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Authors Mirko Jovanović*, Vesna Šuljagić†‡, Vladimir Bančević*‡Vojnosanitetski pregled (2018); Online First October, 2018.

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POSTOPERATIVE URINARY TRACT INFECTION AFTER URETEROSCOPIC LITHOTRIPSY IN PATIENTS WITH ASYMPTOMATIC BACTERIURIA

POSTOPERATIVNA URINARNA INFEKCIJA NAKON URETEROSKOPSKE LITOTRIPSIJE KOD PACIJENATA SA ASIMPTOMATSKOM BAKTERIURIJOM

Mirko Jovanović*, Vesna Šuljagić†‡, Vladimir Bančević*‡

Military Medical Academy, *Urology Clinic, †Department of Infection Control, ‡Medical Faculty, University of Defence, Belgrade, Serbia;

Correspondence to: Mirko Jovanović, MD, Military Medical Academy, Urology Clinic, Crnotravska 17, 11 000 Belgrade, Serbia. +381659760825, E-mail: mirkojov70@gmail.com
Abstract

Background/Aim. Postoperative urinary tract infection is one of the most common infective complications of ureteroscopic lithotripsy. Preoperative asymptomatic bacteriuria is not a contraindication for performing ureteroscopic lithotripsy but it can be a significant risk factor for occurrence of severe forms of postoperative urinary infection. Methods. From January 2010 until December 2014 at the Urology Clinic of the Military Medical Academy 389 patients undergoing ureteroscopic lithotripsy were analyzed, and their postoperative infective complications were monitored. From the group, by means of chi-squared test ($X^2$), the incidence of postoperative urinary infection was analysed in 52 patients with preoperative asymptomatic bacteriuria. Results. Infective complications occurred in 18.7% of patients, and postoperative urinary tract infection in 10% of patients. Out of 52 patients with preoperative asymptomatic bacteriuria, 36.5% had postoperative urinary tract infection ($X^2=46.773$) ($p<0.001$). Discussion. The incidence of a postoperative urinary tract infection following ureteroscopic lithotripsy in our study is 10%, and total percentage of all infective complications is 18.7% which correlate with referent studies showing the percentage of infective complications from 1.7 to 18.3%. Different incidence of infective complications between studies is explained by the fact that a standardised system for registering these complications does not exist yet. In our study, of 36.5% patients that preoperatively had asymptomatic bacteriuria, we registered higher frequency of severe forms of postoperative urinary tract infection, SIRS and sepsis. Conclusion. Preoperative asymptomatic bacteriuria represents a significant risk factor for developing postoperative urinary tract infection following ureteroscopic lithotripsy and is associated with increased risk for occurrence of severe forms of SIRS and sepsis. It is desirable that every patient with indicated ureteroscopic lithotripsy has sterile urine culture, and if this is impossible to achieve, a special caution and an adequate antibiotic therapy and prophylaxis are needed in these patients before and during the surgical procedure.

Key words: ureteroscopy; lithotripsy; infection; bacteriuria; urinary stone.

Apstrakt

Introduction

Ureteroscopic lithotripsy (URS) is one of the most common surgical methods for treating kidney and ureter stone (1). The multicentric study of the Endourological society (Clinical Research Office of the Endourological Society – CROES), which was done at 114 hospitals in 32 countries, with 11,885 patients, founded that the percentage of this procedure success (when the patients loses the stone – stone free rate - SFR) is 85.6%, and the percentage of postoperative complications is 3.5% (2).

According to present studies the frequency of infective complications following the ureteroscopic lithotripsy is between 1.7 and 18.8% (3,4,5).

For patients who have stone in the kidney or ureter it is characteristic that they often have asymptomatic bacteriuria with values from 10,000 to 100,000 colonies per millilitre, but without local and general signs of urinary tract infection, and this condition is explained by existence of bacterial biofilm at the surface of the stone or at the previously placed ureteral JJ stent or at the nephrostomy catheter (6,7). Untreated preoperative urinary tract infection presents absolute contraindication for performing ureteroscopic lithotripsy (1), while it can be done in patients with asymptomatic bacteriuria with the application of a short term preoperative antibiotic therapy recommended in order to mitigate risks for developing possible infective complications (8).

