

THE INFLAMMATORY MEDIATORS IN THE PATHOGENESIS OF METABOLIC SYNDROME

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SUMMARY

The article presents the results of a study of serum levels of IL-6, TNF- α and C-reactive protein (CRP) in patients with metabolic syndrome before and after treatment with rosuvastatin. The study included 20 patients with MS and impaired immune status indicators from 39 to 68 years old (average age 56.8 ± 1.7 years). Patients were prescribed lipid-lowering therapy (rosuvastatin) at 10 mg. The collection of patients was carried out on the basis of the "Immunogen-test" RDC on an outpatient basis and included observation in the dynamics of treatment after 3 months. The cytokines IL-6 and TNF- α were determined in blood serum by the enzyme immunoassay using the reagent kits of Vector-Best CJSC (Novosibirsk, Russia) on an enzyme-linked immunosorbent analyzer StatFax - 2100 (USA). **Conclusions:** In patients with unstable patients with MS, the dynamics of treatment with rosuvastatin showed a significant decrease in blood lipids: total cholesterol by 1.5 times ($p < 0.001$), triglycerides by 1.5 times ($p < 0.01$), low-density lipoprotein cholesterol in 1.8 times ($p < 0.001$), and the atherogenic coefficient was 1.6 times ($p < 0.001$). In addition, the anti-inflammatory effect of rosuvastatin was noted, namely, a significant decrease in the markers of inflammation of CRP by 2 times ($p < 0.01$), IL-6 by 3 times ($p < 0.001$), TNF- α 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.

Metabolic syndrome (MS) is a relationship of pathogenetic disorders, such as: carbohydrate, lipid, purine metabolism, arterial hypertension (AH) and visceral obesity.^[8,10] The frequent combination of visceral obesity, disorders of carbohydrate, lipid metabolism, hypertension and the presence of a close pathogenetic relationship between them served as the basis for their isolation into an independent syndrome, called metabolic syndrome, the prevalence of which is about 20%. MS is considered as a leading risk factor for the development of cardiovascular complications.^[2,10] It should be noted that the mechanisms by which MS increases cardiovascular risks are only partially understood. In the development of these complications, along with well-known traditional cardiovascular risk factors, so-called new factors are important, among which a special place is given to pro-inflammatory mediators, such as cytokines, SVCAM-1, C-reactive protein intercellular adhesion molecules, which are positioned as markers of atherosclerotic risk.^[4] Therefore, the attention of researchers in recent years has been attracted by the study of the activity of immune inflammation, its role in the progression of cardiovascular diseases, which is especially important from the standpoint of the potential reversibility of these changes under the influence of therapy. The dominant role of immunocompetent cells in metabolic dysfunction

suggests the need for the development and implementation of specific, targeted immunotherapy.^[2,4,5,7,8] In this regard, more specific immunometabolic therapeutic methods are required, which will be useful for improving the metabolic profile of adipose tissue and preventing its dysfunction.

THE AIM OF THE STUDY

Study of a non-specific inflammatory process in the dynamics of treatment with a lipid-lowering drug in patients with MS.

MATERIALS AND METHODS

The study included 20 patients with MS and impaired immune status indicators from 39 to 68 years old (average age 56.8 ± 1.7 years). Patients were prescribed lipid-lowering therapy (rosuvastatin) at 10 mg. The collection of patients was carried out on the basis of the "Immunogen-test" RDC on an outpatient basis and included observation in the dynamics of treatment after 3 months.

The study did not include patients with complex disorders of the rhythm and conduction of the heart; chronic heart failure III-IV FC (NYHA); after myocardial infarction or cerebral stroke; renal and hepatic insufficiency; thyroid dysfunction, type 1 and

type 2 diabetes; oncological and immunopathological diseases.

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); Decrease in 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, blood pressure $\geq 130 / 85$ mmHg.; fasting plasma glucose > 5.6 mmol / L.^[10]

Blood sampling was carried out in the early morning hours, from the cubital vein in the horizontal position of the patient, after 12 hours of fasting. The lipid spectrum — total cholesterol, triglycerides (TG), high lipoprotein cholesterol (HDL cholesterol), very low (VLDL cholesterol), low (LDL cholesterol) density, highly sensitive C-reactive protein (hsCRP), fasting glucose was determined on a biochemical autoanalyzer Randox "(Great Britain).

