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FEATURES OF THE COURSE OF GOUT IN THE PRESENCE OF METABOLIC SYNDROME

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ABSTRACT: The purpose of this study is to study the features of the course of gout in combination with metabolic syndrome (MS) and to assess the impact of an integrated therapeutic approach on the course of joint syndrome and the dynamics of metabolic disorders. 89 patients with primary chronic gout were examined, verified based on the classification criteria of S. Wallace et al., mainly men – 74 (86.0%), average age 57.35 ± 12.41 years, median duration of the disease at the time of treatment 5.0 (2.0–10.0) years. MS was detected in 63 % of patients with primary chronic gout. The age of gout onset is significantly lower in patients with gout in combination with MS – 47.51 ± 11.03 years ($p < 0.001$). In the main group, there was a high frequency and duration of gout exacerbations per year ($p < 0.01$ and $p < 0.05$, respectively). The maximum serum uric acid (MC) values were detected in the gout group in combination with MS, and have strong direct correlations with the duration of the disease ($R = 0.31$ at $p < 0.05$), as well as the frequency exacerbations over the past year ($R = 0.37$ at $p < 0.001$). Against the background of allopurinol therapy, all patients showed a decrease in the frequency and duration of exacerbations, in the "MK level control" group, the frequency (median 1.0 [0.0-2.5]) and duration (median 2.5 [0.0–4.0]) of exacerbations were significantly lower compared with the "no MK level control" group ($p < 0.01$). Among the patients who reached the target values of serum MC in the control period, there was a significantly greater decrease in such indicators as cholesterol, low-density lipoproteins and triglycerides.

Keywords: Gout, metabolic syndrome, hyperuricemia, highly sensitive C-reactive protein.

INTRODUCTION

The relationship between gout and hypertension, renal pathology, and cardiovascular diseases has been studied since the end of the 19th century, but in the 20th century, interest in this problem arose again, but in the light of new priorities of modern medicine – the impact on reducing morbidity and mortality from cardiovascular disasters. Numerous modern studies have described a high prevalence of MS among patients with gout – more than 60%, increasing with age by 10-15%. As one of the reasons for such a high prevalence of MS in patients with gout, the close association of individual metabolic disorders with hyperuricemia is considered. On the other hand, there is accumulated data on the mutual effect of hyperuricemia and individual metabolic disorders, their relationship with markers of inflammation, such as highly sensitive C-reactive protein, interleukin-6, and α-factor of tumor necrosis suggest a negative effect of comorbid pathology on the nature of joint syndrome in gout. Research affecting this The question is currently practically non-existent. There are few data indicating the negative impact of MS on the parameters of the course of gout due to an increase in chronic forms of the disease, an aggravation of the parameters of the joint syndrome in the form of the formation of frequent and prolonged exacerbations. Understanding gout as a metabolic disease characterized by a high risk of cardiovascular

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diseases, its combination with MS, which affects the course of joint syndrome, makes it necessary to develop an integrated approach to the treatment of this category of patients. The aim is to study the features of the course of gout in combination with MS and to evaluate the effect of an integrated therapeutic approach on the course of joint syndrome and the dynamics of metabolic disorders.

MATERIALS AND METHODS OF RESEARCH

The study included 89 patients with primary chronic gout. The diagnosis of gout was verified based on the classification criteria of S. Wallace et al. The examination of patients was carried out during the initial examination and during the control period of observation (12 months). The study group was dominated by men – 74 (86.0%), the average age was 57.35 ± 12.41 years, the median duration of the disease at the time of treatment was 5.0 (2.0–10.0) years. The average age of gout onset was 50.74 ± 11.91 years old, 39 (43.8%) patients were diagnosed with tofous gout, 50 (56.2%) patients suffered from a non-tofous form of the disease. Among the concomitant pathologies, arterial hypertension, chronic kidney disease, nephrolithiasis, coronary heart disease were most often detected, the overwhelming number of patients consumed alcohol and did not follow a diet. At the time of the initial examination, 59 (66.29%) people received hypouricemic therapy with allopurinol, the dose of the drug varied from 50 to 300 mg per day. All patients were evaluated for clinical signs of MS according to the criteria of the second revision of the IOC. MS was diagnosed in 56 (63.0%) patients with gout. Based on this, all patients were divided into 2 groups to be compared: the main group – gout in combination with MS, the comparison group – isolated gouty arthritis. The median waist circumference (FROM) for men was 98 (95.0–102.0) cm, for women – 88 (86.0–90.0) cm. Abdominal type of obesity was diagnosed in 38 (67.85%) patients with obesity and in 18 (32.15%) patients with low body weight. Among the other criteria of the metabolic syndrome, arterial hypertension was detected in all patients, hypertriglyceridemia was detected in 38 (82.60%) men and 6 (60.0 %) women, a violation of carbohydrate metabolism was noted in 26 (46.42%) patients. Clinical research methods included the assessment of joint syndrome and MS parameters. The severity of gout was assessed based on a patient's survey and a retrospective analysis of anamnestic data. To all patients The level of MC, creatinine, and fasting glycemia was studied, and the lipid spectrum was determined: total cholesterol (OH), triglycerides (TG), high-density lipoprotein cholesterol (HDL cholesterol), low-density lipoprotein cholesterol (LDL cholesterol). Quantitative measurement of highly sensitive C-reactive protein (hf-CRP) in blood serum was carried out using a highly sensitive immunometric test on an IMMULITE analyzer. The results of the study were processed using an IBM-compatible a computer with a Pentium processor using Microsoft Office Excel 2007 and the Statistica 6.0 statistical software package.

