Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 4300 - 4304
Received 16 February 2021; Accepted 08 March 2021.

The State of the Main Clinical Laboratory Parameters in Metabolic Syndrome during Statin Therapy

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SUMMARY: The aim of this work was to study the effectiveness of lipid-lowering therapy with rosuvastatin in patients with metabolic syndrome (MS). For this purpose, 86 patients with AH of I-III degree and MS aged from 27 to 70 years were examined. It was found that lipid-lowering therapy significantly reduced the level of not only lipids, but also pro-inflammatory cytokines, which in turn confirms their pleiotropic (anti-inflammatory) effect. The data obtained are consistent with the results of a number of studies in which the anti-inflammatory effect of statins is carried out through the suppression of the activity of a number of cytokines, such as TNF-α, IFN-gamma, IL-6, and hsCRP levels. As a result of the obtained lipid-lowering therapy, patients with MS showed a significant decrease in the level of lipid spectrum parameters: total cholesterol by 1.5 times, triglycerides by 1.5 times, low-density lipoprotein cholesterol by 1.8 times, and the atherogenic coefficient by 1.6 times, which indicates a highly effective hypolipidemic effect of rosuvastatin. Along with this, in patients with MS in the dynamics of treatment with rosuvastatin, there was a significant decrease in markers of inflammation CRP by 2 times, IL-6 by 3 times, TNF-a by 2.1 times, which confirms their pleiotropic (anti-inflammatory) effect.

Keywords: metabolic syndrome, obesity, diabetes mellitus, hypertension, statins, anti-inflammatory effect.

Topicality. Current epidemiological data indicate a steady increase in persons with metabolic syndrome (MS). Currently, MS, along with arterial hypertension (AH), atherosclerosis and type 2 diabetes mellitus, is recognized as one of the metabolic pandemics of the 21st century. One of the most discussed processes in recent years that consolidate the components of MS and associated diseases is subclinical chronic inflammation [1, 10]. The interpretation of the importance of inflammation in the above diseases has now expanded significantly and covers not only local inflammatory reactions, but also systemic inflammation, which, unlike local, is more demonstrative and available for research in a clinic. Intensive immunological studies in recent years have made it possible to identify common features in the pathogenesis of a number of diseases that have different clinical manifestations, but in the pathogenesis of which immunocompetent cells, regulatory molecules and their receptors are involved [7,9,13,15].

Atherogenic dyslipidemia associated with MS is characterized by low concentrations of high density lipoprotein cholesterol (HDL), elevated triglyceride (TG) levels; and the predominance of small particles of low density lipoprotein cholesterol (LDL-C) [3,8]. Many patients may also have elevated levels of LDL-C, which increases the risk of cardiovascular disease [2,4].

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Statins, in turn, are considered the most effective and well-tolerated agents for the treatment of dyslipidemia, and they are also recognized as first-line therapy for lowering cholesterol levels [3,5,6,7]. By lowering LDL cholesterol and triglycerides and raising HDL cholesterol, they have been shown to reduce cardiovascular morbidity and mortality in large outcome studies in different populations [8,10]. In addition, statins have "pleiotropic" effects, such as reducing oxidative stress and regulating inflammatory responses, and these effects may improve other risk factors associated with metabolic syndrome [11]. Moreover, the available evidence suggests that highly sensitive C-reactive protein (CRP), a biomarker of inflammation, is a strong, independent predictor and is associated with an increased risk of cardiovascular events [5,14,16]. Rosuvastatin selectively and reversibly competitively inhibits the HMG-CoA reductase enzyme. This enzyme converts HMG-CoA to mevalonic acid in the cholesterol biosynthetic pathway, which is the rate-limiting step in cholesterol synthesis. Thus, rosuvastatin reduces the synthesis of sterols in the liver, which, in turn, leads to a decrease in the concentration of hepatocellular cholesterol. Hepatocytes respond to this decrease in intracellular cholesterol concentration by increasing the synthesis of LDL receptors, which promotes the reuptake of LDL by the liver from the bloodstream. The end result of this process is increased fractional catabolism of LDL, which lowers the concentration of LDL-C and total serum cholesterol [2,5,10,13].
The aim of this work was to study the state of the main clinical and laboratory parameters of inflammation in MS against the background of hypolipidemic therapy with rosuvastatin in patients with metabolic syndrome.

