Review

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Prophylactic Antimicrobial Therapy and Antimicrobial Stewardship in Urologic Surgery

Hee Jo Yang

Department of Urology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea

Postoperative infectious complications are a worrying problem for surgeons. Urological surgery has a higher risk of postoperative urinary tract infection than other surgeries because of the common use of various types of catheters. Due to the recent increase in antibiotic resistance, antimicrobial stewardship recommends using appropriate antibiotics for a suitable period. It is generally advocated that prescribing antibiotics in the absence of infection is equivalent to the inappropriate use of antibiotics. Based on numerous studies reported by several academic societies, appropriate use of antibiotics before surgery has been suggested. It was confirmed that using antibiotics according to these guidelines reduces the use of antibiotics without increasing the incidence of postoperative infectious complications. Furthermore, endourological surgery reports have proved the efficacy of antibiotics given once before surgery. Differences in antibiotic resistance by region must be taken into consideration when selecting the appropriate antibiotic type.

Keywords: Anti-bacterial agents; Postoperative complications; Urinary tract infections

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Correspondence to: Hee Jo Yang
https://orcid.org/0000-0002-7195-806X
Department of Urology, Soonchunhyang University Cheonan Hospital, 8 Soonchunhyang 2-gil, Dongnam-gu, Cheonan 31151, Korea
Tel: +82-41-570-2376, Fax: +82-41-570-3723
E-mail: c78154@schmc.ac.kr

INTRODUCTION

With an increasing crisis of antibiotic resistance worldwide, an antimicrobial stewardship program (ASP) has been proposed as an important method to reduce or prevent antibiotic resistance [1]. ASP supports the appropriate use of antibiotics through optimal usage including dosing, duration of treatment, and route of administration [2].

Surgical site infection and postoperative urinary tract infection (UTI) are common complications of surgery. Postoperative UTIs often occur in association with catheter indwelling. Retention of a catheter results in a 3% to 7% occurrence of bacteriuria per day [3]. The urology department particularly has a wide array of surgeries and urethral catheters are often used post-operatively, thereby increasing the possibility of UTI and infection at the surgical site. Depending on the operation, an infection may occur in up to 1.8% of ureteroscopic lithotripsy (URSL) [4] and up to 35% of percutaneous nephrolithotripsy (PCNL) [5] cases. It is well known that the use of preoperative antibiotics reduces the incidence of postoperative infectious complications [6]. However, in the current era of increasing antibiotic resistance and limited availability of new drugs, the use of antibiotics should be restricted. Several academic societies have published guidelines for appropriate prophylactic use of antibiotics in urologic surgery.

EFFECTIVENESS OF THE ANTIBIOTIC STEWARDSHIP PROGRAM

Although generally agreed that antibiotics should be used only when required, surgeons are largely concerned about the occurrence of infection-related complications after surgery and often consider the use of prophylactic antibiotics before surgery. In 2016, Cai et al. [7] evaluated the occurrence of antibiotic resistance and postoperative complications before and after adapting the EAU (European Association of Urology) guideline in a tertiary urological institution. They reported that reducing the use of antibiotics according to the EAU guideline showed no difference in the proportion of patients with postoperative symptomatic UTI (p=0.27) compared to before adapting the guidelines. Moreover, the prevalence of antibiotic-resistant urinary tract pathogens was reduced. They emphasized the importance of antibiotic stewardship programs and recommended adherence to guidelines.

PREOPERATIVE PREPARATION

All patients undergoing planned surgery should be evaluated for a complete medical history, appropriate physical examination, urine culture, and susceptibility test. In the event of any risk factors (such as advanced age, immunodeficiency, diabetes, obesity, and smoking) liable for infection after surgery, administration of prophylactic antibiotics before surgery should be considered. There are no guidelines that have established the minimum risk factors for advocating the use of antibiotics. Preoperative treatment is recommended for factors that can be corrected before surgery, such as chronic bacteriuria, voiding difficulties, urinary tract obstruction, and impaired urinary flow [8].

The UTI EAU Panel has not recommended any drugs against the present and susceptible bacterial pathogens and antimicrobials for specific surgeries, due to significant differences between Europe and other countries. In principle, prophylactic antibiotics should not be drugs that are often used to treat infections. In cases of clinically obvious urinary tract obstruction and UTI, a urine culture test should be confirmed before surgical treatment, and relief of obstruction and treatment for UTI should precede the surgery [9].

However, accuracy of the urine culture test performed before surgery is often doubted. Mariappan and Loong [10] have compared mid-stream urine, stone culture results, and renal pelvis urine culture results of patients who have undergone surgical treatment for obstructive ureteral stones. The mid-stream culture test showed a lower positive predictive value (0.62) and a lower negative predictive value (0.42) compared to the urine culture test of the renal pelvis.

