RESEARCH ARTICLE

INDONESIAN JOURNAL OF CANCER

The Profile of Ciprofloxacin-Resistant Bacteria in the Rectum of Patients Undergoing Transrectal Ultrasound-Guided Prostate Biopsy, Its Relation to Post-Biopsy Infection and Alternative Prophylactic Antibiotics

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ARTICLE INFO

Received : 05 July 2020
Reviewed : 24 July 2020
Accepted : 03 November 2020

Keywords:
ultrasonography, biopsy, prostatic hyperplasia, drug resistance, antibiotic

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ABSTRACT

Background: Fluoroquinolone has been routinely given as a prophylactic antibiotic to patients undergoing transrectal ultrasound (TRUS)-guided prostate biopsy. Currently, there is no data on the profile of fluoroquinolone-resistant bacteria, its association with post-biopsy sepsis, and alternative prophylactic antibiotics.

Methods: A cross-sectional study was conducted in patients undergoing TRUS-guided prostate biopsy at Urology Clinic, Cipto Mangunkusumo National Central General Hospital between August and December 2015. Specimens were taken from rectal swabs prior to biopsy. Gram-negative bacilli and Gram-positive cocci were characterized on the Vitek®2 using GN and GP cards (BioMérieux, USA). Antimicrobial susceptibility testing was done by Kirby Bauer disc diffusion method. Post-biopsy infection was monitored within one week after biopsy by telephone call and diagnosed by clinical examination.

Results: A total of 52 patients aged 52-80 years were enrolled. Sixty-six isolates grew from 52 swabs; 14 swabs among them grew 2 isolates. The commonest pathogen was *Escherichia coli* (78.8%), followed by *Klebsiella pneumoniae* (13.6%), *Enterococcus faecium* (3.0%), *Acinetobacter haemolyticus, Morganella morganii* subsp. *morganii,* and *Enterococcus faecalis* (1.5%), respectively. Ciprofloxacin-resistant bacteria were found in 33 (50.0%) isolates which were predominated by *E. coli*. Meanwhile, 90.4% and 96.2% of isolates were sensitive to amoxicillin-clavulanate and ampicillin-sulbactam, respectively. Post-biopsy infection was established in 7 patients requiring no hospitalization.

Conclusions: The proportion of ciprofloxacin-resistant bacteria in the rectum among patients undergoing prostate biopsy was 50.0%. *Escherichia coli* is the commonest resistant pathogen to fluoroquinolone. The recommended alternatives for prophylactic antibiotics are amoxicillin-clavulanate and ampicillin-sulbactam. Routine pre-biopsy rectal swab cultures should also be encouraged.

INTRODUCTION

Transrectal ultrasound (TRUS)-guided prostate biopsy is the standard technique for obtaining a histological diagnosis of prostatic carcinoma [1]. The commonest indications for TRUS biopsy are a raised prostate specific antigen (PSA) level and/or an abnormal digital rectal examination. According to recent estimates, approximately one million TRUS biopsies are performed annually in the United States [2]. Although generally considered as a safe and well-tolerated procedure, post-biopsy complications are reported in up to 50% of cases, which include pain, hematuria, hematospermia, urinary retention, and infection [3].

A variety of infectious complications may occur following TRUS biopsy, ranging from asymptomatic bacteriuria or urinary tract infection (UTI) to prostatitis, bacteremia, and severe sepsis [3]. Acute prostatitis was reported to occur in 1.3% of patients after the first biopsy and 6.8% after repeated biopsy [4]. The reported incidence of UTI after TRUS biopsy typically ranges between 2% and 6% with approximately 30%–50% of these patients having accompanying bacteremia [5,6]. Bacteremia is frequently accompanied by severe sepsis, which has an overall incidence of 0.1%–2.2% following TRUS biopsy [3].

The primary mechanism of post-TRUS biopsy sepsis is likely to be direct inoculation of bacteria from the rectal mucosa by the biopsy needle into the prostate, blood vessels, or urinary tract. This is supported by high reported rates of bacteremia (16%–75%) and bacteriuria (36%–53%) immediately post-procedure in the absence of prophylactic antibiotics and the fact that most infections manifest clinically within 3 days of TRUS biopsy [7]. In addition, pre-existing infection or inflammation may also contribute to post-biopsy infections although the value of routine urine culture and pre-biopsy treatment of asymptomatic bacteriuria remains controversial [3].

