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Activation of persistent pathogenic microflora after ascending pyelolithotripsy and the recurrence rate of nephrolithiasis

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персистуюча патогенна мікрофлора, пієлолітотрипсія, рецидив нефролітіазу

SUMMARY

We've studied the activation of persistent pathogenic microflora in 28 patients after retrograde pyelolithotripsy and the frequency of recurrence of kidney stones during the year under the conditions of traditional drug treatment in the early and late postoperative periods. We've studied the recurrence of kidney stones during the year under conditions of use in another group of patients (26 patients), in addition to traditional drug treatment, phytouroantiseptic (herbal extract BNO 1045). It has been confirmed that persistent pathogenic microflora is found in the structures of urinary stones, which is released after operative crushing of stones and reverses into active forms that are insensitive to the main groups of antibiotics, which long-term support a chronic inflammatory process in the kidneys, and is the cause of exacerbation of chronic pyelonephritis and relapse. It has been proven that the use of a phytouroantiseptic (herbal extract BNO 1045) in the complex treatment is the effective method for eliminating the infectious and inflammatory process in the kidneys caused by persistent pathogenic microflora, for decreasing the level of uric acid in the blood and normalization of urine's pH, which leads to effective prevention of stone relapse.

РЕФЕРАТ

Активация персистующей патогенной микрофлоры после восходящей пиелолитотрипсии та частота рецидиву нефролітіазу. Ухаль М. І., Пустовойт І. П., Семанів О. М., Дюльгер В. І., Єрґієва Т. С. У 28 хворих проведено дослідження активації персистуючої патогенної мікрофлори після ретроградної пієлолітотрипсії та частоту рецидиву сечокам'яної хвороби протягом року за умов традиційного медикаментозного лікування в ранньому та пізньому післяопераційному періодах. В іншій групі хворих (26 пацієнтів) проведено дослідження

рецидиву сечокам'яної хвороби протягом року за умов використання, крім традиційної медикаментозної терапії, фітоуроантисептика (BNO 1045). Підтверджено, що в структурах сечових каменів знаходиться персистуюча патогенна мікрофлора, яка звільняється після оперативного дроблення каменів і реверсує в активні низькочутливі до основних груп антибіотиків форми, які тривалий час підтримують хронічний запальний процес у нирках, і є причиною загострення хронічного пієлонефриту та рецидиву. Доведено, що застосування в комплексному лікуванні фітоуроантисептика (BNO 1045) є ефективним методом ліквідації інфекційно-запального процесу в нирках, обумовленого персистуючою патогенною мікрофлорою, зниженням у крові сечової кислоти та нормалізації рН сечі, що зумовлює до ефективної профілактики рецидиву сечокам'яної хвороби.

INTRODUCTION

Persistence is a strategy for pathogenic and opportunistic microorganisms to survive in the host, evading both host antibacterial defense factors (inflammatory reaction, phagocytosis and antibody production) and antibacterial drugs (Falagas et al., 1995; Bukharin, 1999). Persistence of bacteria in the urinary tract is one of the most important goals for the successful treatment of urinary tract infections (UTIs). This is due to the lack of protective anti-infective mechanisms on artificial materials (catheters, drains, urinary stones, prostheses, etc.), as well as the adhesion of microorganisms on the surfaces of urine salt crystals with the formation of biofilms (Choong et al., 1999; Choong et al., 2001). The high adaptation of microorganisms in biofilms fixed on catheters, drains, as well as to changing features of survival is especially evident in antibiotic therapy, making worthless the entire classes of antibiotics due to the selection of resistant strains of microorganisms (Morris et al., 2001). It is known that the infectious inflammatory process in the kidneys plays one of the key roles in the development, progression and recurrence of urolithiasis after removal of kidney and ureteral stones. Thus, pathogenic bacteria and phagocytic leukocytes secrete lysosomal and proteolytic enzymes, cationic proteins and other biologically active factors into the cavity of the pelvicalyceal system. This leads to coagulation of the protective protein substances of urine, disruption of the colloidal balance of urine (supersaturation), and also contributes to the formation of a bacterial-protein-leukocyte complex, which adheres to salt crystals of urine, causing their sedimentation and aggregation with the development of struvite ($MgNH_4PO_4 \cdot 6H_2O$) or carbonate apatite ($Ca_{10}(PO_4)_6CO_3$) stones (Ukhal et al., 2002; Vashchula et al., 2007; Suleimanov et al., 2010; Romanova et al., 2011).