URETEROSCOPIC LITHOTRIPSY

Ureteroscopic stone surgery is a rapidly increasing endoscopic surgery in Korea [11]. Post-operative infection is one of the most feared complications of URSL. A multicenter study by the Clinical Research Office of the Endourological Society (CROES) reported the following incidences of infectious complication after URSL surgery: fever 1.8%, UTI 1.0%, and sepsis 0.7% [12]. In another multicenter study on the use of prophylactic antibiotics in endoscopic surgery for renal stones, antibiotics were administered to all patients. Infectious complications occurred in 31 patients (7.7%), fever in 18 patients (4.4%), systemic inflammatory response syndrome (SIRS) in 7 patients (1.7%), and sepsis in 3 patients (0.7%) [13]. Furthermore, subgroup analysis of CROES revealed that rates of postoperative UTI and fever were not reduced by prophylactic antibiotics when the urine culture was negative before surgery [14].

A recent meta-analysis study examined 4,591 patients from 11 studies [15]. Although the risk of febrile UTI after surgery (odds ratio [OR], 0.82; 95% confidence interval [CI], 0.40-1.67; p=0.59) did not differ with the administration of prophylactic antibiotics, patients who received a single dose of prophylactic antibiotics had significantly lower risks of pyuria (OR, 0.42; 95% CI, 0.25-0.69; p=0.0007) and bacteriuria (OR, 0.25; 95% CI, 0.11-0.58; p=0.001) post-surgery.

In another randomized clinical trial study on ureteroscopic nephrolithotripsy, no difference was obtained in the SIRS according to ciprofloxacin dose [16]. However, in the absence of prophylactic antibiotics, the likelihood of SIRS was higher in patients with a stone size >200 mm^2 (no prophylactic antibiotics, 18%; single dose, 4.3%, p=0.036; two doses, 5.5%, p=0.044). In addition, studies reported that administration of fosfomycin as a prophylactic antibiotic showed higher efficacy, higher safety, and lower cost than commonly used antibiotics [17].

Table 1. Recommendations for procedures (reproduced from guidelines)

Procedures	AUA guidelines (2019)	EAU guidelines (2022)
Ureteroscopy	Yes	Yes
Percutaneous nephrolithotomy	Yes	Yes (single dose)
Transurethral resection of prostate	Yes	Yes
Transurethral resection of bladder tumor	Yes	Yes, in high risk

AUA: American Urological Association, EAU: European Association of Urology.

Because of the potential risk of infectious complications due to the presence of infected stones and the low risk associated with the use of a single dose of prophylactic antibiotics, one needs to consider antibiotic prophylaxis in URSL for the treatment of urolithiasis (Table 1).

PERCUTANEOUS NEPHROLITHOTRIPSY

PCNL is a recommended treatment for large-sized kidney stones which damage the urothelium by directly puncturing the kidney. Fever is known to occur in 21% to 39.8% of patients after PCNL [5]. In addition, sepsis has been documented in 0.3% to 9.3% of patients after PCNL [5]. Positive preoperative urine culture results are associated with an increased risk of postoperative infection. However, even if the midstream urine culture is negative, the presence of bacteria in the stone or urine from the renal pelvis cannot be ruled out. One study reported positive cultures for renal pelvis urine and stones in approximately one-third of the patients with negative mid-stream urine cultures [18].

The PCNL study of CROES compared 162 patients who underwent the procedure with and without preoperative prophylactic antibiotics [19]. All patients had a negative preoperative midstream urine culture test. No significant differences were obtained for the risk factors related to stones between the two groups. The incidence of fever (2.5 vs. 7.4%, respectively) and other complications (1.9 vs. 22%, respectively) were low in patients who used prophylactic antibiotics.

In a meta-analysis study by Yu et al. [20], the use of a single dose of prophylactic antibiotic before surgery significantly reduced sepsis (OR, 0.31; 95% CI, 0.20-0.50; p <0.00001) and febrile episodes (OR, 0.26; 95% CI, 0.14-0.48; p<0.0001). In addition, the presence of bacteria in culture tests for stones and urine in the renal pelvis significantly reduced after prophylaxis. Another meta-analysis study analyzed the effects of single and multiple doses of prophylactic antibiotics [21]. No differences were obtained in postoperative fever between the two groups (OR, 0.96; 95% CI, 0.44-2.13; p=0.93), but multiple antibiotic administration resulted in a lowered incidence of SIRS (OR, 1.81; 95% CI, 1.30-2.53; p=0.0005). The study concluded that single-dose prophylactic antibiotics are effective in PCNL and multiple dosing may reduce postoperative infection-related complications in high-risk patients (Table 1).

TRANSURETHRAL RESECTION OF THE PROSTATE

The use of prophylactic antibiotics has been studied most for transurethral resection of the prostate (TURP) compared to other urological surgeries. The meta-analysis study of Berry and Barratt [22] reported that the prophylactic use of antibiotics in low-risk patients reduces the incidence of bacteriuria from 26% to 9.1% and sepsis from 4.4% to 0.7%. In addition, in a meta-analysis of 4,694 patients from 28 studies, Qiang et al. [23] reported that prophylactic antibiotics reduce the incidence of bacteriuria, fever, and sepsis. A single dose of prophylactic antibiotic also imparted a preventive effect, and no differences were obtained according to the type of antibiotic administered. However, although there is insufficient evidence for using prophylactic antibiotics in holmium laser enucleation of prostate of photo-vaporization of the prostate other than TURP, the results are not expected to be significantly different from TURP (Table 1).