Strong evidence exists to support the use of prophylactic antibiotic prior to TRUS biopsy [8,9]. Fluoroquinolones are still the most frequently used antibiotic for prophylaxis in TRUS-guided prostate biopsy [7]. Prophylactic antibiotic with fluoroquinolones is recommended in several international guidelines to prevent infections in patients undergoing TRUS-guided prostate biopsy [10,11]. They are particularly useful due to their broad spectrum of activity against intestinal flora and high prostatic tissue levels obtained after oral administration [12].

Cipto Mangunkusumo National Central General Hospital (CMNCGH) is one of the top referral hospitals in Jakarta with 990 beds, which makes it the largest general and teaching hospital in Indonesia. Infection due to resistant bacteria to ciprofloxacin was recently suspected due to the increasing number of hospitalized cases with post-biopsy infection. However, the profile of fluoroquinolone-resistant bacteria in the rectum at the time of biopsy is not known. Therefore, this study was aimed to obtain the bacterial and antibiogram profile of rectal swabs among patients undergoing TRUS-guided prostate biopsy, the following incidence of post-biopsy infections at CMNCGH, and alternative prophylactic antibiotics.

METHODS

Study Design and Subjects

This was a cross-sectional study in male patients undergoing TRUS-guided prostate biopsy at the Urology Department between August and December 2015. Patients were included if they were willing to undergo a rectal swab prior to a prostate biopsy. All patients gave their written consent before enrolment. Ethical approval letter number 766/UN2.F1/ETIK/2015 was issued by the Ethical Committee for Medical Research, Faculty of Medicine, Universitas Indonesia. The minimum sample size was calculated by estimating a population proportion with specified absolute precision [13]. The anticipated population proportion was 14%. The required sample size at 95% confidence level and 10% absolute precision were 47. Clinical assessment was done on each patient, and the patients' data were collected from their medical records including current urinary tract catheterization, the presence of diabetes mellitus, the history of UTI, hospital admission, fluoroquinolone, and other antibiotic treatments received in the past 6 months, and previous prostate biopsy.

Rectal Swab Procedure and Microorganism Culture

The prophylactic antibiotic ciprofloxacin 500 mg tablet was given 1 hour before biopsy and then, after biopsy, the patient was given a prescription for another 5 tablets of ciprofloxacin 500 mg to be taken every 12 hours. About one hour before TRUS-guided prostate biopsy, the urologist obtained a rectal swab by using a sterile swab inserted into the rectum. The swab was then put into the Stuart transport medium and was brought to the laboratory in less than one hour. In the laboratory, the swab was streaked onto sheep blood agar and MacConkey agar and then dipped into the thioglycolate broth. After overnight incubation at 35°C in ambient air, a single grown colony was identified with VITEK® 2 GN for Gram-negative bacilli and VITEK® 2 GP for Gram-positive cocci. VITEK® 2 Gram-negative bacilli identification was controlled with *Stenotrophomonas maltophilia* ATCC 17666 and Gram-positive cocci were controlled with *Enterococcus casseliflavus* ATCC 700327. Antibiotic susceptibility testing was done by disc diffusion method according to Kirby Bauer. *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, and *Pseudomonas aeruginosa* ATCC 27853 were used as quality control bacteria for antibiotic susceptibility testing. The interpretation of susceptibility testing was based on the 2014 Clinical Laboratory Standards Institute guidelines.

The susceptibility testing included 17 antibiotics, i.e. ciprofloxacin, levofloxacin, gentamicin, amikacin, ampicillin-sulbactam, cephalothin, cefotaxime, amoxicillin-clavulanate, ceftriaxone, ceftazidime, cefoperazone, piperacillin-tazobactam, cefepime, imipenem, doripenem, meropenem, and ertapenem. The panel test for *Enterococcus faecium* and *Enterofoccus faecalis* consisted of 7 antibiotics, i.e. ciprofloxacin, levofloxacin, ampicillin, teicoplanin, linezolid, vancomycin, and fosfomycin.

