Review Article

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Antimicrobial prophylaxis for ureterorenoscopic surgery

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ABSTRACT

The necessity of antimicrobial prophylaxis (AMP) for ureterorenoscopy is undisputed. Most guidelines state that single AMP is sufficient for ureteroscopy, but indiscriminate antibiotic use is common. Except for transurethral resection of prostate and prostate biopsy, there is a lack of well-performed studies investigating the need and duration of antibiotic prophylaxis in endourology. Although single dose AMP is a widely accepted principle, still multiple-dose regimens are used in some centers. A systematic review was done to know the AMP for ureteroscopy using PubMed articles and Urological Association guidelines. It was concluded that a single dose AMP is necessary for ureterorenoscopic surgery. Either a fluoroquinolone or a combination of ampicillin and aminoglycoside can be used as prophylactic antibiotic.

Keywords: Antimicrobial prophylaxis, Endourology, Ureterorenoscopy, Urinary tract infection

INTRODUCTION

Uncomplicated ureteroscopy is a clean-contaminated procedure.1 Symptomatic urinary tract infections (UTIs) are possible post-operative complications of ureteroscopic interventions with the risk of ascending pyelonephritis, or other inflammable complications.2 Hence, prophylactic use of antibiotic is needed during perioperative period.² However, indiscriminate antibiotic use increases environmental selection pressure, favoring emergence of antimicrobial resistant bacteria that can cause surgical site infections, resulting in administration of more antibiotics, an increase in the cost of care, and a prolonged hospital stay.³ Except for transurethral resection of the prostate (TURP) and prostatic biopsy, there is a lack of well-performed studies investigating the need and duration of antibiotic prophylaxis in urologic interventions.⁴ Although singledose antimicrobial prophylaxis (AMP) is a widely accepted principle, still multiple-dose regimens are used in some centers.5 A systematic review was done using words "AMP for ureterorenoscopy," "AMP in urology," "Urological Association guidelines" and conclusions were drawn about AMP during ureterorenoscopy.

DISCUSSION

Definitions

Surgical AMP in ureteroscopy entails treatment with an antimicrobial agent before and for a limited time after the procedure to prevent bacteremia and secondarily prevention of post-operative bacteriuria.⁶ Post-operative UTIs are the main concern for morbidity in patients after ureteroscopy.^{7,8}

Bacteriuria, defined as bacteriuria >10³ or >10⁴ colonyforming units (CFU)/ml in symptomatic UTI and >10⁵ CFU/ml in asymptomatic bacteriuria within 30 days postoperatively is a frequent primary outcome in urologic procedure studies.⁴ In terms of UTIs after ureteroscopy, the more current literature is fairly consistent in showing the post-operative incidence to be <2%.⁵ Ureteroscopy has a risk of UTI due to several factors, including increased trauma to the mucosa, increased duration and/or degree of difficulty of most ureteroscopic procedure, increased pressure of irrigants, and manipulation or resection of infected material.⁶

Principles of surgical AMP^{10,11}

- 1. Surgical AMP is the periprocedural systemic administration of an antimicrobial agent intended to reduce the risk of post-procedural local and systemic infections. AMP is only one of several measures thought to reduce surgical site infection (SSI). Others include bowel preparation, pre-operative hair removal, antiseptic bathing, hand washing protocol, double gloving and sterile preparation of the operative field.
- 2. The potential benefit of surgical AMP is determined by three considerations: Patient related factors (ability of the host to respond to bacterial invasion), procedural factors (likelihood of bacterial invasion at the operative site) and the potential morbidity of infection.

Risk factors are important in the pre-operative assessment of the patient. They are related to:

- General health of the patient as defined by American Society of Anesthesiology score P₁-P₅ (Table 1)
- General risk factors
- Special risk factors associated with an increased bacterial load
- Type of surgery and surgical field of contamination
- Expected level of surgical invasiveness, duration and technical aspects.

General patient related risk factors that may influence the risk for SSI:¹¹ older age, deficient nutritional status, impaired immune response, diabetes mellitus, smoking, extreme weight, coexisting infection at a remote site, lack of control of risk factors

Special risk factors associated with increased bacterial load:¹¹ Long pre-operative hospital stay, history of recurrent urogenital infections, colonization with microorganisms, long-term drainage, urinary obstruction, urinary stone.