TRANSURETHRAL RESECTION OF BLADDER TUMOR

Endoscopic transurethral resection of bladder tumors (TURBt) is a first-line procedure for the diagnosis, staging, and treatment of visible tumors [24]. According to the World Health Organization, TURBt is classified as a clean-contaminated wound [25]. To date, evidence suggests that, unlike TURP [22], UTI rates were lower after TURBt [26]. In a recent meta-study about post-operative infection complications after TURBt, only 49 of the 1,536 study participants (3.2%) developed a UTI after surgery [27]. As a result, the European Society of Urology presented a weak recommendation for

the use of prophylactic antibiotics before a TURBt procedure, in patients at high risk of postoperative sepsis [28].

Recently, Bausch et al. [27] examined 7 studies involving 1,725 patients and analyzed the incidence of UTI and asymptomatic bacteriuria after surgery. They reported that the use of prophylactic antibiotics showed no benefit. However, their study had some limitations; the study did not evaluate potential risk factors such as age, operation time, tumor size, and preoperative midstream urine culture. Nevertheless, since the use of prophylactic antibiotics carries the risk of unwanted side effects and the risk of emerging multidrug-resistant pathogens, they should be used only when essential (Table 1).

CLEAN PROCEDURES

A urological procedure is considered clean if the surgical site is uninfected, there is no entry into the genitourinary tract, there is no evidence of inflammation, and an aseptic technique is followed. Examples include simple nephrectomy, planned scrotal surgery, vasectomy, or varicocelectomy [29]. Most guidelines recommend prophylactic use of antibiotics only in patients with risk factors. Several studies on radical nephrectomy have also confirmed that the rate of infectious complication is low after prophylactic antibiotic use, where third-generation cephalosporins were the primary antibiotics used [30-32]. The use of antibiotics was recommended in patients with risk factors based on data from non-urology studies [33,34]. Moreover, if the duration of surgery is longer than the half-life of the antibiotics, a short re-injection interval may be required to maintain an appropriate antibiotic concentration in the body [35].

CLEAN-CONTAMINATED PROCEDURES

Examples of clean-contaminated procedures in urology include prostatectomy, partial nephrectomy, and partial cystectomy [17]. It is essential for all patients undergoing clean-contaminated procedures to get antimicrobial prophylaxis. These recommendations are derived from data showing reduced infectious complications in prostatectomy using prophylactic antibiotics [36-40].

However, in actual practice, antibiotics are often abused after surgery for urogenital cancer, which is largely associated with hospital-acquired *Clostridium difficile* colitis. Efforts are needed to encourage greater adherence to an evidence-based approach for postoperative care [41].

PROCEDURES INVOLVING INTESTINE

Depending on the amount of spillage, urological procedures involving the intestine can be considered either clean or contaminated [29], and all patients should receive antibiotic prophylaxis. A recent systematic review study from Japan reported that administering prophylactic antibiotics before surgery is necessary. However, the use of antibiotics after surgery was inconclusive [42].

PROCEDURES INVOLVING PROSTHETICS

Since prosthetic infection has serious consequences, all patients undergoing such procedures should receive antimicrobial prophylaxis. However, recommendations were mainly drawn from non-urological data [43,44]. Recent studies of infected penile prosthesis suggest that 14-38% of infections were caused by microorganisms that could not be treated with standard prophylactic antibiotics, thereby suggesting additional antibiotics application [45].

VAGINAL SURGERY

Prophylactic antibiotics are also recommended for vaginal surgery, such as surgery for urinary incontinence. One recently reported systematic review and meta-analysis evaluated the role of prophylactic antibiotics for mid-urethral sling surgery [46]. Although there was considerable clinical heterogeneity among the articles used in the meta-analysis, prophylactic antibiotics were found to be ineffective in reducing the incidence of bacteriuria/UTI in women who underwent the surgery. Accordingly, the authors suggested that preoperative antibiotic prophylaxis for UTI prevention may not be necessary for mid-urethral sling alone.

CONCLUSIONS

In the field of urology, patients with a positive urine culture test before surgery should be administered relevant

antibiotics. In addition, repeated urine cultures should be done before surgery. In ureteroscopy and PCNL, single prophylactic antibiotic therapy is appropriate, although it is not adequate for high-risk patients. Although large data exists on the use of antibiotics in surgery, it is difficult to select the most appropriate antibiotic, especially in endoscopic surgery. Further research will help us find the safest way to reduce increasing antibiotic resistance and deliver the greatest benefit to the patient.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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