THE RESULTS AND THEIR DISCUSSION

The analysis of the main parameters of the course of gout, depending on the presence of MS, was carried out. The data is presented in the table. 2. In the main group and the comparison group, chronic arthritis with or without the formation of tofuses prevailed, about 70% of patients on average for each sample. The age of gout onset was significantly lower in patients of the main group and amounted to 47.51 ± 11.03 years ($p < 0.001$), while the total duration of the disease did not significantly differ. The total number of topuses at the time of

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the initial appeal in both samples it turned out to be similar. The main differences were revealed in the analysis of the articular syndrome. Thus, the course of gout in patients of the main group was characterized by a higher frequency of 3.0 (2.0–5.0) and a duration of 7.0 (3.5–8.5) attacks, which was significantly higher ($p < 0.01$ for frequency and $p < 0.05$ for duration of exacerbations) compared with the control group. Thus, it was noted that the presence of MS in patients with gout may predispose to an earlier onset of the disease, as well as worsen the course of joint syndrome by increasing the frequency and duration of exacerbations. In order to identify the mechanisms contributing to the aggravation of the course of gout in combination with MS, the levels of MC and hf-CRP in patients of the main group and the comparison group were studied. In the study of serum MC levels in patients of the main group, this indicator was significantly higher ($p < 0.01$) and ranged from 222.0 to 762.0 (median 510.25 [441.0–593.0]) mmol/L. The level of MC in patients with gout significantly influenced the course of the disease. In both groups, higher MC scores led to an increase in the frequency and duration of exacerbations. It should be noted that in patients with gout without MS, prolonged exacerbations (14 weeks or more) They were detected at a level of MK 354.9 (316.8–393.0) mmol/l, which is significantly lower than in patients of the main group ($p < 0.05$). The number of affected joints throughout the disease increased with an increase in the level of MC in both compared groups (correlation coefficient $R = 0.22$, $p < 0.05$). In addition, in patients without MS with recurrent arthritis in the presence of tofuses, the serum level of MC significantly increased ($p < 0.05$). Serum levels of HF-CRP in patients The main group ranged from 0.12 to 37.4 (median 2.98 [1.45–5.85]) mg/l and was significantly higher than in the comparison group ($p < 0.001$). The distribution of hf-CRP in patients with gout ranged from 0.12 to 38.4 (median 2.3 [1.0-4.11]) mg/l, the majority of patients – 56 (63.0%) – had an hf–CRP level of less than 3.0 mg/l. Taking into account the peculiarities of the distribution of the trait, the division of patients into groups was carried out according to the quartile size of hf-CRP. The first group consisted of 56 (63.0%) patients with an hf-CRP level of less than 3.0 mg/l, in The second group included 33 (37.0%) patients with a concentration of hf-CRP of more than 3.0 mg/l. The age of gout onset in patients with an hf-CRP level of more than 3.0 mg/l was slightly lower than in patients with an hf-CRP level of less than 3.0 mg/l ($p = 0,05$). In the group of patients with a large number of exacerbations, significantly higher rates of HF-CRP were detected per year ($p < 0.05$). The level of hf-CRP increases with the chronic course of gout, the formation of tofuses and reflects the high frequency of exacerbations per year. In patients without MS, the level of hf-CRP increased with a longer duration of the disease, while as in MS, the indicators of hf-CRP did not depend on the duration of the disease. During the correlation analysis, the strongest direct correlation was noted for the level of MC and the duration of the disease ($R = 0.31$ at $p < 0.05$), as well as the frequency of exacerbations over the past year ($R = 0.37$ at $p < 0.001$). Also, during the work, the main components of MS were studied in patients of the main group and the comparison group. According to the recommendations of the International Diabetes Federation, Abdominal obesity is considered as the main criterion for MS. In patients with gout without metabolic syndrome, body weight, BMI, waist circumference they were significantly lower in comparison with those in the main group ($p < 0.001$). Fatness (BMI ≥ 30 kg/m2) in the main group was observed in 38 (67.85%) patients, in other cases excess body weight was found. The prevalence of additional signs of MS It was high in both groups compared, however, the identification of abdominal obesity as the main criterion of MS and two additional signs made it possible to diagnose this pathology only in 56 patients suffering from gout. Among the additional signs of MS, according to the study, arterial hypertension was detected (79.77%), and for patients with MS this value was

