

Perioperative cultures and the role of antibiotics during stone surgery

Piruz Motamedinia¹, Ruslan Korets¹, Gina Badalato¹, Mantu Gupta^{1,2}

¹Department of Urology, Columbia University, College of Physicians and Surgeons, New York, NY 10032, USA; ²Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA

Correspondence to: Mantu Gupta, MD. Chairman of Urology, Mount Sinai Roosevelt and Mount Sinai St. Luke's Hospitals; Director of Endourology, Mount Sinai Health Care System; Professor of Urology, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA. Email: drmantugupta@gmail.com.

Abstract: Urinary tract infection and urosepsis are the most common complications associated with the procedures urologists employ to manage stone disease. Recommendations regarding antibiotic prophylaxis and utilization of perioperative urine and stone culture prior to shockwave lithotripsy (SWL) or endoscopic intervention have evolved overtime. We sought to provide readers with a comprehensive consensus regarding these most recent recommendations.

Keywords: Antibiotic prophylaxis; stone culture; urosepsis

Submitted Oct 10, 2013. Accepted for publication Jun 25, 2014.

doi: 10.3978/j.issn.2223-4683.2014.07.01

View this article at: <http://dx.doi.org/10.3978/j.issn.2223-4683.2014.07.01>

Shockwave lithotripsy (SWL)

The guidelines pertaining to pre-operative SWL prophylaxis have been subject to change and controversy over the last several years.

The AUA Best Practice Policy guidelines on antibiotic prophylaxis published in 2008 recommended pre-operative antibiotic prophylaxis for all patients undergoing SWL (1). This recommendation was based on a 1997 meta-analysis by Pearle and Roehrborn (2) combining data from eight randomized controlled trials (RCT), which included 854 patients (3-10). Their study found that the post-SWL UTI rate for the placebo/no-prophylaxis patients was 5.7% (range, 0-28%) compared to 2.1% (range, 0-7.7%) for patients who were given pre-procedural prophylaxis. The relative risk of UTI with prophylaxis was 0.45 (P=0.0005).

The EAU based their contemporaneous recommendations on a narrower list of RCTs that focused on the effects on antibiotic prophylaxis rather than the treatment itself (11). Along with follow-up studies they found that the rates of post-SWL symptomatic UTI and asymptomatic bacteriuria were low both with and without prophylaxis (12). Their ultimate recommendation is against antibiotic prophylaxis

prior to SWL in patients without stents or positive urine cultures.

Since the time of the original AUA guideline statement, Lu and colleagues re-examined the available data in their own meta-analysis including nine RCT (1,364 patients) (13). Lu showed that antibiotic prophylaxis did not significantly reduce the risk of fever (RR =0.36, P=0.31) or overall asymptomatic bacteriuria (RR =0.77, P=0.17). There was a trend toward protection against UTI (RR =0.54, P=0.05); however, there was no difference in UTI rates for patients with pre-operative ureteral stents (RR =0.85, P=0.75). Interestingly, despite the differing conclusions, only five studies (675 patients) overlapped between the two analyses.

Honey and colleagues corroborated Lu's findings as they prospectively examined pre- and post-procedural urine cultures in their patients undergoing SWL (14). Their general practice was to check a urine culture two weeks prior to and a urinalysis the day of SWL. Antibiotic prophylaxis was provided to patients with nephrostomy tubes, a history of infected stones, recent instrumentation, or dipstick positive for nitrites or leukocytes. They did not routinely provide prophylaxis on the basis of an indwelling stent alone. For the purposes of this study, they additionally

checked a urine culture the day of SWL and 3 days post-procedure. They found that about 6% of asymptomatic patients had a positive urine culture the day of SWL. Only one patient (0.3%) developed a symptomatic UTI post-procedure while asymptomatic bacteriuria occurred in 2.8%. Patients with indwelling ureteral stents were more likely to have asymptomatic bacteriuria but UTI did not occur. Based on their extremely low UTI rate, they concluded that universal antibiotic prophylaxis prior to SWL did not seem necessary. Additionally, they found that a day of urine dipstick negative for leukocytes or nitrites was very specific (95.9%) with a high negative predictive value for a negative urine culture.

The AUA guidelines were revised last year given Lu and Honey's findings and currently do not recommend antibiotic prophylaxis for patients undergoing SWL, which is in line with EAU recommendations (1). Given the overall consensus patients undergoing SWL with a negative urine culture should not receive antibiotics (1,11). Special consideration should be given to patients at increased risk for infection which the AUA defines as patients with advanced age, anatomic anomalies of the urinary tract, poor nutritional status, smoking, chronic corticosteroid use, immunodeficiency, externalized catheters, distant coexistent infection, or prolonged hospitalization.

