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EVALUATION OF THE EFFECT OF STANDARD TREATMENT AND CHOLESTEROL ABSORPTION INHIBITORS ON RENAL FUNCTION IN STABLE ANGINA PECTORIS

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ABSTRACT

There is sufficient information on the diagnosis and treatment of ischemic heart disease (IHD), but in comorbid conditions, including renal dysfunction (RD), there is some difficulty in stabilizing the main disease and restoring kidney function, regardless of the presence of diabetes in the anamnesis. Taking into account existing risk factors (RF) and comorbid conditions in this group of patients, early detection of changes in kidney function and selection of drugs with nephroprotective and cardioprotective effects are currently considered one of the urgent problems in medicine.

INTRODUCTION

Cardiovascular disease (CVD) is one of the main causes of death and disability among the population of all countries, including Uzbekistan. According to the report of the experts of the World Health Organization (WHO), confirmed by statistical analysis, more than 2/3 of the observed deaths caused by this group of diseases were caused by IHD. Among the comorbid diseases observed in patients with CKD, chronic kidney disease (CKD) is particularly important, and it is one of the leading CKD groups that cause and aggravate cardiovascular diseases. [5, 17, 18].

Heart and kidney diseases have "traditional" factors such as general arterial hypertension (AH), diabetis, obesity, dyslipidemia, and "non-traditional" factors such as hyperhydration, anemia, phosphorus-calcium metabolism disorders, systemic inflammation, and hypercoagulation, which together have a pathogenetic effect on the development of CVD. Epidemiological and population studies show that even the earliest subclinical impairment of kidney function affects the development of CKD and their complications and mortality as an independent risk factor. It increases the number of cardiorenal complications, resulting in premature death [1, 3, 5, 11, 16]. According to the USRDS (The United States Renal Data System) American registry, among the population over 65 years of age diagnosed with RD, coronary atherosclerosis (16.5% vs. 42.5%) and myocardial infarction (MI) (2% vs. 10 %) is more common [6,13, 14].

When RD is detected in patients with CKD, regardless of the type of existing comorbid conditions, it is necessary to stabilize the main disease and eliminate factors that have a negative effect on kidney function. When treating this group of patients with drugs, drugs with nephroprotective and cardioprotective effects are usually selected [4, 7, 11, 13]. The effectiveness of the use of statins, which are among the drugs proven to be effective in the treatment of this disease, is shown by their pleiotropic, i.e., improvement of endothelial activity, vasodilation, antiproliferative, immunosuppressive properties, antiischemic and antithrombotic, and anti-inflammatory effects. Statins prevent glomerulosclerosis by reducing the accumulation of lipids in the kidney tissue and the proliferation of mesangial cells. At the same time, in order to reduce the side effects of drugs (especially severe myopathies), it is reasonable to reduce the daily amount of statins and use them together with ezetimibe. Ezetimibe, in turn, reduces low density lipoproteins by 15-22% by preventing the absorption of exogenous and endogenous cholesterol in the small intestine. The combined use of drugs of this group increases the effectiveness of treatment and reduces low density lipoproteins by 25-58% [1, 5, 9, 10, 13, 15].

Taking the above into account, we devoted ourselves to the evaluation of the effectiveness of cholesterol absorption inhibitor ezetimibe along with standard treatment and early diagnosis of RD in patients with stable angina pectoris.

Material and methods

In 2020-2022, 167 patients with stable angina pectoris II-III-IV FC with an average age of 61.47±8.42, who were treated in the cardiology and cardiorehabilitation departments of the multidisciplinary clinic of the Tashkent Medical Academy, participated in this research. 112(67.1%) of them were men (average age 61.29±8.3 years) and 55(32.9%) were women (average age 61.85±8.7 years). The diagnosis was based on the classification criteria adopted by the European Society of Cardiology (ESC Guidelines for the diagnosis and management of chronic coronary syndromes). All patients were followed up in an outpatient setting for 6 months after inpatient treatment. Electrocardiography (ECG), Holter monitoring, echocardiography (ExoKG) were performed before and after treatment, as well as biochemical blood analysis. In order to evaluate kidney function, blood creatinine, cystatin S, fetuin A (FA), and urine proteinuria and fetuinuria were determined. Alternatively, eGFR was calculated based on serum creatinine and cystatin C.