The traditional classification of surgical procedures according to Cruse and Foord¹¹ into clean, clean-contaminated, contaminated, and dirty operations does not apply to endourological interventions. However, members of the European Association of Urology expert group considers these procedures as clean-contaminated because urine culture is not always a predictor of bacterial presence, and the lower genitourinary tract is colonized by microflora, even in the presence of sterile urine.¹¹

3. Surgical AMP is recommended only when potential benefit exceeds the risks and anticipated costs.

Clearly SSIs are associated with poorer patient outcomes and increased costs.¹⁰ It has been demonstrated in a variety of settings that surgical AMP, by reducing the incidence of SSIs, reduces costs. Conversely, excess and/or inappropriate use increase costs, which is reversed by measures to improve compliance with evidence-based recommendations.¹¹

Prophylactic antimicrobial use is associated with financial, personal-health, and public health costs. Costs vary widely with the antimicrobial agent selected and also according to the setting in which the administration occurs. Another important factor is

variation in the duration of AMP. A single pre-operative administration has less total associated cost than a cycle of three administrations during the 24 h perioperative period.¹⁰

The personal health risk of prophylactic antimicrobial administration include allergic reactions, which vary from minor rashes to anaphylaxis and suppression of normal bacterial flora, which can lead to clostridium difficile colitis, colonization and infection with resistant organisms and other adverse effects. In general, the financial costs of prophylaxis are controlled using the least expensive and safest efficacious agent for the shortest duration that is consistent with good clinical practice.¹⁰

The public health risk of AMP relates to the induction of bacterial resistance in the patient and in the community microbial reservoir. Antimicrobial usage has had a clear impact on the emergence of resistant bacterial strains. A substantial cause of the emergence of these resistant strains is the overuse (treatment when none is needed and prolonged therapy exposures) of antimicrobial agents for all indications. Data are suggesting that fluoroquinolone resistance is rising in areas of high use support the contention that microbial resistance is directly related to repetitive exposure of microbes to unique antimicrobial agents. It is likely that the appropriate use of AMP (indication specific and of limited duration) would limit these resistance trends.¹⁰

- 4. The antimicrobial agent used for prophylaxis should be effective against the disease-relevant bacterial flora characteristic of the operative site. Cost, convenience and safety of the agent also should be considered. The common pathogens expected during ureteroscopy are *Enterobacteriaceae*, Enterococci and Staphylococci.¹¹
 - The fluoroquinolones are generally efficacious, have a long half-life, are inexpensive (when used as a single dose) and are rarely associated with allergic reactions. ¹⁰ Ciprofloxacin achieves peak serum level by 1 h after oral administration and has a half-life of 3.9 h.⁶
- The duration of surgical AMP should extend throughout the period in which bacterial invasion is facilitated and/ or is likely to establish an infection.

For prophylactic antimicrobial administration to be optimally effective timing and dosing are critical. Oral ciprofloxacin should be given approximately 1 h before the intervention. This allows antibiotic to reach a peak concentration at the time of highest risk during the procedure and an effective concentration shortly afterward. Additional doses are required intra-operatively if the procedure extends beyond two half-lives of the initial dose.

Published literature suggests that AMP is unnecessary upon termination of an ureteroscopic procedure. ¹⁰ Thus, AMP should be a single dose or at least discontinued within 24 h of the end of procedure. ¹⁰ Misuse of antimicrobials is associated with bacterial resistance, morbidity and increased health care costs. ¹⁰

AMP recommendations for ureteroscopy (Table 2): The use of oral fluoroguinolones as a prophylactic agent in ureteroscopy and other endourological procedures is a special situation. This antimicrobial regimen is rarely used for prophylaxis outside of urologic surgery.¹⁰ Many studies comparing oral ciprofloxacin to intravenous cephalosporins in variety of endourological procedures have found no difference in the incidence of post-operative bacteriuria between two groups, and costs were lower in the ciprofloxacin groups owing to the simpler use of oral rather than intravenous administration.¹⁰

Various studies on AMP for ureteroscopy

Moslemi et al.³ did a comparative evaluation of prophylactic single-dose intravenous antibiotic with post-operative antibiotics in elective urologic surgery, which included ureterorenoscopy also. They had 74 patients in Group 1 who received single intravenous cefazolin and 75 patients in Group 2 who received cefazolin post-operatively also. No patient in either group developed post-operative UTI, and they concluded that the protocol of use of single dose antibiotic decreased the amount of antibiotics used without increasing perioperative infection rate.

Takahashi et al. 12 did a study to establish a standard protocol for surgical antimicrobial agents for patients who received transurethral ureterolithotripsy (TUL). They retrospectively reviewed the medical charts of patients who received TUL. From October 2002 to December 2003, 4 doses of AMP were done, and from January 2004 to December 2004, single prophylaxis was done. Of 135 patients with TUL, 66 were in single AMP group and 69 in 4 dose AMP group. No statistically significant difference was found

Table 1: General physical status defined by ASA.1

Category	Clinical evaluation		
P_1	A normal patient		
P_2	A patient with a mild systemic disease		
P_3	A patient with a severe systemic disease		
P_4	A patient with a severe systemic disease that is a constant threat to life		
P ₅	A moribund patient who is not expected to survive with or without the operation		

ASA: American Society of Anesthesiology

in the incidence of post-operative fever between the two groups. Their study showed that single AMP was effective for patients receiving a TUL operation.