URS

A 2003 RCT by Knopf *et al.* that included 113 patients found a single prophylactic oral dose of fluoroquinolone prior to ureteroscopy reduced the incidence of post-operative bacteriuria (1.8% *vs.* 12.5%, $P=0.02$) (15). There were, however, no incidences of symptomatic UTI. This study guided the AUA Best Practice Policy in recommending antibiotic prophylaxis prior to ureteroscopy for the management of stone disease (1). The guideline committee states that the potential risk of bacteriuria is 30% and UTI ranges from 4-25% without prophylaxis. There is no difference in efficacy between oral fluoroquinolone and intravenous cefazolin (16).

With regard to post-operative prophylaxis for patients with stents, Ramaswamy and Shah retrospectively reviewed their experience between two groups that had received different post-procedural prophylaxis (17). The first group was covered with fluoroquinolones for 1 week post-ureteroscopy until stent removal, while the second group received 3 days of cephalexin immediately prior to ureteral stent removal within 1 week of surgery. They observed no

differences in asymptomatic bacteria or symptomatic UTI rates (2% for both groups). Unfortunately, this series did not examine whether any antibiotics post-ureteroscopy were indicated or not.

A Korean group reviewed their experience with infectious complications following ureteroscopy and identified several risk factors (18). They noted an overall UTI rate of 3.8%. Furthermore, they found hydronephrosis, bacteriuria, and an indwelling ureteral stent or nephrostomy tube was associated with an increased risk of post-procedural fever. Administration of antibiotics after the procedure was not as effective as pre-procedural prophylaxis.

Moreover, there has been increased interest in stone cultures and their increased sensitivity over voided urine in predicting UTI or sepsis. The bulk of the literature has focused on stone cultures in patients undergoing PCNL. However, in a recent publication, one group also examined their role in patients undergoing ureteroscopic procedures. Eswara and colleagues retrospectively reviewed their experience with stone cultures in patients undergoing ureteroscopy ($n=274$) or PCNL ($n=54$) (19). They found that while pre-operative urine cultures were only positive at some point in 7% of patients, stone cultures were positive in 29%. Their overall sepsis rate was about 3-4% for all patients. In patients with positive stone cultures, the sepsis rate was significantly higher at 8% compared to only 1% in those who had negative stone cultures. Ultimately, urine cultures had a sensitivity of 11% versus 64% in stone cultures and there was a concordance of 64% between the stone culture pathogen and the one causes sepsis compared to only 9% of pre-operative urine cultures. Despite the correlation of stone cultures and post-operative infection, their utilization in guiding clinical practice is limited in that it takes several days following the removal of the stone for cultures to results. They are most helpful following the development of UTI to help guide antibiotic choice.

PCNL

Antibiotic prophylaxis

PCNL is ideal for large, complex (staghorn) stones. The most common composition for staghorn stones is struvite (20), which results from the presence of urea-splitting organisms in the urinary tract. Large non-struvite stones may also harbor bacteria. Additionally, PCNL, while minimally invasive, still traverses through skin, retroperitoneal and renal tissue to access the urinary tract

and stone and utilize large volumes of irrigation relative to ureteroscopy. These factors taken together make a strong case for pre-operative antibiotic prophylaxis.

The practice of prophylaxis was reinforced by the CROES group, who retrospectively identified 162 patients from multiple institutions who underwent PCNL without pre-operative antibiotics and matched them to patients who did receive antibiotics (21). All patients had negative pre-operative urine cultures and matching was based on infectious risk factors such as diabetes, nephrostomy tubes and staghorn stones. They found that antibiotic prophylaxis led to fewer fevers (2.5% vs. 7.4%) and other complications (1.9% vs. 22%) and higher stone free rate (86.3% vs. 74%).

Other studies that compared limiting antibiotics to pre-operative prophylaxis versus continuing until nephrostomy tube removal have found no difference in infection related outcomes (22-24). Bag and colleagues randomized high-risk patients (stone ≥ 2.5 cm and/or hydronephrosis) to immediate pre-operative antibiotic prophylaxis versus one week or nitrofurantoin plus prophylaxis prior to PCNL. The patients who received nitrofurantoin were more likely to have sterile pelvic urine (RR =4.95) and stone cultures (RR =3.64), and less likely to have endotoxemia (RR =0.22) or experience SIRS (RR =0.31).

Stone cultures

There is little disagreement that prior to endourological procedures, including PCNL, a pre-operative urine culture should be obtained and confirmed to be sterile. In the event of bacteriuria, culture specific treatment prior to proceeding with the intended procedure is recommended; the goal being to prevent urosepsis resulting from the instrumentation and manipulation the urinary tract.

