

The Role of Antibiotic Prophylaxis in Percutaneous Nephrolithotomy

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Postoperative sepsis is the most common cause of mortality after percutaneous nephrolithotomy (PCNL) procedures. Studies investigating the use of antibiotics in PCNL patients have shown that prophylactic antibiotic regimens can reduce the rate of postoperative infectious complications. In addition, several studies have identified risk factors for sepsis development that can help guide antibiotic treatment and perioperative care overall. This has led the American Urological Association to recommend antibiotic prophylaxis for PCNL as a best practice policy statement. However, despite prophylaxis, postoperative sepsis has continued to remain the leading cause of mortality in PCNL patients. In addition, multiple antibiotic protocols exist within the guideline realms. This review assesses the development and role of antibiotic prophylaxis for PCNL procedures.

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KEY WORDS

Percutaneous nephrolithotomy • Antibiotic prophylaxis • Urosepsis

Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure designed to remove large volume upper urinary tract stones. It is extremely effective, yielding high stone-free rates.¹ However, complications of varying degrees occur; rates of complications range from 18.30% to 83%.^{1,2} Sepsis has been reported in 0.3% to 7.6% of cases.²⁻⁴

The occurrence of sepsis is a seminal event, as it is the most common cause of perioperative mortality in PCNL patients.^{4,5} Antibiotic prophylaxis has been recommended for patients subjected to PCNL to avert these infectious complications, as profiled in an American Urological Association (AUA) Best Practice Policy Statement.⁶ Multiple studies have

shown that, in patients with negative preoperative urine culture results, antibiotic prophylaxis can reduce the incidence of postoperative sepsis.⁷⁻¹³ However, there are significant variations in the type, dose, duration, and timing of such therapy, which is often based on physician preference or geographic location.

Infectious Complications of PCNL

The use of prophylactic antibiotics in PCNL patients was first limited to those who were determined to be at high risk for infection, such as the immunosuppressed or those with positive preoperative urine culture results. However, a 1986 article by Charton and associates¹⁴

predicted its occurrence based on risk factors. There have been numerous studies investigating potential risk factors for the development of postoperative infection in PCNL patients. However, the primary endpoints have differed among studies, with a variation of the use of fever or SIRS as criteria for infection. Multiple studies have used fever as an endpoint in identifying risk factors. An initial study by Doğan and associates⁷ identified operative time and amount of irrigation used during PCNL as risk factors for fever. Sharifi Aghdas and colleagues²⁴ found that female sex, use of nephrostomy tube, and positive preoperative urine culture results were associated with higher rates of post-PCNL fever. Subsequent

found that a longer operative time and larger stone burden were more frequently associated with SIRS. Numerous other studies identified additional factors including number of access tracts, intraoperative blood transfusion, female sex, and hydronephrosis.^{1,3,19,20,27-30} Overall, from review of this literature, the most common risk factors associated with post-PCNL infection are positive preoperative urine culture results, positive intraoperative renal pelvis urine culture results, positive stone culture results, and prolonged operative time. Some of the aforementioned factors reflect stone complexity.

Use of Antibiotic Prophylaxis

Several studies completed in the past 25 years have confirmed that such antibiotic therapy in patients with negative preoperative urine culture results does reduce the risk of postoperative infectious complications. The initial studies investigating this practice were largely conducted in Europe. One observational study, conducted in 1989 by Baude and associates,³¹ described the use of cefotiam on the day of surgery and postoperatively for 2 days, which resulted in a lower urinary tract infection (UTI) rate after PCNL.³¹ Another observational study, in 1990, demonstrated a reduction in UTIs after PCNL using prophylactic aminoglycosides or cephalosporins.³⁰ One of the first prospective cohort studies, conducted in 1994 by Darenkov and coworkers,¹² described the use of ciprofloxacin for percutaneous/endourologic surgery in three groups consisting of intravenous (IV) ciprofloxacin (day of procedure), oral ciprofloxacin (3-5 d before procedure), and no antibiotic therapy. Those administered antibiotics then remained on oral

