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Treatment and Prevention of Urolithiasis in patients with stones of various locations

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ABSTRACT

The study goal was to find the most optimal approach to the treatment of patients with urolithiasis. The study involved 4014 patients with stones of different localization. Patients with benign prostatic hyperplasia (BPH) were investigated with IPSS, PSA, and uroflowmetry. 3175 ureteropyeloscopies were performed. Separately, we studied the results of treatment of 427 patients with ureterolithiasis in combination with BPH, which underwent ureterolithotripsy. Percutaneous nephrolithotripsy was performed in 412 patients, most of the procedures were performed according to the classical technique. The other research purpose was prophylaxis optimization of the recurrent urolithiasis. 152 patients participated in the experimental part. Some of the patients were taken from the clinical part of the study. All patients were with recurrent calcium oxalate urolithiasis. Patients were divided into two groups: the 1st group (74 patients) did not receive treatment during the follow-up period, the second group (42 patients) received treatment in the volume of thiazide diuretics, water load, citrate mixtures, calcium preparations inside. During the entire follow-up (6 months), all patients underwent a comprehensive urological examination. Eventually have been estimated that surgery should not be the final stage of treatment of the urolithiasis. Urolithiasis requires constant monitoring of patients, and the priority task of a urologist is to prevent recurrent stone formation. This is achieved through the appointment of adequate conservative therapy, which includes thiazide diuretics, citrate mixtures, calcium preparations, water intake in adequate amount, and if necessary, magnesium preparations. The final choice of conservative treatment depends on the type of stone. The change in the concentration of crystallization inhibitors (bikunin and osteopontin) is a predictor of an early relapse of the urolithiasis, which can be used in monitoring patients in the postoperative period.

Keywords: recurrent urolithiasis, nephrolithotripsy, ureteroscopy, urolithiasis markers, urolithiasis and infravesical obstruction

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INTRODUCTION

Urolithiasis has been increasing progressively in recent years, especially in patients with calcium oxalate stones (about 70-80% of all stones)^[1]. Most urologists provide patients with vague recommendations in terms of the prevention of stone formation after surgical removal of stones. Such treatment mode does not affect the etiopathogenic mechanisms of the underlying disease, which leads to a relapse of urolithiasis.

Alexander Randall formulated the hypothesis that the starting point for the formation of a stone is a plaque on the altered mucosa of the wall of the renal pelvis system in the 40s of the XX century ^[1, 2, 3]. In terms of wide distribution of percutaneous nephrolithotripsy, ureterolithotripsy interest to the hypothesis of Randall has been growing for a while, as these methods allow to directly observe these structures. It is assumed that Randall's "plaques" are the basement for the formation of the stones. This basement is a center of crystallization around which new crystals are formed, which leads to the formation of a stone that eventually detaches from the wall and enters the renal pelvis system of the kidney^[4]. Thus Randall's plaques are a predictor of stone formation. There is still a question about the search for markers of stone formation, allowing non-invasively determine the likelihood of recurrence^[5].

There are many studies dedicated to the problem of kidney stone disease management. Scarpa et al. concluded that patient with benign prostatic hyperplasia (BPH) had more complications (acute prostatitis and pyelonephritis) after ureteroscopy in compare with patients without BPH^[12]. The likewise conclusion was made by Kim^[11]. He proposed to use simultaneous transurethral resection of the prostate and ureteroscopy to decrease the likelihood of complications after surgery.

Bikunin and osteopontin are well known substances that expresses in urinary tract system. Despite these markers were investigated many years ago, there role is still unclear in pathogenesis of kidney stone disease. A lot of studies has shown that bikunin and osteopontin change their concentration in regard of urolithiasis activity^[13]. Here is conducted attempt to evaluate the change of concentration of bikunin and osteopontin during treatment

(hydrochlorothiazide, citrates, increased water intake), and by so far there is no studies related to such problem. One of the latest work performed in 2018 by Icer et al^[14] determined that osteopontin concentration correlates with activity of stone disease.

Objective: to find the most optimal approach to the treatment of patients with urolithiasis and to formulate the need for disease monitoring, which will allow to find out the way of stone disease relapse prevention in the future.

MATERIALS AND EXPERIMENTS

The study is divided into two parts: clinical and experimental. In the clinical part, have been used 3 independent studies, the purpose of which was to improve the results of treatment of patients with a different location of the stones in the renal pelvis and in the ureter with the help of the most effective approaches to treatment. In the experimental part, we tried to answer the question of how to optimize the prevention of urolithiasis recurrence.