Materials and research methods. The study involved 86 patients with AH of I-III degrees and MS aged from 27 to 70 years (mean age 57.7 ± 0.62 years). Of these, 48 are men and 38 are women. Among the examined patients, 44 (51%) patients had obesity of I and II degrees, which was also diagnosed based on the assessment of the patient's body mass index. The remaining 42 (49%) patients had grade III obesity. Abdominal obesity as measured by waist circumference (WC) was detected in 64 (74.4%) patients. Hypercholesteremia (HCS) was detected in 60 (69.8%) patients. Dyslipidemia (DLP) was observed in 73 (84.9%) patients, hypertriglyceridemia (HTG) was detected in 67 (77.9%) patients.
The collection of material was carried out in the cardiology department of the City Clinical Hospital No. 7 in Tashkent from 2015 to 2017. The study was carried out within the framework of the current grant of the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan "Development and implementation of algorithms for immunodiagnostics and immunotherapy in metabolic syndrome" for 2018-2020.
The diagnosis of hypertension was established according to the recommendations of the All-Russian Scientific Society of Cardiology 2004. MS criteria were established in accordance with the recommendations of the International Diabetic Foundation (IDF, 2005): central obesity: waist circumference ≥ 94 cm in men and ≥ 80 cm in women in combination with any two of the following 4 factors: triglycerides (TG)> 1.7 mmol / L (65.73 mg / dL); lowering high-density lipoprotein cholesterol (HDL cholesterol) <1.0 mmol / L (38.67 mg / dL) in men and <1.3 mmol / L (50.26 mg / dL) in women, BP ≥ 130/85 mmHg.; fasting plasma glucose> 5.6 mmol / L [3.6].

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Patients with MS received basic standard therapy according to the "Recommendations of All-Russian Scientific Society of Cardiologists for the diagnosis and treatment of MS" [13,15]. Lipid-lowering therapy was rosuvastatin 10 mg daily; patients were re-examined in dynamics after 3 months.

The study did not include patients with complex heart rhythm and conduction disorders; chronic heart failure III-IV FC (NYHA); have had myocardial infarction or cerebral stroke; renal and hepatic impairment; thyroid dysfunction, type 1 and type 2 diabetes mellitus; oncological and immunopathological diseases.

RESEARCH RESULTS AND THEIR DISCUSSION.

In recent decades, more and more data have been accumulated on the importance of immunological mechanisms in the development of a particular pathology, in particular, MS is of particular interest. The results of the study showed that of the 96 examined patients, 37 patients with MS (mean age 56.8 ± 1.7 years) were found to have impaired immune status indicators.

As a result of the obtained lipid-lowering therapy, patients with MS showed a significant decrease in the level of lipid spectrum parameters: total cholesterol by 1.5 times ($p < 0.001$), triglycerides by 1.5 times ($p < 0.01$), low-density lipoprotein cholesterol by 1, 8 times ($p < 0.001$), also the coefficient of atherogenicity 1.6 times ($p < 0.001$), which indicates a highly effective hypolipidemic effect of rosuvastatin.

To assess the significance of immune-mediated reactions in patients with MS, we studied clinical and immunological markers of inflammation: CRP and pro-inflammatory cytokines before treatment, and in the dynamics of treatment.

According to the results of studies by many authors, patients with MS have a predisposition to the development of an inflammatory state, manifested by an increase in the level of CRP. Increased serum CRP is associated with an increased risk of atherosclerosis, type 2 diabetes mellitus, MS and associated complications [1,5,9,13]. According to our study, the baseline CRP level in patients with MS was 5.6 ± 0.8 g / L. After the received lipid-lowering therapy, there was a significant decrease in treatment dynamics by 2 times ($p < 0.01$), which amounted to 2.7 ± 0.5 g / l. One of the reasons for the increase in CRP is considered to be an excess of adipose tissue producing anti-inflammatory cytokines [1,12]. In this regard, we were interested in studying the content of cytokines in the blood involved in the pathogenesis of the inflammatory process. According to the obtained data, the initial level of IL-6 was 30.4 ± 4.9 pg / l. As a result of the received therapy, there was a significant decrease in 3 times ($p < 0.001$) and amounted to 10.1 ± 1.7 pg / l. Comparative analysis of the level of TNF-a showed a significant decrease in treatment dynamics by 2.1 times ($p < 0.01$).

The results of our study showed that the applied lipid-lowering therapy significantly reduced the level of not only lipids, but also pro-inflammatory cytokines, which in turn confirms their pleiotropic (anti-inflammatory) effect. The data obtained are consistent with the results of a number of studies in which the anti-inflammatory effect of statins is carried out through the suppression of the activity of a number of cytokines (TFN-α, IFN-gamma, IL-6, etc.) and the level of hsCRP [10,14,17].

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CONCLUSION

Thus, as a result of the obtained lipid-lowering therapy in patients with MS, there was a significant decrease in the level of lipid spectrum parameters: total cholesterol by 1.5 times ($p < 0.001$), triglycerides by 1.5 times ($p < 0.01$), low lipoprotein cholesterol. density 1.8 times ($p < 0.001$), and atherogenic coefficient 1.6 times ($p < 0.001$), which indicates the highly effective hypolipidemic effect of rosuvastatin. Along with this, also in patients with MS in the dynamics of treatment with rosuvastatin, there was a significant decrease in markers of CRP inflammation by 2 times ($p < 0.01$), IL-6 by 3 times ($p < 0.001$), TNF-a by 2.1 times ($p<0.01$), which confirms their pleiotropic (anti-inflammatory) action.

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