ARC Journal of Urology
Volume 1, Issue 2, 2016, PP 15-19
www.arcjournals.org

Prospective Randomized Controlled Study of the Results of Medication with Oral Ciprofloxacin versus Oralcefixime to Prevent Transient Bacteraemia and Adverse Events from Trans-Rectal Prostatic Biopsy

Thuchchai Pipitpanpipit, M.D.

Division of Urology, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
doctorpeep@gmail.com

Assoc. Prof. Pitak Santanirand, Ph.D.

Clinical Microbiology Unit, Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
pitak_san@mahidol.ac.th

Assoc. Prof. Wisoot Kongchareonsombat, M.D.

Division of Urology, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
wisoot2002@gmail.com

Abstract:

Purpose: *To study whether changing antibiotic prophylaxis from oral ciprofloxacin to oral cefixime has affected transient bacteraemia and adverse events in men undergoing trans-rectal prostatic biopsy.*

Materials and Methods: *One hundred patients with suspected prostate cancer who underwent out-patient surgery at Ramathibodi hospital were randomly assigned to one of the following groups: One group was administered oral ciprofloxacin, and the second group received oral cefixime. Afterward, the patients underwent trans-rectal prostatic biopsy within 24 hours to detect transient bacteraemia, and they were monitored for adverse reactions over a 14-day period.*

Results: *In the group treated with oral cefixime, transient bacteraemia 2% was detected, and in the group receiving the drug oral ciprofloxacin, no transient bacteraemia was. Both rates of transient bacteraemia did not vary with statistical significance ($p>0.05$). Adverse effects were found in both patient groups after the examination, including acute urinary retention, hematuria, rectal bleeding, vasovagal syncope and hematospermia. They did not differ significantly ($p>0.05$). Except for dysuria, the two groups differed significantly ($p<0.05$).*

Conclusion: *Cefixime is not an effective antimicrobial agent compared with ciprofloxacin in preventing post-trans-rectal prostatic biopsy transient bacteraemia and it appears to show a high rate of dysuria after trans-rectal prostatic biopsy. Until a more suitable, effective oral prophylactic agent is found, quinolone-based antibiotics should remain the antibiotic of choice for men undergoing trans-rectal prostatic biopsy.*

Keywords: *Antibiotic prophylaxis; trans-rectal prostatic biopsy; ciprofloxacin; cefixime; transient bacteraemia*

1. INTRODUCTION

Prostate cancer incidence rates have increased in recent years. In the United States of America (USA), accounting for the most common of all new cases of cancer in males, prostate cancer is the second leading cause of cancer death in American men, behind only lung cancer (1). In Thailand, prostate cancer is the eighth commonly diagnosed cancer (2), and the numbers of cases have gradually increased.

Trans-rectal prostatic biopsy is the mainstay method used for the diagnosis of prostate cancer (3). Although it is generally considered a safe procedure, complications secondary to biopsy have been some of the most common adverse events encountered in practice. Trans-rectal prostatic biopsy related to sepsis and septicaemia around 13% to 20% (4). Bacteria that cause these infections are Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Enterococcus (5, 6).

Pre-procedural antibiotic prophylaxis is recommended for all patients. This concept is based on the fact that 16% to 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 (7). Currently, many urologists use prophylactic antibiotic therapy to minimize infective complications after trans-rectal prostatic biopsy, but such therapy does not completely eliminate infection. The reported infection rate varies considerably in studies using different antibiotic regimens (8-13). Nowadays, we prescribe the oral form of ciprofloxacin because the drug, also called fluoroquinolone, is broad spectrum and penetrates the prostate gland well. Patients took the drug one day before undergoing biopsy, and they were then given ciprofloxacin for four days, but we found an infectious complication does not decrease. Moreover, the prevalence of the antibiotic resistance rate in E. coli is rapidly rising in Thailand (14) and also across the world (15-16).

The objective of this study is to compare the efficacy of antibiotic prophylaxis with ciprofloxacin versus cefixime (both oral administration) to determine effective regulation in the future.