Although according to the patient's complaints, anamnesis, clinical and laboratory tests, no specific symptoms of RD were observed, when eGFR was calculated based on serum creatinine and cystatin C, RD was detected in 33.5% of them. Based on the recommendations of the European Society of Cardiology, patients were prescribed angiotensin-converting enzyme inhibitor (ACE-I), ß-adrenoblocker, anetiagrigant, statin, nitrate, diuretic, antiarrhythmic drugs, if necessary, taking into account existing clinical symptoms, XO and comorbid conditions. Ezetimibe 10 mg along with rosuvastatin 20 mg was recommended to balance hypercholesterolemia and dyslipidemia.

Results and discussion

In control group, eGFR was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration, 2021) formula based on blood creatinine and cystatin C, and based on the obtained results, they were divided into 2 groups. The first group consisted of 111 (66.5%) patients with eGFR ≥ 90 ml/min/1.73 m2, and the second group consisted of 56 (33.5%) patients with eGFR ≤ 89 ml/min/1.73 m2. Table 1 shows information about other indicators and their differences in relation to eGFR.

Table 1.

Information about patients under supervision

Indicators	All pateients n=167 та		p
	eGFR ≥ 90 ml/minute/1,73 м^2 (n=111)	eGFR ≤ 89 ml/minute /1,73 м^2 (n=56)	
Men, n(%)	91 (81,9%)	21 (37,5%)	X^2=33.34 P<0.001
Women, n(%)	20 (18.1%)	35 (62,5%)	X^2=33.34 P<0.001
Average age	58,6±0,71	67,16±0,97	P<0.05
Diabetes, n (%)	17 (15.3%)	20 (35,7%)	X^2=8.98 P<0.001
Smokers, n (%)	22 (19.8%)	8 (14,3%)	X^2=0.774 P>0.05
History of myocardial infarction, n (%)	13 (11,7%)	6 (10%)	X^2=0.037 P>0.05
Arterial hypertension was present in the anamnesis, n (%)	91 (82%)	50 (89,3%)	X^2=33.34 P<0.001
Proteinuria, n (%)	54 (48,6%)	47 (83,9%)	P<0.05

According to the data presented in Table 1 above, in the first group, men made up 81.9%, women made up 18.1%, and a highly reliable difference was found between them (X2=33.34 P<0.001). On the contrary, in the second group, women (62.5%) were the majority compared to men (37.5%) (X^2=33.34 P<0.001). At the same time, the percentage of women older than 50 years in the second group was high (r<0.005). This result is precisely related to the fact that IHD and AH are observed more often among women older than 50-60 years. When analyzing the comorbid conditions identified in patients, in the first and second groups, respectively, those suffering from QD were 15.3% /35.7% (P<0.001), those with AG were 73.4% /79.5% (p<0.01). , anemia - 23.4% /41.0% (r<0.001), those who had a stroke in their anamnesis 10.2 /12.8%, those who had an MI 24.2% /35.9% (r<0.001), comorbidity index (CI) was 7.3/8.7 points (r<0.001). The results showed that eGFR was 89 ml/min/1.73 m2 or less in patients with significantly higher comorbid conditions.

PU was detected in 48.6% of patients in the first group, and in 83.9% of patients in the second group (P<0.001). This result also indicates that there is a change in kidney function in the second group of patients.

When eGFR was calculated based on creatinine and cystatin C, the results obtained between the two groups of patients were convincingly different, and the proportion of patients with RD was found to be even higher (p < 0,001) (Table 2).

Table 2.

Comparative analysis of kidney function indicators and biochemical analysis results in groups (n = 167).

