A Comparative Study of Oral Medication to Prevent Transient Bacteremia and Adverse Events from Transrectal Prostatic Biopsy: Ciprofloxacin versus Cefixime

Thuchchai Pipitpanpipit MD*, Pitak Santanirand PhD**, Wisoot Kongchareonsombat MD*

** Division of Urology, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
*** Clinical Microbiology Unit, Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Objective: *To study the transient bacteremia and adverse events of changing antibiotic prophylaxis from oral ciprofloxacin to oral cefixime in (patients) undergoing transrectal prostatic biopsy.*
Material and Method: *One hundred patients with suspected prostate cancer underwent outpatient surgery at Ramathibodi Hospital were randomly assigned to two groups. The first group was prescribed oral ciprofloxacin, and the second group received oral cefixime. Blood culture tests were routinely performed within 24 hours after transrectal prostatic biopsy in all patients, and they were monitored for adverse reactions over a 14-day period.*
Results: *Transient bacteremia was detected in 2% of the participants in the group with oral cefixime, and none in the group receiving oral ciprofloxacin, but the rate of transient bacteremia of the two groups was no varied with statistical significance ($p>0.05$). Adverse effects, including acute urinary retention (AUR), hematuria, rectal bleeding, vasovagal syncope, and hematospermia, were found in both patient groups after the procedure. They did not differ significantly ($p>0.05$). Dysuria was found in the group treated with oral cefixime and it differ significantly ($p<0.05$).*
Conclusion: *Cefixime is likely not the antibiotic of choice compared with ciprofloxacin in preventing post-transrectal prostatic biopsy transient bacteremia, and it appears to show a high rate of dysuria after transrectal prostatic biopsy. Until a more suitable, effective oral prophylactic agent is found, quinolone-based antibiotics should be the antibiotic of choice for patient undergoing transrectal prostatic biopsy.*

Keywords: *Antibiotic prophylaxis; transrectal prostatic biopsy; ciprofloxacin; cefixime; transient bacteremia*

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Prostate cancer incidence rates have increased in recent years. Transrectal prostatic biopsy is the mainstay method used for the diagnosis of prostate cancer[1]. Although it is generally considered a safe procedure, complications secondary to biopsy may occasionally be encountered in practice. Transrectal prostatic biopsy was related to sepsis and septicemia in approximately 13%-20% of cases[2]. Bacteria that cause these infections are Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Enterococcus[3,4]. The prevalence of the antibiotic resistance rate in E. coli is rapidly rising in Thailand[5] and also around the world[6,7].

Pre-procedural antibiotic prophylaxis is recommended for all patients. This concept is based on the fact that 16%-100% of cases of biopsy with no prophylaxis presented either asymptomatic bacteriuria or transient bacteremia, increasing the risk for infectious complications, such as urinary tract infection (UTI), sepsis, and Fournier's syndrome[8]. Currently, many urologists use prophylactic antibiotic therapy to minimize infectious complications after transrectal prostatic biopsy, but such therapy does not completely eliminate infection. The reported infection rate varies in studies using different antibiotic regimens[9-14]. At present, the authors prescribed the oral form of ciprofloxacin because it is a broad-spectrum antibiotic that penetrates the prostate gland well. Patients took the drug one day before undergoing biopsy, and continued for four days.

Correspondence to:
Kongchareonsombat W, Division of Urology, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University 270, Rama VI Road, Ratchathewi, Bangkok 10400, Thailand.
Phone: +66-2-2011315, Fax: +66-2-2011316
E-mail: wisoot2002@hotmail.com

The objective of the present study was to compare the efficacy of antibiotic prophylaxis with ciprofloxacin versus cefixime (both orally administered) on determine effective regulation in the future. prevent of transient bacteremia and adverse symptoms from past transrectal prostate biopsy.

Materials and Method

From June 2014 to June 2015, at the Urologic Clinic,Ramathibodi Hospital, 100 patients entered the study after giving informed consent. The inclusion criteria were: (i) digital rectal examination positive; (ii) prostatic specific antigen (PSA) level >4 ng/ mL; (iii) age between 55- 85 years old; and (iv) acceptance and signed informed consent form. The exclusion criteria were: (i) immunodeficiency, (ii) coagulopathy, (iii) UTI, (iv) receiving an antibiotic within one week before, (v) indwelling , eatheter (vi) heart intervention history, (vii) refused signing informed consent form, and (viii) allergy to ciprofloxacin or cefixime.

The 100 patients were randomize assigned into two groups, using computer-generated random numbers. An enema was administered to each patient the day before biopsy. Oral prophylactic antibiotics were administered to each patient 30-60 minutes before the procedure. In group 1 were 50 patients (mean age 67.7 years), each received a single dose of ciprofloxacin (500 mg). In group 2 were 50 patients (mean age 69.7 years), each of whom were given a single dose of cefixime (200 mg). The authors used an extended 12-core biopsy technique and collected blood cultures within 24 hours Post biopsy. The patients were instructed to take medicine continuously for four days after the procedure. The follow-up was made at 14 days while the pathological report and patient's adverse reactions (if any) were recorded.

