

Brief Original Article

The use of antibiotic prophylaxis in patients undergoing urologic procedures in an academic hospital Surabaya: A retrospective study

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Abstract

Introduction: Prophylactic antibiotics in urological procedures are essential to prevent postoperative infections. A different approach in selecting antibiotic prophylaxis according to the type of procedure is needed.

Methodology: A retrospective study was carried out at an academic hospital in Surabaya, Indonesia, by collecting medical records of patients who underwent urologic procedures within 2019- 2020, including microbiological data.

Result: One hundred seventy-nine urological procedures were assessed. Antibiotic prophylaxis was administered in the clean-contaminated and clean procedures (93.2% and 6.8%, respectively). Ceftriaxone was commonly used (69.3%), single-dose, one day before the surgery. Gram-negative bacteria were widely found in the urinary culture of patients (75.2%). *E. coli*, *K. pneumoniae*, and *P. aeruginosa* were dominating with low susceptibility to cephalosporins. ESBL-producing bacteria were *E. coli* (64%) and *K. pneumoniae* (89%).

Conclusions: The 3rd generation cephalosporins (ceftriaxone) are mostly used in urological procedures despite the low susceptibility against this antibiotic in cultured *E. coli*, *P. aeruginosa*, and *K. pneumoniae*. The aminoglycosides have relatively good activity and have been suggested in several guidelines for urologic procedures, such as prostate and urinary tract stone procedures. It is crucial to consider the incision site, type of procedure, and bacterial profile in the hospital to propose antibiotic prophylaxis guidelines.

Key words: antibiotic prophylaxis; urologic procedure; infection.

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Introduction

Antibiotic prophylaxis usage in urologic surgery is essential to prevent surgical site infection. The principles of selecting antibiotic prophylaxis in urology are the same as in other surgeries. However, there are still many differences, mainly depending on the type of procedure or which organ is involved and local practices [1-3]. The infections related to urologic procedures can be caused by different bacteria depending on the location of the incision. Guidance in determining the choice of prophylactic antibiotics in urology may vary because it is necessary to consider the procedure type, organ involved, and the institutional antibiotic susceptibility profile. Prophylaxis choice

needs to be evaluated for efficacy based on resistance profiles and post-operative complication rates [4].

Earlier studies have shown that antibiotic prophylaxis policies in Indonesia need to be improved. A study in India by Kakkar *et al.* estimated that 30-50% of antibiotics were used in hospitals for postoperative prophylaxis, and 30-90% of antibiotics were administered inappropriately [1,5]. A study conducted by Hadi *et al.* in Indonesia presented an audit of antibiotic prescriptions at two teaching hospitals in Indonesia. It showed that 21% were appropriate prescriptions, while 42% for most surgical prophylaxis were considered unnecessary [6]. Another study by Megawati *et al.* showed another example of irrational

antibiotic prophylaxis with 98.2% in surgery at a hospital in Semarang, Indonesia [7].

In an academic hospital Surabaya-Indonesia, the surgical prophylaxis guidelines recommend using cefazolin for clean-contaminated surgery, including urologic procedures [6]. However, the use of antibiotic prophylaxis in urologic procedures has not been evaluated yet in Indonesia. Therefore, we planned to conduct surveillance on antibiotic use in patients undergoing urologic surgeries in our hospital and compare the findings to the existing guidelines and literature.

Methodology

We carried out a retrospective study by collecting data from medical records. The data source was taken from medical records of patients undergoing urologic procedures in 2019-2020 and microbiology results of urinary specimens. This study is under ethical clearance issued by the ethical committee of Dr. Soetomo Academic General Hospital (ref. no. 0634/LOE/301.4.2/X/2021). Data were analyzed using descriptive statistics.