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highlighted the susceptibility of patients with negative urine culture results who were considered low risk, showing that 35% had signs of postoperative infection. Subsequent studies confirmed that signs of infection (such as fever) are common, occurring in 2.8% to 32.1% of patients.¹⁵⁻¹⁷ Fortunately, the progression to severe sepsis and systemic inflammatory response syndrome (SIRS) is rare (0.3%-4.7%).^{15,18-21} Despite this low risk of sepsis, O'Keeffe and colleagues⁵ first reported the significance of such progression; they encountered a 66% mortality rate in those who developed postoperative sepsis after PCNL. Since then, multiple studies have identified sepsis as the leading cause of death after PCNL.^{2,22,23}

Risk Factors for Infection

With sepsis established as an important complication of PCNL, focus has shifted to trying to

studies also showed that history of a previous ipsilateral PCNL, diabetes, and positive renal pelvis urine and stone culture results were also risk factors for fever.²⁴⁻²⁷ Although fever may be an indicator of post-PCNL infection, it could be related to atelectasis. Many studies, therefore, chose to focus on the occurrence of SIRS as a true indication of postoperative infection. SIRS was diagnosed when a patient met two of the following four criteria: body temperature $< 36^{\circ}\text{C}$ or $> 38^{\circ}\text{C}$, heart rate > 90 beats/min, respiratory rate > 20 breaths/min or $\text{PCO}_2 < 32$ mm Hg, and leucocyte count $> 12 \times 10^3$ cells/mm³ or $< 4 \times 10^3$ cells/mm³. Mariappan and associates²⁸ showed that stone culture and renal pelvis cultures obtained intraoperatively were more predictive of postoperative SIRS as compared with bladder urine cultures. Similar to the previously mentioned studies on fever, Dogan and coworkers²⁵

ciprofloxacin postoperatively for 1 week. Postoperative UTI rates were significantly lower in the IV ciprofloxacin (0%) and oral ciprofloxacin (17%) groups as compared with control subjects (40%). A prospective study using historical control subjects by Mariappan and associates³² demonstrated a reduction in SIRS

recommends administering a first- or second-generation cephalosporin or an aminoglycoside with metronidazole or clindamycin. Alternatives include ampicillin/sulbactam or a fluoroquinolone. The European Association of Urology (EAU) antibiotic guidelines endorse giving either a second- or third-generation cephalosporin,

difference in postoperative SIRS events between the two antibiotics with 13 (13.7%) and 17 (17.7%) patients developing SIRS in the ampicillin/sulbactam and cefuroxime groups, respectively.⁸ Overall, these studies suggest that there is no difference between the recommended antibiotics in preventing postoperative infection in PCNL patients.

A prospective study using historical control subjects ... demonstrated a reduction in SIRS in patients with negative preoperative urine culture results who were administered ciprofloxacin for 1 week prior to PCNL.

in patients with negative preoperative urine culture results who were administered ciprofloxacin for 1 week prior to PCNL. Bag and colleagues¹³ performed a prospective, randomized controlled study in which patients with negative preoperative urine culture results took nitrofurantoin for 1 week before PCNL; the incidence of SIRS was significantly lower. A case control study by Gravas and coworkers¹⁰ concluded that, in patients with negative preoperative culture results, antibiotic prophylaxis led to decreased rates of fever and other postoperative complications. However, there was some question as to whether the administration of antibiotics in the perioperative setting in those patients with negative preoperative culture results was necessary. In a randomized, double-blind, prospective study by Fourcade and colleagues,³³ patients either received no antibiotic or a single dose just before PCNL. They reported that antibiotic therapy did not reduce infectious complications. However, it should be noted that this study was underpowered.

