathology of the microcirculatory bed of the myocardium and coronary vasospasm. According to the WHO definition, atherosclerosis is a variable combination of changes in the inner lining (intima) of the arteries, including the accumulation of lipids, complex carbohydrates, fibrous tissue, blood components, calcification and concomitant changes in the middle shell (media). For a long time, atherosclerosis can proceed asymptotically, only eventually leading to angina pectoris, chronic cerebrovascular insufficiency, intermittent lameness, or to the immediate manifestation of myocardial infarction, ischemic stroke, sudden death. As a result of the formation and growth of ASB, gradual stenosis of the coronary, cerebral and other arteries occurs. However, often the first manifestation of coronary heart disease is a myocardial infarction or sudden death due to the rupture of an atherosclerotic plaque that does not obstruct the lumen of the artery.

In addition to hypercholesterolemia, which leads to the development of atherosclerosis, risk factors for the development of coronary artery disease include hypertension, diabetes mellitus, physical inactivity, obesity, smoking, burdened family history. Preventive and therapeutic measures aimed at correcting risk factors can reduce the likelihood of atherosclerosis and its complications.

An early trigger of atherogenesis is damage to the endothelium by various factors acting from the side of the artery lumen. These same factors cause the release of singlet oxygen, which is accompanied by the oxidation of LDL. Oxidized LDL





penetrates into the subintimal space and is captured by macrophages. Reactive oxygen species (ROS) act on endothelial cells (EC) and cause their activation. Activated ECS produce cell adhesion molecules and chemokines.

Keywords: coronary heart disease, statins, atorvastatin, C-reactive protein

INTRODUCTION

Over the past decades, the principles of treatment of patients with chronic coronary heart disease (CHD) have undergone significant changes, which has led to a significant reduction in mortality from CHD and the frequency of its non-fatal complications in developed countries. The reason for the changes in international clinical guidelines was the results of a number of large randomized trials (4S, CARE, LIPID, HPS, ASCOT-LLA). It has been shown that regular statin intake for 5-6 years reduces the number of recurrent cardiovascular complications (CVD): acute myocardial infarction (MI), unstable angina and death by 25-40%, ischemic strokes - by 25-30%. A 25-30% reduction in total cholesterol (OHC) and low-density lipoprotein cholesterol (LDL cholesterol) by 30-35% was associated with a reduced risk of MTR.

The need to prescribe statins in high-risk patients [with concomitant arterial hypertension (AH), high hyperlipidemia, diabetes mellitus (DM), various forms of coronary artery disease, stroke] has been proven in studies such as HPS, PROSPER, SPARCL, CARDS, etc.. The main purpose of using statins is to reduce the risk of developing CVD and improve the survival of patients.

The results of these studies made it possible to determine the target levels of LDL cholesterol for patients of various risk categories, which is reflected in European and Russian clinical guidelines. The register included all persons with a diagnosis of hypertension, coronary heart disease, chronic heart failure (CHF), atrial fibrillation, who turned to district therapists or cardiologists of one of the randomly selected in the 1-clinic SamMU 2021. (n=82). Severe hypercholesterolemia was detected in 28 people (44%), of whom high and very high cardiovascular risk were 83.7% of patients were referred. At the same time, statins were recommended only by 17.8%, mainly in moderate doses. Only one patient was prescribed atorvastatin at a dose of 40 mg / day. They did not achieve the target values of LDL cholesterol. In addition to the unsatisfactory situation with the appointment of statins by doctors, there is a problem of low adherence to treatment by patients with cardiovascular diseases (CVD), which is fraught with serious consequences. Violation of the statin therapy regimen by patients who have suffered a myocardial infarction (MI) leads to an increase in





mortality. Factors, the factors affecting adherence to prescribed treatment are few and insufficiently studied. The analysis of the prescribability of statins, the compliance of therapy with modern clinical recommendations, its effectiveness and patients' adherence to prescribed treatment remains relevant.

The aim of the study was to evaluate the frequency of prescribing, efficacy and adherence to statin treatment in patients with coronary artery disease, confirmed by coronary angiography (CAG) data.

