ANTIBIOTIC PROPHYLAXIS FOR TRANSRECTAL NEEDLE BIOPSY OF THE PROSTATE

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Abstract :

Objectives: Transrectal needle biopsy of the prostate is essential for the diagnosis of prostate carcinoma, but there is no unanimity of opinion on the antibiotic prophylaxis for that procedure. This study was designed to explore appropriate prophylactic antimicrobial regimens.

Methods: Sixty patients undergoing prostate biopsy were assessed for any overt febrile infection. In the first 30 cases constituting Group 1, ceftibuten (CETB) was administered orally at 200 mg b.i.d. for 3 days, beginning on the day of biopsy, which was also the day of admission (2-3 hours before biopsy). As no serious adverse events were seen among those patients, CETB was administered at 200 mg b.i.d. orally for only one day, the day of admission, in the latter 30 cases (Group 2), and the clinical responses of the groups were compared.

Results: None developed a fever post-biopsy in Group 1, while there were 2 patients (6.7%) who developed a fever at $\geq 38^{\circ}$ C in Group 2. There was no statistically significant intergroup difference in incidence of fever.

Conclusions: The prophylactic antibiotic regimens administered in Groups 1 and 2 were considered to be comparable in efficacy.

Key words : prostate biopsy, infection, prostate carcinoma

INTRODUCTION

For histopathological diagnosis of prostate carcinoma, needle biopsy of the prostate is essential and the number of biopsy cases has been rapidly increasing with the recent widespread use of prostate-specific antigen (PSA) as a laboratory marker. Methods of prophylactic antibiotic medication for the transrectal needle biopsy of the prostate vary from institution to institution. Reported incidences of infection in relation to antibiotic prophylaxis have also varied, ranging widely from a significant reduction in positive urine culture rate to no such reduction; there is no standard method established to date[1-4]. Determining the sufficient antibiotic dosage in the practice of transrectal needle biopsy of the prostate will help prevent overtreatment as well as provide medicoeconomical benefits.

We conducted a prospective controlled study to compare the efficacy of a 3-day versus a single-day prophylactic oral antibiotic regimen.

MATERIAL AND METHODS

The study population consisted of 60 patients who underwent transrectal needle biopsy of

the prostate at our institute between October 2001 and August 2002 because of suspected prostate carcinoma from elevated serum PSA or on rectal examination, or for histologic verification of the lesion on account of a previous diagnosis. Patients with known hemorrhagic diathesis, patients with untreated urinary tract infection prior to the biopsy, and those with an indwelling urethral catheter were excluded from the study.

The biopsy was performed by transrectal puncture with a Monopty-Gun® (Bard, 18G) under transrectal echographic guiding (Bruel & Kjaer, 7 MHz probe), following an intrarectal injection of 10 mL of 10% popidone-iodine solution. The ultrasound probe was sterilized with a solution made up by adding 1000 mL of distilled water to 3 mL of Detergicide® (dimethyl benzyl ammonium, 44%; and inert ingredients, 56%), and then covered with a surgical glove. Xylocaine Jelly® was used as a lubricant for intrarectal insertion of the probe. Each patient was instructed to relieve himself on the morning of the day of biopsy. The number of puncture sites in each case was at the discretion of the attending surgeon and ranged from six to ten.

In the first 30 cases, ceftibuten (CETB) was administered orally at 200 mg b. i. d. for 3 days, beginning on the day of biopsy, which was the day of admission (2-3 hours before biopsy) (Group 1). As no serious adverse events, including pyrexia, were seen among those patients, CETB was administered at 200 mg only twice orally, once at 2-3 hours before and once at 3-5 hours after prostate biopsy in the latter 30 cases (Group 2), and the clinical responses of the groups were compared.

The following factors were examined: (1) the degree of pyuria in urine sediments before biopsy and the morning following biopsy, (2) the presence or absence of gross hematuria persisting for $\geq$12 hours post-biopsy, (3) the presence or absence of fever at $\geq$38° C, (4) the presence or absence of rectal bleeding persisting for $\geq$12 hours post-biopsy, (5) urine culture obtained the morning following biopsy, (6) the presence or absence of newly developed, post-biopsy perineal pain requiring analgesic medication, and (7) the presence or absence of any newly developed, post-biopsy lower urinary tract symptoms. As for lower urinary tract symptoms, each patient was asked to fill out a questionnaire on the morning of the day following biopsy. If any one of the five symptoms: miction pain, nocturia, protraction, retardation, and sense of incompleteness, was present, the patient was rated as having lower urinary tract symptom(s).