Methods

The research was done at the Urology Clinic of the Military Medical Academy through retrospective analyses of medical records of 389 patients, male and female, who had pneumatic and laser ureteroscopic lithotripsy from January 2010 until December 2014 in ureter or kidney, by a semirigid and/or a flexible ureteroscope. During preparations for ureteroscopic lithotripsy the detailed anamnesis was taken from all the patients, physical examination, laboratory tests – sedimentation, complete blood screen analyses, biochemical analyses, microscope exam of urine sediment and urine culture were done.
In patients who developed infective complications, their gradation was done according to Modified Clavien Classification system-MCCS. According to MCCS all infective complications following ureteroscopic lithotripsy in this study were divided to 4 degrees or gradus: Gradus I – temporary febrile condition not requiring additional treatment besides applying antipyretics, Gradus II – postoperative urinary tract infection, non-obstructive pyelonephritis, SIRS or sepsis requiring applying additional antibiotics, and with sepsis requiring also inotropic drugs, Gradus III – obstructive sepsis requiring applying additional endoscopic procedures and multi pharmacological treatment and Gradus IV – severe sepsis (IVа) and septic shock (IVб) requiring staying and treating patients in the intensive care unit (9).

The criteria of the International conference for sepsis and organs collapsing and Guidelines for using inovative therapies in sepsis of the American College of Chest Physicians and Society of Critical Care, established in 1992, where sepsis is defined as presence and verification of infection source and SIRS, were used in this study. The existence of two or more criteria is characteristic for SIRS: body temperature > 38 or < 36ºС; heart rhythm > 90/min; respiration rate number > 12/min or partial pressure СО2 < 32 mmHg; leukocytosis > 12000 or < 4000/mm3. Organ dysfunction is characteristic for severe sepsis and acute circulatory collapse with persistent arterial hypotension is characteristic for septic shock (10,11).

All data in the study were processed in SPSS 20.0 (IBM corporation) software package. The chosen level of importance, i.e. possibility of the first type mistake is 0.05. The examinees were classified in two groups. In the first group the patients with preoperative asymptomatic bacteriuria that were subjected to pneumatic or laser ureteroscopic lithotripsy and did not have postoperative urinary infection would be analysed. In the second group the patients with preoperative asymptomatic bacteriuria that were subjected to pneumatic or laser ureteroscopic lithotripsy and had postoperative urinary infection would be analysed.

**Results**

The study comprised 389 patients, 200 (51.4%) male and 189 (48.6%) female, with unilateral ureteral or kidney calculosis, that had one or more stones in clearly defined levels of upper urinary tract in which the stone was located (kidney, upper ureter, middle ureter and lower ureter), that were subjected to ureteroscopic lithotripsy by a semirigid and/or a flexible instrument. The patients without preoperative urinary tract infection were analysed.

Average age of the patients in this study was 55. The youngest patient was 13 and the oldest 92. Average Body Mass Index (BMI) was 26 (minimum 14 and maximum 37). Average size of the stone was 13 mm, and in 94 (24.2%) patients lithotripsy was performed in the kidney and in 295 (75.8%) patients in the ureter. Laser lithotripsy was performed in 237 (60.9%) patients, and breaking by a pneumatic probe in 152 (39.0%) patients. Average duration of surgery was 40 minutes, the shortest one lasted 5 minutes, the longest one 185 minutes. A semirigid ureteroscope was used in 357 (91.7%) patients, a flexible one in 28 (7.2%), and in 4 (1.1%) patients the both types of ureteroscope were used.

Infective complications in this study developed in 73 (18.7%) patients, and postoperative urinary tract infection in 39 (10%) patients. Temporary febrile condition not requiring additional treatment besides applying antipyretics occurred in 34 (8.7%) patients.
Postoperative urinary tract infection, according to definitions of the Section of Infection in Urology of the European Association of Urology (11) and International conference for sepsis and organ collapsing and Guidelines for using inovative therapies in sepsis of the American Chest Physicians and Society of Critical Care (10), had 39 (10%) patients. In these patients the treatment implied using antipyretics, additional antibiotic therapy, additional infusion inotropic and supportive therapy, and in 2 (0.4%) patients additional procedures were performed - placing JJ stent and percutaneous nephrostomy catheter. In Table 1 the incidence of infective complications and postoperative urinary infections and the treatment method are shown.