MATERIALS AND METHODS

The analysis was carried out on the basis of register data PROGNOSIS OF coronary heart disease, a directional diagnosis of "coronary heart disease", which was performed AS. When analyzing patient medical histories, 128 patients met the selection criteria. The analysis included data from 110 patients in whom, according to the results of CAG, stenosis of at least one coronary artery (CA) $\geq 50\%$ was detected. During the visit, the patient was examined, including a survey, examination, biochemical blood analysis with the determination of lipid profile parameters: OHS, LDL cholesterol, high-density lipoprotein cholesterol (HDL cholesterol), triglycerides (TG). All patients at the visit filled out a questionnaire that included questions about their social status, available risk factors, information about medications currently being taken, and adherence to prescribed treatment. Adherence to statin therapy was assessed in 61 patients who came to visit an average of 3.9 years after discharge, who filled out a special questionnaire. After 3.9 years (from 0.76 to 6.52), the fate of 551 patients (86%) was determined. The analysis included data from 110 patients in whom, according to the results of CAG, stenosis of at least one coronary artery (CA) $\geq 50\%$ was detected. In 2020, out of 110 patients, 82 were alive, and the vital status of 90 people could not be established. In 2020, all 82 patients who lived at that time were interviewed by phone for taking statins and invited to the PM State Medical Center for a follow-up visit (61 people came to visit, and 21 patients refused for various reasons). During the visit to GNIC PM, the patient was examined, including a survey, examination, biochemical blood analysis with the determination of lipid profile parameters: OHC, LDL cholesterol, high-density lipoprotein cholesterol (HDL cholesterol), triglycerides (TG). All patients filled out a questionnaire during the visit, which included questions about their social status, existing risk factors, information about medications currently being taken and adherence to prescribed treatment.





RESULTS

Of the 110 patients included in the analysis, there were 86 men (78.4%; average age 57.7 ± 0.4 years), 24 women (21.6%; average age 60.3 ± 0.7 years). The average age of patients who were assessed for adherence to statin therapy in 2020 was 62 years old (from 39 to 88 years old). Most of these patients had higher education and continued to work. One third of the patients were invalidity pensioners. Almost half of the patients ($n=35$) were eligible for preferential medication, but only 21 people (60.9%) used the right to discharge preferential medications. Out of 61 people, 35 (57.8%) had a history of MI, cerebral stroke or revascularization procedures. As can be seen, only a small part of patients (10.3%) diagnosed with chronic coronary heart disease received statin therapy before reference hospitalization. Due to the small number of patients receiving statins, the effectiveness of therapy at this stage was not evaluated. 85.5% of patients were discharged from the PM hospital. statins are prescribed. However, statins were prescribed in inadequate doses, which was a possible reason for the lack of achievement of target blood lipid levels in most patients, despite a significant increase in the frequency of statin prescribing upon discharge from the hospital. Thus, the frequency of achieving the lipid spectrum targets among patients discharged from the hospital ($n=550$) for OHS <4.5 mmol/l was 23.6%, LDL cholesterol <2.0 mmol/l – 6.3% , HDL CHOLESTEROL $>1.0-1.2$ mmol/l – 53.5%, TG <1.7 mmol/l – 61.8%. Evaluation of statin intake after discharge from the hospital was carried out using a telephone survey of surviving patients ($n=82$), all of them, according to international and national clinical guidelines for the diagnosis and treatment of coronary heart disease, were shown statin therapy. However, according to the results of a telephone survey, 3.9 years after discharge, only 63.6% (52 out of 82) of patients took statins. In addition, an analysis of the effectiveness and adherence to statin therapy was conducted in 61 patients who showed up for a follow-up visit. Before the reference hospitalization, only 4 received statins (7.6%) of 61 patients. Upon discharge from the clinic, statins were prescribed to 53 (86.5%) patients, mainly original simvastatin ($n=25$; 40.9%) and atorvastatin ($n=16$; 25.7%). After 3.9 years (on average), 41 out of 61 patients (67.3%) continued taking statins at the control visit stage. Of these, only one in five of those who were prescribed the original atorvastatin continued taking this particular drug, taking the original simvastatin was continued by 39% of patients, 5 patients (8%) were recommended the original rosuvastatin. The rest of the patients took various generic statins. The improvement in the situation with the appointment and reception of statins (from 7.6% at reference hospitalization to 67.3% at a control visit) led to the regular





achievement of the target values of lipid parameters in a larger number of patients with coronary heart disease: almost 2 times more patients achieved the target values of the lipid profile for OHS (from 18.2 to 40.6%) and LDL<2.5 mmol/l (from 16.5 to 40%), however, the total percentage of patients who reached the target level LDL cholesterol<2.0 mmol/did not exceed 16%.