Post-Biopsy Assessment

After the biopsy procedure, patients were discharged and then monitored by phone on day-3 and day-7. They were asked whether they had a fever and/or pain after being biopsied. If there were a fever and pain, they were asked to come to the outpatient urology clinic for further assessment. Post-biopsy infection was diagnosed by the urologist who did the biopsy.

Statistical analysis

The characteristics of the study subjects, distribution of isolated pathogens, and antibiogram data were presented descriptively. The relationship between risk factors and post-biopsy infection was tested using Fisher's exact test. A *P* value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS software version 17.0 for Windows PC (SPSS Inc., Chicago, IL, USA).

RESULTS

Demography

Patients' characteristics

A total of 52 male patients were enrolled in this study. Patients' mean age was 67.2 + 7.8 years, ranging from 52 to 80 years. Most patients (96.2%) received outpatient care. Other characteristics are shown in **Table 1**. Sixty-six bacterial isolates grew from the 52 rectal swabs obtained; 14 among them grew two bacteria. All patients had Escherichia coli isolate, while *Klebsiella pneumoniae* was the second commonest bacterium (**Table 2**).

Antimicrobial susceptibility

Thirty-three isolates (50.0%) were resistant to ciprofloxacin (**Table 3**). The commonest ciprofloxacin-resistant bacterium was *E. coli* (47.0%). More than 90% of *E. coli* isolates were sensitive to ampicillin-sulbactam and amoxicillin-clavulanate. Among 9 isolates of *K. pneumoniae*, 8 were sensitive to ampicillin-sulbactam and amoxicillin-clavulanate (**Table 4**).

Table 1. Characteristics of the study subjects (n=52)

Characteristics	n	%
Age < 60 years	8	15.4
Urinary catheterization	6	11.5
History of UTI in the last 3 months	3	5.8
Type of care		
In-patient	2	3.8
Out-patient	50	96.2
History of diabetes mellitus	7	13.5
History of fluoroquinolone use in the past 6 months	5	9.6
History of other antibiotic use in the past 6 months	3	5.8
History of previous prostate biopsy	2	3.8
Histopathological prostatitis	7	13.5

Table 2. Isolated organisms from rectal swabs (n=66)

Organism	n	%
Escherichia coli	52	78.8
Klebsiella pneumoniae	9	13.6
Enterococcus faecium	2	3.0
Acinetobacter haemolyticus	1	1.5
Morganella morganii subsp. *morganii*	1	1.5
Enterococcus faecalis	1	1.5

*sum of percentage may not be 100% due to rounding

Table 3. Bacterial susceptibility against ciprofloxacin

Bacteria	n	Susceptible	Intermediate	Resistant
Escherichia coli	52	19 (36.5%)	2 (3.8%)	31 (59.7%)
Klebsiella pneumoniae	9	7 (77.7%)	2 (22.3%)	-
Enterococcus faecium	2	-	2	-
Acinetobacter haemolyticus	1	1	-	-
Morganella morganii subsp. *morganii*	1	-	-	1
Enterococcus faecalis	1	-	-	1

Table 4. Bacterial susceptibility against ciprofloxacin, ampicillin sulbactam and amoxicillin-clavulanate

Bacteria	n	Ciprofloxacin	Ampicillin sulbactam	Amoxicillin clavulanate
Escherichia coli	52	19 (36.5%)	50 (96.2%)	47 (90.4%)
Klebsiella pneumoniae	9	7 (77.7%)	8 (88.9%)	8 (88.9%)
Enterococcus faecium	2	0 (0%)	2 (100%)	2 (100%)
Acinetobacter haemolyticus	1	1 (100%)	1 (100%)	1 (100%)
Morganella morganii subsp. *morganii*	1	0 (0%)	1 (100%)	1 (100%)
Enterococcus faecalis	1	0 (0%)	1 (100%)	1 (100%)

P-ISSN: 1978-3744 E-ISSN: 2355-6811

The *E. coli* antibiogram showed high resistance to fluoroquinolones (59.6% to ciprofloxacin, 57.7% to levofloxacin) and to third-generation cephalosporins (34.6% to cefoperazone, 32.7% to ceftriaxone, and 30.8% to cefotaxime). All of *E. coli* isolates were susceptible to meropenem or ertapenem and showed very high susceptibility to imipenem (98.1%), doripenem (98.1%), piperacillin-tazobactam (96.2%), and ampicillin-sulbactam (96.2%) (**Table 5**).

