

# Ciprofloxacin infusion versus third generation cephalosporin as a surgical prophylaxis for percutaneous nephrolithotomy: a randomized study

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**Introduction** Percutaneous nephrolithotomy (PCNL) is considered a clean-contaminated surgical procedure. The American Urological Association has recommended different preoperative antimicrobial prophylaxis for various urological procedures to prevent surgical site infections, postoperative fever, and possible sepsis. The European Association of Urology (EAU) antibiotic guidelines endorse giving either a second or third-generation cephalosporin, trimethoprim-sulfamethoxazole, fluoroquinolone or aminopenicillin with a  $\beta$ -lactamase inhibitor. The aim of the present study is to prospectively compare two different protocols of antibiotic prophylaxis in PCNL.

**Material and methods** Successfully consented patients with sterile urine preoperatively who were awaiting percutaneous nephrolithotomy were randomized into two groups. The first group (n = 41) was given a single dose of 200 mg ciprofloxacin infusion, while group two (n = 43) was given 2 mg of cefotaxime divided into 2 doses; during induction of anesthesia and 12 hours later. The occurrence of perioperative infection-related events would be compared in both groups.

**Results** Both groups had similar age, sex, Body Mass Index, and stone composition. No statistical difference was found regarding stone size, stone culture, irrigation fluid volume, operative time and urine pelvis culture result in both groups (Table 2). Two patients (5%) developed postoperative fever in the 1<sup>st</sup> group compared to 12 patients (28%) in the second group (p = 0.02).

**Conclusions** A prophylactic regimen consisting of a single dose ciprofloxacin infusion during induction of surgery showed a higher efficacy as a preoperative antibacterial preparation, compared to cefotaxime, in protection against postoperative fever in patients undergoing PCNL.

**Key Words:** Body Mass Index  $\leftrightarrow$  extracorporeal shock wave lithotripsy  $\leftrightarrow$  non-contrast computed tomography  $\leftrightarrow$  percutaneous nephrolithotomy  $\leftrightarrow$  urinary tract infection

## INTRODUCTION

Kidney stone management has been achieved through different minimally invasive modalities [1]. The invention of extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy (PCNL) and retrograde renal surgery have achieved lower morbidity and maximal nephron preservation compared to open renal surgeries [2]. PCNL has provided a satisfactory solution for renal calculi larger than 2 cm,

however, bleeding and infection [3] sequelae are the most serious complications.

Infectious complications are the most common with an overall incidence of fever of 10.5%, but only 0.3–2.5% of patients develop septic shock [4]. As a clean-contaminated surgery, the American Urological Association (AUA) has recommended a single dose of antibiotic prophylaxis for patients subjected to PCNL, to reduce infectious complications [5].

There is a significant variation in the type, dose, duration, and timing of such prophylaxis which is often based on physician preference, patient's comorbidities and geographic location [6]. Our aim was to detect the difference between a single dose of 200 mg ciprofloxacin infusion iv versus 2 mg of cefotaxime 2 mg divided into 2 doses, as a preoperative surgical prophylaxis before PCNL.

## MATERIAL AND METHODS

After institutional review board approval, successfully consented PCNL patients were included in a randomized controlled study. We excluded patients that were younger than 18 years old and immunocompromised. A detailed preoperative evaluation and routine laboratory investigations were conducted. Patients with a negative pre-operative urine culture or a culture-specific treatment of infection, with no antibiotics in the last week before surgery, were included. The radiographic evaluation consisted mainly of non-contrast computed tomography (NCCT). Patients were randomized into two groups based on a computer-generated random table. The first group was given a single dose of 200 mg ciprofloxacin infusion versus 2 mg of cefotaxime divided into 2 doses, 30 minutes before induction of anesthesia and 12 hours later, for the second group.

Under general anesthesia, a ureteric catheter was inserted and used for opacification of the collecting system after which the patient was placed into the prone position and the desired calyx was accessed; Alken metal telescopic dilators were utilized for tract dilatation and PCNL was commenced using a 26F, Storz® Nephroscope. At the end of the procedure, a 6–26 Fr., double J stent was inserted with the removal of the nephrostomy tract sheath.

A charts review was planned to identify baseline demographic variables, medical history, 1<sup>st</sup> 48 hours' fever incidences, and other desired postoperative variables, while intra-operative ones were recorded prospectively during surgery. Wilcoxon's signed-rank test and Fisher's exact test for univariate analysis were utilized as well as logistic regression for multivariate analysis.

