Feasibility of Percutaneous Nephrolithotomy in Positive Urine Culture: A Single Center Retrospective Study

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Purpose: To determine the efficacy and safety of PCNL in patients with positive urine culture without an any other risk factors prior to surgery, and to define an optimal pre-operative antibiotic regimen for these patients.

Materials and methods: The study included 269 consecutive PCNL cases. These cases were divided into 2 groups according pre-operative urine culture results: sterile (group 1, n=166) and positive (group 2, n=103). Patients with risk factors linked to infection complications were excluded from study. All patients underwent PCNL in the prone position. In group 1, the antibiotic regimen included parenteral injection 30 minutes prior to operation and for 3 days after surgery. Group 2 was given antibiotics 24 hours before PCNL as well as 30 minutes before PCNL and then for 3 days following surgery. On the first day after the operation low dose CT and common blood count were performed on all patients to determine residuals, hematomas, blood loss, and inflammatory markers.

Results: Mean age, stone size, failed ESWL, and prior nephrostomy tube insertion were higher in group 2. Although rate of pre-stented patients was equal in groups. No significant differences were observed between group 1 and 2 in regard to operative time (74,3 ± 26,9 vs 70,2 ± 26,5 min, P = .52), length of stay (3,9 ± 1,2 vs 3,8 ± 1,6 days, P = .24), SIRS (6,0% vs 7,8% patients, P = .07), and leukocyte levels exceeding 10*10*9 (77 (46,4%) vs 49 (47,6%) P =.11). Moreover, there was no sepsis or hemotransfusion in either group. Stone-free rates were also similar (78,9% vs 77,7%, P = .35).

Conclusion: 24-hours continuous antibiotic administration before the operation (paying respect to specific resistance bacterial features) can be considered as alternative to 1-week treatment and allow to perform PCNL with sufficient safety in selected patients. Infected urine is not an independent risk factor of post-operative infections complications after PCNL in low risk patients with kidney stones.

Keywords: lithotripsy; nephrolithiasis; nephrostomy; PCNL; SIRS; stent; urine culture

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the most efficient treatment for large staghorn calculi[1,2]. Furthermore, PCNL has spread widely in the past decade in developing countries because of its cost-efficacy compare to flexible ureteroscopy[3].

According to recent data, post-PCNL inflammatory complications occur between 10,8 and 43% of patients, with sepsis occurring in 0,3%-9,3% of patients postoperatively[4,5]. In an effort to avoid these complications, current AUA and EAU guidelines do not recommend the surgical management of kidney stones when the patient has a positive urine culture[4,6,7]. Upper urinary tract drainage (JJ-stent or nephrostomy tube) and antibacterial therapy are recommended in such cases with subsequent PCNL[4,6,7]. There is little guidance, however, in regard to the proper duration of antibacterial treatment. Recent publications have indicated a 7-day preoperative treatment with ciprofloxacin or nitrofurantoin is sufficient, but more data needs to be obtained[8,9].

Furthermore, obtaining a sterile urine culture is not always possible prior to PCNL. In fact, several circumstances indicate PCNL could be performed in patients with positive urine cultures[2,10]. Reasons for this approach may be: patients living in rural, outlying areas with an insufficient level of medical care, a previously unsuccessful antibacterial treatment, or an intolerance of JJ-stents or nephrostomy tubes. We have not found special guidelines to assist in treating these kinds of patients. Thus, in this study we sought to determine the efficacy and safety of PCNL in patients with positive urine culture without a signs of significant urinary tract infection (UTI) prior to surgery, and to define an optimal pre-operative antibiotic regimen for these patients.

MATERIALS AND METHODS

Study population

Two hundred and fifty-four patients were enrolled in this study. Data from 428 consecutive PCNLs performed on these 388 patients was retrospectively reviewed from a prospectively maintained electronic hospital database. The study was approved by the medical ethics committee of Saint-Petersburg State University. Patients underwent PCNL at Department of Urology of Saint-Petersburg University clinic between March 2013 and April 2018. 159 cases performed to 134 patients

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Table 1. Basic Characteristics of PCNL Patients.

