

Brief Original Article

A short course of antimicrobial therapy for asymptomatic bacteriuria is safe and effective before urologic procedures

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Abstract

Introduction: In the presence of asymptomatic bacteriuria (ASB) before the urological procedure, the duration of antimicrobial treatment is controversial. This study aims to evaluate whether a short course of antimicrobial therapy is safe and effective in cases with ASB before urological procedures.

Methodology: We retrospectively reviewed adult patients who had ASB before undergoing several urological procedures between 2011 and 2019. The patients received a single dose of an appropriate parenteral antibiotic, determined by antimicrobial sensitivity testing, 30 to 60 minutes before the urological procedure. If a urinary catheter was placed post-procedure, a second dose was given.

Results: A total of 293 patients who had ASB before undergoing several urological procedures were included in the study. The total number of procedures was 328. Female/male ratio was 92 (31.4%)/201 (68.6%). The mean age was 63.7 ± 14.9 years. The most common isolated microorganisms were *Escherichia coli* (155 [47%]), *Klebsiella pneumoniae* (38 [11.6%]), and *Pseudomonas aeruginosa* (28 [8.5%]). The most common antimicrobial used was ertapenem. A second dose antimicrobial was given for 290 procedures due to a urinary catheter after a urological procedure. The mean hospitalization time was 3.97 ± 3.42 days. None of the patients developed infectious complications.

Conclusions: This study has demonstrated that a single dose of parenteral antimicrobial drug administered 30-60 minutes before the urologic procedures and a second dose in the presence of a post-procedure catheter, was adequate to prevent post-procedure septicemia and urinary tract infection.

Key words: Antimicrobial; asymptomatic bacteriuria; infectious complications; urological procedures.

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Introduction

Asymptomatic bacteriuria (ASB) is seen in some healthy female populations and many women or men with genitourinary tract abnormalities [1]. ASB can be defined as the colonization of the microorganism in the urinary system. Although in many clinical situations ASB is harmless, many patients with ASB are treated unnecessary [2-4]. Especially, long-term antimicrobial therapy of ASB may select for superinfection with more antimicrobial-resistant microorganisms, the increased risk of drug-drug interaction and side effects, prominent collateral damage, including bacterial vaginosis, vaginal candidiasis and *Clostridium difficile*-associated disease, increase in cost and negatively affect the quality of life. It is crucial to identify the special clinical settings for which screening of ASB is beneficial and treatment [4-6].

Asymptomatic bacteriuria treatment is recommended only in pregnant women or the patients

before undergoing urologic surgical procedures associated with mucosal trauma by the Infectious Diseases Society of America (IDSA) [1]. However, a recent study from the Netherlands suggested that selected low-risk pregnant women might not have treatment due to the low ratio of complications [7]. Similarly, two recent studies have shown that ASB screening and treatment before urological procedures do not affect the development of postoperative infectious complications [8,9].

In the presence of ASB before the urological procedure, the duration of antimicrobial treatment is important to prevent the undesired effects of antimicrobials. Although short-course treatment may not eradicate the microorganism from the urinary system, it can prevent bacteremia and sepsis. In our previous study, a single dose of antimicrobial was given to 31 patients 30 to 60 minutes before the surgical procedure and a second dose if a catheter was placed

postoperatively, and none of the patients had no severe infectious complications [10]. We reviewed the effectiveness of single or two-dose antimicrobial treatment, and post-procedure infectious complications in a large group of patients in the current study.

Methodology

We retrospectively reviewed adult patients who had ASB before undergoing several urological procedures between 2011 and 2019 in Pamukkale University Hospital in Denizli, Turkey. This study was conducted on the approval of the Medical Ethics Committee of Pamukkale University, Denizli, Turkey (date: 27 May 2020; resolution number: 10) and adhered to the principles of the Declaration of Helsinki.

Urologic procedures included transurethral surgery of the prostate (TURP), transurethral resection of bladder tumor (TURBT), or ureteroscopy (including lithotripsy), double J insertion and exchange, cystostomy insertion, urethra dilation, nephrostomy tube insertion or exchange, retrograde pyelography, extracorporeal shock wave lithotripsy (ESWL), ureterorenoscopy, urethra resection, bladder fistula repair, cystectomy, nephrectomy, urethroplasty, prostatectomy, transrectal biopsy, urodynamic study (UDS), cystoscopy and intravesical bacille Calmette–Guerin (BCG) therapy.