Table 1. Characteristics of the subjects that underwent the urologic operation.

| Characteristic | N (%) |
|-------------------------------------|------------|
| Age (years) | |
| 0-20 | 39 (21.8) |
| 21-40 | 21 (11.7) |
| 41-60 | 75 (41.9) |
| > 60 | 44 (24.6) |
| Male sex | 115(64.2) |
| Preoperation stay (days) | |
| 0-3 | 46 (25.7) |
| 4-7 | 51 (28.5) |
| 7-14 | 55 (30.7) |
| > 14 | 27 (15.1) |
| Postoperation stay (days) | |
| 0-3 | 82 (45.8) |
| 4-7 | 60 (33.5) |
| 7-14 | 22 (12.3) |
| > 14 | 15 (8.4) |
| Secondary diagnosis | |
| CKD | 28 (15.6) |
| Infection | 19 (10.6) |
| DM | 10 (5.6) |
| Hypertension | 4 (2.2) |
| Hemophilia | 1 (0.6) |
| Surgeon | |
| Urologist | 114 (63.7) |
| Resident | 65 (36.3) |
| Antibiotic prophylaxis usage | 161 (89.9) |

Results

We collected data from 179 patients undergoing urologic surgeries from 2019 to 2020. Most of the patients were aged 41-60 years of age; nine patients were under five years old. The average length of stay (LOS) was 16 days. Preoperative stays vary depending on the patient's condition; 55 (30.7%) of them are between 7-14 days. Postoperative stays ranged from 1 to 62 days; most patients (45.8%) stayed for 0-3 days (Table 1). The clean-contaminated procedure was performed in 164 patients; the clean procedure was conducted in 14 patients, and there was one contaminated procedure. Among the clean-contaminated and clean procedures, antibiotic prophylaxis was given in 93.2% and 6.8%, respectively (Table 2). The type of urologic procedure conducted in our hospital mainly included: placing a double-J stent, retrograde pyelography (RPG), cystoscopy, percutaneous nephrolithotomy (PCNL), ureterorenoscopy (URS), transurethral resection of the prostate (TURP), and transurethral resection of the bladder (TURB).

Ceftriaxone was often given as prophylaxis (69.3%) if the urinary culture did not reveal bacterial growth before the surgery. Other antibiotic choices were amikacin (6.1%), cefoperazone-sulbactam (6.1%), cefazolin (3.4%), and ciprofloxacin (1.1%). All of these antibiotics were given according to the urinary culture result. The majority of antibiotics prescribed belonged to the "watch" category (94%), and there was no "reserve" antibiotic given as prophylaxis. Prophylaxis antibiotic was given as a single dose in most patients (n = 103). Fifty-five patients received more than a one-day antibiotic (Figure 1). This condition was usually also for therapeutic purposes.

Table 2. Characteristic of antibiotic prophylaxis usage.

| The type of surgery | N (%) |
|------------------------------|------------|
| Clean-contaminated | 150 (93.2) |
| Clean | 11 (6.8) |
| Open procedure | 39 (24.2) |
| Endoscopic procedure | 113 (70.2) |
| Both open and endoscopic | 9 (5.6) |
| Urinary culture | |
| Positive urinary culture | 69 (42.9) |
| Negative culture | 92 (57.1) |
| Number of isolates | 105 (65.2) |
| Gram-negative | 79 (75.2) |
| Gram-positive | 24 (22.9) |
| Fungi | 2 (2) |
| ESBL producer | 30 (18.6) |
| <i>Escherichia coli</i> | 22 (73.3) |
| <i>Klebsiella pneumoniae</i> | 8 (26.6) |

ESBL: extended spectrum beta-lactamase.

The urine culture was performed in all patients (n = 179); 69 patients had a positive result and yielded 105 isolates (Table 2). Gram-negative bacteria were commonly found in the urinary culture of patients (75.2%). *E. coli*, *K. pneumonia*, and *P. aeruginosa* are the most prevalent bacteria found with low susceptibility to cephalosporins. ESBL-producing bacteria found were *E. coli* and *K. pneumonia* (Table 2, 3, and Figure 2).

