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THE OCCURRENCE OF METABOLIC SYNDROME AND ITS EFFECT ON CARDIOVASCULAR RISK IN PATIENTS WITH GOUT

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ABSRTACT

Goal. To study the prevalence of metabolic syndrome (MS) and the total risk of cardiovascular diseases (CVD) among patients with gout, depending on the presence of MS.

Material and methods. The study included 56 patients (82% men and 18% women) with verified primary chronic gout and MS (main group). The average age was 53.3±10.9 years; the median duration of gout was 5.74 (2.0-8.5) years. The main group was dominated by men (82%). The comparison group consisted of 30 patients with MS who do not suffer from gout and other inflammatory diseases. Men also dominated among the surveyed (73.3%). The average age was 55.3±12.5 years. For all patients, MS parameters were evaluated, the level of uric acid, creatinine, fasting glycemia was determined, lipid spectrum parameters were determined [total cholesterol (OHC), triglycerides (TG), high-density lipoprotein cholesterol (HDL cholesterol), low-density lipoprotein cholesterol (LDL cholesterol)], quantitative measurement of highly sensitive C-reactive protein in blood serum by a highly sensitive immunometric test. The total risk of CVD was calculated according to the SCORE and PROCAM scales.

Results. The incidence of arterial hypertension and hypertriglyceridemia was the same in the compared groups of patients with MS, regardless of the presence of gout ($p<0.001$). The decrease in HDL cholesterol was more typical for patients of the main group in comparison with

patients with isolated MS (50% vs. 23.3%; $p<0.01$). The total risk of CVD in patients of the main group was significantly higher compared to the isolated MS group (SCORE: 7.05% [3.84-9.03%] vs. 2.73% [1.71-4.97%], $p<0.01$; PROCAM: 13.2% [6.55-23.0%] vs. 11.75% [7.0-17.5%], $p<0.05$). The strongest positive associations were found between the PROCAM risk values and uric acid levels in patients of both groups compared (correlation coefficients 0.13 and 0.25, respectively).

Conclusion. The high prevalence of the main risk factors in patients with gout was revealed. The main contribution to the increase in the risk of CVD on the SCORE and

PROCAM scales is made by the levels of OHC, LDL cholesterol and TG. A higher risk of CVD on the SCORE scale was found in patients with gout in combination with MS compared with patients with isolated MS ($p<0.01$). This fact suggests that it is the combination of metabolic disorders developing in both gout and MS that provide an increase in the total risk of CVD.

Keywords: gout, metabolic syndrome, hyperuricemia, highly sensitive C-reactive protein, cardiovascular risk.

INTRODUCTION

Cardiovascular diseases (CVD) are the cause of 38% of all deaths in North America and the most common cause of death for European men aged less than 65 years, and the second most common cause of death for women. Assessment and modification of correctable CVD risk factors [arterial hypertension (AH), obesity, smoking] effectively reduces the risk of cardiovascular events. Metabolic syndrome (MS), also known as syndrome X or insulin resistance syndrome, is a combination of various metabolic disorders, each of which is an independent risk factor for CVD. The presence of MS is associated with an increased risk of CVD and type 2 diabetes mellitus. The identification of MS in combination with the assessment of a 10-year risk of CVD can be used to identify groups of patients who need not only lifestyle modification, but also require specific drug therapy.

Rheumatological patients with chronic inflammatory diseases have a high risk of CVD, as well as higher morbidity and mortality from them. MS may provide an additional link between accelerated atherosclerosis and inflammation in these diseases. In subsequent years, the relationship between insulin resistance, individual metabolic disorders and their contribution to the risk of CVD was studied. MS is considered as an independent risk factor for CVD and atherogenesis due to an increase in free fatty acids, triglycerides, a decrease in high-density lipoprotein cholesterol (HDL) and apolipoprotein B, abdominal obesity, IR, disorders of carbohydrate metabolism and hypertension. Currently, there are three main definitions of MS proposed by the World Health Organization, the National Cholesterol Education Program (original and modified) and the criteria of the International Diabetes Federation. Although these criteria are widespread, there is still debate about some of them. Thus, the greatest criticism is caused by the reduction of the criterion of abdominal obesity for men – waist circumference from 102 cm to 94 cm in the recommendations of the International Diabetes Federation. As it turned out, this underestimation of indicators led to an increase in the number of patients with MS in epidemiological studies, while

