



## Effect of Combined Therapy of Atorvastatin with Milk Thistle Extract on the Functional State of the Liver in Patients with CHD

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**Abstract:** Coronary heart disease (CHD) remains the leading cause of death in industrialized countries and with a growing trend in developing countries. The most significant risk factor is hypercholesterolemia. While the most effective drug is statins. Statin therapy is usually well tolerated, but side effects may occur, including elevated liver enzymes, aminotransferases. In this regard, the appointment of statins, together with hepatoprotective drugs, such as: milk thistle extract reduces the side effects of lipid-lowering therapy in patients with CHD.

**Key words:** CHD, statins, milk thistle extract, liver, ALT, AST.

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According to the WHO, cardiovascular diseases (CVDs) continue to be one of the leading causes of death among the adult population in all developed countries of the world, including Uzbekistan. Standardized mortality rates per 100,000 people in 2012 made 754.2 in Uzbekistan and 706.9 in Karakalpakstan, while the mortality rate from cardiovascular diseases amounted to 308.9 and 268.5 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 won 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 cytotoxicity 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 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 connection the aim of our study was to investigate the parameters of liver function in patients with stable angina II-III on the background of combined therapy with atorvastatin and milk thistle extract.

**Materials and methods.** The study included 80 patients with stable angina pectoris I-III. All patients were divided into 2 groups. 42 patients with stable angina pectoris of I-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 38 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- BMI, waist volume (WV), increased level of CHB and HDL-C) and instrumental (ECG, veloergometry, EchoCG and Holter monitoring) research methods.

All patients received stable angina medications according to the standards: antianginal drugs, B-blockers, ACE inhibitors, statins, anticoagulants, antiaggregants. All patients were prescribed atorvastatin 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 we performed OAC, OAM, 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 indices were determined by EchoCG.

To evaluate the functional state of the liver after 3 months of therapy with atorvastatin together with milk thistle extract and standard treatment without milk thistle all examined subjects underwent the above laboratory and instrumental studies.

**Results of the study:** against the background of therapy with atorvastatin 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 value of cytolysis markers: after 3 months the mean level of ALT decreased to  $46,25 \pm 3,12$  ME/l ( $p < 0,05$ ), AST to  $37,13 \pm 3,65$  ME/l ( $p < 0,05$ ) in 31 (73,8%) patients, in 11 (26,2%) patients there was stabilization of liver enzymes level. In the 1st group of the study, after the conducted therapy in patients lipid profile indicators improved: in the majority of 33 (78,5%) patients there was observed a normalization of the level of OS, HDL cholesterol, and in 9 (21,5%) the decrease of LDL cholesterol was reached.

Also, 24 (75%) patients included in group 2 of the study had improved lipid spectrum and had a tendency to increase the mean value of cytolysis markers in 9 (28,1%) patients in group 2 and to stabilize in 23 (71,9%) patients. At use of a combination of milk thistle extract and atorvastatin 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 atorvastatin, we can conclude that this combination can be recommended for the treatment of dyslipidemia in patients with CHD. Simultaneous use of domestic milk thistle with atorvastatin 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 the parameters of plasma lipid spectrum in the studied both groups before and after the treatment are presented in Table 1.

**Table 1. Dynamics of lipid metabolism and cytotoxicity markers.**

Indicator	Before the start of 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 compared to baseline data.

**Conclusion.** The use of statins in the treatment of patients with CHD belonging to the group of very high risk of CHD is the "gold standard" in the treatment of this category of patients. The use of milk thistle in patients with CHD has a favorable effect both on liver function and lipid metabolism in comparison with group 2 patients 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. Patients with stable angina pectoris FK 2-3 should be recommended statin therapy (atorvastatin 20 mg 1 tablet in the evening after meals) in combination with milk thistle (milk thistle extract 1 tablet 2 times daily with meals, for 1-3 months).

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