In the period from 2012 to 2017, 4014 patients with stones of different localization in the renal pelvis and ureter, as well as with ureteral stones in combination with BPH were treated. There were 2612 men (65%) and 1407 women (35%). All patients underwent a comprehensive laboratory examination, urine culture, ultrasound of the upper and lower urinary tract, if necessary, transrectal ultrasound, CT of the abdomen. Patients with BPH were performed IPSS, PSA and uroflowmetry.

We performed 3175 ureteroscopies for the stones of different localization. Ureteropyeloscopy was performed urgently in patients with renal colic, due to the presence of ureteral stone. A rigid Karl Storz ureteroscope was used for ureteropyeloscopy.

Separately, we studied the results of treatment of 427 patients with ureterolithiasis in combination with BPH, who underwent ureterolithotripsy as well. Patients with ureteral stones in combination with BPH were divided into two groups: 215 patients two weeks before the ureteroscopy were performed stenting of the upper urinary tract, 212 patients were without prior stenting. Patients on admission to the clinic were prescribed uroantiseptics and α -blockers. The location of stones was as follows: 264 patients (62%) had stone in the lower third, 120 patients (29%) - in the middle third, 43 patients

(9%) - in the upper third of the ureter. The calculus was located in the pelvic ureter segment in 3 patients, and in the upper group of kidney pelvis system in 2 patients.

Percutaneous nephrolithotripsy was made in 412 patients. Most of nephrolithotripsies were performed according to the classical method in the case of 401 (97.3 percent). Mininephrolithotripsy was performed in 11 cases (2.7 per cent). Single-stage nephrolithotripsy was performed in 11 cases on both kidneys without complications. Two-stage nephrolithotripsy was done in 7 cases. In several cases (23 patients) nephrolithotripsy was performed from 2-3 approaches due to complex renal pelvis system structure.

Experimental part of the study was dedicated to prevention of future episodes of kidney stone disease. The study involved 82 patients with recurrent calcium oxalate urolithiasis. Patients were also divided into two groups: group 1 (74 patients) did not receive treatment during the follow-up period, group 2 (78 patients) received treatment in the amount of thiazide diuretics [6], water load, citrate [10], calcium preparations (per os). All patients underwent a comprehensive urologic examination, including urine microscopy after centrifugation for determination of crystallization process intensity (lithos-test) and analysis of blood and urine for potential markers of stone formation (bikunin, osteopontin) during the entire observation period (6 months) every two months[7]. The activity of stone formation was measured on a scale from 0 to 3 with the help of lithos-test. Eventually the concentration of stone formation markers compared in the two groups with each other.

RESULTS

The results of the clinical part

Nephrolithotripsy results: the average age of the patients was 56 years. The range of the stone size was from 10 mm to 32 mm, the density did not exceed 967 HU. The oxalic stones were found in 67% of cases, the urate ones were in 12%, and the mixed stones were in 22%. Location of stones: in the pelvis was noted in 55%, in cups and pelvis - in 25% of cases, in the upper third of the ureter - in 10% of cases, staghorn stones - in 10%. No complications were observed during the procedures. Percutaneous nephrolithotripsy in combination with ureterolithotripsy was performed in 12 patients.

In the postoperative period, the urinary tract was drained through the nephrostomy drainage. In case of significant changes in the mucous membrane at the site of the calculus, the internal stent was also placed along with the nephrostomy. In 12 cases, nephrostomy was not implemented. All patients received antiseptic and antibiotic medications on admission to the clinic. Urine culture was also performed. The growth of pathological microflora was noted in 18% of cases (74 patients): *E. coli* - 35%, *Proteus* - 12%, *Enterococcus sp.* (15%), others - 38%. Here is provided list of complications: acute non-obstructive pyelonephritis - 3 patients, migration of calculus fragments - 3 patients, perforation of the pelvis and ureter - 2 patients, 3 patients had bleeding, which required conversion to open surgery. The average duration of the surgery was 122 minutes.

Ureteroscopy results: ureteroscopy was performed in 3175 patients, there were 2095 men and 1080 women, the average age was 56 ± 7.8 years. Location of stones: in the upper third of the ureter - 456 patients, in the middle third of the ureter - 734 patients, in the lower third of the ureter - 1985 patients. There were no periurethritis and complications during ureteroscopy. The procedure was performed under epidural anesthesia. The upper urinary tract was drained for 2-3 days with a ureteral catheter, followed by insertion of ureteral stent, which was removed 14-30 days after surgery. After the removal of the stent, all patients underwent an ultrasound examination to detect the presence of a BPH.