All isolates of *K. pneumoniae* showed susceptibility to levofloxacin, amikacin, imipenem, doripenem, meropenem, and ertapenem (**Table 6**). The isolate of *Acinetobacter haemolyticus* showed no resistance to all antibiotics tested and intermediate resistance to cefoperazone. The isolate of *Morganella morganii* subsp. *morganii* showed resistance to ciprofloxacin, cephalothin, amoxicillin-clavulanate, and intermediate resistance to levofloxacin.

Only seven antibiotics were tested to the *Enterococci.* The two isolates of *Enterococcus faecium* showed intermediate resistance to ciprofloxacin but were sensitive to ampicillin, teicoplanin, vancomycin, and fosfomycin. One isolate was resistant to linezolid and another one had intermediate resistance to levofloxacin. The isolate of *Enterococcus faecalis* showed resistance to ciprofloxacin and levofloxacin. This isolate was sensitive to ampicillin, teicoplanin, linezolid, vancomycin, and fosfomycin.

Resistant *E. coli* isolates were of special concern. From the 31 resistant isolates, none was sensitive to levofloxacin, but all were sensitive to carbapenems. Additionally, these isolates showed high susceptibility to amikacin (93.5%), ampicillin-sulbactam (93.5%), piperacillin-tazobactam (93.5%), amoxicillin-clavulanate (83.9%), and gentamicin (80.6%). However, sensitivity to other antibiotics was much higher in ciprofloxacin-sensitive *E. coli* isolates. The use of fluoroquinolone in the past six months tended to be associated with ciprofloxacin resistance (**Table 7**).

Post-biopsy infection

Post-biopsy fever was observed in 7 (13.5%) patients; 5 of them had resistant isolate to ciprofloxacin. No clinical factor was associated with infection. However, a history of fluoroquinolone treatment in the past 6 months tended to increase the risk of post-biopsy infection (**Table 8**).

Table 5. Antibiogram of *Escherichia coli* (n=52)

Antibiotic	Susceptible	Intermediate	Resistant
Ciprofloxacin	19 (36.5 %)	2 (3.8 %)	31 (59.6 %)
Levofloxacin	20 (38.5 %)	2 (3.8 %)	30 (57.7 %)
Gentamicin	46 (88.5 %)	0	6 (12.8 %)
Amikacin	47 (90.4 %)	5 (9.6 %)	0
Ampicillin-sulbactam	50 (96.2 %)	2 (3.8 %)	0
Cephalothin	11 (21.2 %)	18 (34.6 %)	23 (44.2 %)
Cefotaxime	32 (61.5 %)	4 (7.7 %)	16 (30.8 %)
Amoxicillin-clavulanate	47 (90.4 %)	4 (7.7 %)	1 (1.9 %)
Ceftriaxone	34 (65.4 %)	1 (1.9 %)	17 (32.7 %)
Ceftazidime	44 (84.6 %)	3 (5.8 %)	5 (9.6 %)
Cefoperazone	29 (55.8 %)	5 (9.6 %)	18 (34.6 %)
Piperacillin-tazobactam	50 (96.2 %)	2 (3.8 %)	0
Cefepime	43 (82.7 %)	7 (13.5 %)	2 (3.8 %)
Imipenem	51 (98.1 %)	1 (1.9 %)	0
Doripenem	51 (98.1 %)	0	1 (1.9 %)
Meropenem	52 (100 %)	0	0
Ertapenem	52 (100 %)	0	0

