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Original Article

Efficacy of two-time prophylactic intravenous administration of tazobactam/piperacillin for transrectal ultrasound-guided needle biopsy of the prostate

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ABSTRACT

Background: Prevalence of fluoroquinolone (FQ)-resistant *Escherichia coli* has been recently increasing worldwide. We analyzed the incidence and characteristics of acute bacterial prostatitis after transrectal ultrasound-guided needle prostate biopsy (TRUSP-Bx) with prophylactic tazobactam/piperacillin (TAZ/PIPC) treatment as an alternative regimen.

Methods: A total of 391 patients who underwent TRUSP-Bx were included in the study. All patients received intravenous TAZ/PIPC (4.5 g) 30 minutes before and 6 hours after TRUSP-Bx.

Results: Acute bacterial prostatitis developed in six patients (1.5%); the frequency of its occurrence was significantly higher in patients in whom rectal disinfection was not performed ($P < 0.05$). These six patients developed clinical symptoms of acute bacterial prostatitis a median of 24 hours after the biopsy. *Escherichia coli* was isolated in urine or blood bacterial cultures in four cases, and *Klebsiella pneumoniae* in two cases. All of the isolated organisms showed excellent sensitivity to TAZ/PIPC.

Conclusions: The incidence rate of acute prostatitis with prophylactic TAZ/PIPC was consistent with those reported previously with FQ-based regimens, despite the favorable sensitivity of isolated organisms. Two-time regimen of TAZ/PIPC may not always prevent the post-TRUSP-Bx infection, possibly due to the pharmacokinetic characteristics of TAZ/PIPC. However, if each case was considered individually to select the best setting and frequency of dosage of TAZ/PIPC, this can be an optimal prophylaxis in the era of widespread FQ-resistant microorganisms.

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Introduction

Transrectal ultrasound-guided needle prostate biopsy (TRUSP-Bx) is generally accepted as a standard procedure for the diagnosis of prostate cancer. Bacterial infection is one of the most serious complications associated with TRUSP-Bx. The incidence of bacterial complications, such as acute prostatitis, ranges from 1% to 5% [1–3]. Therefore, pre-procedure antibiotic prophylaxis is usually performed to reduce the risk of bacterial infection. Because fluoroquinolones (FQs) have a broad spectrum of activity against a majority of Gram-negative bacteria and exhibit excellent prostatic tissue bioavailability [4–6], they are widely used as antibiotic prophylaxis with TRUSP-Bx.

However, prevalence of FQ-resistant *Escherichia coli* has been recently increasing worldwide [7–10], and a trend of increasing resistance to FQs has also been observed in Japan [7,8]. Actually, some previous reports have demonstrated emergence of FQ-resistant *E. coli* infections following TRUSP-Bx after prophylactic use of FQs [11,12]. Therefore, other prophylactic antibiotic regimens need to be considered to decrease the risk of infectious complications of TRUSP-Bx in the era of widespread FQ-resistant microorganisms.

In the present study, we evaluated the prophylactic efficacy of intravenous tazobactam/piperacillin (TAZ/PIPC) for use with TRUSP-Bx. We analyzed the incidence rate, clinical characteristics,

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and bacterial cultures of acute bacterial prostatitis occurring after TRUSP-Bx with prophylactic TAZ/PIPC administration.

Materials and methods

A total of 391 patients who underwent TRUSP-Bx at Ishikawa Prefectural Central Hospital, Kanazawa, Japan between January 2010 and August 2012 were included in our study. The indications for TRUSP-Bx were as follows: elevation of serum prostate-specific antigen levels or aberrant findings on digital rectal examination (DRE) based on the criteria of a mass prostate-specific antigen examination in Kanazawa City as described previously [13]. Before the prostate biopsy, all patients underwent urinalysis, DRE, and transrectal ultrasound to confirm the absence of signs of urinary tract infections. All biopsies were TRUSP-Bx, and an automatic biopsy gun with an 18-gauge needle was used to obtain 8-core biopsies. None of the patients received an enema before the biopsy. Disinfection of the rectum by using an iodine swab was at the discretion of the attending physician. All patients were administered intravenous TAZ/PIPC (4.5 g) twice: 30 minutes before the biopsy and 6 hours after it. All patients were hospitalized at our institution for one night to observe any possible complications, such as hematuria, fever, urinary retention, and anal bleeding. Patients without signs of these complications were discharged the following morning.