	Parameter	Group 1 (n=166)	Group 2 (n=103)	*P*-value
1	Age, years	49.5 ± 12.7	55.3±14.1	.63
	Male/female	91/76	42/61	< 0.01
2	Right/left	71/96	53/50	.03
3	Stone size in lager dimension, mm	17.0 ± 7.1	21.3 ± 13.4	.02
4	Stone density, HU	1191.2 ± 385.2	1130.9 ± 443.5	.07
7	Previously inserted stent	41 (24.7%)	26 (25.2%)	.06
8	Previously inserted nephrostomy	6 (3.6%)	26 (25.2%)	< 0.01
10	Failed ESWL	33 (19.9%)	30 (29.1%)	< 0.01

with defined risk factors, that can lead to inflammatory complications, such as staghorn stones, hydronephrosis, upper urinary tract abnormalities, kidney insufficiency, a solitary kidney, any kind of immunodeficiency, diabetes mellitus, morbid obesity and after any kind of urinary diversion were excluded from study. The rest of 269 PCNLs performed on 254 patients that considered to be low-risk patients were divided into two groups: group 1 (n=166, 61,7%) with sterile urine, and group 2 (n=103, 38,3%) with positive urine culture. All of these patients were non-obstructive and without significant UTI or fever. The stones and associated renal anatomy were evaluated with contrast computer tomography images. In subjects with bilateral PCNL procedures, each kidney was considered separately with respect to residual fragments, re-interventions, and complications. Standard preoperative investigation (laboratory tests, ECG, etc.) were normal in all patients. Specimens for bacteriologic evaluation were derived from midstream urine samples or from a nephrostomy tube. Urine culture performed within a month before the operation in each particular patient. Informed consent was obtained from all individual participants included in the study. Major indications for nephrostomy tube and stent insertions were renal colic and/or UTI manifestation caused by obstructive calculi. Stone size (larger dimension), density and a detailed history including past renal surgery (especially failed ESWL), nephrostomy/stent insertion and duration, and UTI were obtained for all patients (**Table 1**).

Surgical technique

All PCNL were performed by three expert surgeons. After induction of general endotracheal anesthesia, an 6F ureteral catheter or stent was placed using a cystoscope in the lithotomy position. The patient was then turned prone. Percutaneous access was performed by surgeon using an 18-gauge needle under ultrasound and fluoroscopic guidance. Following successful puncture, an ultra stiff hydrophilic guidewire was inserted to the collecting system and the tract was dilated using an Amplatz dilator until a 20- or 30-Fr Amplatz sheath could be placed. Nephroscopy was conducted under low pressure and stones were disintegrated using ultrasound, pneumatic, or laser lithotripsy. The stone fragments were removed with forceps. In some cases, when residual fragments were suspected, we performed a final inspection of the kidney with a fiber-optic flexible cystoscope. A 12-Fr nephrostomy tube was placed at the end of each procedure.

Antibacterial prophylaxis for patients with sterile urine consisted of a single-dose intravenous broad-spectrum antibiotic (cephalosporinum 3rd generation, or fluoroquinolone) when the patient was anesthetized prior to the procedure, and was continued for 3 days postoperatively. For patients with positive urine cultures, antibiotics based on the sensitivity profile of the bacteria were continuously provided for one day before the surgery, at the time of anesthesia induction, and continued for 3 days postoperatively. All antibiotics were given continuously in a standard dosage considering patient's age and renal function according to local treatment protocols.

Outcome assessment

Our primary outcomes were SIRS rate, leucocytes level on common blood count and length of stay. Secondary outcomes included stone-free rate, operative time, post-operative haematoma, and average hemoglobin drop level (difference between pre- and postoperative level on 1 day).

A complete blood count and low-dose CT were performed in all the patients on post-operative day one. Patients were considered stone free if residual stones were $\leq$ 4 mm.

Statistical analysis was performed using an independent sample t-test, and a chi-square test. Statistical significance was set at a p-value of <0,05. We performed all statistical analyses using the SPSS statistical software package (Version 15.0 for Windows, SPSS, Inc).

Table 2. Intra- and postoperative parameters, complications and results of treatment.