Table 6. Antibiogram of ***Klebsiella pneumoniae (n=9)***

Antibiotic	Susceptible	Intermediate	Resistant
Ciprofloxacin	7 (77.7 %)	2 (22.3 %)	0
Levofloxacin	9 (100 %)	0	0
Gentamicin	8 (88.9 %)	0	1 (11.1%)
Amikacin	9 (100 %)	0	0
Ampicillin-sulbactam	8 (88.9 %)	0	1 (11.1 %)
Cephalothin	7 (77.7 %)	0	2 (22.3 %)
Cefotaxime	6 (66.6 %)	1 (11.1 %)	2 (22.3 %)
Amoxicillin-clavulanate	8 (88.9 %)	1 (11.1 %)	0
Ceftriaxone	7 (77.7 %)	1 (11.1 %)	1 (11.1 %)
Ceftazidime	7 (77.7 %)	1 (11.1 %)	1 (11.1 %)
Cefoperazone	7 (77.7 %)	0	2 (22.3 %)
Piperacillin-tazobactam	7 (77.7 %)	2 (22.3 %)	0
Cefepime	7 (77.7 %)	1 (11.1 %)	1 (11.1%)
Imipenem	9 (100 %)	0	0
Doripenem	9 (100 %)	0	0
Meropenem	9 (100 %)	0	0
Ertapenem	9 (100 %)	0	0

Table 7. Clinical factors associated with ciprofloxacin-resistant isolates

Variables	Ciprofloxacin		*P* value[1]
	R (n=31)	S (n=21)	
Current urinary catheterization			
Yes	4 (12.9%)	2 (9.5%)	1.000
No	27 (87.1%)	19 (90.5%)	
History of UTI in the past 3 months			
Yes	3 (9.7%)	0	0.264
No	28 (90.3%)	21 (100%)	
Type of hospital care			
In-patient	2 (6.5%)	0	0.509
Out-patient	29 (93.5%)	21 (100%)	
Presence of diabetes mellitus			
Yes	4 (12.9%)	3 (14.3%)	1.000
No	27 (87.1%)	18 (85.7%)	
Fluoroquinolone use in the past 6 months			
Yes	6 (19.4%)	0	0.070
No	25 (80.6%)	21 (100%)	
Other antibiotics in the past 6 months			
Yes	3 (9.7%)	0	0.264
No	28 (90.3%)	21 (100%)	
Previous prostate biopsy			
Yes	2 (6.5%)	0	0.509
No	29 (93.5%)	21 (100%)	
Histopathological prostatitis			
Yes	5 (16.1%)	2 (9.5%)	0.687
No	26 (83.9%)	19 (90.5%)	

[1]Fisher's exact test

Table 8. Factors associated with post-biopsy infection

Variables	Infection (+) n=7	Infection (-) n=45	*P* value*	OR	95% CI
Resistant to fluoroquinolones					
Yes	5 (16.7%)	25 (83.3%)	0.687	1.827	0.320 – 10.443
No	2 (9.1%)	20 (90.9%)			
History of UTI in the past 3 months					
Yes	1 (33.3%)	2 (66.7%)	0.358	3.583	0.280 – 45.796
No	6 (12.2%)	43 (87.8%)			
Current urinary catheterization					
Yes	2 (33.3%)	4 (66.7%)	0.1801	4.100	0.592 – 28.380
No	5 (10.9%)	41 (89.1%)			
Type of hospital care					
In-patient	7 (14.0%)	43 (86.0%)	1.000	-	-
Out-patient	0	2 (100%)			
Presence of diabetes mellitus					
Yes	1 (14.3%)	6 (85.7%)	1.000	1.083	0.110 – 10.643
No	6 (13.3%)	39 (86.7%)			
Fluoroquinolone in the past 6 months					
Yes	2 (40.0%)	3 (60.0%)	0.129	5.600	0.746 – 42.012
No	5 (10.6%)	42 (89.4)			
Other antibiotics in the past 6 months					
Yes	0	3 (100%)	1.000	-	-
No	7 (14.0%)	42 (85.7%)			
Previous prostate biopsy					
Yes	0	2 (100%)	1.000	-	-
No	7 (14.0%)	43 (86.0%)			

*Fisher's exact test

DISCUSSION

This is the first study in Indonesia to evaluate the resistant pattern of bacterial isolates in the rectum of male patients prior to TRUS-guided prostate biopsy. In this current study, *E. coli* was the most frequently found rectal flora (78.8%). A similar study in Hong Kong found that *E. coli* was the commonest isolated organism (89.8%) [13]. While in Korea, *E. coli* was found in 76% of cases with positive rectal swabs [15]. A US study in 1,274 patients found 31 (2.4%) cases presented with post-biopsy infections. Positive cultures from blood or urine showed 89% among the isolates were *E. coli* bacteria and 90% of them were fluoroquinolone-resistant [7]. Another study found that *E. coli* was the commonest pathogen (75%) in cases with post-biopsy infections [16].