Patient background characteristics data were analyzed using the t test and chi-squared test. The frequency of complications was assessed using the chi-squared test and Fisher's exact test, and the latter procedure was also used to compare urine sediment findings. For these statistical analyses, the Stat View Program for Windows (Version 5.0; SAS, Cary, NC, USA) was used.

RESULTS

Patient Background Characteristics

There was no significant difference between Groups 1 and 2 in respect of age, prostate volume, serum PSA level, or number of biopsy specimens collected (Table 1). The disease was diagnosed histologically as prostate carcinoma on biopsy in 8 of the 30 patients of Group 1, and in 15 of the 29 patients of Group 2 excluding a patient whose lesion had

Table 1. Patients' characteristics

Variables	Group 1 N = 30	Group 2 N = 30	P value
Age (years)	67.93±7.74	68.07±4.52	N.S.
Prostate volume (ml)	44.38±28.64	36.48±16.22	N.S.
Serum PSA (ng/ml)	46.38±120.18	36.22±80.73	N.S.
No. of cores	6.07±0.36	6.37±0.91	N.S.

NS: not significant

already been histologically verified. Thus, the cases diagnosed as prostate carcinoma were prone to be more frequent in Group 2 though the intergroup difference did not attain the level of statistical significance.

Pyuria (Table 2)

Degrees of pyuria before biopsy, on the day following biopsy and on Day 14 post-biopsy are shown in Table 2. Day 14 post-biopsy data from 2 patients in Group 1 who had undergone a transurethral resection of the prostate (TUR-P) were excluded from the assessment. In Group 2, there were 2 patients in whom hematuria interfered with leukocyte counting in urine sediment on the day following biopsy, and 2 other patients lacking in urine sedimentation data on Day 14 post-biopsy; data from these cases were excluded from the respective assessments. No statistically significant difference was noted between the two groups as to degree of pyuria before biopsy, on the day following biopsy, or on Day 14 post-biopsy.

Urine Culture

There were 2 patients each in Groups 1 and 2 whose urine cultures proved positive for bacterial growth. Cultures of urine from a Group 1 patient grew *Enterococcus faecalis* (10^4/mL) and *Pseudomonas aeruginosa* (10^4/mL), but urinalysis on the day following biopsy showed no evidence of pyuria. In the other Group 1 patient, *Enterococcus faecalis* (10^6/mL) was detected in the urine, and urine sediment on the day following biopsy revealed pyuria (50 to 99 white blood cells/HPF). In Group 2, *Enterococcus faecalis* (10^3/mL) was demonstrated in urine from one patient, and methicillin-resistant *Staphylococcus aureus* (MRSA) (10^5/mL) in urine from

Table 2. Comparison of the degree of pyuria

Degree of pyuria	Group 1 (No. of patients)			Group 2 (No. of patients)		
	BB	ODF	OD14	BB	ODF	OD14
<1/HPF	21	21	24	25	20	19
1~4/HPF	7	5	2	4	4	7
5~9/HPF	2	1	2	1	1	1
10~19/HPF		1			2	
20~29/HPF						1
30~49/HPF					1	
50~99/HPF		1				
100</HPF		1				
Total	30	30	28	30	28	28

BB: before biopsy, ODF: on the day following biopsy, .
OD14: on day 14 post-biopsy

Table 3. Comparison of complications

	No. of patients		P value
	Group 1	Group 2	
Hematuria	13	10	N.S.
Fever (>38℃)	0	2	N.S.
Rectal bleeding	1	1	N.S.
Perineal pain	2	0	N.S.
LUTS	9	9	N.S.
Urine culture proved positive	2	2	N.S.

another patient. Both patients had pyuria (10-19 and >100 white blood cells/HPF, respectively). The patient with MRSA in urine culture had been diagnosed as having prostate carcinoma prior to the biopsy, which the patient received solely for the purpose of assessing the therapeutic response. None of the 4 patients with positive urine cultures

developed a fever.