The microbiology profile for the three most common bacteria showed high resistance to ceftriaxone and cefazolin. Ciprofloxacin has better susceptibility against *P. aeruginosa* than ceftriaxone or cefazolin (71.4% vs. 0% or 52.9%). Amikacin has the best in vitro activity against *Escherichia coli* (susceptibility, 97%), whereas levofloxacin, cefotaxime, and ceftazidime

have the lowest potency against *E. coli* (susceptibility: 21.2%, 24.2%, and 24.2% respectively). *K. pneumoniae* was highly susceptible to amikacin (100%) and resistant to most cephalosporins. Gentamicin showed good susceptibility against the three bacteria (Table 3).

We categorized the recommendations for antibiotic prophylaxis based on the type of urological procedure (Table 4). The comparison of the guidelines, including our hospital guidelines, is described in Table 5.

Discussion

In this study, cephalosporins are often used as an empirical treatment in our hospital since it is the most feasible and included in the hospital antibiotic use guidelines. This condition may be implicated in the development of ESBL-producing bacteria.

Figure 1. The type of antibiotic used and the duration of surgical prophylaxis.

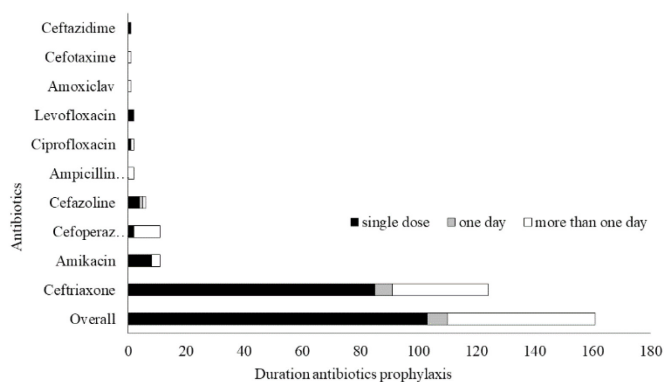


Figure 2. Microbiology profile-based urinary culture result (among 69 patients, 105 isolates).

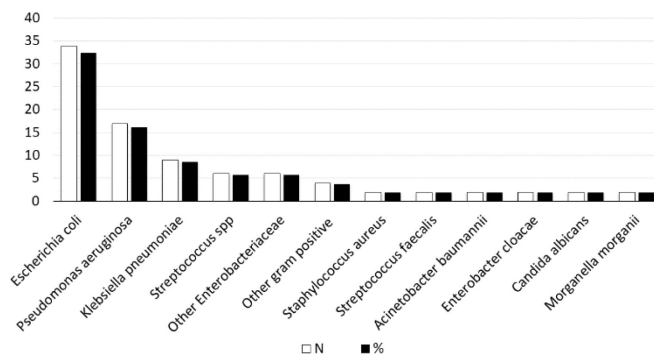


Table 3. Antibiotic susceptibility profile of bacterial isolates from urinary specimen.

| | <i>Escherichia coli</i> (n = 34) | <i>Pseudomonas aeruginosa</i> (n = 17) | <i>Klebsiella pneumoniae</i> (n = 9) |
|-----|-------------------------------------|---|---|
| AMC | 43.8% | 0% | 12.5% |
| CTX | 24.2% | 0% | 11.1% |
| CAZ | 24.2% | 52.9% | 11.1% |
| CRO | 26.5% | 0% | 11.1% |
| FEP | 28.1% | 25% | 11.1% |
| SCF | 66.7% | 70.6% | 22.2% |
| PTZ | 87.9% | 70.6% | 37.5% |
| SAM | 29% | 0% | 11.1% |
| IMI | 96.9% | 80% | 66.7% |
| MEM | 93.9% | 82.4% | 75% |
| AZT | 27.3% | 25% | 22.2% |
| CIP | 25% | 71.4% | 28.6% |
| LEV | 21.2% | 25% | 22.2% |
| AK | 97% | 80% | 100% |
| FOS | 88.2% | 50% | 50% |
| TGC | 80.6% | 7.7% | 12.5% |
| GEN | 60.6% | 100% | 75% |

AMC: Amoxicillin; CTX: Cefotaxime; CAZ: Ceftazidime; CRO: Ceftriaxone; FEP: cefepime; SCF: Cefoperazone-sulbactam; PTZ: Piperacillin-tazobactam; SAM: Ampicillin-sulbactam; IMI: Imipenem; MEM: Meropenem; AZT: Azithromycin; CIP: Ciprofloxacin; LEV: Levofloxacin; AK: Amikacin; FOS: Fosfomycin; TGC: Tigecycline; GEN: Gentamicin; Total bacteria: n = 60.

