Extended Antimicrobial Use in Patients Undergoing Percutaneous Nephrolithotomy and Associated Antibiotic Related Complications

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Purpose: Despite global concern about antibiotic related complications the duration of antibiotic therapy at percutaneous nephrolithotomy varies based on individual physician practice. We evaluated perioperative antibiotic related complications in patients who received extended antimicrobial therapy at percutaneous nephrolithotomy.

Materials and Methods: We reviewed the records of 227 consecutive patients treated with percutaneous nephrolithotomy from 2009 to 2013. Patients with positive urine or stone cultures received extended antimicrobial treatment. All others received 7 days of empirical therapy preoperatively and postoperatively. Adverse antibiotic related events were recorded for up to 3 months.

Results: The median duration of antibiotic therapy was 14 days (IQR 14–34). Perioperatively 143 (63%), 67 (30%), 75 (33%) and 41 patients (18%) received nitrofurantoin, trimethoprim/sulfamethoxazole, fluoroquinolones and other antibiotics, respectively. Antibiotic related complications developed in 23 patients (10%) at a median of 12 days (IQR 8–19). Common complications included rash in 7 cases (3%), gastrointestinal upset in 6 (3%) and Clostridium difficile colitis in 1 (0.4%). Trimethoprim/sulfamethoxazole was associated with an increased likelihood of an adverse event ($p = 0.04$) but patient age, gender, and therapy type (therapeutic vs prophylactic) and duration were not. Finally, antibiotic and multidrug resistance developed in 4 (36%) and 3 patients (27%), respectively, who experienced a urinary tract infection.

Conclusions: We report a low rate of adverse antibiotic related events in patients treated with percutaneous nephrolithotomy who received extended perioperative antibiotic therapy. Exposure to trimethoprim/sulfamethoxazole was the only identifiable risk factor for a complication. These findings should be considered when counseling patients on the risks of perioperative antimicrobial therapy at percutaneous nephrolithotomy.

Key Words: kidney; nephrostomy, percutaneous; antibiotic prophylaxis; complications; trimethoprim-sulfamethoxazole combination

Abbreviations and Acronyms

MDR = multidrug resistance

PCNL = percutaneous nephrolithotomy

SIRS = systemic inflammatory response syndrome

UTI = urinary tract infection

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THE use of PCNL to manage complex renal calculi has almost doubled in parallel with the increasing incidence of urolithiasis.[1] PCNL represents a clean contaminated procedure with unique infectious risks due to intermixing blood from the renal parenchymal tract and urine from the affected kidney.[2–4] Large stones treated with PCNL are more likely

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to harbor bacteria and endotoxins, resulting in a greater risk of infectious complications,[5–7] including a 4.5-fold increased risk of SIRS in patients with a positive stone culture.[2] Thus, despite its minimally invasive nature the estimated overall complication rate of PCNL is as high as 21%.[8] Specifically the risk of postoperative fever was reported to be high as 32%[9] with SIRS developing in up to 37% of patients[2] and sepsis developing in 1% to 5%.[9]

Currently the AUA (American Urological Association) recommends 24 hours or less of perioperative antibiotic prophylaxis.[10] However, these recommendations were challenged by studies suggesting that extended duration preoperative antibiotic therapy even in the setting of a negative preoperative urine culture may decrease the risk of infectious complications postoperatively.[11–13] Specifically 2 studies independently verified that 1 week of preoperative antimicrobial therapy in patients with a negative urine culture decreased the risk of fever, SIRS and sepsis postoperatively.[12,13]

Despite the potential advantages of such a therapeutic approach clinicians have questioned the wisdom of extended antibiotic use due to concern about adverse antibiotic complications such as Clostridium difficile colitis[14] and antimicrobial resistance. Furthermore, there remains a lack of evidence evaluating the association between extended perioperative therapy and antibiotic related complications.[15]

It has been our practice to treat all patients undergoing PCNL with an extended course of perioperative antibiotics. We present our experience with a regimen of extended antibiotic therapy in patients undergoing PCNL, including short-term antibiotic related complications and antimicrobial resistance.

MATERIAL AND METHODS

After receiving institutional review board approval we reviewed the records of all consecutive PCNLs performed by a single surgeon (AEK) between January 2009 and May 2013. Patients with a negative preoperative urine culture, no risk factors for recurrent UTIs and no contraindications received 7 days of prophylactic antimicrobial therapy preoperatively. Patients with a positive preoperative urine culture or a history of chronic bacterial colonization, including neurogenic bladder, urinary catheterization, urinary diversion or recurrent UTIs, received extended duration targeted therapeutic antimicrobial therapy before PCNL.

We hypothesized that indwelling catheters, urothelial mucosal injury and small infected residual stone debris or blood products pose a postoperative risk of ongoing infectious complications. As such, patients with a negative stone culture received an additional 7 days of prophylactic antimicrobial therapy. Patients with a positive stone culture received an extended course of therapeutic antibiotics based on sensitivity analysis, including 2 to 6 weeks for nonstruvite infected stones and 3 months for struvite composition, comprising 1 month of treatment and 2 months of suppression. This practice changed in October 2013 when we decreased antibiotic treatment time from 6 to 2 weeks in patients with nonstruvite stones who were infected secondarily. In patients with extensive resistance who required intravenous antibiotics a peripherally inserted central catheter was placed and they were treated per protocol.

Followup included metabolic evaluation and urinalysis with culture between 6 and 12 weeks. Any patient with a residual stone on postoperative imaging underwent a secondary stone procedure. Stone fragments obtained through the percutaneous tract at PCNL using a no touch technique were sent for aerobic bacterial and fungal cultures. The no touch technique was previously validated at our institution and demonstrated a sterile working environment without stone contamination.[16]

The clinical characteristics of each patient were recorded, including antibiotic exposure and therapy duration. Perioperative antibiotic and infectious related complications were evaluated up to 3 months postoperatively. MDR was defined as acquired nonsusceptibility in 3 or more antimicrobial categories.[17] SIRS was defined as 2 or more conditions, including temperature greater than 38C or less than 36C, heart rate greater than 90 beats per minute, respiratory rate greater than 20 breaths per minute and white blood count greater than 12,000 or less than 4,000/mm^3.[18]

We used the 2-sample Student t-test and the chi-square test to assess differences. All reported p values were 2-sided with $p < 0.05$ considered statistically significant. Statistical analysis was done with SAS®, version 9.3 and JMP®, version 9.

RESULTS

From 2009 to 2013 PCNL was performed in 227 consecutive patients, of whom 23 (10%) experienced a total of 26 antibiotic related complications a median of 12 days (IQR 8–19) after therapy initiation. A total of 105 patients (46%) were exposed to more than 1 antibiotic in the perioperative period. Median antibiotic therapy duration was 14 days (IQR 14–34). During this treatment course 143 patients (63%) received nitrofurantoin, 67 (30%) received trimethoprim/sulfamethoxazole and 75 (33%) received fluoroquinolone. Intravenous antibiotic therapy was required in 11 patients (4.8%) with complications not associated with the central line. Of 67 patients with a positive stone culture 44 (66%) had a positive urine culture preoperatively. The concordance between stone culture antibiotic sensitivity profiles and the preoperative antibiotic was high with appropriate antibiotics administered in 47 patients (72%).