Acute bacterial prostatitis caused by TRUSP-Bx was diagnosed using these criteria: core body temperature > 38°C, the presence of leukocytes in the urine sediment, the isolation of any microorganisms from urine or bladder cultures, and tenderness of the prostate found on DRE within 7 days of the biopsy. Before the initiation of antibiotic treatment, all microorganisms isolated from urine or blood cultures were tested for antibiotic susceptibility. The minimum inhibitory concentration (MIC) was measured using the broth microdilution method, based on the criteria of the Clinical and Laboratory Standards Institute (CLSI). Drug susceptibility was determined based on the breakpoint MIC established by the CLSI.

We recorded the clinical characteristics and results of bacterial cultures in patients diagnosed with acute bacterial prostatitis. In addition, all patients were divided into two groups as follows: patients with acute bacterial prostatitis after TRUSP-Bx (Group 1) and patients without bacterial complications after TRUSP-Bx (Group 2). We then analyzed the risk factors for acute bacterial prostatitis after TRUSP-Bx.

The Chi-square test was used to compare patients' background characteristics between the two groups. The Mann-Whitney *U* test was used for comparison of the age distribution between the two groups. In all analyses, which were performed using the SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA), $P < 0.05$ was considered statistically significant.

Results

A total of 391 patients, 333 undergoing a first biopsy and 58 undergoing a second biopsy, were enrolled in this study. None of the patients had any definite clinical signs of a urinary tract infection before the biopsy based on urinary analysis. The patients' background characteristics in Group 1 and Group 2 are shown in Table 1. Acute bacterial prostatitis after TRUSP-Bx occurred in six patients (1.5%). There was no significant difference between Group 1 and Group 2 in patients' background characteristics regarding median age, median prostate volume, prevalence of diabetes mellitus, and the median International Prostate Symptom Score, and past histories of TRUSP-Bx. Enforcement of rectal disinfection was significantly lower in Group 1 than in Group 2 ($P < 0.05$).

Table 2 summarizes the data from the six patients who developed acute bacterial prostatitis after TRUSP-Bx. The median age of the patients was 66 years (range, 54–74 years). These patients developed clinical symptoms of acute bacterial prostatitis a median of 24 hours after the biopsy (range, 6–168 hours). *E. coli* was isolated in four cases, and *Klebsiella pneumoniae* in two cases from their bacterial cultures. For the treatment of the infections, cephalosporins were used in four patients, carbapenems in one patient, and FQs in one patient. All patients received immediate antibiotic administration, and the median duration of treatment was 7 days. All patients were successfully treated without incidence of septic shock or death.

Drug susceptibility of the bacterial isolates to a wide range of antibiotics was also evaluated (Table 3). One isolate was of an extended-spectrum β-lactamase producing bacteria. All bacteria isolated from blood and/or urine of the patients with acute bacterial prostatitis showed excellent sensitivity to TAZ/PIPC. In addition,

Table 1
Patients' characteristics and comparisons between Group 1 and Group 2.

Categories	Group 1 ($n = 6$)	Group 2 ($n = 385$)	*P*
	Acute prostatitis	No bacterial complications	
Median age (range)	66 (54–74)	68 (51–88)	0.2
Median prostate volume (mL)	21.4	27.9	0.33
Rate of diabetes mellitus (%)	0 (0.0)	70 (18.2)	0.25
Median IPSS score	11.5	13.0	0.33
Rate of rectum sterilization (%)	2 (33.3)	312 (81)	0.0035
No. of re-biopsy	2 (33.3)	55 (14.3)	0.19

IPSS, international prostatic symptoms score.

Table 2
Details of patients with acute bacterial prostatitis after transrectal prostate needle biopsy.

No.	Age (yr)	Biopsy numbers	Interval [a]	Therapy	Culture		Isolated organisms
			(hr)	Antibiotics (g/d) × d	Urine	Blood	
1	60	1	6	MEPM 1.5 g × 7	−	+	*Escherichia coli*
2	68	2	24	SBT/CPZ 2 g × 9	+	−	*E. coli*
3	74	1	168	CAZ 2 g × 9	+	+	*E. coli*
4	64	1	6	CTM 3 g × 6	−	+	*Klebsiella pneumoniae*
5	68	1	24	LVFX 500 mg × 7	−	+	*E. coli*
6	54	2	72	CTRX 2 g × 5	−	+	*K. pneumoniae*

[a] Interval from biopsy to appearance of acute bacterial prostatitis.
CAZ, ceftazidime; CTM, cefotiam; CTRX, ceftriaxone; LVFX, levofloxacin; MEPM, meropenem; SBT/CPZ, sulbactam/cefoperazone.

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