PREVALENCE OF FLUOROQUINOLONE - RESISTANT ENTEROBACTERIACEAE IN THE NORMAL RECTAL FLORA OF PATIENTS UNDERGOING TRANSRECTAL PROSTATE BIOPSY IN PHRAMONGKUTKLAO HOSPITAL, THAILAND

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Abstract

Background: Despite routine use of antimicrobial prophylaxis, the incidence of infections after transrectal ultrasound-guided prostate biopsy has increased over the last 2 decades. Notably, a rising incidence of postbiopsy infections from fluoroquinolone-resistant Enterobacteriaceae had been reported over the same period. Many authors have studied the rectal flora reservoir to select the most appropriate prophylaxis antibiotics.

Objectives: The study aimed to determine the prevalence of fluoroquinolone-resistant and extended spectrum β-lactamase producing isolates at Phramongkutklao Hospital, Thailand and to identify the risk factors predicting the carriage of these organisms.

Methods: Men undergoing transrectal ultrasound-guided prostate biopsy were prospectively enrolled between February and October 2015. Rectal swab culture was obtained before antimicrobial prophylaxis and prostate biopsy. Univariate and multivariate analyses were performed to identify the independent risk factors associated with antimicrobial-resistant flora.

Results: In total, 99 patients underwent biopsy, of whom 38 (38.4%) had antimicrobial-resistant rectal flora, with 26 (26.3%) presenting fluoroquinolone-resistant rectal flora and 12 (12.1%) having both fluoroquinolone-resistant rectal flora and extended spectrum β-lactamase. The incidence of postbiopsy infections was 6.1%. The use of antibiotics in the past 6 months was found in 23.7% of the resistant group vs.6.6% of the sensitive group (odds ratio = 4.86, p = 0.030), with the previous biopsy history being 31.6 and14.8% (odds ratio = 3.17, p = 0.036), respectively. Postbiopsy infections occurred in13.2 and1% (odds ratio = 10.69, p = 0.045) of patients in the resistant and sensitive groups, respectively.

Conclusion: The prevalence of fluoroquinolone-resistant rectal flora increased among patients undergoing transrectal prostate biopsy at Phramongkutklao Hospital, Thailand. A history of antibiotics in the past 6 months, previous biopsy, and postbiopsy infections were associated with antimicrobial resistance. Culture-directed prophylaxis antibiotics may reduce postbiopsy infections after transrectal prostate biopsy

Keywords : Biopsy, Fluoroquinolone, Prostate, Risk factors, Thailand

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Introduction

Transrectal ultrasound-guided prostate biopsy (TRUS-Bx) is the gold standard procedure for diagnosing prostate cancer, which is the most commonly diagnosed cancer and the second leading cause of cancer deaths among American men. In 2014, it has been estimated that 233,000 men would be diagnosed with prostate cancer and 29,480 would die of this disease.[1] Approximately 800,000 biopsies are performed in the US alone annually.[2] Although generally considered a safe procedure, complications can sometimes occur, including urinary tract infection, prostatitis, bacteremia, sepsis, hematuria, rectal bleeding, and hematospermia.[3] In a larger series, the postbiopsy infection (PBI) rate ranged from 0.1 to 7%.[4–6] Clear evidence showed that prophylactic antimicrobials reduced the rates of PBIs after TRUS-Bx.[6] Currently, the antimicrobial prophylaxis regimen, as recommended by the American Urological Association, is a single dose of fluoroquinolone(FQ) before TRUS-Bx, with cephalosporin or trimethoprim-sulphamethoxazole or aminoglycosides as alternatives.[7]

Despite routine use of antimicrobial prophylaxis, the incidence of PBI after TRUS-Bx has increased over the last two decades.[8–10] Notably, a rising incidence of PBI from FQ-resistant *Escherichia coli* has been reported over the same period, leading many to conclude that the recent rise in infectious complications is related to FQ-resistance.[10–12] Most PBIs arise from the direct inoculation of bacteria from the rectal mucosa into the urinary tract and prostatic vessels. Many authors have studied the rectal flora reservoir of patients undergoing TRUS-Bx to select the most appropriate prophylaxis antibiotics to reduce PBI.[13–18]

Based on this practice, the rates of rectal carriage have ranged from 10.6 to 22% for FQ-resistant flora in the US and Europe.[17, 19–21] In Asia, the prevalence of these organisms has ranged from 26.7 to 40.4%.[22, 23] Studies of the risk factors associated with FQ-resistant bacteria have shown a relation to diabetes, history of antibiotic use in the last three months, hospitalization, previous prostate biopsy, indwelling of urinary catheter, and use of steroids.[17,19] Our study aimed to determine the prevalence of FQ resistant rectal flora and extended spectrum β-lactamase (ESBL)-producing isolates at Phramongkutklao Hospital, Thailand, and to identify the risk factors predicting the carriage of these organisms.