Antibiotic of Choice

Several antibiotics have been suggested for prophylaxis. The AUA best practice statement

trimethoprim-sulfamethoxazole, fluoroquinolone or aminopenicillin with a β -lactamase inhibitor.³⁴ Like many of the other urologic prophylactic regimens, the antibiotics recommended in these guidelines are based on the usual bacterial pathogens found in the genitourinary tract and skin. The effectiveness of many of these antibiotics in the setting of PCNL has been established in the studies previously mentioned.^{10,12,31,32} Few studies have investigated the superiority of one specific regimen over another. One study by Demirtas and associates¹¹ investigated the difference in postoperative occurrence of SIRS between IV ciprofloxacin and IV ceftriaxone (third-generation) prophylaxis. In this study, antibiotics were started on the day of procedure in PCNL patients with negative urine culture results. Results showed no difference between the antibiotics with 15.5% (7/45) and 8.8% (4/45) of patients developing SIRS in the ciprofloxacin and ceftriaxone groups, respectively. Another prospective, randomized study compared IV ampicillin/sulbactam and IV cefuroxime (second-generation) in a similar patient population undergoing PCNL. This investigation again did not observe any significant

Timing and Duration of Therapy

The optimal timing, dosing, and duration of a prophylactic antibiotic regimen for PCNL procedures has also been a point of discussion. The AUA best practice policy statement currently recommends that a one-time dose on the day of the procedure is sufficient.⁶ The EAU guidelines are less definitive in concluding that a short course is adequate but that the "length of time is to be determined."³⁴ These policies are based on previous studies comparing the timing and duration of therapy: specifically, the need to continue antibiotics until nephrostomy tube removal. The first prospective study to investigate the duration of therapy was performed by Doğan and associates⁷ in 2002. In this study, PCNL patients in one group were administered a single 200-mg dose of ofloxacin during anesthesia induction, whereas those in the comparison group were given 400 mg of ofloxacin daily from the day of procedure until nephrostomy tube removal. Results showed no differences between the two groups with respect to postoperative fever, bacteremia, or bacteriuria. Subsequent studies in 2012 and 2013 confirmed the effectiveness of the single-dose antibiotic regimen. A prospective, randomized study by Seyrek and coworkers⁸ investigated three different durations of

antibiotic therapy for PCNL using either cefuroxime or sulbactam-ampicillin. The first group had a single dose of the chosen antibiotic administered at time of anesthesia induction, the second group had the antibiotic given both at time of induction and 12 hours after the initial dose, and the third group had antibiotics administered at time of induction and then either every 6 hours (sulbactam-ampicillin) or 8 hours (cefuroxime) until the time of nephrostomy tube removal. There were no differences among the three groups in the development of postoperative SIRS. A subsequent prospective study by Tuzel and associates⁹ compared the use of a single dose of ceftriaxone at time of procedure against a regimen of a preprocedural dose with subsequent antibiotic administration until the time of nephrostomy tube removal. Again, there were no differences between the groups in occurrence of postoperative fever or bacteriuria. Overall, it appears that a single dose of a broad-spectrum antibiotic just prior to PCNL provides effective prophylaxis against infectious complications.

Conclusions

Postoperative sepsis after PCNL is a rare but critical complication serving as the leading cause of death in PCNL patients. Despite negative preoperative urine culture results, a large percentage of patients still have postoperative infection. The administration of prophylactic antibiotics tailored to urinary tract and skin flora significantly decreases the occurrence of postoperative infectious complications. A prophylactic regimen consisting of a single dose during induction on the day of surgery is sufficient. ■