Urine cultures were obtained 48 to 72 hours before the urological procedure. ASB was defined as the isolation of $\geq 10^5$ colony-forming units/mL in the absence of symptoms or signs of urinary tract infection (UTI) such as fever, dysuria, frequency, urgency, pelvic or flank pain, costovertebral angle tenderness. Because of the retrospective design of the study, antimicrobial susceptibility was determined using Clinical and Laboratory Standards Institute criteria in 2011-2015 [11] and the European Committee on Antimicrobial

Susceptibility Testing criteria in 2016-2019 [12]. According to antimicrobial sensitivity test results, a single dose of appropriate parenteral antibiotic was given to the patients 30 to 60 minutes before the urological procedure. If the patients had a post-procedure urinary catheter, a second antimicrobial dose was given following the recommended dose interval. All patients were followed clinically for the signs of UTIs and sepsis after the procedure. The patients were also evaluated for UTIs and sepsis on the 14th day after discharge in the outpatient clinic. Additionally, the medical records of all patients were checked for symptoms and signs of infections.

Statistics

Data are shown as numbers and percentages. Continuous variables with normal distribution are given as the mean \pm standard deviation. All analyses were done with SPSS, version 23 (IBM, Chicago, IL, USA).

Results

The study included a total of 328 urological surgical procedures which were performed in 293 patients with ASB. Female/male ratio was 92 (31.4%)/201 (68.6%). The mean age was 63.7 ± 14.9 years. The urologic procedures were shown in Table 1. The most common isolated microorganisms were *Escherichia coli* (155 [47%]), *Klebsiella pneumoniae* (38 [11.6%]), and *Pseudomonas aeruginosa* (28 [8.5%]) (Table 2). The most common antimicrobial used was ertapenem because of the frequent occurrence of extended-spectrum beta-lactamase (ESBL) producing *E. coli* and *K. pneumoniae* at 66% (109/166) and 86% (37/43) respectively (Table 3). A second dose antimicrobial was given for 290 procedures due to the presence of a urinary catheter after the procedure.

Post-procedural 66 urine cultures were obtained. Microorganisms were isolated in 21 (32%) urine

Table 1. Urologic procedures.

Urologic procedures	N = 328 (%)
Double J insertion and exchange	45 (13.7)
Nephrostomy tube insertion or exchange	32 (9.8)
Transurethral resection of bladder tumor	42 (12.8)
Transurethral prostatic resection	35 (10.6)
Ureteroscopy (including lithotripsy)	27 (8.2)
Urethra Dilation	26 (7.9)
Cystoscopy	25 (7.6)
Retrograde pyelography	16 (4.9)
Urethroplasty	10 (3.0)
Urodynamic study	10 (3.0)
Other*	60 (18.3)

*: Urethra resection, bladder fistula repair, cystectomy, nephrectomy, extracorporeal shock wave lithotripsy, radical prostatectomy, transrectal biopsy, intravesical bacille Calmette–Guerin therapy.

Table 2. Isolated microorganism causing asymptomatic bacteriuria before the urological procedures.

Microorganism	N= 328 (%)
<i>Echerichia coli</i>	154 (47)
<i>Klebsiella pneumoniae</i>	38 (11.6)
<i>Pseudomonas aeruginosa</i>	28 (8.5)
<i>Candida</i> species	28 (8.5)
<i>Enterococcus faecalis</i>	25 (7.6)
<i>Enterococcus faecium</i>	12 (3.6)
Polymicrobial	13 (4.0)
Other*	30 (9.2)

*: *Citrobacter freundii*, *Staphylococcus aureus*, *Serratia marcescens*, *Acinetobacter* spp., *Stenotrophomonas maltophilia*, *Burkholderia cepacia*, *Morganella morganii*, *Enterobacter* spp., *Streptococcus agalactiae*, coagulase- negative *Staphylococcus* spp.

cultures. All of these patients were asymptomatic. These microorganisms were the same species and had the same antimicrobial sensitivity pattern to those isolated from pre-procedure urine cultures with three exceptions. None of the patients developed infectious complications during the hospitalization and 14 days after discharge. The mean hospitalization time was 3.97 ± 3.42 days.

Discussion

Our study showed that a single dose or two doses of antimicrobial therapy was effective in preventing severe infectious complications such as upper UTI and septicemia following urological procedures in patients with pre-procedure ASB. We had previously come to this conclusion in a small prospective study including 31 procedures [10]. That study showed that short-course treatment (one or two doses) of ASB resulted in a significantly shorter length of stay and cost of antimicrobial therapy, while long term treatment was associated with subsequent isolation of a greater number of resistant microorganisms [10]. Incompatible with our previous findings, in our current study, no infectious complications developed over 300 procedures.

The Infectious Diseases Society of America recommended ASB should be detected and treated before undergoing endourologic surgical procedures associated with mucosal trauma [1]. However, two recent studies have reported that ASB screening and treatment before urological procedures did not alter the development of postoperative infectious complications [8, 9]. In both studies, antimicrobial prophylaxis was given according to the European Association of Urology (EAU) guidelines [13]. However, no information has been provided on whether the antimicrobial given in prophylaxis was effective to the microorganism isolated from pre-procedural urine culture [8,9]. Antibiotic administered as prophylaxis before surgery might be effective for the microorganism isolated from a urine culture, which, we believe that, also reflects the case in our study.