the frequency of CVD and, more importantly, mortality from CVD is significantly higher among patients with a waist circumference of more than 102 cm than more than 94 cm.

At the end of the XX century, taking into account the main priorities of modern medicine in the fight against CVD, there was renewed interest in studying the relationship between gout and hypertension, renal failure and cardiovascular pathology.Thus, MS was detected in 62.8% of patients with gout and only in 25.4% without this disease, while the prevalence of MS was mainly associated with high detection of hypertension, excess body weight and diabetes in patients. In addition, the prevalence of MS increased with the age of patients, and amounted to 70% in the group of patients older than 40 years.

In addition to the obvious connection of MS and insulin resistance syndrome with gout, the relationship of hyperuricemia with individual components of MS has been widely studied in the last decade. First of all, the relationship between hypertension and hyperuricemia is interesting. Thus, hypertension is detected in 20-50% of patients with gout, while gouty arthritis is observed among 20-40% of patients with GOUT. Uric acid, firstly, can cause direct stimulation of the renin-angiotensin system in the kidneys, secondly, it inhibits vascular synthesis of NO, which is a potential vasodilator, thirdly, it stimulates the proliferation of smooth muscle cells in the vascular wall, thereby increasing vasoconstriction, and fourth, it causes kidney damage (interstitial nephritis or damage tubules), indirectly leading to the development of hypertension.

Thus, the role of hyperuricemia in the development of hypertension is undeniable, but the study of this problem requires conducting a larger study among patients with essential hypertension and gout to address the need for correction of hyperuricemia in the absence of gouty arthritis.

In addition to the effect of hyperuricemia on the formation of coronary atherosclerosis, a number of studies have shown a close relationship of this factor with the development of atherosclerotic lesions of the carotid arteries, stroke, preeclampsia and vascular dementia. Thus, the problem of studying the role of hyperuricemia and MS in the development and progression of CVD is very relevant.

The purpose of the study: to study the prevalence metabolic syndrome in patients with gout, and the total risk of CVD in patients with gout, depending on the presence of metabolic syndrome.

MATERIALS AND METHODS

We have investigated the main components MS, such as hypertension, obesity, impaired carbohydrate metabolism and lipid spectrum in patients with gout and in the control group (MS without gout). The study included 86 patients. The main group included patients with primary chronic gout, and MS, established according to the criteria of the IOC (n=56). The main group was dominated by men (82%; n=46), the average age of patients was 53.3±10.9 years, the median duration of the disease at the time of treatment was 5.7 [2.0-8.5] years. The comparison group was formed from 30 volunteers with MS without gout and other immuno-inflammatory process. Among the examined individuals of the control group, men also prevailed (73.33%; n=22), the average age of patients was 55.3±12.5. Thus, the main group and the comparison group had no significant differences in age and gender (men predominated in all groups, the average age of patients >50 years). For all patients, the parameters of the metabolic syndrome were evaluated, the level of uric acid, creatinine, fasting glycemia was determined, lipid spectrum parameters were determined: total cholesterol (OH), triglycerides (TG), HDL cholesterol, low-density lipoprotein cholesterol (LDL cholesterol), quantitative measurement of highly sensitive C-reactive protein (hf-CRP) in blood serum by a highly sensitive immunometric test. The total risk of CVD was calculated according to the SCORE and PROCAM.