In recent years, a large positive experience has been gained in the use of a herbal preparation based on a special composition of herbal components BNO – rosemary leaves, lovage root and aerial parts of centaury – (active substance of Canephron® N) in the metaphylaxis of urolithiasis and the treatment of

infectious and inflammatory diseases of the urinary tract. Due to the influence on the pathogenicity factors of the bacterial flora (anti-adhesive effect), anti-inflammatory effect and improvement of urodynamics, the medicinal product provides an effective management of pathogenic flora in the urinary tract. In addition, the medicinal product affects the main non-specific links in the pathogenesis of the formation of urinary calculi, namely: reduces the saturation of urine with crystal-forming substances; increases the concentration of magnesium ions in the urine as a natural inhibitor of crystallization; helps to maintain the urine pH within physiologically optimal values (6.2–6.4). But the effectiveness of this approach for the treatment of UL associated with the persistence of pathogenic microflora in the urinary tract has not been studied enough.

Study objective: To confirm the activation of persistent pathogenic microflora after retrograde pyelolithripsy, to study the recurrence rate of nephrolithiasis when using a herbal preparation based on lovage root, rosemary leaves and aerial parts of centaury to increase the efficacy of anti-relapse therapy for urolithiasis in chronic pyelonephritis caused by persistent pathogenic microflora.

MATERIALS AND METHODS

The study observed 54 patients after retrograde pyelolithripsy with chronic pyelonephritis in remission. Depending on the chosen further treatment, they were divided into 2 parallel groups: the treatment group (26 patients) received standard antibiotic treatment in the postoperative period, diet therapy and a herbal preparation based on the above herbal composition (BNO 1045) for 3 months. In the control group, patients received only antibiotic treatment and diet.

The efficacy endpoints were: the recurrence rate of stone formation in the urinary tract and signs of activation of persistent pathogenic microflora.

The exclusion criteria were:

- acute pyelonephritis;
- chronic renal insufficiency;
- severe somatic diseases that can affect the prognosis of treatment.

In all patients, stones were localized in the renal pelvis. Stone sizes ranged from 23 to 18 mm

(mean, 19.8±1.8 mm). The age of the patients was from 22 to 68 years. There was no acute pyelonephritis in the studied patients before surgery.

In both groups of patients, the tests were conducted with a special focus on identifying the rate of development and progression of the infectious and inflammatory process after pyelolithotripsy, as well as the recurrence of urolithiasis.

RESULTS AND DISCUSSION

According to clinical manifestations, laboratory and functional tests performed before pyelolithotripsy, all patients of the first and second groups had chronic pyelonephritis. Bacteriuria ranged from 103 to 104 per 1 mL of urine. At the same time, in urine cultures during this period, *E. coli* was detected in 67%, *Enterobacter agglomerans* – in 15%, *S. Aureus* – in 10%, *S. Epidermidis* – in 8%. Sensitivity to the main types of antibiotics ranged from ++ to +++.

After lithotripsy, with a standard bacteriological test of stone fragments and urine, the bacterial microflora in the cultures differed significantly from the results of urine cultures before surgery. Yes, *E. coli* was already cultured in 70%. *Proteus mirabilis* was cultured in 20% of patients and *Klebsiella pneumoniae* in 5%, which were not cultured in urine before lithotripsy.