References

- Olvera-Posada D, Taïlly T, Alenezi H, et al. Risk factors for postoperative complications after percutaneous nephrolithotomy (PCNL) in a tertiary referral centre. *J Urol*. 2015;194:1646-1651.
- Michel MS, Trojan L, Rassweiler JJ. Complications in percutaneous nephrolithotomy. *Eur Urol*. 2007; 51:899-906.
- Koras O, Bozkurt IH, Yonguc T, et al. Risk factors for postoperative infectious complications following percutaneous nephrolithotomy: a prospective clinical study. *Urolithiasis*. 2015;43:55-60.
- de la Rosette J, Assimos D, Desai M, et al; CROES PCNL Study Group. The Clinical Research Office of the Endourological Society Percutaneous Nephrolithotomy Global Study: indications, complications, and outcomes in 5803 patients. *J Endourol*. 2011;25:11-17.
- O'Keeffe NK, Mortimer AJ, Sambrook PA, Rao PN. Severe sepsis following percutaneous or endoscopic procedures for urinary tract stones. *Br J Urol*. 1993;72:277-283.
- Wolf JS, Bennett CJ, Dmochowski RR, et al; Urologic Surgery Antimicrobial Prophylaxis Best Practice Policy Panel. Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol*. 2008;179:1379-1390.
- Dogan HS, Sahin A, Cetinkaya Y, et al. Antibiotic prophylaxis in percutaneous nephrolithotomy: prospective study in 81 patients. *J Endourol*. 2002;16:649-653.
- Seyrek M, Binbay M, Yuruk E, et al. Perioperative prophylaxis for percutaneous nephrolithotomy: randomized study concerning the drug and dosage. *J Endourol*. 2012;26:1431-1436.
- Tuzel E, Aktepe OC, Akdogan B. Prospective comparative study of two protocols of antibiotic prophylaxis in percutaneous nephrolithotomy. *J Endourol*. 2013;27:172-176.
- Gravas S, Montanari E, Geavlete P, et al. Postoperative infection rates in low risk patients undergoing percutaneous nephrolithotomy with and without antibiotic prophylaxis: a matched case control study. *J Urol*. 2012;188:843-847.
- Demirtas A, Yildirim YE, Sofikerim M, et al. Comparison of infection and urosepsis rates of ciprofloxacin and ceftriaxone prophylaxis before percutaneous nephrolithotomy: a prospective and randomised study. *ScientificWorldJournal*. 2012;2012:916381.
- Darenkov AF, Derevianko II, Martov AG, et al. [The prevention of infectious-inflammatory complications in the postoperative period in percutaneous surgical interventions in patients with urolithiasis]. *Urol Nefrol (Mosk)*. 1994;24-26.
- Bag S, Kumar S, Taneja N, et al. One week of nitrofurantoin before percutaneous nephrolithotomy significantly reduces upper tract infection and urosepsis: a prospective controlled study. *Urology*. 2011;77:45-49.
- Charton M, Vallancien G, Veillon B, Brisset JM. Urinary tract infection in percutaneous surgery for renal calculi. *J Urol*. 1986;135:15-17.
- Seitz C, Desai M, Häcker A, et al. Incidence, prevention, and management of complications following percutaneous nephrolitholapaxy. *Eur Urol*. 2012;61:146-158.
- Tefekli A, Altunrende F, Tepeler K, et al. Tubeless percutaneous nephrolithotomy in selected patients: a prospective randomized comparison. *Int Urol Nephrol*. 2007;39:57-63.
- Osman M, Wendt-Nordahl G, Heger K, et al. Percutaneous nephrolithotomy with ultrasonography-guided renal access: experience from over 300 cases. *BJU Int*. 2005;96:875-878.

MAIN POINTS

- Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure designed to remove large volume upper urinary tract stones. However, the occurrence of sepsis is a seminal event because it is the most common cause of perioperative mortality in PCNL patients.
- Antibiotic prophylaxis is recommended for patients subjected to PCNL to avert these infectious complications. Multiple studies have shown that, in patients with negative preoperative urine culture results, antibiotic prophylaxis can reduce the incidence of postoperative sepsis.
- Female sex, use of nephrostomy tube, and positive preoperative urine culture results were associated with higher rates of post-PCNL fever. Subsequent studies also showed that history of a previous ipsilateral PCNL, diabetes, and positive renal pelvis urine and stone culture results were also risk factors for fever.
- The optimal timing, dosing, and duration of a prophylactic antibiotic regimen for PCNL procedures is subject to debate. The American Urological Association has determined that a prophylactic regimen consisting of a single dose during induction on the day of surgery is sufficient.