The results of the study were processed using the Statistica 8.0 statistical software package (Statsoft Inc., USA). The statistical analysis was preceded by a check of quantitative features for the normality of the distribution using the Shapiro-Wilk criterion. Statistical analysis was carried out by nonparametric methods – comparison by the Mann-Whitney method (for 2 independent groups) and correlation analysis by the parametric method.

RESULTS

According to the recommendations of the International Diabetes Federation, abdominal obesity is considered as the main criterion for MS. The weight of patients in the main group ranged from 71.0 to 170.0 kg, the control group – from 82.0 to 106.0 kg. In the main group, the body mass index (BMI) ranged from 23.0 to 52.0 kg/m^2, in the isolated MS group – from 29.05 to 40.39 kg/m^2.

Body weight in the group of patients with MS without gout was significantly lower than that in the main group ($p<0.05$). Obesity (BMI≥30 kg/m2) in the main group was observed in 38 (67.85%) patients, in other cases excess body weight was found. The distribution of patients by degrees of obesity was as follows: obesity of the I degree - in 26 (46.4%) patients, II degree - in 8 (14.3%), III degree – in 4 (7,1%).

In the comparison group without gout, obesity was detected in 18 (60.00%) patients: I degree of obesity was determined in 15 (50.0%) patients, the second degree – in 2 (6.7%) and grade III – in 1 (3.3%) patient. Abdominal type of obesity (waist circumference >94 cm for men and >80 cm for women), was equally often detected in patients with excess body weight in the main group and the MS group without gout. It should be noted that grade II and III obesity was more often diagnosed in patients with gout - 14.3% and 7.17% compared with 6.7% and 3.3% for patients without gouty arthritis.

Thus, hypertension and hypertriglyceridemia were detected in patients with MS regardless of the presence of gout ($p<0.001$). The decrease in HDL cholesterol was more typical for patients of the main group compared with patients with isolated MS ($p<0.01$). At least one additional sign of MS was detected in all the examined patients. In 13 (23.2%) patients of the main group and 1 (3.3%) of the MS group without gout, all 5 additional signs were identified. Patients in the main group were more likely to have more than 3 additional signs of MS compared to the MS group without gout: 28 (50.0%) and 10 (33.3%) patients, respectively. Also as part of the study for all patients without CVD – 68 people, the individual risk of developing CVD was assessed according to the SCORE and PROCAM scales. All patients in both groups compared were older than 40 and younger than 65 years. The main risk factors assessed, based on the recommendation for these scales, were the age and gender of patients, smoking, systolic blood pressure, diabetes mellitus, hereditary history of early CVD, as well as the levels of OHC, HDL, LDL, TG.

The total risk of CVD on the SCORE scale in patients of the main group was significantly higher in comparison with the group of isolated MS ($p<0.01$ for SCORE and $p<0.05$ for PROCAM). Thus, the presence of gout in patients with MS increases the risk of CVD according to evaluation scales, which may be due to lipid metabolism disorders occurring in these patients and closely correlating with the severity of hyperuricemia.

When assessing the frequency of occurrence of vascular events (coronary heart disease, acute cerebral circulatory disorders, chronic heart failure), as well as type 2 diabetes mellitus it was found that this pathology prevails in patients of the gout group in combination with MS. So, IBS It was detected in 9 (16.1%), among them 3 (5.4%) patients had a history of myocardial infarction (MI). Acute cerebrovascular accident (ONMC) in the anamnesis occurred in 2 (3.6%) patients. Type 2 diabetes mellitus at the initial examination was noted in 9 (16.1%) of patients, while only two received drug therapy. In the MS group without gout, 11 (36.7%) people had various disorders of carbohydrate metabolism, including 2 (6.7%) – type 2 diabetes mellitus, coronary

heart disease it was found in 7 (23.3%) patients. There were no patients with an indication of ONMC in the anamnesis.