Ureteroscopy results in patients with BPH: The average age of the patients was 65 years, the average volume of the prostate was 58 cc, the PSA level in all patients was within normal values. The IPSS index averaged 14, the quality of life index was 2. The incidence of complications in the first group (urolithiasis without BPH) was 3.2%: acute non-obstructive pyelonephritis - 3 patients, prostatitis - 2 patients, stone migration - 2 patients. In the second group (urolithiasis in combination with BPH), the complication rate was 10.3%: ureteral perforation - 7 patients, stone migration - 6 patients, bleeding - 5 patients, acute pyelonephritis - 2 patients, prostatitis - 2 patients. The duration of the surgery in the second group was longer on average by 25

minutes compared with the same indicator in the first group.

The results of the experimental part

After 6 months of treatment and follow-up, the concentration of bikunin was significantly higher in the 1st group (74 patients) where patients did not receive treatment during the entire observation period compared to the 2nd group (78 patients) who were prescribed therapy: 6.1 ± 0.81 mg / ml vs 3.3 ± 0.86 ng / ml. The concentration of osteopontin was significantly higher in the group of patients receiving treatment - 3.4 ± 0.36 ng / ml vs 2.4 ± 0.39 ng / ml, respectively. Nephrocalcin concentration did not significantly change in both groups: 9.7 ± 2.9 ng / ml vs 12.9 ± 2.5 ng / ml, respectively, for the 1st and 2nd groups. In the 1st group, stone formation activity was significantly higher than in the 2nd group after 6 months of observation (86% of patients of the 1st group had 2-3 stone formation activities, while only 12% of patients from the 2nd group had similar stone formation activity). None of the patients from the 2nd group had a recurrence of urolithiasis disease during the observation period, while 12 people from the other group had an episode of renal colic in the anamnesis.

DISCUSSION

Modern methods of surgical treatment can significantly reduce the time of hospitalization and treatment of patients with ureterolithiasis. The frequency of complications is 2%, most of which are inflammatory in nature and can be easily stopped by antibacterial therapy. Changes of the ureteral wall mucosa require postoperative draining of the upper urinary tract by ureteral stent. In addition, as shown by the experimental part of the study, the administration of adequate therapy in the postoperative period (calcium supplements, thiazide diuretics, water load, citrate mixtures) contributes to the epithelialization of the mucous membrane, as evidenced by the change in the concentration of stone formation inhibitors such as bikunin and osteopontin. Changing of the bikunin concentration can be determined as negative feedback. The smaller the activity of stone formation during the treatment process, which is confirmed by the data of the Lithos-test, the less the expression of bikunin in the transitional cell epithelium becomes. As for osteopontin, an increase in the concentration of

this inhibitor of stone formation is due to the fact that osteopontin is the main component of the calcium-oxalate stone matrix. Accordingly, as the number of crystallization points decreases, the concentration of the free fraction of osteopontin will increase.

Considering the obtained statistically reliable results, pre-stenting of the upper urinary tract before performing ureteroscopy in patients with ureterolithiasis in combination with BPH is a reasonable approach, as it allows to reduce the number of postoperative complications and the time of surgery. The use of nephrolithotripsy and its varieties is the "gold standard" in the treatment of patients with kidney stones, the upper third of the ureter, and staghorn stones. Modern tools can improve the quality of nephrolithiasis treatment, especially complicated with staghorn stones.

The results of the experimental part of the study led to the preliminary conclusion that a high concentration of stone formation inhibitors, as a compensatory reaction to an increase in the activity of urolithiasis disease, is a predictor of rapid stone formation. Measurement of stone formation activity with the help of Lithos-test and markers of stone formation (bikunin and osteopontin) can be used as screening of the urolithiasis disease for the purpose of early prescribing of adequate therapy to avoid the recurrence of the urolithiasis disease in the future.

CONCLUSION

In this study, the results of urolithiasis surgical treatment were analyzed in terms of absence or presence of the BPH. BPH complicates the ureteroscopy by means of increasing time of surgery, making the access to ureter much more difficult due to inadequate visualization. Placement of stent in the upper urinary tract seems to be a solution. Stenting decreases the number of infectious complications and provide additional time to evaluate patient before radical treatment. This study provides the evidence of stenting benefit before ureteroscopy after one-two week pretreatment of the patient with concurrent kidney stone disease and BPH.

Experimental part of study shows that it is not appropriate to leave the patient with kidney stone disease without further recommendations. Such method will lead to relapse of the disease. It is obvious that monitoring of urolithiasis have

to be constant on the outpatient basis, and urologists need markers to monitor the disease as PSA for BPH. Osteopontin and bikunin are the available markers that can be used during monitoring of kidney stone disease activity. The change in the concentration of crystallization inhibitors (bikunin and osteopontin) is a predictor of a fast recurrence of urolithiasis disease, which can be used in patient screening in postoperative period.

