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Risk Factors for Recurrence of Stone Formation in Patients with Nephrolithiasis and Post-COVID Syndrome Undergoing Metaphylactic Treatment

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Today, the problem of urolithiasis (UL) as a metabolic disorder characterized by the formation of stones in the kidneys, remains extremely relevant due to its prevalence in urological practice (ranking second only to urinary tract infections), its tendency toward frequent recurrence (30–80%), and serious complications, especially among individuals of working age, remains extremely relevant. UL can lead to renal failure, disability, and mortality among patients [1–3]. Thus, this problem is not only medical but also economic and social.

This issue has become particularly relevant following the COVID-19 pandemic, when, regardless of the severity of the illness, the viral infection is accompanied by complications affecting various organs and systems of the body, including the kidneys and urinary tract [4–5]. The term “post-COVID syndrome” (PCS) is used to describe patients who have not returned to their baseline health and functioning 6 months after recovering from COVID-19.

As is known, the following main risk factors for kidney stone formation are currently considered: oversaturation of blood serum and urine with stone-forming metabolites, particularly uric acid, oxalic acid, and calcium; an imbalance in the ratio of crystallization and precipitation activators and inhibitors in urine; and specific changes in urine output and pH.

The aim of the study was to analyze the dynamics of changes in the main risk factors for recurrent stone formation in patients with nephrolithiasis (NL) and PCS during metaphylactic treatment, as determined by measuring the concentrations of calcium, oxalic acid, and uric acid.

Materials and Methods. The study included 96 patients with NL; of these, 44 patients constituted the experimental group, consisting of patients with NL and PCS (group 1); 52 patients constituted the comparison group, consisting of patients with NL who underwent treatment at the State Institution “Academician O. F. Vozianov Institute of Urology of the National Academy of Medical Sciences of Ukraine” during the pre-study period (group 2). The mean age of patients in

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group 1 was $43,6 \pm 6,1$ years; there were 27 men (61,4%) and 17 women (38,6%). The mean age of patients in group 2 was $45,8 \pm 7,2$ years; there were 29 men (55,8%) and 23 women (44,2%).

Control group - 28 generally healthy individuals with normal urine test results and no history of organic kidney disease. Renal function was preserved in both patient groups, and the kidney stones did not cause acute urinary tract obstruction. Examination of patients, as well as determination of concentrations of calcium, oxalic acid, and uric acid - the primary risk factors for kidney stone formation - were performed in patients urine prior to stone removal and 5-7 months (on average 6 ± 1 month) after stone removal while undergoing metaphylactic treatment [6]. Urine for analysis was collected after spontaneous urination (urine from the bladder). Calcium and uric acid concentrations in urine were expressed in mmol/L, and oxalic acid concentration in urine was expressed in mg/L. Serum uric acid concentration (mmol/L) and oxalic acid excretion in 24 - hour urine (mg/day) were also determined.

Research results. Analysis of the results showed that, in terms of mineral composition, 73,1% of the removed calculi in patients from the comparison group consisted of oxalates in various proportions; 6 calculi (11,5%) were a mixture of uric acid (more than 20%) and wevelite; 4 stones (7,7%) consisted of uric acid (100%), and another 4 stones (7,7%) consisted of a mixture of oxalates (predominantly weddelite) with hydroxyapatite (from 15%). In patients from the study group, 65,8% of the removed calculi were also oxalates in various proportions. Calculi containing uric acid (6 mixed with wevellite and 6 monomolecular) accounted for 29,2%. Thus, while oxalate stones were the most common in both groups, the composition of the removed stones varied: in the group of patients with post-COVID syndrome, the proportion of uric acid stones increased to 29,2% compared to 19,2% (11,5%+7,7%) in the comparison group.

It should be noted that pharmacological metaphylactic therapy was initiated in patients from both groups even before stone removal. Personalized anti-relapse treatment was prescribed after stone removal and a comprehensive examination of the patient, taking into account the individual characteristics of the disease course.

The results of examinations of patients in Groups 1 and 2 following stone removal and metaphylactic treatment at 6 ± 1

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months showed a certain trend toward normalization of all parameters studied. Thus, in patients from the comparison group, diuresis increased on average from $1,12 \pm 0,24$ L/day after treatment to $1,63 \pm 0,3$ L/day, i.e., it increased by 45,5%. The concentration of oxalic acid in urine decreased from $52,4 \pm 6,7$ mg/L after treatment to $42,4 \pm 7,0$ mg/L, i.e., it decreased by an average of 19%. Daily oxalic acid excretion increased from $58,4 \pm 3,39$ mg/day to $69,1 \pm 3,9$ mg/day after treatment ($p < 0,05$), i.e., it increased by an average of 18,3%. Serum uric acid concentration decreased from $0,52 \pm 0,02$ mmol/L to $0,472 \pm 0,013$ mmol/L after treatment ($p < 0,05$), representing an average decrease of 9,2%. The concentration of uric acid in urine decreased from $5,65 \pm 0,70$ mmol/L before treatment to $5,03 \pm 0,70$ mmol/L after treatment, representing an average decrease of 11%. It was found that in the urine of patients in the experimental group, diuresis increased on average from $1,3 \pm 0,2$ L/day after treatment to $1,54 \pm 0,35$ L/day, i.e., an increase of 18,5%. The concentration of oxalic acid in urine decreased from $55,8 \pm 4,2$ mg/L after treatment to $47,84 \pm 4,4$ mg/L, i.e., it decreased by an average of 14,3%. Daily oxalic acid excretion increased from $72,5 \pm 5,8$ mg/day to $77,5 \pm 7,1$ mg/day following treatment, representing an average increase of 6,9%. Serum uric acid concentration decreased from $0,611 \pm 0,038$ mmol/L to $0,558 \pm 0,025$ mmol/L after treatment, i.e., it decreased by an average of 8,7%. The concentration of uric acid in urine decreased from $6,05 \pm 0,35$ mmol/L after treatment to $5,47 \pm 0,30$ mmol/L, i.e., it decreased by an average of 9,6%. No significant differences in serum and urine calcium levels were found between the groups before and after treatment.

Thus, in patients with NL and PCS, the dynamics of changes in risk factors for disease recurrence following stone removal and subsequent prophylactic treatment over a period of 6 ± 1 month indicates a slowing of the normalization process compared to the control group; that is, in patients with PCS, the efficacy of long-term treatment is reduced, which requires the development of more effective metaphylactic treatment regimens to prolong the relapse-free period.

Conclusions. The efficacy of six-month metaphylactic treatment in patients with NL and PCS is lower due to a slower rate of normalization of risk factors for disease recurrence compared to Group 2; this is particularly true for serum uric acid levels.

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