Indicators	eGFR ≥ 90 ml/min/1,73 м^2 (n=111)	eGFR ≤ 89 ml/min/1,73 м^2 (n=56)	P
Creatinine, (mmol/l)	65,8±6,9	91,4±7,7	p<0,05
Cystatin C (mg/l)	1,2±0,01	1,3±0,02	p<0,05

eGFR based on creatinine, based on ml/min/1.73m2.	99,9±1,6	79,9±1,4	p<0.001
eGFR based on cystatin C, based on ml/min/1.73m2	91,8±1,6	72,4±1,3	p<0.001
Proteinuria (g/l)	0,005±0,018	0,017±0,048	p>0,05
Fetuina-A in blood, ng/ml	227,2±16,06	216,3±15,5	p>0,05
Fetuina-A in urine, ng/ml	30.4±1.6	72.4±4.8	p<0.001

In the first group of patients, serum creatinine was 65.8±6.9 mmol/l, cystatin C was 1.2±0.01 mg/l, and in the second group these indicators were on average 91.4±7.7 mmol/l and was 1.3±0.02 mg/l (p<0.05). eGFR calculated based on serum creatinine was 99.9±1.6 in the first group and 79.9±1.4 ml/min/1.73m2 in the second group (P<0.001). When this index was calculated based on cystatin C, it was 91.8±1.6 and 72.4±1.3 ml/min/1.73m2, respectively, and it was found to be significantly lower than the first method (r<0.05). According to the results, when eGFR was calculated on the basis of cystatin S, compared to those determined on the basis of creatinine, there were 7.2% more people with RD (r<0.05), those with eGFR ≥ 90 ml/min/1.73 m2 had 59.3% (99), ≤ 89 ml/min/1.73 m2 was 40.7% (68) (p<0.05).

The amount of FA in the blood was 227.2±16.06 ng/ml in the first group, and 216.3±15.5 ng/ml in the second group. This indicator was significantly lower (r<0.001) in both groups compared to the control group (324.7 ± 18.5) mg/l. FA levels were found to be lower in all patients with stable angina pectoris compared to healthy controls (p<0,001). At the same time, when the patients were analyzed in groups, it was observed that FA in the blood of the first group of patients was higher than that of the second group, but this difference was not convincing (r>0.05). It was observed that the amount of FA in the blood of all patients decreased in accordance with the reduction of eGFR (Diagram 1)