## RESULTS

Between February and October 2016, 84 patients were successfully enrolled in our study. Both groups showed similar results regarding different demographic variables and preoperative clinical variables (Table 1).

Both groups showed similar irrigation fluid volume and the number of tracts with a statistically insignificant difference ( $p = 0.6, 0.5$ ). Two (5%) patients in the ciprofloxacin group developed postoperative fe-

**Table 1.** Preoperative demographics

Variable	Ciprofloxacin Group	Cefotaxime Group	P value
Number	41	43	N/A
Age (Mean &SD)	51 ±12	50 ±11	0.7
Sex			
M	21 (51%)	19 (44%)	0.3
F	20 (49%)	24 (56%)	
BMI (Kg/m <sup>2</sup> )	31 ±10	31.4 ±8	0.6
Stone Size (Cm)	3.1 ±0.58	2.9 ±0.7	0.7
Diabetes	6 (15%)	5 (12%)	0.9
Hypertension	4 (10%)	5 (12%)	0.8
Composition			
Ca Ox	15 (37%)	16 (37%)	0.9
Ca P	12 (29%)	11 (26%)	0.6
Uric A	7 (17%)	7 (16%)	0.8
Others	7 (17%)	9 (21%)	0.5
Pre-op positive urine culture that required preoperative treatment	25 (58%)	17 (40%)	0.1
Degree of hydronephrosis			
Grade 0	2 (5%)	2 (5%)	0.6
Grade 2	21 (51%)	18 (42%)	
Grade 3	16 (39%)	19 (44%)	
Grade 4	2 (5%)	4 (9%)	

SD – standard deviation; M – male; F – female; BMI – body mass index; Ca – calcium; Ox – oxylate; P – phosphate

ver compared to 12 (28%) patients in the cefotaxime group ( $p = .002$ ).

Twelve patients in the ciprofloxacin group (29%) and 14 patients in cefotaxime group (33%) had a positive stone culture with a statistically insignificant difference ( $p = 0.6$ ).

Urine pelvic culture was positive in 7 patients in the ciprofloxacin group and 10 patients in cefotaxime group ( $p = 0.4$ ) (Table 2).

Mean operative time was similar in both groups without a statistically significant difference ( $p = 0.8$ ) (Table 2).

Table 3 shows the different isolated microorganisms across both groups according to the type of sample cultured. Table 4 shows the Incidence of SIRS, fever, and sepsis in preoperative culture positive and negative patients.

## DISCUSSION

PCNL has replaced the traditional open surgical approach for the management of large renal calculi >2 cm [7]. Generally, PCNL has a limited incidence of serious complications, in which postoperative sepsis is the most severe [8], with a low reported incidence of urinary sepsis (0.3–1%), but a high mortality rate [9]. Different factors have been found to increase the risk of postoperative sepsis, including patient age, stone

**Table 2.** Intraoperative and postoperative results

Variable	Ciprofloxacin Group	Cefotaxime Group	P value
Postoperative fever	2 (5%)	12 (28%)	0.002
Wash volume (liters)	15 ±10	16 ±9	0.6
Operative time (minutes)	92 ±36	89 ±42	0.8
Number of tracts	1 (1–3)	1 (1–2)	0.5
Hospital stay (days)	1 (1–3)	1 (1–4)	0.7
Stone culture (positive)	12 (29%)	14 (33%)	0.6
Urine pelvic culture (positive)	7 (17%)	10 (23%)	0.4

**Table 3.** Distribution of microorganisms between different samples and antibiotic groups

Organism	Preoperative		Pelvic urine Cipro Cefotax		Stone culture Cipro Cefotax	
	Cipro	Cefotax	Cipro	Cefotax	Cipro	Cefotax
E. coli	15	12	3	4	6	8
Staphylococcus	2	1	1	1	2	1
Pseudomonas	2	1	1	1	1	2
Enterococcus	1	2	1	0	0	1
Acinetobacter	2	0	0	2	1	0
Proteus	1	0	0	0	0	1
Others	2	1	1	2	2	1

**Table 4.** Incidence of SIRS, fever and sepsis in preoperative culture positive and negative patients

	Preop Culture positive Cefotaxime	Preop Culture negative Cefotaxime	P-Value	Preop Culture positive Cipro	Preop Culture negative Cipro	P-Value
SIRS	10	7	0.1	8	4	0.08
Fever	7	5	0.09	1	1	0.9
Sepsis	0	0	1	0	0	1

burden [10], stone culture [11], renal pelvis culture [12], previous history of urinary tract infection [13] or indwelling catheters [14], immunocompromise [15], neurogenic bladder [16] and irrigation fluid pressure [17].