Shigemura et al.¹³ investigated whether the occurrence of SSI could be decreased by a shorter duration of prophylactic antibiotic medications. 389 patients were included in the study. A group of 362 patients from the immediate post period in whom no specific AMP protocol was used were used as control. They found a significantly lower SSI occurrence in the study group (3/389, 0.77%) than the control group (14/362, 3.87's) (p = 0.0111).

Higuchi et al. 14 did a study to know the efficacy of a single dose of AMP for prevention of post-operative infection in a total of 788 patients undergoing urological surgery that included 380 endoscopic instrumental operations. They observed UTI in 12 (3.2%) and remote infection in 1 (0.3%) patients after endoscopic instrumental operation. They concluded that single dose regimen of AMP was effective and feasible for the prevention of UTIs in endoscopic instrumental procedures.

Yamamoto et al.15 did a study in which a single dose AMP was administered parenterally for prevention of perioperative infection in a total of 206 urological surgeries including 114 endoscopic instrumental procedures between January and December 2007 and SSI, UTI and remote infection were prospectively surveyed. UTI was observed in three cases (2.7%) after endoscopic instrumental procedures. They concluded that a single dose regimen at AMP was effective for prevention of UTI in endourology.

Bootsma et al.4 conducted a systematic literature review about antibiotic prophylaxis in urologic procedures and found low evidence favoring the use of antibiotic prophylaxis for therapeutic ureteroscopy. They also concluded that except for TURP and prostate biopsy, there is a lack of well-performed studies investigating the need for antibiotic prophylaxis in urologic interventions.

Knopf et al.² did a prospective study to settle the question whether a perioperative single shot prophylaxis in connection with ureteroscopic stone removal has an influence on the rate of post-operative UTIs and inflammable complications or not. 113 patients were included in a prospectively randomized study. In 57 patients 250 mg levofloxacin per oral was given 60 min prior to ureteroscopy, 56 patients

Table 2: Urology association guidelines.

	First choice	Alternative	Duration
AUA guidelines ¹⁰	Fluoroquinolone TMP-SMX	Aminoglycoside+ampicillin amoxicillin+clavulunate 1 st /2 nd generation cephalosporin	<24 h
EAU guidelines ¹¹	TMP+SMX 2 nd /3 rd Generation ce Amino penicillin Fluoroquinolones	2 nd /3 rd Generation cephalosporin Amino penicillin	

TMP: Trimethoprim, SMX: Sulfamethaxozole, EAU: European Association of Urology, AUA: American Urological Association

had no prophylaxis. Post-operatively, symptomatic UTI or inflammable complications of the urogenital tract were found in neither of the two groups. In the group without prophylaxis, the rate of the post-operative significant bacteriuria was significantly higher than in the group with prophylaxis (seven patients 12.5%) versus one patient (1.8%) (p=0.026). They concluded that a single shot prophylaxis using 250 mg levofloxacin per oral can be considered as cheap, the patient not burdened and the preferred manner of peri operative antibiotic prophylaxis in ureteroscopic stone removal.

Grabe¹⁶ reviewed studies on infections complications and antibiotic prophylaxis in common urological instrumentation. He found limited clear-cut evidence for giving definite standards regarding antibiotic prophylaxis for most urological interventions. He found that correctly administered oral prophylaxis is as effective as intravenous prophylaxis.

Zanetti et al.¹⁷ in a review on current clinical evidence in prophylaxis and antibiotic therapy for infections and urolithiasis found excellent results with oral fluoroquinolones in prophylaxis concerning post-operative infection control after ureteroscopy. They also found that prophylaxis should be administered only for a limited amount of time.

Shokeir and Al Ansari¹⁸ reviewed pathogenesis, prevention and management of iatrogenic infection in urological practice. They found that in endourological procedures antibiotic prophylaxis is indicated in cases of infected stones, pre-operative UTIs or prolonged procedures.

Esposito¹⁹ did a review on single dose antibiotic prophylaxis in endourology and found out numerous clinical studies that have clearly shown that appropriately timed single shot prophylaxis is as effective as multiple dose prophylaxis.

CONCLUSION

Antimicrobial propylaxis is a necessity for ureterorenscopy as it is a clean contaminated procedure. A single preoperative dose of either fluoroquinolone or a combination of ampicillin and aminoglycoside is preferred for prophylaxis.

Abbreviations

AUA: American Urological Association ASA: American Society of Anaesthesiology

AMP: Antimicrobial prophylaxis CFU: Colony forming units

EAU: European Association of Urology

Ml: Milliliter, MG: Milligrams

RI: Remote infection SSI: Surgical Site Infection SMX: Sulfamethaxozole

TURP: Transurethral resection of prostate

TMP: Trimethoprim

TUL: Transureteral ureterolithotripsy

UTI: Urinary tract infection

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