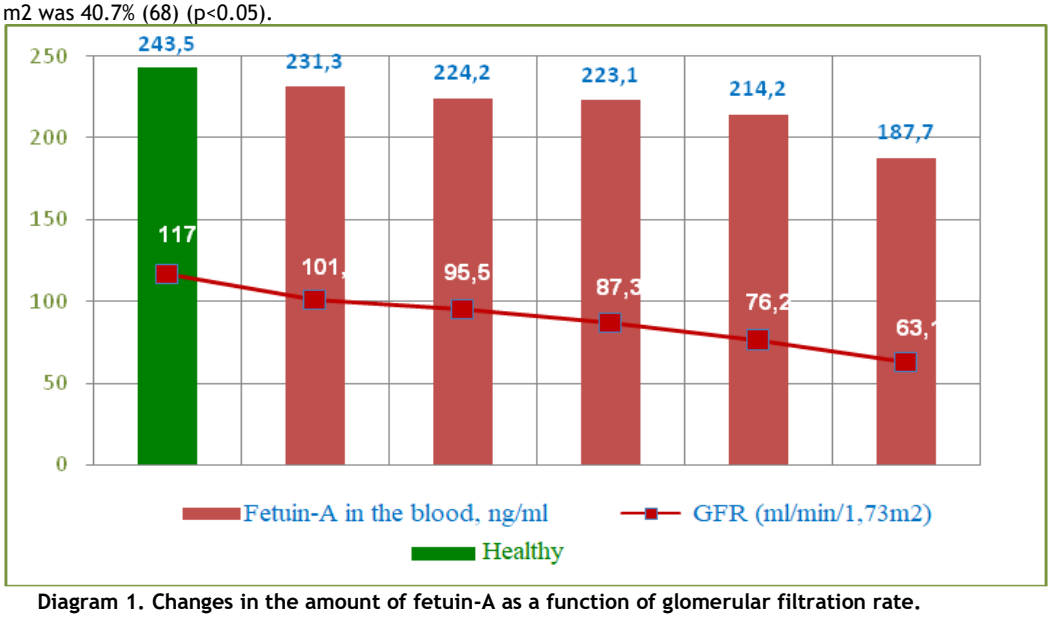

Diagram 1. Changes in the amount of fetuin-A as a function of glomerular filtration rate.

30.4±1.6 ng/ml FA in the first group and 72.4±4.8 ng/ml FA in the second group were found in urine. In this case, fetuinuria was 2.4 times higher in patients with eGFR ≤ 89 ml/min/1.73 m2 compared to those with eGFR ≥ 90 ml/min/1.73 m2 (r<0.001). eGFR ≤89 ml/min/1.73 m2, AH ≥140/90 mm.rt.st. It was found that patients with 12% of patients in the first group had PU and 27% had fetuinuria, while in the second group these indicators were 87% and 69%, respectively (P<0.001). According to this result, the decrease of FA in the blood of patients with high risk group and comorbidity index (CI) and the observation of fetuinuria indicate that their kidney function has worsened. Based on the above data, it can be concluded that fetuinuria has a longer duration than proteinuria, that is, it occurs in the early stages of the main disease, and it is important as the first sign of RD.

To determine the efficacy of monotherapy (rosuvastatin 20 mg) and combination therapy (rosuvastatin + ezitimibe 20/10 mg) and its effect on RD factors in patients with CKD with GFR≤89 ml/min/1.73 m2. they were divided into two groups using the random selection method. Rosuvastatin 20 mg was recommended to the first group, rosuvastatin 20 mg + ezitimibe 10 mg to the second group. As a result of treatment, positive clinical progress was observed in both groups. Angina attacks were not observed in 42.9% of the 1st group and 60.7% of the 2nd group of patients (r<0.001). During this period, the AH level in both groups was within the normal range.

After six months of treatment, OCH-16.6%, TG - 27.7%, LDLP-18.6% (P<0.001) decreased in patients of group 1, in group 2 these indicators decreased by 23.8%, 50%, respectively. , decreased by 18.4% (r<0.001) (Chart 2). At the same time, LDLP increased by 27% (P<0.05) in group 1 and by 33.1% (P<0.001) in patients in group 2, while AH decreased by 12.2% and 23.8%, respectively. (P<0.05).