Conflict of interest

None.

REFERENCES

1. Saeed R. Khan, Douglas E. Rodriguez, Laurie B. Gower, Manoj Monga. Association of Randall's Plaques with Collagen Fibers and Membrane Vesicles. *Journal of Urology*. V.187, №3, 2012 Mar, pp.1094–1100.
2. Emmanuel Letavernier, Sophie Vandermeersch, Olivier Traxer, Mohamed Tligui, Laurent Baud, Pierre Ronco, Jean-Philippe Haymann, and Michel Daudon. Demographics and Characterization of 10,282 Randall Plaque-Related Kidney Stones. A New Epidemic? *Medicine (Baltimore)*. Vol. 94, №10, 2015 Mar, pp. 566.
3. Khan S.R., Canales B.K. Unified theory on the pathogenesis of Randall's plaques and plugs. *Urolithiasis*. Vol. 43, №1, 2015 Jan, pp.109-123.
4. Lulich J.P., Osborne C.A., Carvalho M., Nakagawa Y. Effects of a urolith prevention diet on urine compositions of glycosaminoglycans, Tamm-Horsfall glycoprotein, and nephrocalcin in cats with calcium oxalate urolithiasis. *Am J Vet Res*. Vol. 73, №3, - 2012 Mar, - pp.447-451.
5. Michel Daudon, Vincent Frochot. Crystalluria. *Clinical Chemistry and Laboratory Medicine (CCLM)*. Vol. 53, №2, November 2015, pp.1479–1487.
6. Arrabal-Martín M., González-Torres S. Treatment with hydrochlorothiazide and alendronate in patients with stones and bone mineral density loss. Evolution of bone metabolism and calciuria with medical treatment. *Arch Esp Urol*. Vol.69, №1, 2016 Jan-Feb, pp. 9-18.
7. Tsuji H., Shimizu N., Nozawa M., Umekawa T., Yoshimura K., De Velasco M.A., Uemura H., Khan S.R. Osteopontin knockdown in the kidneys of hyperoxaluric rats leads to reduction in renal calcium oxalate crystal deposition. *Urolithiasis*. Vol.42, №3, 2014 Jun, pp.195-202.
8. Zharikov A.Y., Motin Y.G., Zverev Y.F., Lampatov V.V., Bryukhanov V.M., Talalaeva O.S. Expression of renal crystallization inhibitors in experimental nephrolithiasis. *Bull Exp Biol Med*. Vol.153, №2, 2012 Jun, pp.279-82.
9. Malihi Z., Wu Z., Stewart A.W. Hypercalcemia, hypercalciuria, and kidney stones in long-term studies of vitamin D supplementation: a systematic review and meta-analysis. *Am J Clin Nutr*. Vol.104, №4, 2016 Oct, pp.1039-1051.
10. Barbera M. The importance of citrates in treatment and prophylaxis of calcium oxalate urinary stones. *Arch Ital Urol Androl*. Vol.88, №4, 2016 Dec, pp.343-344.
11. Kim S.C., Tinmouth W.W., Kuo R.L., Paterson R.F., Lingeman J.E. Simultaneous holmium laser enucleation of prostate and upper-tract endourologic stone procedures // *J Endourol*. 2004 Dec, - Vol.18, №10, - pp. 971-975.
12. Scarpa R.M., De Lisa A., Porru D., Usai E. Large benign prostatic hyperplasia means impossible ureteroscopy: myth or reality? // *Eur Urol*. 2000 Apr, - Vol.37, №4, - pp. 381-385.
13. Igci M., Arslan A, Igci Y.Z., Gogebakan B., Erturhan M.S., Cengiz B., Oztuzcu S., Cakmak E.A., Demiryurek A.T. Bikunin and α 1-microglobulin/bikunin precursor (AMBP) gene mutational screening in patients with kidney stones: a case-control study // *Scand J Urol Nephrol*. 2010 Dec, - Vol. 44, №4, - pp. 13-9. doi: 10.3109/00365599.2010.497768. Epub 2010 Jul 5.
14. Icer M.A., Gezmen-Karadag M., Sozen S. Can urine osteopontin levels, which may be correlated with nutrition intake and body composition, be used as a new biomarker in the diagnosis of nephrolithiasis? *Clin Biochem*. 2018 Sep, - Vol.60, - pp. 38-43. doi: 10.1016/j.clinbiochem.2018.08.001. Epub 2018 Aug 13.

