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Optimization of Functional State of the Liver in Patients with Chd on the Background of Rosuvastatin Intake

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ABSTRACT

In 2019, 18.6 million people died of cardiovascular diseases (CVDs) worldwide. Coronary heart disease (CHD) is the leading cause of death from CVDs. One of the main risk factors for atherosclerosis and its complications is hyperlipidemia. The progress achieved is due in no small part to the emergence of a new class of hypolipidemic drugs belonging to the group of statins - HMG-CoA reductase inhibitors. Statins are the most effective means of combating atherosclerosis, having proven the ability to slow or completely stop its progression. Usually, statin therapy is well tolerated, but side effects can develop, including elevation of hepatic enzymes - aminotransferases. In this regard, the administration of statins together with hepatoprotective drugs, such as milk thistle extract leads to a decrease in the side effects of hypolipidemic therapy in patients with CHD.

According to the WHO, cardiovascular diseases (CVD) continue to be one of the leading causes of mortality among adult population in all developed countries of the world, including Uzbekistan. In 2012 standardized mortality rates per 100,000 people in Uzbekistan made 754.2 and in Karakalpakstan 706.9, respectively, while cardiovascular disease accounted for 308.9 and 268.5 deaths respectively. In European Union countries direct and indirect economic losses connected with cardiovascular diseases make annually about €192 billion [1,2,3]. Numerous epidemiological studies have demonstrated the relationship between the incidence of atherosclerosis, coronary heart disease and some risk factors. Dyslipidemia is one of the main causes of atherosclerosis and coronary heart disease (CHD).

Statins have deservedly gained the first place in the list of modern drugs for hypolipidemic therapy. Long-term clinical experience with statins has convincingly demonstrated that long-term statin therapy is generally quite safe [4,5]. The issue of safety of long-term statin therapy in patients with baseline impaired liver function is less clear. Since there are many patients with such disorders, the issue of prevention of side effects of statins in this group of patients is still quite relevant. Taking into account the increase of cytolysis markers during hypolipidemic therapy, administration of hepatoprotective drugs leads to reduction of side effects of statins. Milk thistle extract is one of the traditional hepatoprotective agents, which make up a whole

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complex of antioxidant bioflavonoids called silymarin. In fact, it turned out that taking this medicinal plant in an accessible and traditional form is both cheap and effective [6,7,8].

Purpose of the study: in this regard, the aim of our study was to investigate liver function parameters in patients with stable angina II-III on the background of combined therapy with rosuvastatin and milk thistle extract.

Materials and methods. 90 patients with stable angina II-III were included in the study. All patients were divided into 2 groups. 44 patients with stable angina II-III functional class (FC) who received standard therapy together with milk thistle extract were included into the main group (I group). The control group included 46 patients with CHD who received only basic therapy without milk thistle extract. The study was conducted in the departments of cardiology and cardiac rehabilitation of 3 clinics of Tashkent Medical Academy. Verification of the diagnosis was based on clinical and laboratory (body mass index-IMT, waist volume (WV), increased level of CH and HDL-C) and instrumental (ECG, veloergometry, EchoCG and Holter monitoring) research methods.

All patients were treated with drugs for stable angina according to the standards: antianginal drugs, B-blockers, ACE inhibitors, statins, anticoagulants, antiaggregants. All patients were prescribed rosuvastatin 20 mg in the evening after dinner, and patients in the main group took milk thistle extract (30 mg silymarin) for 3 months. (1 tablet 2 times a day, with meals).

All patients before and after treatment, along with general clinical tests had OAC, AML, biochemical blood tests, including ALT, AST level, total bilirubin, Serological screening for viral hepatitis (HBsAg, anti-HCV), blood lipid spectrum (triglycerides, total cholesterol, HDL-C, LDL-C), coagulogram, ECG, Holter monitoring were studied. Intracardiac hemodynamic parameters were determined by EchoCG.

To assess the functional status of the liver after 3 months of therapy with rosuvastatin together with milk thistle extract and standard treatment without milk thistle, all examined people underwent the above laboratory and instrumental studies.

Results of the study: against the background of therapy with rosuvastatin together with milk thistle extract after 3 months the liver transaminases values were observed in comparison with the initial indices, there was a tendency to decrease the mean level of cytolysis markers: after 3 months the mean level of ALT decreased to 46,25+3,12 ME/l ($p<0,05$), AST to 37,13+3,65 ME/l ($p<0,05$) in 32 (73,8%) patients, in 12 (26,2%) patients there was stabilization of liver enzymes level. In the 1st group of research, after the conducted therapy in patients lipid profile indexes have improved: in the majority of 35 (78,5%) patients normalization of level of OS, HDL cholesterol, and in 9 (21,5%) decrease of LDL cholesterol has been reached. Also, in 34 (75%) patients included in group 2 of the study, the lipid spectrum improved and a tendency to increase the mean value of cytolysis markers was observed in 13 (28,1%) patients in group 2 and to stabilize in 33 (71,9%) patients. At use of a combination of milk thistle extract and rosuvastatin it was possible to achieve a reliable decrease of LDL cholesterol and triglycerides levels, which is extremely important in patients with CHD. Taking into account the results of the study on the combined use of milk thistle extract and rosuvastatin, it can be concluded that this combination can be recommended in the treatment of dyslipidemia in patients with CHD. The simultaneous use of domestic milk thistle extract with rosuvastatin in patients with initially elevated levels of cytolysis markers leads to a significant decrease in the level of liver transaminases in patients with CHD, which is of interest in the development of methods to improve the effectiveness and safety of hypolipidemic therapy.

The results of comparative analysis of plasma lipid spectrum parameters in the studied two groups before and after the treatment are presented in Table 1.

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Table №1. Dynamics of lipid metabolism parameters and cytolysis markers.

Indicator	Before treatment		After 30 days of treatment	
	Group I	Group II	Group I	Group II
ALT IU/l	55,18+2,15	54,25+1,82	46,25+3,12*	55,35+2,92
AST IU/l	48,43+2,65	48,15+1,24	37,13+3,65*	49,25+2,14
Triglycerides mmol/l	3,18+1,52	3,14+1,48	2,16+0,35*	2,53+0,62
Total cholesterol mmol/l	6,81+1,28	6,75+1,18	5,24+0,86	5,48+0,53
LDL cholesterol mmol/l	4,26+1,19	4,05+1,65	3,26+1,02*	3,84+0,85
HDL cholesterol mmol/l	0,90+0,31	0,89+0,28	1,38+0,25	1,12+0,32

*Note: *-r<0.05 in comparison with the initial data.*

Conclusion. The use of statins for treatment of patients with CHD belonging to very high risk group is "gold standard" in treatment of this category of patients. Use of milk thistle in patients with coronary heart disease favorably influenced both on liver function and lipid exchange in comparison with patients of the 2nd group, who received only basic therapy without milk thistle. Having a membrane-stabilizing and cytoprotective effect, milk thistle protects hepatocytes from oxidative stress products and interrupts membrane lipid peroxidation reactions. Thus, combined therapy with statins and milk thistle in patients with CHD can achieve an effective reduction of total cholesterol and LDL cholesterol with simultaneous leveling of side effects of statins by low and medium doses of statins. Therefore, the combination of statins and milk thistle in the treatment of dyslipidemia in patients with CHD is justified and promising. The patients with stable angina II-III should be recommended statin therapy (rosuvastatin 20 mg 1 tablet in the evening after meal) in combination with milk thistle (milk thistle extract 1 tablet 2 times daily with meal, during 1-3 months).

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