	Parameter	Group 1 (n=166)	Group 2 (n=103)	*p*-value
1	Operative time, min	74.3 ± 26.9	70.2 ± 26.5	.52
2	Access size			
	20 Ch	48 (28.9%)	31 (30.1%)	.62
	30Ch	118 (71.1%)	72 (69.9%)	.47
4	SIRS on 1-2 postoperative day	10 (6.0%)	9 (8.7%)	.07
5	Average hemoglobin drop level (difference between pre- and postoperative level on 1 day), g/L.	11.2 ± 5.3	12.8 ± 6.7	.17
6	Leukocytes level in CBC exceeding 10*109 on 1 post-operation day	77 (46.4%)	49 (47.6%)	.41
7	Postoperative hematoma (≥100 ml)	4 (2.4%)	2 (1.9%)	.09
8	Length of stay (days)	3.9 ± 1.2	3.8 ± 1.6	.67
9	Stone-free rate (no or less than 4 mm residuals)	131 (78.9%)	80 (77.7%)	.35

Table 3. Postoperative complications in groups according to modified Clavien Score.

	Group 1 (n=166)	Group 2 (n=103)	*P* value
None	142 (85.5%)	83 (80.6%)	.83
Grade I	14 (8.4%)	12 (11.7%)	.09
Grade II	9 (5.4%)	7 (6.7%)	.86
Grade IIIA	2 (0.7%)	1 (1.0%)	.96

RESULTS

Mean patient age, stone size, stone density, previously inserted stent, nephrostomy and stent duration time, and failed ESWL rates were similar in groups, although left-side disease and male gender was more common in group 1.

Furthermore, group 2 had a higher prevalence of patients with previously established nephrostomy tracts when compared to group 1 (25,2% vs 3,6%, respectively; $P < .01$). The Enterobacteriaceae and Enterococci bacteria accounted for about half of all detected pathogens in group 2. Klebsiella and Proteus accounted for 10% each. The rest of the results were presented by Pseudomonas, staphylococci and streptococci. Mixed flora was observed in 5 (5%) patients of the second group. Multi-resistant bacteria were noticed in 13 (12,6%) patients. Reserve antibiotic such as carbapenems, vancomycin etc. were used for treatment according sensitivity range. No patients with super-resistant bacteria were observed in our study. We found no significant difference in the operative time, the sizes of accesses and the length of hospital stay between the two groups. Intra- and post-operative bleeding did not require any interventions, and no hemotransfusion was needed in either group. Comparative intra- and postoperative results shown in **Table 2**.

There was also no statistical difference for infection-related complications between the two groups. Clinical and laboratory data correlated with these data: systemic inflammatory response syndrome (SIRS) rates and leukocyte level on postoperative day one were similar in both groups. Of note: patients with fever were included in SIRS group as fever is element of this syndrome. There was no sepsis (as a life-threatening complication, required intensive care) following any PCNL in either group, and stone-free rates were similar between groups. Postoperative complications according to modified Clavien score are shown in **Table 3**. No grade IIIB-V complications were noticed.

Two patients from group 1 and one patient from group 2 required second-look flexible nephroscopy under local anesthesia for 5-8 mm residual stones. No severe complications Grade IIIB-V were noted in both groups.

DISCUSSION

There is overwhelming clinical experience and expert consensus that a preoperative urine culture should be obtained and confirmed to be sterile prior to PCNL; therefore in patients with positive urine culture, antibiotic treatment prior to PCNL is recommended[7]. According to several studies, a positive preoperative urine culture has been associated with increased infectious risk[2,10,11]. According to EAU and AUA guidelines, obtaining a negative urine culture is one of the requirements for PCNL alongside the insertion of any type of drainage tube in the case of obstruction followed by subsequent antimicrobial therapy and a secondary PCNL session at a later date even if there were no clinical signs of active infection[4,6]. In non-complicated patients in the absence of obvious infection there is a variety of options as there is no defined standard for preoperative antibiotic regimen[12,13,14].