18. Shoshany O, Margel D, Finz C, et al. Percutaneous nephrolithotomy for infection stones: what is the risk for postoperative sepsis? A retrospective cohort study. *Urolithiasis*. 2015;43:237-242.
19. Erdil T, Bostanci Y, Ozden E, et al. Risk factors for systemic inflammatory response syndrome following percutaneous nephrolithotomy. *Urolithiasis*. 2013;41:395-401.
20. Kumar S, Bag S, Ganesamoni R, et al. Risk factors for urosepsis following percutaneous nephrolithotomy: role of 1 week of nitrofurantoin in reducing the risk of urosepsis. *Urol Res*. 2012;40:79-86.
21. Chen L, Xu QQ, Li JX, et al. Systemic inflammatory response syndrome after percutaneous nephrolithotomy: an assessment of risk factors. *Int J Urol*. 2008;15:1025-1028.
22. Lewis S, Patel U. Major complications after percutaneous nephrostomy-lessons from a department audit. *Clin Radiol*. 2004;59:171-179.
23. Vorrakitpokatorn P, Permtongchuchai K, Raksamani E, Phettongkam A. Perioperative complications and risk factors of percutaneous nephrolithotomy. *J Med Assoc Thai*. 2006;89:826-833.
24. Sharifi Aghdas F, Akhaviadegan H, Aryanpoor A, et al. Fever after percutaneous nephrolithotomy: contributing factors. *Surg Infect (Larchmt)*. 2006; 7:367-371.
25. Dogan HS, Guliyev F, Cetinkaya YS, et al. Importance of microbiological evaluation in management of infectious complications following percutaneous nephrolithotomy. *Int Urol Nephrol*. 2007;39:737-742.
26. Gonen M, Turan H, Ozturk B, Ozkardes H. Factors affecting fever following percutaneous nephrolithotomy: a prospective clinical study. *J Endourol*. 2008;22:2135-2138.
27. Draga ROP, Kok ET, Sorel MR, et al. Percutaneous nephrolithotomy: factors associated with fever after the first postoperative day and systemic inflammatory response syndrome. *J Endourol*. 2009;23:921-927.
28. Mariappan P, Smith G, Bariol SV, et al. Stone and pelvic urine culture and sensitivity are better than bladder urine as predictors of urosepsis following percutaneous nephrolithotomy: a prospective clinical study. *J Urol*. 2005;173:1610-1614.
29. Lojanapiwat B, Kitirattrakarn P. Role of preoperative and intraoperative factors in mediating infection complication following percutaneous nephrolithotomy. *Urol Int*. 2011;86:448-452.
30. Hallmann B, Menzel G, Ruttloff J. [Perioperative chemoprophylaxis in percutaneous nephrolitholapaxy]. *Z Urol Nephrol*. 1990;83:475-479.
31. Baude C, Long D, Chabrol B, et al. [Antibiotic prophylaxis with cefotiam in percutaneous nephrolithotomy]. *Pathol Biol (Paris)*. 1989; 37(5 Pt 2):673-676.
32. Mariappan P, Smith G, Moussa SA, Tolley DA. One week of ciprofloxacin before percutaneous nephrolithotomy significantly reduces upper tract infection and urosepsis: a prospective controlled study. *BJU Int*. 2006;98:1075-1079.
33. Fourcade RO. Antibiotic prophylaxis with cefotaxime in endoscopic extraction of upper urinary tract stones: a randomized study. The Cefotaxime Cooperative Group. *J Antimicrob Chemother*. 1990;26(suppl A): 77-83.
34. Grabe M, Bjerklund-Johansen TE, Botto H, et al. EAU guidelines on urological infections 2013. Presented at: 28th Annual EAU Congress; March 15-19, 2013; Milan, Italy.