The kidney ultrasound in patients of the control group who received no herbal preparation showed

that a sufficiently significant amount of salt urine crystals and microliths up to 1-1.5 mm continued to appear in the renal pelvis and calyces on Day 30 after pyelolithotripsy.

The kidney ultrasound in patients of the treatment group who received the claimed herbal preparation showed that salt crystals and microliths were practically not detected in the renal pelvis and calyces on Day 30 of treatment.

The urinary sediment examination in patients of both groups performed on Days 3 and 7 after lithotripsy detected leukocyturia, proteinuria, bacteriuria and salt crystals. At the same time, sensitivity to the main types of antibiotics was very low in patients of both groups and did not exceed one +.

In 21 patients of the control group (75%) who received no claimed herbal preparation, significant leukocyturia and bacteriuria remained on Days 15 and 30 after the surgery and reached 104-105, respectively. In the urine cultures of these patients, the microflora in almost all cases coincided with pathogenic microorganisms that were cultured after lithotripsy. In the long-term study period (12 months) after surgery, 4 of 21 patients (19%) of the control group with an inflammatory process caused by the postoperative period of persistent pathogenic microflora had recurrent kidney stones.

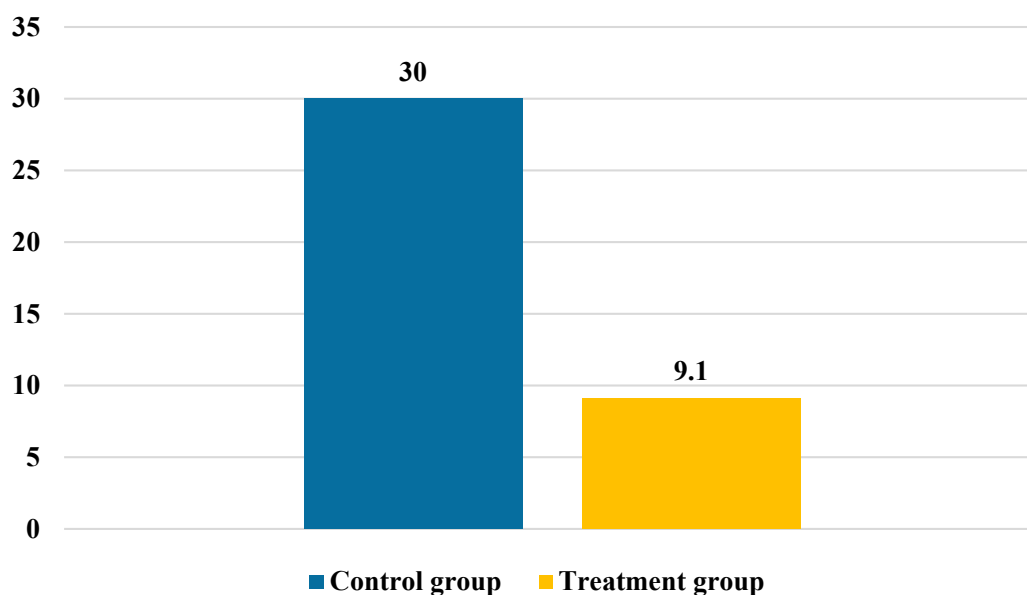
Comparative tests of changes of uric acid and urine pH in the blood of patients of both studied groups are given in Table.

Dynamics of changes of uric acid and urine pH in the blood of patients under conditions of conventional drug treatment and in patients under conditions other than conventional drug treatment using a phyto-urinary antiseptic

Study time schedule	Before treatment		On Day 30
	in patients of both groups	Patients of the control group	Patients of the treatment group using a phyto-urinary antiseptic
Uric acid in blood, $\mu\text{mol/L}$	490.0±40.0	380.0±21.0	230.0±24.0*
Urine pH	5.8±0.1	6.2±0.3	6.8±0.2*

In the study of the rate of exacerbation of chronic pyelonephritis and recurrence of urolithiasis in the long term (within a year) in patients of the treatment group using the claimed phyto-urinary antiseptic, an exacerbation of a chronic infectious and inflammatory process in the kidneys was detected in

9.1%, and recurrence of urolithiasis within a year was not found in any of these patients. The higher effectiveness of prevention of exacerbation of chronic pyelonephritis compared with patients who received no phyto-urinary antiseptic is clearly seen in Figure.