2. MATERIALS AND METHODS

Between June 2014 and 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) from 55-85 years old; and (iv) acceptance or informed consent form. The exclusion criteria were: (i) immunodeficiency; (ii) coagulopathy; (iii) UTI; (iv) took an antibiotic within one week before biopsy; (v) on urinary catheter; (vi) heart intervention history; (vii) refused informed consent form; and (viii) allergy to ciprofloxacin or cefixime.

The 100 patients were randomized into two groups, using computer-generated random numbers. The enema was administered on the day before biopsy was required. Oral prophylactic antibiotics were administered to all patients 30-60 minutes before the procedure. Patients in group 1 (50, mean age 67.7 years) received ciprofloxacin. In group 2, 50 patients (mean age 69.7 years) were given cefixime. During biopsy, sterile technique and local anaesthetic were applied. We used extended 12-core biopsy technique and collected blood culture within 24 hours. The volunteers were informed that complications are especially serious events, and they were instructed to take medicine continuously for four days after the procedure. The volunteers were also told to make appointments 14 days later for the biopsy results and were followed up on for complications.

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

3. 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.

Table1. *Characteristics of the Study*

	Ciprofloxacin	Cefixime	p-Values
Mean age (years)	67.70 +/- 7.3	69.70 +/- 7.9	0.19
No. of patients	50	50	

Transient bacteraemia was recorded for one patient (2%, Enterococcus) in group 2; the patient did not develop true bacteraemia. No significant difference was found between the two groups as shown in Table 2.

Table2. *Percentage of Transient Bacteraemia*

	Ciprofloxacin (No., %)	Cefixime (No., %)	p-Values
Negative	100 (50)	98 (49)	1.00
Positive	0 (0)	2 (1)	

Dysuria was significantly higher in the cefixime group; there were no cases in group 1, and there were seven cases (14%) in group 2 as shown in Table 3. In terms of other complications, including acute

urinary retention, hematuria, rectal bleeding, vasovagal syncope and hematospermia, no significant difference was found between the groups (p>0.05).

Table3. *Adverse Events*

	Ciprofloxacin (No., %)	Cefixime (No., %)	p-Values
AUR •No •Yes	 47(94.0) 3(6.0)	 47(94.0) 3(6.0)	1.00
Hematuria •No •Yes	 43(86.0) 7(14.0)	 47(94.0) 3(6.0)	0.32
Rectal bleeding •No •Yes	 50(86.0) 0(14.0)	 48(96.0) 2(4.0)	0.50
Vasovagal syncope •No •Yes	 47(94.0) 3(6.0)	 48(96.0) 2(4.0)	1.00
Hematospermia •No •Yes	 49(98.0) 1(2.0)	 49(98.0) 1(2.0)	1.00
Dysuria •No •Yes	 50(100) 0(0)	 43(86.0) 7(14.0)	0.01*

**significant, p<0.05*

In both groups, the most common pathology was benign prostatic hyperplasia (BPH) (48.8% and 53.6%, respectively) as shown in Table 4.

Table4. *Pathologic Reports*

	Ciprofloxacin (No., %)	Cefixime (No., %)
BPH	39(48.8)	37(53.6)
HGPIN	17(21.3)	12 (17.4)
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)

4. DISCUSSION

Transient, usually asymptomatic bacteraemia occurs in a wide variety of procedures and manipulations, particularly those associated with mucous membrane trauma, thus increasing the risk for infectious complications, such as UTI, sepsis and Fournier's syndrome (17). Therefore, trans-rectal prostatic biopsy is considered to be a harmful procedure.

Fluoroquinolone antibiotics, such as ciprofloxacin, are the most popular prophylactic agents used in trans-rectal prostatic biopsy (18). Ciprofloxacin has a broad spectrum of activity especially against most gram-negative organisms that cause UTIs (19). 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, we evaluated whether oral cefixime could be used as an effective alternative antibiotic prophylaxis for men undergoing trans-rectal 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 (20). It can also be administered easily in an oral form, and our local resistance data in 2015 showed that ≈65% of coliforms that were isolated from urine samples were resistant to ciprofloxacin, whereas only 25% of coliforms were resistant to cefixime (14).