Methods

We prospectively enrolled all male patients undergoing TRUS-Bx between February and October 2015 at Phramongkutklao Hospital, Thailand. The protocol for the research project was approved by the Institutional Review Board of the Royal Thai Army Medical Department. The exclusion criteria included active urinary tract or intestinal infection at the time of biopsy and coagulopathy.

Informed consent was obtained from eligible patients. Rectal swab culture was obtained before performing antimicrobial prophylaxis and prostate biopsy. For FQ-resistant testing, swabs were directly cultured on both MacConkey agar, with 1mg/L ciprofloxacin, and blood agar plates and incubated at 37°C for 18 h. Antimicrobial susceptibility testing was performed using the agar disk diffusion technique. All patients received a standard empirical prophylactic of FQ. Basic demographic and clinical data were collected from patients undergoing TRUS-Bx during the study period using questionnaires. The history of antibiotic use (less than six months), hospitalization, urethra catheter and previous prostate biopsy within six months was reviewed from medical records. The patients were followed for at least 30 days to check for infectious complications. Infections were defined as lower urinary tract symptoms with fever and positive urine culture (>104 cfu/mL).

Descriptive statistics were used for the patients' demographic and background data. Univariate analyses were performed for variables that were possible predictors of PBIs using Pearson's chi-square test and Student's t-test. Variables were considered eligible for inclusion in a multivariate logistic regression model when they had a p value of <0.05.

Results

In total, 99 patients undergoing TRUS-Bx at Phramongkutklao Hospital between February and October 2015 were enrolled in the present study. The demographic data of the patients are shown in **Table 1**. Rectal swab culture showed that 94.9% (n= 94) involved *Escherichia coli*, followed by *Klebsiella spp*. (4.1%, n= 4) and *Enterococcus faecalis* (1%, n= 1). In total, 38.4% (n= 38) of patients carried antimicrobial-resistant rectal flora, of whom 26.3% (n= 26) had FQ-resistant rectal flora and 12.1% (n= 12) had both FQ-resistant rectal flora and ESBL. The incidence of PBI was 6.1% (n= 6). The characteristics of the patients who developed PBI are shown in **Table 2.**

Table 1 Characteristics of transrectal ultrasound-guided biopsy of prostate patients

Parameters	Number	Percent
Age		
Mean ± SD		67.25 ± 8.07
Range (Min-Max)		49–84
PSA		
Mean ± SD		24.98 ± 62.62
Median		9.81
Range (Min-Max)		2.06–500
Diabetes		
Yes	17	17.2
History of ATB use (<6 months)		
Fluoroquinolone	10	10.1
Cephalosporin	3	3.0
Past admission		
Yes	4	4.0
History of urethra catheter		
Yes	5	5.1
The frequency of TRUS-Bx		
1	78	78.8
2	18	18.2
3	3	3.0
The number of biopsy cores		
12	89	89.9
>12	10	10.1

SD, standard deviation; PSA, prostate-specific antigen; ATB, antibiotic; TRUS-Bx, transrectal ultrasound-guided biopsy

Table 2 Characteristics of patients with postbiopsy infection

Characteristics	Postbiopsy patient					
	1	**2**	**3**	**4**	**5**	**6**
Age, y	55	68	67	56	68	73
PSA, ng/ml	6.6	15	6.79	53	11.5	8.07
Rectal swab culture	*E. coli*	*E. coli*	*E. coli*	*E. coli*	*E. coli*	*E. coli*
FQ-resistant	+	+	+	+	-	+
ESBL	-	-	+	+	-	-
Urine culture	*Klebsilla*	*E. coli*	*E. coli ESBL*	*E. coli ESBL*	*E. faecalis*	*E. coli*
Blood culture	-	-	-	-	-	-