As is known, metabolic disorders developing in gout due to hyperuricemia and insulin resistance syndrome, in particular, the most important of them – hypertension, lipid and carbohydrate metabolism disorders, obesity – are closely associated with atherosclerosis and are considered as independent risk factors for CVD. This fact undoubtedly obliges us to regard gout as a general medical problem, which is characterized by a high risk of fatal cardiovascular catastrophes associated with atherosclerosis.

Considering the relationship of individual indicators of lipid metabolism, as well as hypertension and age with the levels of hf-CRP and uric acid in patients with gout, the correlations of these indicators with the values of the total risk of CVD on the SCORE and PROCAM scales were evaluated. The average levels of hf-CRP for patients of the main group were 2.98 [1.45-5.85] mg/l, for the comparison group – 1.69 [1.13-2.3] mg/l.

The low values of the correlation coefficients are probably due to the small number of patients sampled and reflect rather weak connections between the studied parameters. At the same time, the strongest positive associations were found between the risk values on the PROCAM scale and the level of uric acid in patients of both groups compared. This pattern is most likely explained by the influence of uric acid levels on the concentration of TG, regardless of the presence of MS or gout in the examined patients. In turn, an increase in TSH significantly increases the risk of CVD on the PROCAM scale ($p<0,01$). Thus, the study revealed a high prevalence of the main risk factors in patients with gout. The main contribution to the increase in the risk of CVD on the SCORE and PROCAM scales is made by the levels OHS, LDL cholesterol and TG, the concentration of which, in turn, is significantly higher with higher total

values of CVD risks calculated according to evaluation scales.

DISCUSSION

The study confirms a fairly high prevalence of metabolic syndrome in patients with gout. In the study, only patients with gout and multiple sclerosis were included in the main group, which accounted for approximately 60% of all examined patients with gout, which generally corresponds to most literature data. According to the study, arterial hypertension (100%) and hypertriglyceridemia (78.6%) were identified among additional signs of metabolic syndrome in patients with gout. According to our results, when studying the serum level hf-CRP in patients of the main group, this

indicator was 2.98 (1.45-5.85) mg/l and was also significantly higher than in the group of isolated MS – 1.69 [1.13-2.3] mg/l ($p<0.01$).

Our data also indicate a high prevalence of CVD among patients with gout – 19.6%, which, however, is somewhat lower than in the study by H.J.Janssen. At the same time, it is interesting that this indicator turned out to be comparable with that of patients with gout, which, apparently, can be explained by the small sample size. As for additional signs of multiple sclerosis and generally accepted risk factors for CVD, the data from this study also differ somewhat from the results the study described above. According to our data, arterial hypertension was detected in 100% of patients with gout and in 93.3% of patients with multiple sclerosis without gout, obesity - in 67.9% and 60% of the examined, respectively. This indicator is significantly higher than in known epidemiological studies, and is most likely due to the fact that, unlike the work of X. J. Janssen, we studied only patients with metabolic syndrome.

As for the prevalence of type 2 diabetes mellitus, in this case our data are comparable with the literature data and reveal approximately 3-fold prevalence of this pathology in patients with gout.

CONCLUSION

Thus, patients with chronic rheumatic diseases, including those suffering from gout, have an increased risk of morbidity and mortality from CVD. Among them, a high prevalence of traditional risk factors and MS is revealed. These data suggest that chronic inflammation can be considered as one of the key factors contributing to the development of MS and progression of atherosclerosis. Aggressive treatment of the underlying disease and correction of inflammation, Thus, patients with chronic rheumatic diseases, including those suffering from gout, have an increased risk of morbidity and mortality from CVD. Among them, a high prevalence of traditional risk factors and MS is revealed. These data suggest that chronic inflammation can be considered as one of the key factors contributing to the development of MS and progression of atherosclerosis. Aggressive treatment of the underlying disease and correction of inflammation, as well as the elimination of traditional risk factors can reduce the incidence and mortality of CVD. The evaluation of the MS criteria, along with the assessment of the 10-year risk of CVD, should be used in order to identify patients who need lifestyle modification and/or drug therapy.

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