Out of total number of patients, 52 (13.4%) were with preoperative asymptomatic bacteriuria, while 337 (86.6%) patients had sterile urine culture. In the group of patients without postoperative urinary infection, in 33 (63.5%) of them asymptomatic bacteriuria was verified before the surgery, and in the group of patients with postoperative urinary infection 19 (36.5%) of them had asymptomatic bacteriuria before the surgery. These data were analysed by chi-squared test which confirmed that there was a statistically highly significant difference between the groups (X^2=46.773; p<0.001).

In 19 patients with postoperative urinary infection, the most common bacteria present in the preoperative urine culture was *Escherichia coli* (52.6%), the second one most common was *Pseudomonas aeruginosa* (21.0%), then mixed bacterial flora with *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Enterococcus faecalis* (10.5%), *Pseudomonas aeruginosa* and *Enterococcus faecalis* (5.3%), *Proteus mirabilis* (5.3%) and *Enterococcus faecalis* (5.3%). In the postoperative urine culture results of these patients the following bacteria were isolated: *Escherichia coli* (43.7%), *Klebsiella species* (17.8%), *Pseudomonas aeruginosa* (15.0%), *Enterococcus faecalis* (13.2%) and *Proteus mirabilis* (10.3%).

Out of 7 patients with sepsis in this study, 5 (1.4%) patients were treated at the urology department. Out of these 5 patients treated at the urology department, 3 (0.9%) patients were receiving antibiotic therapy, infusion solution and drugs for regulating circulatory collapse and cardiorespiratory dysfunction, but it was not necessary to keep them in the intensive care unit. In all three patients the *Staphylococcus coag.* (−) bacteria was isolated in the hemoculture. In the rest 2 (0.5%) patients treated at the urology department, postoperative obstructive pyelonephritis and sepsis were verified and it was necessary to place a JJ stent in one case and a percutaneous nephrostomy catheter in another case besides applying antibiotics therapy.

In 2 (0.4%) patients (out of 7 patients with sepsis) the treatment required monitoring and their staying in the intensive care unit. These two patients were treated in the intensive care unit because of circulatory collapse and cardiorespiratory dysfunction, under diagnosis of severe sepsis and septic shock, with intubation and putting on respiratory device and applying several antibiotics, inotropic drugs and colloid infusion and nutritive solutions simultaneously. In both patients the *Escherichia coli* was isolated from the hemoculture, and the same bacteria was found in the preoperative asymptomatic bacteriuria results.

**Discussion**

The impact of preoperative asymptomatic bacteriuria on development of urinary tract infection in patients following ureteroscopic lithotripsy was being analyzed in this study. Infective complications following ureteroscopic lithotripsy are the most common complications occurring after these procedures (2), which is why it is important to identify
patients with a risk for developing infective complications following the procedure. Reasons for secondary postoperative urinary tract infection may also be dissemination of bacteria from the lower to the upper urinary tract in the course of procedure, also performing procedure on an infectious stone and using irrigation solution under high pressure which generates bacteremia (9). Preoperative antibiotic therapy mitigates the risk of postoperative urinary infection (8).

Infective complications following ureteroscopic lithotripsy comprises: temporary febrile condition not requiring applying additional antibiotic therapy, postoperative urinary tract infection, SIRS and sepsis (8,12,13). Temporary febrile condition requires applying only antipyretics and usually passes spontaneously in 24-48 hours, but postoperative urinary tract infections which comprise also severe forms of postoperative urinary infection – SIRS and sepsis, are complications extending time of the patient’s hospitalizing, requiring expensive antibiotics therapy, requiring even additional procedure sometimes, significantly rising the price of treatment, and in the case of organ dysfunction are life threatening complications (5,14). Even with abiding basic principles in the preoperative preparation of a patient and applying antibiotics prophylaxis in line with recommendations of the Guidelines on Urological Infections – EAU Guidelines, patients frequently get unpredictable severe forms of postoperative urinary tract infections.

