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Original article

Clinical effectiveness and safety of tazobactam/piperacillin 4.5 g for the prevention of febrile infectious complication after prostate biopsy

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ABSTRACT

We investigated the clinical effectiveness and safety of tazobactam/piperacillin (TAZ/PIPC) in a 1:8 ratio, a β-lactamase inhibitor with penicillin antibiotic, for the prevention of febrile infectious complication after prostate biopsy. Each patient received a single dose of TAZ/PIPC 4.5 g, 30 min before the biopsy in Group 1 or TAZ/PIPC 4.5 g twice, once 30 min before and once after the biopsy (just before discharge or 5 h after the biopsy), in Group 2. Estimation of efficacy was performed within 1-month after prostate biopsy. Clinical diagnosis of febrile infectious complication was based on a body temperature elevation greater than 38 °C. Infectious complication after prostate biopsy was detected in 2.5% (4/160 patients) in Group 1 and in 0.45% (2/442 patients) in Group 2. All of the patients with febrile infectious complication had risk factors: 5 patients had voiding disturbance, 2 patients had diabetes mellitus and 1 patient had steroid dosing. In group 1, 88 patients had at least one risk factor and 72 patients had no risk factors. Of the patients with a risk factor, 4 had febrile infectious complication after prostate biopsy, but there was no significant difference between the two groups. In group 2, 87 patients had at least one risk factor and 255 patients had no risk factors. The patients with a risk factor had febrile infectious complication significantly more frequently than did patients without a risk factor ($P = 0.038$). Therefore, TAZ/PIPC appears to be effective as preoperative prophylaxis against the occurrence of febrile infectious complication after prostate biopsy.

1. Introduction

Transrectal ultrasound-guided needle biopsy of the prostate is generally accepted as the standard procedure to detect prostate cancer [1]. One of the complications after transrectal prostate biopsy is infectious complications including those of fever, urinary tract infection, acute prostatitis, epididymitis and bacterial sepsis. When no antimicrobial prophylaxis for transrectal prostate biopsy was administered, bacteremia was reported to occur in 70–100% of patients, and 10.8–18% of patients had an elevated fever [2–4]. Therefore, antimicrobial prophylaxis administered before transrectal prostate biopsy is used to prevent infectious complication. When antimicrobial prophylaxis is used, the infectious complication rate is reported to be reduced to less than 5% [5,6]. For these reasons, the 2013 edition of the European Association of Urology (EAU) guidelines

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Table 1
Patient characteristics.

Characteristic	Group 1	Group 2	*P* value
Number of patients	160	442	
Median age (years)	71 (50–91)	70 (40–91)	0.182
Average PSA value (ng/ml)	41.5 (1.729–2724.5)	31.4 (0.026–5880)	0.346
Average prostate volume (ml)	36.4 (7.8–154)	41.2 (10–219.3)	0.022[a]
Rate of diabetes mellitus (%)	19.4	10.2	0.051

[a] Significant difference $P < 0.05$.

[7] recommends fluoroquinolones, trimethoprim + sulfamethoxazole and metronidazole as preoperative antibiotic prophylaxis against infectious complication after a prostate biopsy. The guidelines recommend using a single dose for low-risk patients, although a prolonged course should be considered for high-risk patients (those with diabetes mellitus, impaired immune system, malnutrition, older age or extreme body weight). Similarly, the American Urological Association (AUA) recommends antimicrobial prophylaxis for all patients undergoing transrectal prostate biopsy [8]. Fluoroquinolone as the first choice and aminoglycoside + metronidazole or clindamycin as alternative antimicrobial agents are recommended for prophylaxis in the AUA guidelines.

By contrast, the Japanese guidelines for prevention of preoperative infections in the urological field were published in 2007 [9]. The antibiotic prophylaxis for prostate needle biopsy recommended is a high dose of oral fluoroquinolones as the first choice and also cephalosporin or tazobactam/piperacillin (TAZ/PIPC) (1:4 ratio) as alternatives in both low- and high-risk patients. The high-risk patients include those with a large prostate (≥75 mL), diabetes, systemic steroid use, high-grade obstruction of the lower urinary tract (IPSS ≥ 20, Q_{max}≤12 mL/s, or residual urine ≥100 mL), and immunocompromised status. Although TAZ/PIPC (1:4 ratio) 2.5 g 3 times a day was recommended, sales of TAZ/PIPC (1:4 ratio) were stopped in Japan, and a study of the clinical effectiveness and safety of TAZ/PIPC (1:8 ratio) 4.5 g to prevent infectious complication was necessary. Therefore, we prospectively examined the efficacy and safety of TAZ/PIPC (1:8 ratio) as preoperative antimicrobial prophylaxis for febrile infectious complication after prostate biopsy.