The proportion of fluoroquinolone-resistant bacteria in this study was high (50.0% for ciprofloxacin), which was mostly predominated by *E. coli.* As a comparison, previous studies in developed countries found a prevalence of 22% in the United States [17], 10.6% in London [9], 19% in Canada [18], and 26.7% in Korea [15].

Uncontrolled use of fluoroquinolone in society could be responsible for the high bacterial resistance to it. In many cities in Indonesia, especially Jakarta, antibiotics can be purchased without prescriptions such as from “drug stores” which usually act as “peoples’ pharmacy”. The availability of over-the-counter antibiotics without prescriptions is found not only in Indonesia but also in other developing countries such as Bangladesh, the Philippines, and Mexico. One contributing factor to it is poverty, i.e. when people cannot get free or cheap health treatment in primary health care, they try to get cheaper costs by getting antibiotics and other drugs over the counter. Self-antibiotic treatment usually led to under dosage and inadequate duration of antibiotic treatment which then contributes to the emergence of multi-drug resistant bacteria.

Another contributing factor is the misuse of antibiotics (including ciprofloxacin) as a “growth promoter” in animal food, especially in poultry. It induced the *Enterobacteriaceae* in the animal gut, especially *Escherichia coli* and *Klebsiella pneumoniae* to become resistant to ciprofloxacin. This ciprofloxacin-resistant *Escherichia coli* and *Klebsiella pneumoniae* could contaminate the raw food material and the cooked food, which is then consumed by people and then becomes the normal flora in human guts. The Indonesian government has already banned the misuse of antibiotics in animal food.

The other contributing factor is ciprofloxacin and levofloxacin (quinolones) are relatively “new” compared to the “old” antibiotics such as amoxicillin-clavulanate and ampicillin-sulbactam which have been available since 40–50 years ago. Therefore, many physicians tend to

In this study, no clinical factor was found to be associated with fluoroquinolone-resistant *E. coli*. The small number of patients with certain clinical characteristics might affect statistical analyses and significance. For example, only two patients had a history of prostate biopsy before and only five patients received fluoroquinolone in the past six months.

A study in Hong Kong found that diabetes mellitus and prior antibiotics within the last five years are significant predictors for fluoroquinolone-resistant bacteria found in rectal swab cultures [14]. Potential risk factors for fluoroquinolone-resistant are hospitalization, diabetes, and prior treatment with fluoroquinolone [3]. The American Urological Association has also stated that the commonest risk factor for fluoroquinolone-resistant bacteria among patients undergoing prostate biopsy is fluoroquinolone exposure during the last 6 months [10]. Besides fluoroquinolone, the *extended-spectrum beta-lactamase* (ESBL)-producing bacteria have also raised awareness. Resistant *E. coli* to the third-generation cephalosporin in this study was also high (above 30%). A study in the US found only 0.64% incidence of ESBL producing bacteria [19]. The reported incidence of ESBL-producing organisms is 0.8%–1.3% [20].

Despite the high proportion of bacterial resistance in this study, infectious complication after the procedure was relatively low (13.5%). However, the reported incidence of UTI after TRUS-guided prostate biopsy was 2%–6% [5,6]. Post-biopsy infections by the ESBL-organism have also been reported and may be co-resistant to fluoroquinolone as well [3,21,22]. Generally, the pathogens are resistant to third-generation cephalosporins but sensitive to carbapenems [23]. A similar pattern was also seen in this study; almost all *E. coli* isolates were sensitive to carbapenems. Of interest, high susceptibility was also observed with ampicillin-sulbactam, piperacillin-tazobactam, and amoxicillin-clavulanate. In contrast, a previous study in the US found that fluoroquinolone-resistant *E. coli* showed 94% resistance to ampicillin and 74% resistance to ampicillin-sulbactam [17]. Another study in Hong Kong found that rectal bacterial isolates showed high resistance to ampicillin (93.6%) and ciprofloxacin (60.7%), but 96.7% were sensitive to amoxicillin-clavulanate and 100% sensitive to piperacillin-tazobactam [14]. Our finding is highly suggestive of using ampicillin-sulbactam and amoxicillin-clavulanate as alternative options for post-biopsy infections resistant to fluoroquinolone. In comparison, a randomized trial in patients with complicated skin and skin structure infections found that tigecycline treatment was equally effective compared to ampicillin-sulbactam or amoxicillin-clavulanate [24]. This older antibiotic combination seems promising as an alternative antimicrobial treatment in patients with fluoroquinolone resistance.