Stones themselves may harbor bacteria that may not manifest in a voided urine culture (25) and techniques to culture stones were described over 40 years ago (26). In a study examining infection rates in patients undergoing PCNL 35% of patients had positive stone cultures, compared with 21% of upper tract and 11% of bladder urine cultures (27). Korets *et al.* found that in patients with negative bladder cultures, about one-third had infected pelvic urine and half had positive stone cultures (28). Stone manipulation and lithotripsy can result in the release of bacteria and contamination of urine with possible systemic transudation resulting in sepsis or systemic inflammatory response syndrome (SIRS). Stone cultures have been shown to be a better predictor of sepsis and SIRS than voided

cultures (19,27-29). Mariappan showed a positive stone culture to have over 80% sensitivity and a positive predictive value of 70% in predicting SIRS (27). Overall, positive stone cultures increased the risk of SIRS 4-fold (27,30). Also, the stone culture pathogen has a higher concordance with the offending bacteria causing sepsis. Eswara found that the urine culture organism on readmission for sepsis correlated with the stone culture in 64% versus preoperative urine culture in only 11% of patients (19).

Along with bacteria, stones contain endotoxins that can potentially result in a systemic immune response clinically similar to sepsis. McAleer and colleagues found higher endotoxin concentrations in infected stones supporting this hypothesis but also raising the question, is it the bacteria or the endotoxins resulting in the reaction (31)?

The greatest limitation of stone cultures is that they are only available after a procedure with some days to allow bacteria growth and speciation and so cannot influence immediate peri-operative treatment. The utility of obtaining stone cultures in clinical practice is to guide antibiotic choice in the event of sepsis following ureteroscopy or PCNL rather than predicting it. Having said this, it is our practice to routinely collect stone cultures from patients undergoing PCNL.

Risk factors for fevers/sepsis/SIRS

Many groups have reviewed their experience with PCNL in an attempt to identify risk factors for post-operative fever, sepsis or SIRS. A positive pre-operative urine culture was associated with increased infectious risk (OR, 2.2-16.7), as were positive pelvic urine (OR, 10.2-24.1) and stone cultures (OR, 4.88-25.6) (22,29,32,33). Other pre-operatively available factors such as female sex, hydronephrosis, pre-operative nephrostomy tube, large or complex stone burden, and a patient with diabetes have all been associated with an increased risk of post-operative fever or sepsis (28,32-34).

Korets and colleagues showed that an increased number of access tracts increased the risk of SIRS (OR, 4.8) (28) when controlling for patient sex, stone culture and composition, while several other groups have found increased operative time to be a risk factor for fever (22,32,34). Dogan also showed volume of irrigation fluid required was a significant predictor (22). These three factors are likely all surrogates for stone size and complexity. It is hard to know whether reducing these intra-operative factors would result in decreased infectious risk given the

retrospective nature of these studies.