Due to the high incidence of mortality with urosepsis, surgical prophylaxis [18] regimen and extended preoperative antibiotics [19, 20] have been studied. Char-ton M et al. [21] studied 107 patients who had sterile urine preoperatively and deliberately did not receive prophylactic antibiotics so that the mechanisms of urinary tract infection after percutaneous nephrolithotomy could be studied. Of these patients, 37 (35%) suffered a postoperative urinary tract infection, usually due to *Escherichia coli*, *streptococcus* or *staphy-*

*lococcus*. This study has confirmed the importance of surgical prophylaxis even in culture free patients undergoing PCNL, to decrease the postoperative fever from 35% to 10%.

Throughout literature [22], and based on American urological association guidelines, it has been recognized that patients with preoperative sterile urine are adequately managed with a single dose of preoperative antibiotic prophylaxis, while those with positive preoperative urine cultures should have at least 5–7 days antibiotic treatment based on urine culture and sensitivity results.

Previous studies regarding antibiotic prophylaxis for PCNL have suggested that 1<sup>st</sup> and 2<sup>nd</sup> generation cephalosporins, aminoglycosides, aztreonam + metronidazole [23] are the antibiotics of choice during induction of anesthesia; while Ampicillin/Sulbactam or fluoroquinolones were chosen as alternative choices by the AUA best practice policy [24]. Demirtas A et al. [25], compared infection rates between patients receiving ciprofloxacin versus ceftriaxone as a surgical prophylaxis prior to PCNL. The results showed no statistical difference between ciprofloxacin and ceftriaxone groups in terms of systemic inflammatory response syndrome (SIRS).

In our study, we chose to compare cefotaxime, the most widely used preoperative cephalosporin in our institution, versus a single ciprofloxacin infusion as preoperative prophylaxis for patients undergoing PCNL. We reported a fever incidence after PCNL as 5% for the ciprofloxacin group and 28% for the cefotaxime group with  $p = 0.02$ .

The conflict between our results and Demirtas study could be attributed to the broader spectrum of ceftriaxone over cefotaxime. In 1989, Baude and associates investigated the use of cefotiam (3<sup>rd</sup> generation cephalosporin) on the day of surgery and postoperatively for 2 days, which resulted in a lower urinary tract infection (UTI) rate after PCNL, but the study control group hadn't received any antibiotic prophylaxis which resulted in an unfair comparison.

In 1994, Darenkov et al. [26], compared the utilization of ciprofloxacin orally and intravenously versus no antibiotic therapy for those undergoing PCNL, and reported superiority for the intravenous regimen over oral, both of which were superior to no antibiotic prophylaxis. Owing to the restricted use of quinolones in pregnant and lactating women, or those less than 18 years of age, comparing quinolones versus a safer antibiotic that fit all of these groups was an important issue that this study missed.

From our results, more evidence has emerged supporting the superiority of quinolones over the cefotaxime group, although both have been equally recommended by the AUA and EAU panels and best practice policy.

In 1990, Fourcade RO [27], investigated the efficacy of a single dose of cefotaxime 1 g, versus no antibiotic, as surgical prophylaxis for patients undergoing endoscopic extraction of urinary tract stones, with the result showing fever occurring in 12 patients in the placebo group and in nine in the cefotaxime group (with no significant difference).

The emergence of more highly resistant strains, especially for cephalosporins, is accelerated by the ample usage of the drug and the transmission of drug-resistant organisms among hospital patients. Mariappan et al. [28] demonstrated that stone and pelvic urine cultures obtained during surgery are better predictors of potential urosepsis than bladder urine culture. Our results have shown no significant difference be-

tween the incidences of positive stone culture or urine pelvic culture in both groups, which eliminated the presence of a biased sample.

## CONCLUSIONS

A prophylactic regimen consisting of a single dose of ciprofloxacin infusion during induction of surgery showed a higher efficacy as a preoperative antibacterial preparation as compared to cefotaxime, in the protection against postoperative infectious complications in patients undergoing PCNL.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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