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100%, and hypertriglyceridemia (73.03%). At least one additional sign of MS was detected in all examined patients, in 13 (23.21%) all 5 additional signs were detected, which also corresponds to the literature data. In the G. Zuliania study, the relationship between elevated levels of hf-CRP, a low grade inflammatory marker, and MS was assessed among 1,044 patients over the age of 65. In general, MS was detected in 31% of the surveyed, while the level of hf-CRP was significantly higher ($p < 0.001$) in the MS group. According to our results, when studying the serum level of 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 comparison group without MS ($p < 0.001$). The accumulated data on the close relationship of hyperuricemia and certain metabolic disorders in gout, including their mutual influence, the association of insulin resistance syndrome and MS with the level of inflammatory cytokines, allow us to make assumptions on the negative effect of comorbid pathology on the nature of joint syndrome in gout. Currently, there are practically no studies addressing this issue, there is only some data on the negative role of MS in the course of gouty arthritis. Thus, in the works it was shown that the development of obesity and hypertension at a young age can contribute to an earlier onset of gout, while at an older age, an increasing range of concomitant diseases is important for the onset of the disease, in which a metabolic disorder is noted. In addition, it has been shown that the presence of insulin resistance syndrome in patients with gout contributes to an earlier chronology of the disease and a greater severity of the joint syndrome (a tendency to prolonged exacerbations, involving a significantly larger number of joints). This fact is explained by significantly higher indices of the serum concentration of MC, correlating with the level of immunoreactive insulin in the group of patients with insulin resistance syndrome. According to the results of our study, the presence of MS in patients with gout predisposed to an earlier onset of the disease. Thus, the age of gout onset was significantly lower in patients of the main group and amounted to 47.51 ± 11.03 years ($p < 0.001$), while the total duration of the disease did not significantly differ. The total number of topuses at the time of the initial appeal in both samples turned out to be similar. The main differences were revealed in the analysis of the articular syndrome. Thus, in the main group, a high frequency and duration of gout exacerbations per year were noted ($p < 0.01$ and $p < 0.05$, respectively). Serum MC values in the study were also maximal in the gout group in combination with MS (510.25 [441.0–593.0] mmol/l) and had strong direct correlations with the duration of the disease ($R = 0.31$ at $p < 0.05$), as well as the frequency of exacerbations over the past year ($R = 0.37$ at $p < 0.001$). Of great interest is the dynamics of the parameters of the course of gout against the background of complex therapy. Thus, against the background of allopurinol therapy, a decrease in the frequency and duration of exacerbations was noted in all patients. However, it should be noted that in the "MK level control" group, the frequency (median 1.0 [0.0–2.5]) and duration (median 2.5 [0.0–4.0]) of exacerbations were significantly lower in comparison with the "no MK level control" group ($p < 0.01$). In our opinion, it seems interesting that The fact is that in patients who reached the target values of serum MC (less than 360 mmol/l) in the control period, there was a significantly greater decrease in such indicators as low-density lipoprotein cholesterol and triglycerides ($p < 0.001$). Special interest The obtained data on the correlation of the dose of allopurinol with the degree of decrease in blood pressure ($R = 0.21$) are presented, so, in the group of patients with target values of MC, the degree of arterial hypertension in the control periods was significantly lower ($p < 0.05$). This effect of allopurinol needs further study to resolve the issue of the possibility of prescribing the drug to correct metabolic disorders in patients with asymptomatic hyperuricemia.

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CONCLUSIONS

In conclusion, it should be noted that for the purpose of a comprehensive analysis of the course of the disease, in addition to evaluating the parameters of the joint syndrome and serum MC concentration, it is advisable to determine hf-CRP, clinical and laboratory signs of MS, and the basis for adequate disease control is the multidisciplinary therapeutic approach: control of MC levels and correction of risk factors for cardiovascular diseases both by medication and and by non-medicinal methods.

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