In conclusion, the current guidelines and practice patterns pertaining to stone surgery have evolved based on emerging clinical data. These recommendations in conjunction with patients' individual risk factors and culture data should help guide ongoing practice patterns.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Wolf JS Jr, Bennett CJ, Dmochowski RR, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol* 2008;179:1379-90.
2. Pearle MS, Roehrborn CG. Antimicrobial prophylaxis prior to shock wave lithotripsy in patients with sterile urine before treatment: a meta-analysis and cost-effectiveness analysis. *Urology* 1997;49:679-86.
3. Claes H, Vandeursen R, Baert L. Amoxicillin/clavulanate prophylaxis for extracorporeal shock wave lithotripsy - a comparative study. *J Antimicrob Chemother* 1989;24 Suppl B:217-20.
4. Menges T, Sablotzki A, Welters I, et al. Concentration of cefamandole in plasma and tissues of patients undergoing cardiac surgery: the influence of different cefamandole dosage. *J Cardiothorac Vasc Anesth* 1997;11:565-70.
5. Gattegno B, Sicard F, Alcaldinho D, et al. Extracorporeal lithotripsy and prophylactic antibiotic therapy. *Ann Urol (Paris)* 1988;22:101-2.
6. Pettersson B, Tiselius HG. Are prophylactic antibiotics necessary during extracorporeal shockwave lithotripsy? *Br J Urol* 1989;63:449-52.
7. Tominaga T, Tomita K, Shibamoto K, et al. Clinical study of urinary tract infection after treatment with extracorporeal shock-wave lithotripter. *Extracorporeal shock-wave lithotripter. Nihon Hinyokika Gakkai Zasshi* 1987;78:1240-5.
8. Ilker Y, Türkeri LN, Korten V, et al. Antimicrobial prophylaxis in management of urinary tract stones by extracorporeal shock-wave lithotripsy: is it necessary? *Urology* 1995;46:165-7.
9. Herrlinger A, Bornhof C, Kuehn R. Antibiotic prophylaxis before extracorporeal shock wave lithotripsy by single-shot application of azlocillin. *Chemioterapia* 1987;6:607-9.
10. Knipper A, Böhle A, Pense J, et al. Antibiotic prophylaxis with enoxacin in extracorporeal shockwave lithotripsy. *Infection* 1989;17 Suppl 1:S37-8.
11. Grabe M, Bjerklund-Johansen TE, Botto H, et al. Guidelines on Urological Infections. *European Association of Urology* 2010;79.
12. Bootsma AM, Laguna Pes MP, Geerlings SE, et al. Antibiotic prophylaxis in urologic procedures: a systematic review. *Eur Urol* 2008;54:1270-86.
13. Lu Y, Tianyong F, Ping H, et al. Antibiotic prophylaxis for shock wave lithotripsy in patients with sterile urine before treatment may be unnecessary: a systematic review and meta-analysis. *J Urol* 2012;188:441-8.
14. Honey RJ, Ordon M, Ghiculete D, et al. A prospective study examining the incidence of bacteriuria and urinary tract infection after shock wave lithotripsy with targeted antibiotic prophylaxis. *J Urol* 2013;189:2112-7.
15. Knopf HJ, Graff HJ, Schulze H. Perioperative antibiotic prophylaxis in ureteroscopic stone removal. *Eur Urol* 2003;44:115-8.
16. Christiano AP, Hollowell CM, Kim H, et al. Double-blind randomized comparison of single-dose ciprofloxacin versus intravenous cefazolin in patients undergoing outpatient endourologic surgery. *Urology* 2000;55:182-5.
17. Ramaswamy K, Shah O. Antibiotic prophylaxis after uncomplicated ureteroscopic stone treatment: is there a difference? *J Endourol* 2012;26:122-5.
18. Sohn DW, Kim SW, Hong CG, et al. Risk factors of infectious complication after ureteroscopic procedures of the upper urinary tract. *J Infect Chemother* 2013;19:1102-8.
19. Eswara JR, Shariftabrizi A, Sacco D. Positive stone culture is associated with a higher rate of sepsis after endourological procedures. *Urolithiasis* 2013;41:411-4.
20. Segura JW, Preminger GM, Assimos DG, et al. Nephrolithiasis Clinical Guidelines Panel summary report on the management of staghorn calculi. The American Urological Association Nephrolithiasis Clinical Guidelines Panel. *J Urol* 1994;151:1648-51.
21. 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;188:843-7.
22. Doğan HS, Sahin A, Cetinkaya Y, et al. Antibiotic

- prophylaxis in percutaneous nephrolithotomy: prospective study in 81 patients. *J Endourol* 2002;16:649-53.
23. Seyrek M, Binbay M, Yuruk E, et al. Perioperative prophylaxis for percutaneous nephrolithotomy: randomized study concerning the drug and dosage. *J Endourol* 2012;26:1431-6.
 24. Tuzel E, Aktepe OC, Akdogan B. Prospective comparative study of two protocols of antibiotic prophylaxis in percutaneous nephrolithotomy. *J Endourol* 2013;27:172-6.
 25. Mariappan P, Loong CW. Midstream urine culture and sensitivity test is a poor predictor of infected urine proximal to the obstructing ureteral stone or infected stones: a prospective clinical study. *J Urol* 2004;171:2142-5.
 26. Nemoy NJ, Staney TA. Surgical, bacteriological, and biochemical management of "infection stones". *JAMA* 1971;215:1470-6.
 27. 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;173:1610-4.
 28. Korets R, Gravarsen JA, Kates M, et al. Post-percutaneous nephrolithotomy systemic inflammatory response: a prospective analysis of preoperative urine, renal pelvic urine and stone cultures. *J Urol* 2011;186:1899-903.
 29. Lojanapiwat B, Kitirattrakarn P. Role of preoperative and intraoperative factors in mediating infection complication following percutaneous nephrolithotomy. *Urol Int* 2011;86:448-52.
 30. Margel D, Ehrlich Y, Brown N, et al. Clinical implication of routine stone culture in percutaneous nephrolithotomy—a prospective study. *Urology* 2006;67:26-9.
 31. McAleer IM, Kaplan GW, Bradley JS, et al. Endotoxin content in renal calculi. *J Urol* 2003;169:1813-4.
 32. Gonen M, Turan H, Ozturk B, et al. Factors affecting fever following percutaneous nephrolithotomy: a prospective clinical study. *J Endourol* 2008;22:2135-8.
 33. Gutierrez J, Smith A, Geavlete P, et al. Urinary tract infections and post-operative fever in percutaneous nephrolithotomy. *World J Urol* 2013;31:1135-40.
 34. 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;77:45-9.

Cite this article as: Motamedinia P, Korets R, Badalato G, Gupta M. Perioperative cultures and the role of antibiotics during stone surgery. *Transl Androl Urol* 2014;3(3):297-301. doi: 10.3978/j.issn.2223-4683.2014.07.01