The incidence of postoperative urinary infection following ureteroscopic lithotripsy in the study is 10%, and the frequency of all infective complications, taking into account also temporary febrile condition is 18.7%. This incidence in our study is in line with the Japanese authors’ (Mitsuzuka et al.) that analyzed factors associated with occurrence of postoperative febrile urinary tract infection following ureteroscopic stone breaking in 153 patients. In their study the incidence of all infective complications is 18.3%, and the incidence of postoperative infective complications requiring additional antibiotics and supportive therapy or endoscopic procedures is 7.8% (12). However, other authors reported lower incidence of infective complications following ureteroscopic procedures. A group of authors from Korea (Sohn et al.) analyzed 531 patients that were subjected to ureteroscopic procedures from 2002 to 2010, including also ureteroscopic lithotripsy (13). In this study the incidence of infective complications is 3.8%. Higher frequency of infective complications in our study can be explained by differences between the groups of patients analyzed and also by different definitions of infective complications and of postoperative urinary infection between the studies. In our study we analyzed only patients that were subjected to ureteroscopic lithotripsy, and the Sohn study comprised also 154 (29.0%) patients that were subjected to diagnostic ureteroscopy. In the study of authors from Korea the infective complications comprised only complications requiring additional antibiotics or other treatment (Gradus ≥ II complications according to MCCS), in comparison with our study, the infective complications Gradus ≥ II are defined as postoperative urinary infections and their frequency in our study is 10%. Also, the difference in frequency of infective complications between these two studies may be due to using different types of ureteroscopes, considering the Sohn analyzed using only semirigid ureteroscope (15). The size of a stone could also have impact on developing postoperative infection, because the average stone size in our study in patients with postoperative urinary infections was 15 mm, which was more than in the studies dealing with complications following ureteroscopy and endourological procedures (5,16).

An absolute contraindication for performing ureteroscopic lithotripsy was untreated urinary tract infection. Preoperative asymptomatic bacteriuria with positive values of
bacteria in urine culture, from 10,000 to 100,000 colonies per ml, but with no local, general and clinic signs of urinary infection, was not an excluding factor because in a number of patients sterile urine culture could not be achieved, which is explained by increasing bacterial colonies at the stone surface or at the ureteral JJ stent and on the nephrostomic catheter which the patients had to wear before the surgery (6,7). 52 (13.4%) patients in our study had preoperative asymptomatic bacteriuria and in these patients an antibiotic therapy was applied 1-12 days preoperatively under the antibiogram results and most frequently a third generation cephalosporin (Ceftriaxon) was used - in 17 (32.7%) patients. In these patients the most frequently isolated bacteria in the preoperative values of urine culture was *Escherichia coli* (40.4%). Among 52 patients with preoperative asymptomatic bacteriuria, a postoperative urinary tract infection had 19 (36.5%) of them. In these patients that postoperatively had urinary infection, the most commonly preoperatively used antibiotics were aminoglycosides (*Amikacin, Gentamycin*), i.e. they were applied in 6 (31.6%) patients, and the most frequently isolated bacteria in the preoperative values of urine culture was also *Escherichia coli* (52.6%). In our study we found statistically significant difference between a group without and a group with postoperative urinary infection following ureteroscopic lithotripsy in comparison to patients that had asymptomatic bacteriuria and patients with sterile urine culture (p<0.001). Moses in its study examined 16.5% patients that had preoperatively positive urine culture and received antibiotic therapy 3-7 days preoperatively (8). Preoperative bacteriuria was examined in other authors’ studies as a risk factor following ureteroscopic lithotripsy. Uchida proved through multivariate analysis that positive preoperative findings of urine culture in patients that were subjected to ureteroscopic laser lithotripsy was associated with higher risk of postoperative SIRS (17). In this study 12.4% patients that were subjected to ureteroscopic laser lithotripsy had positive preoperative findings of urine culture, but with no signs of urinary tract infection. In these patients an adequate antibiotic therapy was applied in duration prescribed by an urologist, but the study did not bring forward the therapy duration. It was proved in the study through a multivariate logistic regression analyses that positive preoperative urine culture was a significant risk factor for occurrence of SIRS following laser ureteroscopic lithotripsy (p=0.005). The patients with preoperative asymptomatic bacteriuria subjected to ureteroscopic lithotripsy were analyzed by Sohn also (13). He examined 20.9% patients with preoperative bacteriuria, and 10.8% of these patients had infective complications (p=0.000). Matsumoto in his study also concluded the preoperative bacteriuria was a statistically significant risk factor for occurrence of infective complications following urologic procedures in the upper urinary tract (18). Blackmur in his analyses of risk factors for developing sepsis following ureteroscopic lithotripsy, which was done with 462 patients, published that 34 (7.4%) patients had sepsis and that positive preoperative findings of urine culture were associated with occurrence of postoperative urosepsis, although an adequate antibiotic preoperative therapy was applied (p<0.001) (15). All these studies showed results in line with our analyses. The work proving the opposite was not found in the existing literature.