Table 4. Studies of antibiotic prophylaxis in urologic procedure.

| Study/Guideline | Year | Country | Treatment | Recommendation of AMP | Evidence GRADE | Route | Dosing | Duration |
|----------------------|------|---------|--------------------|---|----------------|------------|-------------|--|
| Prostate | | | | | | | | |
| Mrkobrada [4] | 2015 | England | TURP | 3rd generation Cephalosporin | ++++ | IV | single-dose | 1-2 hours preoperative |
| Yamamoto [3] | 2016 | Japan | TURP | Penicillin with Beta-lactamase inhibitor (BLI)* or 2nd generation Cephalosporin | ++++ | IV | single-dose | within 72 hours |
| | | | HoLEP/TUEB | First- or second-generation cephalosporins or penicillins with BLIs*, or aminoglycosides | +++ | IV or oral | single-dose | within 48 hours |
| Stone surgery | | | | | | | | |
| Mrkobrada [4] | 2015 | England | ESWL | Fluoroquinolones | +++ | IV | single-dose | 30 minutes before surgery |
| | | | PCNL | Fluoroquinolones, or 3rd generation cephalosporins, or 1st generation cephalosporins, or aminoglycosides | +++ | IV | single-dose | 1 hour before surgery |
| Yamamoto [3] | 2016 | Japan | SWL | Only for high-risk (bacteriuria, infected stone, endoscopic manipulation repeated ESWL history of febrile UTI, stone size ≥ 2 cm) with 2nd- or 3rd-generation cephalosporins, or penicillins with BLIs*, or aminoglycosides, or oral quinolones or ST | ++++ | IV | single-dose | Not mentioned |
| | | | PCNL | First- or second-generation cephalosporins, or penicillins with BLIs*, or aminoglycosides | ++++ | oral | single-dose | preoperative antimicrobial therapy one week |
| | | | TUL | First- or second-generation cephalosporins, or penicillins with BLIs*, or aminoglycosides | ++++ | IV | single-dose | |
| Deng [8] | 2017 | China | URL | Not mentioned | +++ | IV or oral | single-dose | minimal 1 hour before surgery |
| Yu [9] | 2020 | China | PCNL | Fluoroquinolones, or penicillins with BLIs*, or 3rd generation cephalosporins, or 1st generation cephalosporins, or aminoglycosides | ++++ | IV | single-dose | Minimal 1 hour before surgery, maximal seven days (AMP+GEN or CIP) |
| Paediatric | | | | | | | | |
| Yamamoto [3] | 2016 | Japan | Clean | First- or second-generation cephalosporins | ++++ | IV | single-dose | within 24 hours |
| | | | Clean-contaminated | First- or second-generation cephalosporins, or penicillins with BLIs† with oral cephalosporins | ++++ | IV or oral | single-dose | for IV within 72 hours, for oral within seven days |

AMP: ampicilin; BLI: beta-lactamase inhibitors; CIP: ciprofloxacin; ESWL: extracorporeal shock wave lithotripsy; ; HoLEP: Holmium Laser Enucleation of the Prostate; GEN: gentamicin; IV: intavenous; PCNL: percutaneous nephrolithotomy intravenously; TUEB: Transurethral Enucleation with Bipolar Energy; TUL: transurethral uterolithotripsy; TURP: transurethral resection of the prostate; UTI: urinary tract infection.