The present results show that the dysuria rates among men undergoing trans-rectal prostatic biopsy were significantly higher in the group receiving cefixime prophylaxis compared with those who received ciprofloxacin prophylaxis. No difference was found in the transient bacteraemia rate between

these two regimes. This suggests that prophylaxis with cefixime failed to be better either because there was poor absorption of the antibiotic via the gastrointestinal tract or there was a low serum concentration.

Based on the present results, we 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 trans-rectal prostatic biopsy. Until a more suitable, effective oral prophylactic agent is found, quinolone-based antibiotics should remain the antibiotic of choice for men undergoing trans-rectal prostatic biopsy, but this needs to be judged on a case-by-case basis.

5. CONCLUSION

Ciprofloxacin appears to be a superior prophylactic agent to cefixime in men undergoing trans-rectal prostatic biopsy. Changing antibiotic prophylaxis from a quinolone-based regime may therefore be putting our patients at an increased risk for serious infectious complications after trans-rectal prostatic biopsy.

REFERENCES

[1] American Cancer Society, 2012

[2] Cancer in Thailand, Vol. IV, 1998-2000

[3] Heidenreich A, Aus G, Bolla M et al. EAU guidelines on prostate cancer. Eur Urol 2008; 53: 68–80

[4] Webb NR, Woo HH. Antibiotic prophylaxis for prostate biopsy. BJU Int 2002; 89: 824–8

[5] Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for trans-rectal needle biopsy of the prostate: a randomized controlled study. BJU Int 2000; 85: 682–5

[6] Crundwell MC, Cooke PW, Wallace DM. Patients' tolerance of trans-rectal ultrasound-guided prostatic biopsy: an audit of 104 cases. BJU Int 1999;83: 792– 5

[7] Puig J, Darnell A, Bermúdez P et al. Trans-rectal ultrasound-guided prostate biopsy: is antibiotic prophylaxis necessary? EurRadiol 2006; 16: 939–43

[8] Aus G, Hermansson CG, Hugosson J, Pedersen KV. Trans-rectal ultrasound examination of the prostate: complications and acceptance by patients. Br J Urol 1993; 71: 457-9

[9] Desmond PM, Clark J, Thompson IM, Zeidman EJ, Mueller EJ. Morbidity with contemporary prostate biopsy. J Urol 1993; 150: 1425-6

[10] Norberg M, Holmberg L, HaÈggman M, Magnusson A. Determinants of complications after multiple trans-rectal core biopsies of the prostate. ActaRadiolSuppl 1994; 35: 7-21

[11] Aus G, Ahlgren G, Bergdahl S, Hugosson J. Infection after trans-rectal core biopsies of the prostate-risk factors and antibiotic prophylaxis. Br J Urol 1996; 77: 851-5

[12] Collins GN, Lloyd SN, Hehir M, McKelvie GB. Multiple trans-rectal ultrasound-guided prostatic biopsies — true morbidity and patient acceptance. Br J Urol 1993; 71: 460-3

[13] Kapoor DA, Klimberg IW, Malek GH et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during trans-rectal prostate biopsy. Urology 1998; 52: 552–8

[14] National Antimicrobial Resistance Surveillance Center, Thailand, 2015

[15] Michael A. Liss et al. Prevalence and Significance of Fluoroquinolone Resistant Escherichia coli in Patients Undergoing Tran-srectal Ultrasound Guided Prostate Needle Biopsy. J Urol 2011; 185: 1283-1288

[16] Deborah A. Williamson et al. Infectious Complications Following Trans-rectal Ultrasound–Guided Prostate Biopsy: New Challenges in the Era of Multidrug-Resistant Escherichia coli. Clinical Infectious Diseases Advance Access 2013

[17] JV, E. Transient bacteremia and endocarditis prophylaxis. A review. - PubMed - NCBI

[18] Burden HP, Ranasinghe W, Persad R. Antibiotics for transrectal ultrasonography-guided prostate biopsy: are we practising evidence-based medicine? BJU Int 2008; 101: 1202–4

[19] Davis R, Markham A, Balfour JA. Ciprofloxacin. An updated review of its pharmacology, therapeutic efficacy and tolerability. Drugs 1996; 51: 1019–74

[20] Faulkner RD, Bohaychuk W, Lanc RA, et al.: Pharmacokinetics of cefixime in the young and elderly. J AntimicrobChemother 1988; 21(6): 787-794.