PSA, prostate-specific antigen; FQ, fluoroquinolone; ESBL, extend-spectrum β-lactamase producing

FQ-resistance of a patient was not significantly associated with age, mean PSA, DM, past admission, urethra catheter and more than 12 core biopsies. FQ resistance flora significantly differed in recent antibiotic use, previous prostate biopsy and PBIs between the two groups revealed by the univariate analyses. The use of antibiotics in the past six months was found in23.7% of the resistant group vs.6.6% of the sensitive group [odds ratio (OR) = 4.86, $p = 0.030$], with a previous biopsy history being 31.6 and14.8% (OR= 3.17, $p = 0.036$), respectively. PBIs occurred in13.2 and1% (OR= 10.69, $p= 0.045$) of patients in the resistant and sensitive groups, respectively, using multivariate logistic regression analysis. **(Tables 3 and 4).**

Table 3 Univariate comparision of FQ resistance by clinical finding

	FQ-sensitive (%)	**FQ-resistant (%)**	***p*-value**
Mean age	66.85	67.89	0.535
Mean PSA	23.31	27.65	0.739
Diabetes	8 (13.1)	9 (23.7)	0.650
ATB use in 6 months	4 (6.6)	9 (23.7)	0.023*
Past admission	1 (1.6)	3 (7.9)	0.187
Urethra catheter	3 (4.9)	2 (5.3)	0.311
Previous prostate biopsy	9 (14.8)	12 (31.6)	0.034*
>12 cores biopsy	7 (11.5)	3 (7.9)	0.667
Postbiopsy infection	1 (1.6)	5 (13.2)	0.019*

* $p < 0.05$, PSA, prostate-specific antigen; ATB, antibiotics; FQ, fluoroquinolone

Table 4 Multivariate analysis of FQ resistance by clinical finding

	OR (95% CI)	***p*-value**
Diabetes	1.334 (0.385–4.624)	0.649
ATB use in 6 months	4.860 (1.170–20.192)	0.030*
Past admission	5.204 (0.399–67.881)	0.208
Urethra catheter	0.285 (0.023–3.571)	0.330
Previous prostate biopsy	3.173 (1.078–9.334)	0.036*
>12 cores biopsy	0.720 (0.157–3.291)	0.720
Postbiopsy infection	10.688 (1.059–107.83)	0.045*

* $p < 0.05$, FQ, fluoroquinolone; ATB, antibiotic; OR, odd ratios;

Discussion

Currently, the antimicrobial prophylaxis regimen before TRUS-Bx is a single dose of FQ.[7] In the present study, the incidence of PBI was 6.1%; in related studies, the incidence of PBI ranged from 0.1 to 7%.[4–6] The incidence of PBI has been increasing in recent years, along with the rising prevalence of FQ-resistant flora. The prevalence of FQ-resistant rectal flora was 38.4% in the present study. Based on these findings, we suggest that the use of FQ for prophylaxis before TRUS-Bx may not be effective at Phramongkutklao Hospital, Thailand. Alternative ways included adapting the prophylaxis antibiotics to local resistant rates or identifying patients carrying FQ-resistant organisms before the procedure using culturing rectal swabs.

In the present study, we showed that a history of previous TRUS-Bx and recent use of antibiotics were risk factors of FQ-resistant rectal flora. However, these risk factors may overlap among some patients because the patients undergoing biopsy had received the prophylaxis antibiotics too.

We conclude that when patients have an appointment for TRUS-Bx, the most effective method is to perform a rectal swab culture one to two weeks before the biopsy and select a prophylaxis antibiotic using the culture result to decrease the PBI rate. When the hospital is unable to perform a rectal swab culture, the history of the previous biopsy or antibiotic (FQ or cephalosporin) used in the past six months can be used to select the most appropriate antibiotic. The alternatives for prophylaxis antibiotics are aminoglycoside, carbapenem and fosfomycin.

In the present study, we found the following limitations. The first was the limited number of patients in the study; the study had a small sample size. The second was the patient data from hospital records may have underestimated the history of antibiotic use. The prevalence of fluoroquinolone-resistant rectal flora increased among patients undergoing TRUS-Bx at Phramongkutklao Hospital, Thailand. A history of antibiotics in the past six months, previous biopsy and PBIs were associated with antimicrobial resistance. Culture-directed prophylaxis antibiotics may reduce the infectious complications after TRUS-Bx.

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