The rate (%) of exacerbations of chronic pyelonephritis within a year

CONCLUSIONS

1. We have confirmed that in the structures of urinary stones there is a persistent pathogenic microflora which is released after the operative lithotripsy and reverses into active forms that are low-sensitive to the main types of antibiotics, which long-term support a chronic inflammatory process in the kidneys and is the cause of exacerbation of chronic pyelonephritis and recurrence of urolithiasis.

2. The recurrence rate of nephrolithiasis in chronic pyelonephritis, caused by persistent pathogenic microflora, is quite high already a year after pyelolithotripsy, which should be taken into account when planning metaphylaxis of kidney stones through long-term outpatient use of medicinal products which are

not nephrotoxic, affect bacterial infection and stone formation factors.

3. The use of the original complex herbal preparation containing extracts of rosemary leaves, aerial parts of centaury and lovage root in complex treatment and on the long-term outpatient basis, starting from the early postoperative period, is an effective method to eliminate the infectious and inflammatory process in the kidneys, caused by persistent pathogenic microflora, a decrease of uric acid in the blood and normalization of urine pH, which leads to effective prevention of recurrence of urolithiasis.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

REFERENCES

- Bukharin, O. V. (1999). *Persistence of pathogenic bacteria*. Medicine.
- Choong, S. K. S., Hallson, P., Whitfield, H. N. & Fry, C. H. (1999). The physicochemical basis of urinary catheter encrustation. *Br J Urol Int*, 83, 770-775.
<https://doi.org/10.1046/j.1464-410x.1999.00014.x>
- Choong, S. K. S., Wood, S., Fry, C. H., & Whitfield, H. N. (2001). Catheter associated urinary tract infection and encrustation. *Int J Antimicrob Agents*, 17, 305-310.
[https://doi.org/10.1016/s0924-8579\(00\)00348-4](https://doi.org/10.1016/s0924-8579(00)00348-4)
- Falagas, M. E., & Gorbach, S. L. (1995). Practice guidelines: urinary tract infections. *Infect. Dis. Clin. Pract*, 4, 241-256.
<https://doi.org/10.1097/00019048-199507000-00001>
- Morris, N. S. & Stickler, D. J. (2001). Does drinking cranberry juice produce urine inhibitory to the development of crystalline, catheter-blocking *Proteus mirabilis* biofilms? *Br J Urol Int*, 88, 192-197.
<https://doi.org/10.1046/j.1464-410x.2001.02248.x>
- Romanova, Yu. M., Tiganova, I. G., Khmel', I. A., Alekseeva, N. V., Stepanova, T. V., Shevlyagina, N. V., Didenko, L. V., Goryachev, S. N., &

- Ginzburg, A. L. (2011). Biofilms of Burkholderia cepacia: Characteristics of mutants with modified formation capacity. *Mol. Genet. Mikrobiol. Virusol.* 26(3), 3-10.
<https://doi.org/10.3103/s0891416811030037>
- Suleimanov, S. I., Kadyrov, Z. A., Istratov, V. N., & Romashvili, V. Sh. (2010). The role of the infectious factor in the pathogenesis of urolithiasis. *Clinical laboratory diagnostics*, 7, 18-23.
- Ukhal, M., & Borisov, A. (2002). *The role of activated by accompanying inflammation in kidneys secretory Ig a in the development of urolithiasis. 26-Congress of the Societe Internationale Urologie.* SIU. Stockholm. 312.
- Vashchula, V. I., Lish, E. Ya., & Stankevich, S. I. (2007). Infection in the etiopathogenesis of urolithiasis. *Medical news*, 11.113-118.