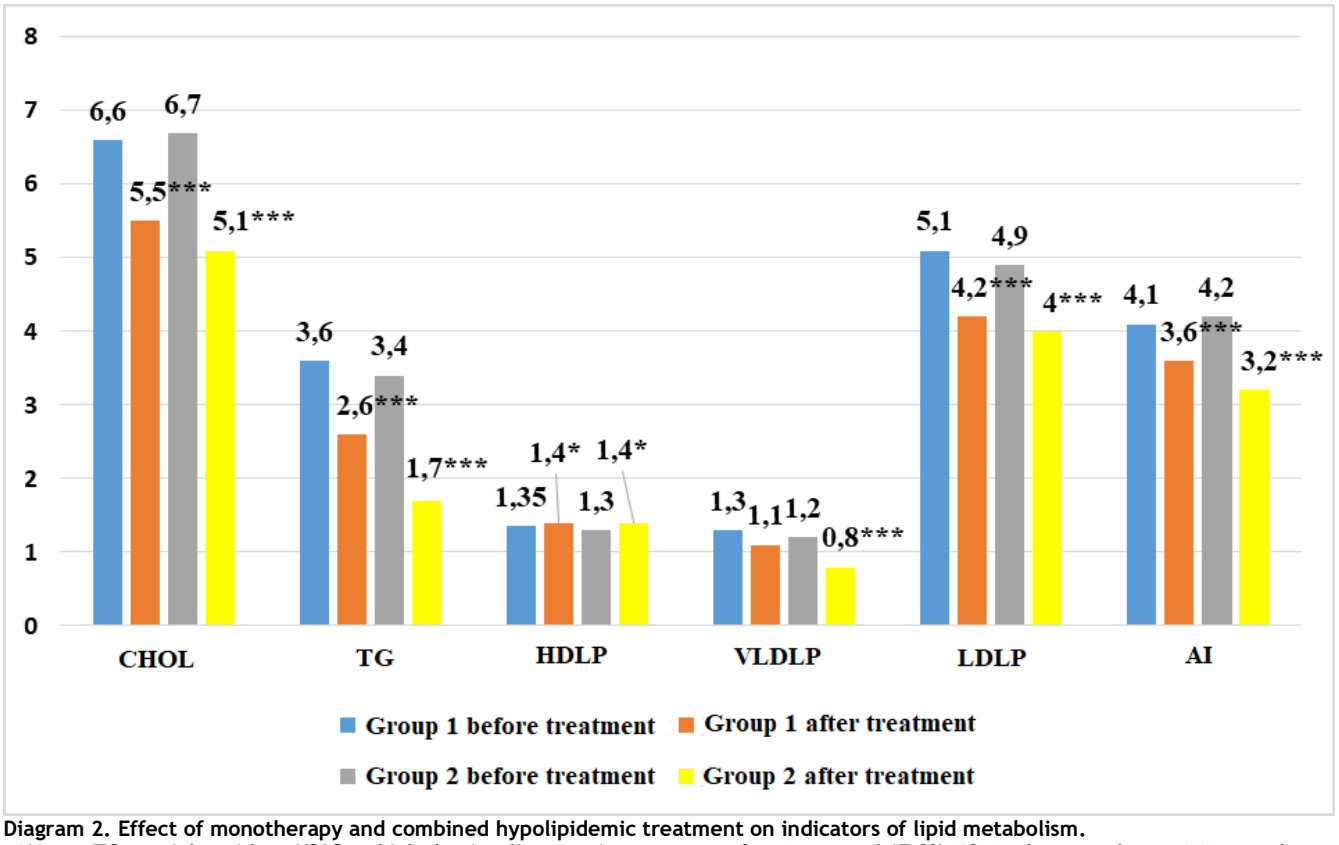

Diagram 2. Effect of monotherapy and combined hypolipidemic treatment on indicators of lipid metabolism.

*Notes: TG - triglycerides. HDLP - high-density lipoproteins. VLDLP - very low density lipoproteins. LDLP - low density lipoproteins. * - reliability of the difference between pre- and post-treatment indicators: * - p<0,05., ** - p<0,01., *** - p<0,001.*

The effect of treatment with a hypolipidemic agent in patients with CKD who received a combination of a statin and a cholesterol absorption inhibitor was reliably higher than in those who received monotherapy. As a result of monotherapy (rosuvastatin 20 mg) and combined (rosuvastatin + ezitimibe 20/10 mg) hypolipidemic treatment, 46.4% (13) in the first group of patients, and 67.9% (19) in the second group) it was observed that PZLP decreased to the target level. The results of the analysis show that combined (rosuvastatin and ezitimibe together) treatment is reliably superior to monotherapy (p <0,001).

As a result of the treatment, there was a positive shift in the factors reflecting the kidney function of both groups of patients. PU decreased by 60% in group 1 and 75% in group 2, but this shift was not significantly different (r>0.05). Serum creatinine decreased by 12.6% and 7.1%, and cystatin-S by 8.3% (P<0.01) and 12% (P<0.001) in both groups, respectively. (Diagram 3).