Immunological studies were carried out in the laboratory of fundamental immunology of the Institute of Human Immunology and Genomics, Academy of Sciences of the Republic of Uzbekistan. The cytokines IL-6 and TNF- α

were determined in blood serum by the ELISA method using reagent kits of Vector-Best CJSC (Novosibirsk, Russia) using an enzyme-linked immunosorbent analyzer Stat Fax - 2100 (USA).

When conducting a statistical analysis of the obtained data, the capabilities of Microsoft Excel spreadsheets and the statistical analysis package Statistica 6.0 were used. The results are presented in the form of arithmetic mean and standard error ($M \pm m$), the statistical significance of the measurements obtained by comparing the average values was determined by Student's t test (t) with the calculation of the probability of error (P) when checking the normality of the distribution using standard methods. If the distribution of the studied variables differed from the normal one, nonparametric methods of analysis were used: the Wilcoxon test for successive measurements and the Mann-Whitney test for two samples. Differences in the compared values were recognized as statistically significant at $p < 0.05$.

THE RESULTS OF THE STUDY

As a result of the therapy, patients with MS showed a significant decrease in the level of lipid 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 ($p < 0.001$), as well as an atherogenic coefficient of 1.6 times ($p < 0.001$), which indicates the highly effective lipid-lowering effect of rosuvastatin.

Table 1: The lipid profile in patients with MS before and in the dynamics of treatment ($M \pm m$).

| N $^{\circ}$ | Indicators | Before treatment (mmol / L) | After treatment (mmol / L) | P |
|--------------|-------------------|-----------------------------|----------------------------|---------|
| | Total cholesterol | 5,8 \pm 0,3 | 3,9 \pm 0,3 | P<0,001 |
| | TG | 2,8 \pm 0,2 | 1,9 \pm 0,2 | P<0,01 |
| | LDL cholesterol | 4,4 \pm 0,2 | 2,4 \pm 0,3 | P<0,001 |
| | HDL cholesterol | 1,0 \pm 0,0 | 1,0 \pm 0,1 | P>0,05 |
| | VLDL cholesterol | 0,4 \pm 0,0 | 0,5 \pm 0,0 | P>0,05 |
| | Kahs | 5,1 \pm 0,3 | 3,0 \pm 0,3 | P<0,001 |

To assess the significance of immuno-mediated reactions in patients with MS, we studied the clinical and immunological markers of inflammation: CRP and pro-

inflammatory cytokines before and in the course of treatment.

Table 2: The level of clinical and immunological markers in patients with MS before and in the dynamics of treatment ($M \pm m$).

| N $^{\circ}$ | Indicators | Before treatment (mmol / L) | After treatment (mmol / L) | P |
|--------------|------------|-----------------------------|----------------------------|---------|
| 1 | IL-6 | 30,4 \pm 4,9 | 10,1 \pm 1,7 | P<0,001 |
| 2 | TNF-a | 21,4 \pm 3,2 | 10,1 \pm 1,5 | P<0,01 |
| 3 | CRP | 5,6 \pm 0,8 | 2,7 \pm 0,5 | P<0,01 |

According to the results of studies of many authors in patients with MS, there is a predisposition to the development of an inflammatory condition, manifested by an increase in the level of CRP. An increase in serum CRP is associated with an increased risk of developing atherosclerosis, type 2 diabetes mellitus, MS and related complications.^[3,5] According to our study, the initial level of CRP in patients with MS was 5.6 ± 0.8 g / L.

After the received lipid-lowering therapy, its significant decrease in the dynamics of treatment was 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.^[6,8] 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 data obtained, the initial level of IL-6 was 30.4 ± 4.9 pg / L. As a result of the therapy received, a significant 3-fold decrease was noted ($p < 0.001$) and amounted to 10.1 ± 1.7 pg / L. A comparative analysis of the level of TNF- α showed a significant decrease in the dynamics of treatment 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 by suppressing the activity of a number of cytokines (TNF- α , interferon γ , IL-6, etc.) and the level of hsCRP.^[6,7,9]

CONCLUSIONS

In patients with MS, the use of rosuvastatin confirms the presence of an anti-inflammatory effect due to a significant decrease in clinical and immunological biomarkers of inflammation.

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