From the other hand, several author[s][15,16] suggested that performing surgery even in presence of hydronephrosis and cloudy urine can, in fact, be safe. Concerning the staged procedure, Sharma et al[17] noticed a higher risk of infection complications in patients with previously inserted nephrostomy tubes: the cause of such complications possibly being a bacterial biofilm on the surface of the tube. We have similar results in our study: there were more patients with nephrostomy in positive urine culture group comparing with sterile urine group – 35 (20,1%) vs 16 (6,3%) respectively. However, in our study previously placed ureteral stents were not found to increase the bacterial stone burden, concluding this option seems to be safer if staged treatment is needed.

Many studies dedicated to duration of antimicrobial prophylaxis in patients with sterile urine[18,19,20], but there are no guidelines how to reach this condition preoperatively. Two studies evaluated the role of 1-week preoperatively-administered antibiotics for the prevention of sepsis/SIRS. It was reported that 1 week of ciprofloxacin prophylaxis before PCNL significantly reduced the risk for urosepsis[8]. The second study investigated the impact of prophylaxis with nitrofurantoin for a week before PCNL and found a significantly lower rate of endotoxemia (17.5 vs 41.9%) and SIRS (19 vs 49%) in the nitrofurantoin group(9). These studies indicate that a 7-day pre-PCNL course of antibiotics may play an important role in the prevention of infective complications in patients at a higher risk for the development of urosepsis and included patients with very large renal calculi and/or hydronephrosis with a higher risk for urosepsis. Keeping in mind growing bacterial resistance and toxic effect of ciprofloxacin and overuse of other antibiotics, more opportune approaches are needed[21]. Our study promotes alternative tactic to long-term antibiotic course.

Some studies indicated that the majority of the stones, including non-infected stones such as oxalate stones, contain bacteria and bacterial toxins that are mediators of SIRS and sepsis[22,23]. Despite careful pre-operative preparation, serious systemic infection can be difficult to predict. The source of the infection is almost always the stone itself, but this is impossible to predict pre-operatively with certainty, although in many cases there will be a high index of suspicion[24]. The main reasons for the development of UTI after PCNL include the release of bacteria from the surgical manipulation, fragmentation of calculi, and the introduction of bacteria through the nephrostomy tract, which traverses through

skin, retroperitoneum, and renal tissues[24]. After stone disruption during ESWL, the square of the stone is increased, possibly leading to the escape of bacteria and endotoxins from the inside of the stone. Probably this could cause a previously negative urine culture to become positive[25]. Indeed, we noticed such a trend in our study: there was a higher prevalence of post-ESWL patients in group 2 compared to group 1 – 51 (29,3%) vs 40 (15,7%) respectively.

In majority of the patients of both group ultrasonic lithotripsy used for stone fragmentation, as we believe that suction effect of the probe during the procedure can eliminate some portion of planktonic bacteria. Although Radfar et al[26] reported no significal difference of success rates and complications between ultrasonic or pneumatic lithotripsy.

Some authors consider the contrast and density of the stone as an additional predictor of SFR and possible complications after PCNL[27]. Of course, this method of evaluation can also be used to assess the likely infectious nature of the stone, which may lead to changes in the therapy both in patients with sterile or infected urine culture.

Several studies investigated the significance of leukocytosis, SIRS and readmission rate following PCNL and any association with postoperative infection[28,29]. Nearly half of the patients in both studies had a leukocytosis and met the criteria for SIRS. In contrast to our study, there was no association between leukocytosis and urine culture.

Of note, negative bladder urine culture does not exclude the presence of bacteria in stones or in urine within the renal pelvis: it was found that in patients with negative bladder cultures, about one-third had infected pelvic urine and half had positive stone cultures(30). Obviously proper source of infection cannot be directly established at preoperative examination both in patients with sterile and infected urine.

CONCLUSIONS

24-hours continuous antibiotic administration before the operation (paying respect to specific resistance bacterial features) can be considered as alternative to 1-week treatment and allow to perform PCNL with sufficient safety in selected patients (without risk factors, that can lead to inflammatory complications, such as staghorn stones, hydronephrosis, upper urinary tract abnormalities, kidney insufficiency, a solitary kidney, any kind of immunodeficiency, diabetes mellitus, morbid obesity and after any kind of urinary diversion). Infected urine is not an independent risk factor of post-operative infections complications after PCNL in low risk patients with kidney stones.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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