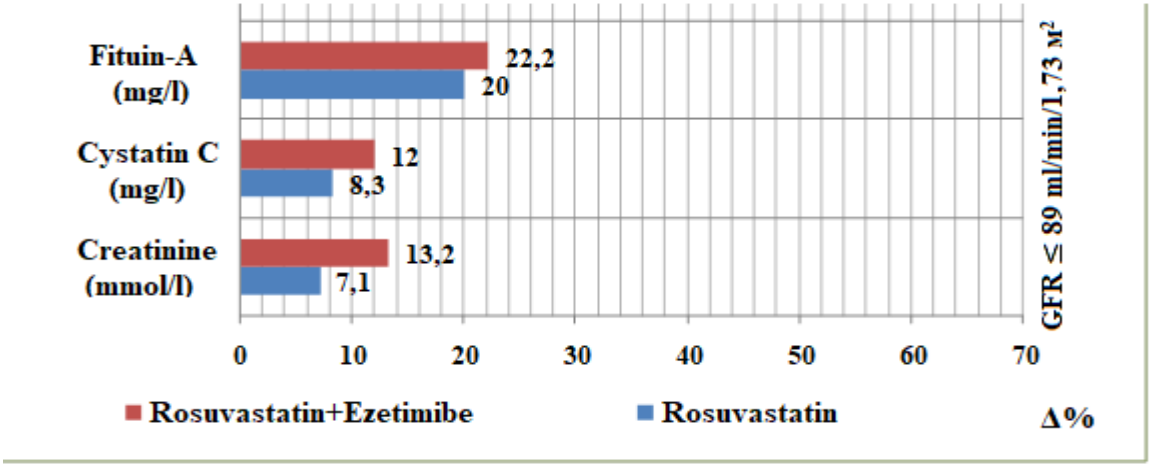

Diagram 3. Effects of monotherapy and combined hypolipidemic treatment on markers of renal dysfunction

In addition, on the basis of standard treatment, isolated and combined hypolipidemic agents had a positive effect on eGFR and were 80.2±1.6 (P<0.05) and 79.4±1.4 (P<0.01) ml/min, respectively, in the groups was 1.73m2 (Table 3).

Table 3

Effects of rosuvastatin and rosuvastatin + ezitimibe on renal function in patients with ischemic heart disease and renal dysfunction

Indicators	eGFR ≤ 89 ml/min/1,73 м^2 (n=56)			
	Розувастатин		Розувастатин + эзитимиб	
	Group 1 (n=28) before treatment	Group 2 (n=28) after treatment	Group 1 (n=28) before treatment	Group 2 (n=28) after treatment
Proteinuria (g/l)	0,005±0,001	0,002±0,002 (60%)	0,004±0,001	0,001±0,004 (75%)
Creatinine, (mmol/l)	74,5±7,5	80,2±5,7 (7,1%)	71,8±7.7	82,8±5,9 (13,2%)*
Cystatin C (mg/l)	1,2±0,02	1,1±0,03* (8,3%)	1,25±0,02	1,1±0,03*** (12%)
Glomerularfiltration rate, ml/min/1.73m2	73,4±1,4	80,2±1,6**	74,6±1,6	79,4±1,4*

*Notes: * - p<0,05., ** - p<0,01., *** - p<0,001.*

CONCLUSION

Based on the results of the treatment, it was confirmed that the combined hypolipidemic agent used in the treatment of patients with chronic angina pectoris, RD has a high efficiency in balancing lipid metabolism and stabilizing kidney function..

In conclusion, the effectiveness of regular use of statins and cholesterol absorption inhibitors in the treatment of patients with stable angina pectoris was shown by a reliable decrease in LDLP, VLDLP, TG, AH, and an increase in the amount of HDLP. In addition, as a result of the treatment, the reduction of creatinine and cystatin C in the blood serum, fetuinuria and PU in the urine, and the increase of FA and eGFR indicate that the treatment has a positive effect on kidney function.

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