Out of 19 patients that preoperatively had asymptomatic bacteriuria and developed infective complications following ureteroscopic lithotripsy, 7 (1.8%) patients were treated for severe postoperative urinary infections with signs of sepsis. All these patients preoperatively received an adequate antibiotic prophylaxis. Sepsis following ureteroscopic lithotripsy is one of the most severe complications. In other studies that analyzed risk factor for developing postoperative urinary infection, the frequency of sepsis was also between 1-
3%. Mitsuzuka in his study reported 1.3% patients with sepsis developed after ureteroscopic lithotripsy (12). In the existing literature only few studies analyzed the frequency of sepsis following ureteroscopic lithotripsy. Geavlete brought forward the data of 1.13% out of 2735 patients with sepsis occurred following ureteroscopic lithotripsy made by a semirigid ureteroscope (19). Eswara analyzed 328 patients that were subjected to endourological procedures, out of which 11 (3.0%) had sepsis (20). However, Blackmur in his analysis of risk factors for developing sepsis after ureteroscopic lithotripsy, in which he examined 462 patients, published data on 34 (7.4%) patients with sepsis (15). This somewhat larger number of patients with sepsis developed following ureteroscopic lithotripsy in the study was explained by the fact the study comprised patients with both sides ureteroscopic lithotripsy also and a great number of patients with cardiovascular illnesses and diabetes associated, high ASA score and larger stones.

Out of these 19 patients in our study that had asymptomatic bacteriuria preoperative and developed postoperative infective complications, the rest 12 (3.1%) patients had postoperative urinary infection and SIRS. Their treatment required applying additional antibiotic therapy according to findings of urine culture, but not infusion and supportive therapy, nor additional endoscopic procedures.

From the above mentioned results it can be observed the patients with asymptomatic bacteriuria preoperative had also higher frequency of severe forms of postoperative urinary infection.

Use of standardized system for infective complications classification (MCCS) enabled easier and more precised comparison with the referent studies. This study should provide initial retrospective analysis of infective complications following ureteroscopic lithotripsy and should in time develop into a prospective multi-centric study that besides preoperative asymptomatic bacteriuria analyzes also some other risk factors and discovers a way to prevent severe infective complications following ureteroscopic lithotripsy.

**Conclusion**

In our study, out of all patients with preoperative asymptomatic bacteriuria, 36.5% patients had postoperative urinary infection which presents a statistically significant number. It was found a statistically significant difference between a group without and a group with postoperative urinary infection developed following ureteroscopic lithotripsy compared to patients that had asymptomatic bacteruria and patients that had sterile findings of urine culture (p<0.001). This result proves that asymptomatic preoperative bacteriuria is a significant risk factor for developing postoperative urinary infection following ureteroscopic lithotripsy and is associated with higher risk for developing severe forms of SIRS and sepsis. This great risk must be taken into account in an observant preoperative preparation of patients for ureteroscopic lithotripsy. It is desirable that all patients indicated with ureteroscopic lithotripsy have sterile urine culture, but if this is impossible to achieve, a special caution and an adequate antibiotic therapy and profilaxa are necessary in these patients before and in the course of operative procedure. Immediate postoperative monitoring is also very important in order to timely prevent severe infective complications.
REFERENCES:


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<tr>
<th>Complication</th>
<th>Patients n (%)</th>
<th>Treatment</th>
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<td>Gradus I</td>
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<tr>
<td>Temporary febrile condition</td>
<td>34 (8,7%)</td>
<td>Antipyretics</td>
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<td>Gradus II</td>
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<tr>
<td>SIRS</td>
<td>32 (8,3%)</td>
<td>Antibiotic therapy</td>
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<td>Sepsis</td>
<td>3 (0,9%)</td>
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<td>Parenteral infusion solution</td>
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<td>Inotropic drugs</td>
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<td>Gradus III</td>
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<td>Obstructive sepsis - pyelonephritis</td>
<td>2 (0,4%)</td>
<td>Endoscopic intervention</td>
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<td>Placement of JJ stent or percutaneous catheter</td>
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<td>Gradus IVa</td>
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<td>Severe sepsis</td>
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<td>Gradus IVb</td>
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<tr>
<td>Septic shock</td>
<td>1 (0,2%)</td>
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\( n \) – number of patients;

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