Complications (Table 3)

Gross hematuria had the highest incidence among the complications encountered; it was noted in 23 of the 60 patients (38.3%), with no significant difference in incidence between Groups 1 and 2. Lower urinary tract symptoms occurred with a relatively high frequency (18/60 cases, 30%), again with no significant intergroup difference.

All Group 1 patients remained afebrile throughout the course, while 2 patients in Group 2 developed a fever. One of these patients received meropenem trihydrate (MEPM) intravenously for 3 days and levofloxacin (LVFX) for the ensuing 14 days; the fever receded after 2 days of the MEPM medication. The other patient was administered LVFX for 14 days and became afebrile 3 days after the start of the antibiotic therapy. No blood culture was performed on these two patients. In these two cases, cultures of urine sampled on the day following biopsy were negative, and neither pyuria nor lower urinary tract symptoms were noted.

DISCUSSION

There is no established method as yet regarding prophylactic antibiotic medication after transrectal needle biopsy of the prostate, and the prophylactic regimens adopted vary from center to center[1-4]. While many reports have documented that new quinolone antibiotics with proven potent activity against enteric bacteria and with satisfactory distribution to tissues of the prostate are selected for this purpose[2-4], we chose CETB, a cephem antibiotic, for the reasons mentioned below. First, regarding drug distribution into prostate tissues, Arakawa et al.[5] reported that a 200-mg oral dose of CETB yielded a prostatic tissue drug concentration of 4.22 μg/mL at 2 hours post-dosing. They investigated the relation between *Escherichia coli* isolates from 10 patients with acute prostatitis and MICs of CETB for those isolates, and found that the MICs were $\geq$3.13 μg/mL for all those *E. coli* isolates, thus providing evidence that CETB may have prophylactic effectiveness. Another reason pertains to drug interactions. Most patients subject to transrectal needle biopsy of the prostate are elderly, not a few of whom are on drugs for other disorders. One hesitates to use new quinolone antibiotics concurrently with such drugs as bronchodilators, antiarrhythmic agents, or magnesium preparations[6, 7]. Furthermore, in case of a post-biopsy febrile infection requiring administration of a non-steroidal antipyretic-analgesic agent, concomitant use of a new quinolone antibiotic has a risk of central convulsion[8], while CETB has no such risk. The fact that CETB costs less than new quinolones is another reason for its selection.

With regard to duration and initiation period of antibiotic prophylaxis, in the United States, drug administration on the day before biopsy or from before biopsy onwards is undertaken in approximately 80% of cases, with the duration of medication being 2 or 3 days in 50% of cases[9]. Based on our previous experience, we started this investigation with a 3-day medication scheme and, upon confirming that no serious adverse event occurred among the first 30 cases studied, the prophylactic regimen was shifted to a single-day medication scheme. Prior to the initiation of this clinical study, we had explored the possibility of setting up a non-medication group to receive no prophylactic regimen. According to a report

of Enlund et al.[10], transrectal needle biopsy of the prostate was performed on 415 patients without antimicrobial prophylaxis, of whom 12 patients (2.9%) developed a fever at ≥38° C, requiring antibiotic refills in 11 patients while the remaining patient attained cure without drug medication. However, fatal complications after transrectal prostatic needle biopsy have also been documented[11, 12]. In view of these reports, we decided not to include a non-medication group in the study. In the present study, there was no complication whose incidence differed significantly between the two groups, and the incidences of complications in these two groups were essentially the same as those reported by other investigators[1-4]. Two patients who developed a fever responded with rapid subsidence to treatment with MEPM or LVFX.

Thus, the prophylaxis against post-transrectal prostatic needle biopsy with CETB at 400 mg q.d. for one day and for 3 days were comparable in efficacy. The data also indicate that treatment with a new quinolone antibiotic may suffice to cope with the problem in patients having developed a fever after the biopsy. A prospective randomized study in three groups of patients, i.e., 3-day regimen, single-day regimen and non-medication, has yet to be pursued.

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