Table 5. The antibiotic prophylaxis guideline of AUA, EUA, and Academic General Hospital Surabaya-Indonesia (AGHS).

| PROSTATE | | | | | | | | | |
|--------------------------------------|-----------|--|-------------|----------------|--|-------------|---------------|------------|-------------|
| | AUA Route | Antibiotic | Duration | EAU Route | Antibiotic | Duration | AGHS Route | Antibiotic | Duration |
| TRPB | IV | Cefazoline or TMP-SMX | Single-dose | IV or oral | TMP or TMP-SMX, 2nd or 3rd gen cephalosporin or penicillin + beta-lactam inhibitor | Single-dose | IV | Cefazoline | Single-dose |
| TURP | IV | Cefazoline or TMP-SMX | Single-dose | IV or oral | TMP or TMP-SMX, 2nd or 3rd gen cephalosporin or penicillin + beta-lactam inhibitor | Single-dose | IV | Cefazoline | Single-dose |
| STONE MANIPULATION | | | | | | | | | |
| | AUA Route | Dosing | Duration | EAU Route | Dosing | Duration | AGHS Route | Dosing | Duration |
| ESWL | IV | TMP-SMX, 1st or 2nd gen cephalosporin | Single-dose | No Prophylaxis | | | IV | Cefazoline | Single-dose |
| NON-ESWL | IV | 1st or 2nd cephalosporin, or Aminoglycoside and metronidazole, or aztreonam and metronidazole, or Aminoglycoside and clindamycin, or aztreonam and clindamycin | Single-dose | IV | TMP or TMP-SMX, 2nd or 3rd gen cephalosporin or penicillin + beta-lactam inhibitor | Single-dose | IV | Cefazoline | Single-dose |
| PEDIATRIC | | | | | | | | | |
| | AUA Route | Dosing | Duration | EAU Route | Dosing | Duration | AGHS Route | Dosing | Duration |
| entry into the urinary tract | IV | Aminoglycoside (Gentamicin) or cephalosporin | Single-dose | IV | Aminoglycoside (Gentamicin) | Single-dose | Not explained | | |
| without entry into the urinary tract | IV | Aminoglycoside (Gentamicin) or cephalosporin | Single-dose | IV | Cefazoline | Single-dose | | | |

AUA: American Urological Association; EAU: European Association of Urology, ESWL, extracorporeal shock wave lithotripsy; IV, intravenous; TURP, transurethral resection of the prostate; TMP: Trimethoprim; TRPB: Transrectal ultrasound-guided prostate biops; SMX: sufamethoxazole; AGHS: Academic General Hospital Surabaya

This study's high ESBL rate of *E. coli* and *K. pneumoniae* may also be related to more extended hospital stays. Patients who stay longer in the hospital are usually admitted from an emergency department which needs prior management and preparation before the surgery, such as malignant cases with a need for supportive treatment or renal failure, which requires hemodialysis before the surgery. Postoperative stay also varies (1-62 days); mostly (45.8%) for 0-3 days. The rest usually need further treatment due to the underlying disease or complication. Complications due to healthcare-associated urinary tract infections include cystitis, pyelonephritis, and urosepsis [15].

Despite following existing guidelines for antibiotic prophylaxis, our urinary culture results showed that cephalosporins had low susceptibility to the most common bacteria. It is in line with a study by Yamasaki in 2015, which stated the high resistance of cephalosporins to UTIs caused by *K. pneumoniae* in Dr. Soetomo Hospital [16]. In Japan and Taiwan, the incidence of pre- or post-surgery UTIs also indicated resistance to cephalosporins and gentamicin [17]. The Japanese Association for Infectious Diseases and the Japanese Society of Clinical Microbiology noted an increase in levofloxacin-resistant *E. coli* from national surveillance data in 2015-2016 [18]. In addition, European studies also showed that the same Gram-negative uropathogens are also highly resistant to cephalosporins and fluoroquinolones [19,20]. The high rate of ESBL-producing bacteria in this study may also give a point to consider choosing antibiotic prophylaxis, which has activity against these bacteria.