We did not find any association between the clinical variable tested and post-biopsy infection. This result could be due to the small sample size and low incidence of risk factors, such as a history of UTI in the last 3 months, urinary catheterization, hospitalization, diabetes mellitus, and prior prostate biopsy. However, the use of fluoroquinolone in the past six months may contribute to the present infection. Our results indicated that all six patients with a history of fluoroquinolone use also showed ciprofloxacin resistance. The statistic did not reach significance due to the small sample size of patients with a history of fluoroquinolone use and zero result in the patient's subgroup without ciprofloxacin resistance.

In comparison, a study in Pakistan involving 158 patients undergoing TRUS-guided biopsy found an infection rate of 12.5%. The rate was significantly higher among patients carrying fluoroquinolone-resistant bacteria than non-carriers (24% vs. 3.5%, $P < .001$). Previous use of fluoroquinolone (OR, 2.54; 95% CI, 1.17–5.49; $P = .019$) and history of hospitalization (OR, 7.85; 95% CI, 2.075–29.744; $P = .002$) were identified as independent risk factors of fluoroquinolone resistance [25]. This study strongly emphasizes the need for appropriate prophylaxis to reduce the post-biopsy infection rate.

Modification of prophylaxis antibiotics might be needed to reduce infectious complications. In Korea, for instance, the previous policy was to give ciprofloxacin 500 mg before 2009, which resulted in an increase in the incidence rate of post-biopsy infection from 0.3% to 2.31%. The addition of intravenous ceftriaxone before biopsy plus fluoroquinolone for more than 7 days after biopsy reduced the infection rate to 0.2% in 2010–2012 [26]. An alternative regimen with piperacillin-tazobactam 4.5 gram 30 minutes before and 6 hours after TRUS-guided biopsy has been proposed in Japan. This regimen showed a similar incidence rate of acute prostatitis with previous fluoro-quinolone-based regimens [27].

Recently, a pre-biopsy screening to identify fluoroquinolone-resistant bacteria using ciprofloxacin-supplemented MacConkey agar has been proposed. Antibiotic prophylaxis was modified in patients showing positive resistant bacteria. This method resulted in reduced post-biopsy sepsis compared to standard empirical antibiotic prophylaxis, but it did not reach statistical significance (0.66% vs. 4.3%; $P = .08$). The alternative antibiotic regimen used in this study was trimethoprim-sulfamethoxazole or cefuroxime depending on their resistance profiles [28].

This study has several limitations. The total sample size was 52 patients, but, with the proportion of ciprofloxacin-resistant bacteria as high as 50%, this result was quite significant for considering alternative antimicrobial prophylaxis in the future. Another limitation of this study was the lack of identification of uropathogenic *Escherichia coli.*

CONCLUSIONS

Ciprofloxacin-resistant bacteria in the rectum are common among patients undergoing prostate biopsy in Cipto Mangunkusumo Hospital. The proportion is found to be as high as 50.0% with *Escherichia coli* as the commonest resistant pathogen. Alternative antimicrobial prophylaxis should be considered in the future; the recommended choices based on the antibiogram profile in this study are ampicillin-sulbactam and amoxicillin-clavulanate. Routine pre-biopsy rectal swab cultures should also be encouraged, both to guide prophylaxis and to plan treatment to reduce the incidence of post-biopsy bacteremia and sepsis.

DECLARATIONS

Competing of Interest

The authors declare no potential conflicts of interest.

Acknowledgment

Not applicable

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