An analysis of the factors influencing adherence to statin therapy showed the following. Men were more committed to the treatment prescribed upon discharge from the GNCPM: 60% of men and only 40% of women continued taking the medications recommended to them in the clinic until the control visit ($p=0.005$). Women were more careful about taking medications: 81% of women and 75% of men (total 76% of patients participating in the study) every day, without omissions, they took the recommended medications. Approximately 12% of patients took only part of the prescribed medications daily, and 2% of patients were inclined to change therapy independently.

According to the survey, the majority of patients (82%) believed that the danger of an increase in cholesterol levels was the development of stroke and heart attack. 43 patients knew their cholesterol levels (70.6%), and 54 people (89.4%) knew about the existence of drugs that reduce cholesterol in the blood. Among the last 38 (69.8%) patients, statins were attributed to them, the rest of the patients classified dietary supplements (dietary supplements), cytoprotectors, vitamins as lipid-lowering drugs.

CONCLUSION

When analyzing the register data, the PROGNOSIS of coronary heart disease a low frequency of statin prescribing (10%) was revealed in patients with stable coronary artery disease in 2017-2020 before hospitalization, and an increase in this indicator to 86.5% at discharge. Thus, hospitalization in a specialized hospital led to an improvement in the quality of treatment of patients with IBS. In Uzbekistan, as well as abroad, there is a discrepancy between real clinical practice and clinical recommendations for treatment and prevention CVD, but gradually this gap is narrowing. In this regard, the results of EUROASPIRE research are indicative I, II, III, which were conducted over 12 years in 8 European countries (14 more European countries participated in the EUROASPIRE III study, including Russia). Their goal was to monitor secondary prevention in patients with coronary artery disease who had undergone acute coronary syndrome, coronary bypass surgery or balloon angioplasty. Over 5 years, the average frequency of statin prescribing in Europe has increased 5-fold: from 10.5% to 55.3%, which is consistent with the results of our study, which, however, were obtained for and data from the REACH registry, in which





58% of outpatient patients with coronary heart disease received statins. In a recently published report on coronary heart disease and CHF, started in 2012, including data from all patients aged 18 and older, in whose outpatient card there is a diagnosis of coronary heart disease or CHF from 74 medical institutions in 23 regions of Uzbekistan, the frequency of statin prescribing for coronary heart disease at the end of 2013 was 35%. Among the patients of the registry in Saratov, the frequency of statin prescribing was 87%. Such a significant difference may be due to the fact that in Saratov, part of the work was performed by Saratov Research Institute of Cardiology. This indicator is almost identical to the frequency of statin prescribing for coronary heart disease in the IHD Prognosis Register, which was created on the basis of the GNIC PM. Thus, in specialized scientific institutions, the quality of therapy recommended for patients with coronary heart disease is significantly higher than in ordinary medical and preventive institutions.

After discharge, almost 20% of patients from the registry PROGNOSIS OF coronary heart disease stopped taking statins prescribed in the hospital, after 3.9 years, 67.3% of patients continued taking these drugs. A similar pattern has been revealed in a number of large studies that have shown that over time, a significant part of patients voluntarily stop taking prescribed therapy. According to the GNIC PM in recent years, the number of CHD patients receiving statins in Russia has reached 28.3%, however, the dosage of the drug is usually initial, or, at best, reaches 50% of the maximum. According to the data, 22.8% of patients continued taking prescribed statins until the end of the first year, 5.6% before three years, and only 1.6% after three years. On average, the percentage of people taking statins did not exceed 5%, and the duration of therapy did not exceed 5 months. The results obtained in our study demonstrate an improvement in the situation with the appointment of statins and the adherence of patients to this treatment: The results of the analysis of the data of the IHD PROGNOSIS registry are consistent with the data of the EUROASPIRE IV study, in which lipid-lowering therapy (mainly statins) was prescribed to 87% of patients with IHD from European participating countries. At the same time, the level of LDL cholesterol < 2.5 mmol/l was reached in 58% of patients, and only in 21% of patients managed to achieve the target level LDL cholesterol < 1.8 mmol/l.

Thus, there is a gradual improvement in the situation with the appointment and adherence to statins in patients with chronic coronary heart disease, but both the frequency of use and the effectiveness of therapy remains insufficient.

The IHD PROGNOSIS register revealed a low frequency of statin prescribing in patients with stable IHD before hospitalization, its significant increase during the stay in a specialized hospital, and a decrease after discharge. The effectiveness of therapy





was low at all stages of follow-up. There remains insufficient adherence of patients to treatment with statins on an outpatient basis.

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