Bacteremia is the presence of bacteria in the bloodstream. It can occur spontaneously, during certain tissue infections, with the use of indwelling GU or IV catheters, or after dental, GI, GU, wound-care, or other procedures[15].

Statistical analysis

Descriptive statistics were used to analyze the data. Data analysis comparing the two treatment groups were assessed from an unpaired t-test and Fisher's exact test. The threshold for statistical significance was set at $p<0.05$.

Results

For males with suspected prostate cancer, 50 patients were classified as group 1 (ciprofloxacin), and 50 patients were classified as group 2 (cefixime). The mean age of the patients was 67.70±7.3 and 69.70 ±7.9 years, respectively. No statistical significance was found between the two groups, as shown in Table 1.

Transient bacteremia (positive blood culture test; the presence of Enterococcus in the blood) was recorded for one patient (2%) in group 2; the patient did not develop true bacteremia (e.g., clinically significant symptoms of fever with chills, flank pain, and alteration of consciousness). No significant difference was found between the two groups, as shown in Table 2. Dysuria was significantly higher in the cefixime group; there was no case in group 1, and seven cases (14%) in group 2. In terms of other complications, including acute urinary retention (AUR), hematuria, rectal bleeding, vasovagal syncope, and hematospermia, no significant difference was found between the groups ($p>0.05$), as shown in Table 2.

In both groups, the most common pathological binding was benign prostatic hyperplasia (BPH) (48.8% and 53.6%, respectively), as shown in Table 3.

Discussion

Transient, usually asymptomatic bacteremia occurs in a wide variety of procedures and manipulations, in particular, those associated with mucous membrane trauma, therefore increasing the risk for infectious complications, such as: UTI, sepsis, and Fournier's syndrome[16]. Therefore, transrectal prostatic biopsy is considered to be a harmful procedure.

Fluoroquinolone antibiotics, such as ciprofloxacin, are the most popular prophylactic agents used in transrectal prostatic biopsy[17]. Ciprofloxacin has a broad spectrum of activity, especially against most gram-negative organisms that cause UTIs[18]. In recent years, there has been increasing microbial resistance to ciprofloxacin and other quinolones worldwide. For this reason, clinicians have been under increasing pressure to shift away from the use of quinolones to that of alternative antibiotics in recent years. In the present study, the authors evaluated

Table 1. Base-line characteristics of 100 men with suspected prostate cancer

	Ciprofloxacin	Cefixime	*p*-value
Mean age (years)	67.70 ±7.3	69.70±7.9	0.19
No. of patients	50	50	

Table 2. Percentage of blood culture test, adverse events, and pathological reports

	Ciprofloxacin n (%)	Cefixime n (%)	*p*-value
Blood culture test			
Negative	100 (50)	98 (49)	1.00
Positive	0 (0)	2 (1)	
Adverse events			
Hematuria			
No	43 (86.0)	47 (94.0)	0.32
Yes	7 (14.0)	3 (6.0)	
Rectal bleeding			
No	50 (86.0)	48 (96.0)	0.50
Yes	0 (14.0)	2 (4.0)	
Vasovagal syncope			
No	47 (94.0)	48 (96.0)	1.00
Ye	3 (6.0)	2 (4.0)	
Hematospermia			
No	49 (98.0)	49 (98.0)	1.00
Yes	1 (2.0)	1 (2.0)	
Acute urinary retention			
No	47 (94.0)	47 (94.0)	1.00
Yes	3 (6.0)	3 (6.0)	
Dysuria			
No	50 (100)	43 (86.0)	0.01*
Yes	0 (0)	7 (14.0)	

*significant, $p< 0.05$

Table 3. Pathological reports

	Ciprofloxacin n (%)	Cefixime n (%)
Benign prostatic hyperplasia (BPH)	39 (48.8)	37 (53.6)
High-grade prostatic intraepithelial neoplasia (HGPIN)	17 (21.3)	12 (17.4)
Atypical small acinar proliferation (ASAP)	3 (3.8)	2 (2.9)
Adenocarcinoma	7 (8.8)	9 (13)
Acute inflammation	5 (6.3)	2 (2.9)
Chronic inflammation	9 (11.3)	7 (10.1)

whether oral cefixime could be used as an effective alternative antibiotic prophylaxis for patient undergoing transrectal prostatic biopsy. Cefixime is a third-generation cephalosporin and is commonly used to treat bacterial infections of the ear, urinary tract, and upper respiratory tract[19]. It can also be administered easily in an oral form, and our local resistance data in 2015 showed that ≈ 65% of coliforms isolated from urine samples were resistant to ciprofloxacin, whereas only 25% of coliforms were resistant to cefixime.