Our results show that amikacin is the best antibiotic sensitive to *E. coli*, *P. aeruginosa*, and *K. pneumoniae* (approximately 97%), based on existing studies in Japan and Europe [17,20]. However, amikacin in the guidelines has not been included as a choice in antibiotic prophylaxis for urological intervention, but it remains an alternative in the event of cephalosporin resistance [3,4,8,9]. In our study, gentamicin has a good susceptibility profile against *E. coli*, *P. aeruginosa*, and *K. pneumoniae*, so it can be an option to give as prophylaxis, as suggested in several studies and guidelines, especially for prostate procedures, stone manipulation, or pediatric surgery. However, patients can have renal function disorders that may not allow for aminoglycoside use.

According to the literature collected, the study by Yamamoto *et al.* stated that prostate procedures such as TURP, HoLEP (holmium laser enucleation of the prostate), TUEB (transurethral enucleation with bipolar) regularly use a single-dose combination of

ampicillin with a beta-lactamase inhibitor or second-generation cephalosporin as a prophylactic antibiotic. The antibiotic administration is started 72 hours before TURP and 48 hours before HoLEP/TUEB [3]. The study of Mrkobrada *et al.* declared that patients undergoing TURP need a single dose of 3rd generation cephalosporin 1-2 hours before surgery [4]. On the other hand, a study by Demitras *et al.* in Turkey showed that only 25.7% of urologists use single-dose antibiotic prophylaxis during transrectal prostate biopsy [11].

Previous studies of stone surgery suggested that second and third-generation cephalosporin, oral fluoroquinolones, or aminoglycosides be given seven days before surgery [3,4,8,9]. However, only the study of Mrkobrada *et al.* stated that ESWL needs antibiotic prophylaxis 30 minutes before surgery and 1 hour before PCNL [4]. The AUA guidelines recommend that cefazolin (first-generation cephalosporin) or trimethoprim-sulfamethoxazole (TMP-SMX) be administered in a single IV dose. Nonetheless, a more elaborate explanation is carried out by the EAU guidelines suggesting the use of TMP/TMP-SMX, 2nd or 3rd generation cephalosporin, or ampicillin-sulbactam with a single dose IV [12].

The guideline from an academic general hospital Surabaya in 2018 stated that in clean procedures with a risk of infection (urologic procedures included), a single-dose, dripped intravenous antibiotic prophylaxis should be given 30-60 minutes before initiation in the operating room within 15-30 minute intervals (dissolved in 100 ml of normal saline in adult) [13]. In this study, it was shown that the antibiotic prophylaxis used followed the hospital local guidelines. However, the policy does not provide any other antibiotic prophylaxis regarding the type of surgery.

The study of Sharma *et al.* demonstrated using a second-generation cephalosporin as a prophylactic antibiotic for urologic procedures [1]. Meanwhile, a study in Korea by Kim *et al.* with 77 patients who underwent transrectal ultrasonography prostate biopsy (TRUS-Bx), exhibited cephalosporins due to the high resistance quinolones associated with *E. coli* in prostate procedures [14].

We have some limitations in our study. Our data collection was mainly based on medical records. In addition, other information related to the procedure, such as surgical site infection incidence, was recorded manually in a separate document; hence we cannot include the incidence of postsurgical wound infection and UTI in patients given prophylactic antibiotics. Nevertheless, this article underlines the need for local guidelines that consider the location of the incision,

whether it passes through the urinary tract or not, and the type of procedure as we face different bacteria or normal flora during the incision. Regarding the antibiotic sensitivity test results, it is necessary to review the selection of relevant antibiotics and conduct a broader range of the study on this issue.

Conclusions

Third-generation (ceftriaxone) is the antibiotic most often used as prophylaxis in urological procedures in a teaching hospital in Indonesia. However, the culture results of urine specimens mainly are gram-negative bacterial bacilli that are highly resistant to this class of antibiotics. Aminoglycosides have an excellent sensitivity against Gram-negative bacteria. It can be used as an option for Antimicrobial prophylaxis. The high ESBL rate in the urine culture is also essential for determining antibiotic prophylaxis. It is necessary to review local guidelines in antibiotic prophylaxis that specifically consider the incision site, type of procedure, local bacterial mapping in the hospital, and monitoring of the surgical site infection.

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