We included miscellaneous urologic procedures. Before some procedures such as TURP, TURBT, ureteroscopy including lithotripsy, which causes mucosal breaching, the patients should be screened and treated for ASB [1,13]. In these procedures, bacteriuria is a well-identified risk factor for postoperative infectious complications [14-17].

The European Association of Urology Guidelines on urological infections accepted that placement/exchanges of nephrostomy tubes and

Table 3. Antimicrobial drugs used for asymptomatic bacteriuria.

Drugs	N = 328 (%)
Ertapenem	107 (32.5)
Ceftriaxone	58 (17.7)
Imipenem	33 (10.1)
Fluconazole	28 (8.5)
Meropenem	16 (4.9)
Ampicillin-sulbactam	10 (3.0)
Piperacillin- tazobactam	10 (3.0)
Teicoplanin	9 (2.7)
Ampicillin	8 (2.4)
Ceftazidime	6 (1.8)
Cefoperazone-sulbactam	5 (1.5)
Dual antimicrobial drugs [#]	21 (6.4)
Other*	17 (5.2)

[#]: Ceftriaxone- linezolid, meropenem - ampicillin-sulbactam, meropenem-amikacin, meropenem-fosfomycin, meropenem -colistin, piperacillin/tazobactam-fluconazole, ertapenem-vancomycin, ertapenem-linezolid, ertapenem-teicoplanin, ceftriaxone-fluconazole, imipenem-fluconazole, imipenem-teicoplanin; *: Trimethoprim-sulfamethaxazole, ciprofloxacin, fosfomycin, cefazolin, cefuroxime aksetil, cefepime, vancomycin, linezolid, daptomycin, amikacin.

internal stents in the presence of ASB are considered as a risk factor for infectious complications. Screening and treatment of ASB before placement/exchanges of nephrostomy tubes and internal stents have been recommended in the EAU guideline [11]. However, there is no recommendation regarding the screening and treatment of ASB in these procedures by IDSA [1]. Also, not much data was found in the literature between the relationship of the presence of ASB before retrograde pyelography and the development of UTI or sepsis. It was reported that febrile infectious complications were more common after the retrograde pyelography or single or double J stenting despite periprocedural antimicrobial treatment if pre-procedural pyuria existed. Unfortunately, ASB has not been screened before the procedures in that study [18]. In our series, appropriate antimicrobial drugs were administered before these urologic procedures in the presence of ASB.

The presence of ASB is generally not considered as a risk factor in diagnostic and therapeutic procedures such as cystoscopy and intravesical BCG therapy, so screening and treatment of ASB are not necessary for these conditions [1, 19]. There are also data showing that intravesical BCG treatment is more effective in the presence of chronic ASB [20, 21]. Although symptomatic UTI after cystoscopy was more common in patients with ASB than in uninfected patients, the incidence was < 4%, so pretreatment antimicrobial therapy does not appear to be necessary [22]. However, we used antimicrobial drugs for ASB before these procedures because of the possibility of performing an

unplanned biopsy and the occurrence of consequent mucosal trauma.

The urodynamic study does not have a risk of breakage of the mucosa, therefore, ASB may not be treated before these procedures. In a previous study, the use of antimicrobial prophylaxis did not alter the post-procedure infectious complication risk, independently of the presence of ASB [23]. However, in another study, single-dose antibiotic prophylaxis before UDS even without ASB, has been shown to reduce the incidence of post-procedure UTI [24]. Also, EAU recommended that antimicrobial prophylaxis should be considered in cystoscopy and urodynamic studies, in case of individual risk factors for UTI such as the presence of ASB [13].

Antimicrobial prophylaxis is recommended for the transrectal prostate biopsy which is accepted as a high-risk class III/contaminated procedure [13, 25]. However, ASB screening and treatment is not routinely recommended before prostate biopsy because of microorganisms causing UTI after the procedure are mostly the members of the rectal flora. When routine antibiotic prophylaxis and enema is performed, it is not beneficial to take routine urine culture before biopsy [26, 27]. However, Lindstedt *et al.* [28] reported that bacteriuria before the biopsy is a major risk factor for post-biopsy infective complications.

The first limitation of our study is that we included miscellaneous urological procedures, however, our large sample size enables us to determine the findings entirely, despite the inclusion of various procedures. The second limitation is the retrospective nature of our study. Prospective randomized studies are needed to evaluate the effectiveness of the short-term treatment of ASB, particularly before procedures in which there is a lack of consensus on ASB screening and treatment, such as cystoscopy and UDS.

Conclusions

We found that a single dose of parenteral antimicrobial drug administered 30-60 minutes before the urologic procedures and a second dose in the presence of a post-procedure catheter, was effective to prevent postprocedure septicemia and UTI. However, further prospective studies are required to determine procedure-specific approaches for ASB screening and treatment.

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