1.1. Patients and methods

This prospective study was approved by the ethics committee of each participating institution and registered with UMIN-CTR (UMIN000003228). This study was a joint research project among the following cooperating medical institutions: Gifu University Hospital, Kobe University Hospital and the University of Occupational and Environmental Health Hospital.

The study protocol was explained thoroughly to the patients or their legal representatives before the start of treatment, and written informed consent was obtained from each patient or their representative. After receiving the agreement for participation in this study from the patients, we investigated patient background characteristics: age, complications, steroid use, prostate volume and voiding disturbance.

The prostate needle biopsy was performed in the usual manner of each institution. Each patient received a single dose of TAZ/PIPC 4.5 g, 30 min before the biopsy in Group 1 or TAZ/PIPC 4.5 g twice, once 30 min before and once after the biopsy (just before discharge or 5 h after the biopsy), in Group 2.

Evaluation of the efficacy of the treatment was done within 1 month after the prostate biopsy. At the consultation, all patients were investigated as to the duration of fever, chills and/or dysuria, and urinalysis, WBC and CRP in plasma, and urine culture testing were performed. The definition of febrile infectious complication was based on the presence of a body temperature elevation of greater than 38 °C. Differences between the two groups of patients were compared using the Fisher exact test and the Student *t*-test. A value of $p < 0.05$ was considered to be statistically significant.

2. Results

Of the 602 patients who underwent prostate biopsy, 160 patients (transrectal biopsy: 146 patients, transperineal biopsy: 9 patients, transrectal + transperineal biopsy: 5 patients) had received TAZ/PIPC 4.5 g once a day (Group 1) from April 2009 to December 2010 and 442 patients (transrectal biopsy: 438 patients, transperineal biopsy: 2 patients, transrectal + transperineal biopsy: 2 patients) had received TAZ/PIPC 4.5 g twice a day from January 2010 to March 2012 (Group 2). The characteristics of the patients are summarized in Table 1. There was a significant difference in prostate volume between the two groups. Febrile infectious complication after prostate biopsy was detected in 2.5% (4/160 patients) in Group 1 and 0.45% (2/442 patients) in Group 2, and the difference between the two groups was significant ($P = 0.0457$). All of the patients with febrile infectious complication had underwent transrectal prostate biopsy and had risk factors: 5 patients had voiding disturbance, 2 patients had diabetes mellitus and 1 patient used steroid (Table 2). In Group 1, 88 patients had at least one risk

Table 2
Clinical and microbiologic characteristics of patients with febrile infectious complication.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Group	1	1	1	1	2	2
Age (years)	77	60	71	67	75	82
Prostate volume (ml)	17.5	57	46.6	31.4	51.5	10
Complications	DM, cerebral infarction, HTN	DM, pneumonia	–	–	–	Lung cancer
Steroid	–	–	–	–	–	+
Voiding disturbance	+	+	+	+	+ (urinary retention)	–
Culture	ESBL-producing*E. coli*	NG	NG	*A. baumannii*	NG	NG
Treatment	TAZ/PIPC 4.5 g × 2/ day × 5 days →LVFX 500 mg × 1/ day × 9 days	TAZ/PIPC 4.5 g × 2/ day × 2 days →PZFX 300 mg × 1/ day × 3 days →LVFX 500 mg × 1/ day × 9 days	TAZ/PIPC 4.5 g × 2/ day × 2 days →LVFX 500 mg × 1/ day × 7 days	MEPM 0.5 g × 2/ day × 4 days →LVFX 500 mg × 1/ day × 11 days	TAZ/PIPC 4.5 g × 2/ day × 3 days →LVFX 500 mg × 1/ day × 5 days	PZFX 500 mg × 1/ day × 6 days →LVFX 500 mg × 1/ day × 14 days

DM diabetes mellitus, ESBL extended spectrum beta lactamase, HTN hypertension, LVFX levofloxacin, MEPM meropenem, NG No growth, PZFX pazufloxacin, TAZ/PIPC tazobactam/piperacillin.