The present result showed that dysuria rates among patient undergoing transrectal prostatic biopsy were significantly higher in the group receiving cefixime prophylaxis compared with those received ciprofloxacin prophylaxis. No difference was found in the transient bacteremia rate between these two regimes. These findings may suggest that prophylaxis with cefixime is inferior to the other because of poor absorption via the gastrointestinal tract or low serum concentration. However, the findings might be misleading because of small sample size.

Conclusion

Ciprofloxacin appears to be a superior prophylactic agent to cefixime in patient undergoing transrectal prostatic biopsy. Changing antibiotic prophylaxis from a quinolone-based regime may, therefore, be putting our patients at increased risk for

serious infectious complications after the biopsy.

What is alredy known on this topic?

Quinolone-based antibiotics are the antibiotic of choice for patient undergoing trans-rectal prostatic biopsy.

What this study adds?

Based on the present results, the autors feel that cefixime is not an effective antimicrobial agent compared with ciprofloxacin in preventing post-trans-rectal prostatic biopsy transient bacteraemia, and it appears to show high rate of dysuria after the biopsy.

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Potential conflict of interest

None.

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โครงการวิจัยศึกษาสุ่มเปรียบเทียบผลการให้ยาเพื่อป้องกันการติดเชื้อในกระแสเลือด และผลแทรกซ้อนจากการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนัก ระหว่าง Ciprofloxacin กับ Cefixime ชนิดรับประทาน

ธัชชัย พิพิธพันธ์พิพิท, พิทักษ์ สันตนิรันดร์, วิสูตร คงเจริญสมบัติ

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบการป้องกันการติดเชื้อในกระแสเลือด และผลแทรกซ้อนจากการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนัก ในผู้ป่วยที่ได้รับยา Ciprofloxacin (500 มิลลิกรัม) ชนิดรับประทาน และผู้ป่วยที่ได้รับยา Cefixime (200 มิลลิกรัม) ชนิดรับประทาน*

วัสดุและวิธีการ: *ศึกษาในผู้ป่วยจำนวน 100 คนที่สงสัยมะเร็งต่อมลูกหมาก ที่แผนกผู้ป่วยนอก โรงพยาบาลรามาธิบดี มาแบ่งโดยใช้วิธีการสุ่มออกเป็น 2 กลุ่มๆ ละเท่าๆ กัน ได้แก่ กลุ่มผู้ป่วยที่ได้รับยาก่อนการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนักเป็น Ciprofloxacin (500 มิลลิกรัม) ชนิดรับประทาน และกลุ่มผู้ป่วยที่ได้รับ Cefixime (200 มิลลิกรัม) ชนิดรับประทาน ผู้ป่วยจะต้องได้รับการตรวจเพื่อเพาะเชื้อในกระแสเลือดภายใน 24 ชั่วโมงหลังการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนัก และนัดมาตรวจติดตามผลแทรกซ้อนจากการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนักภายใน 14 วัน*

ผลการศึกษา: *ผลการเกิดการติดเชื้อในกระแสเลือด ของผู้ป่วยทั้ง 2 กลุ่มไม่ต่างกันอย่างมีนัยสำคัญทางสถิติ (p-value >0.05) โดยพบผู้ป่วยร้อยละ 2 ในกลุ่มที่ได้รับ Cefixime (200 มิลลิกรัม) ชนิดรับประทาน และไม่พบเลยในกลุ่มที่ได้รับ Ciprofloxacin (500 มิลลิกรัม) ชนิดรับประทาน อาการแทรกซ้อนจากการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนัก ได้แก่ อุจจาระมีเลือดปน, ปัสสาวะมีเลือดปน, อสุจิมีเลือดปน, วิงเวียนศีรษะ, และปัสสาวะค้าง พบในผู้ป่วยทั้ง 2 กลุ่ม โดยไม่ต่างกันอย่างมีนัยสำคัญทางสถิติ (p-value >0.05) ยกเว้นอาการปัสสาวะแสบขัดซึ่งพบเฉพาะกลุ่มที่ได้รับ Cefixime (200 มิลลิกรัม) ชนิดรับประทาน ซึ่งมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (p-value <0.05)*

สรุป: *การใช้ยา Cefixime (200 มิลลิกรัม) ชนิดรับประทาน ไม่สามารถลดการเกิดการติดเชื้อในกระแสเลือด หลังการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนัก และพบว่ามีอัตราการเกิดปัสสาวะแสบขัดสูงกว่าผู้ป่วยที่ได้รับ Ciprofloxacin (500 มิลลิกรัม) ชนิดรับประทาน ดังนั้นยากลุ่ม Quinolone-based ยังคงเป็นยาที่เหมาะสมที่สุดสำหรับให้ก่อนการตัดชิ้นเนื้อต่อมลูกหมากผ่านอัลตราซาวด์ทางทวารหนัก*