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Culture Directed Prostate Biopsy: Culture Sensitivity Pattern and Infectious Complications: A Prospective Study

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Abstract

Introduction

Overall incidence of infectious complications following Transrectal Ultrasound (TRUS) guided prostate biopsy is 11%.It ranges from simple UTI to severe sepsis and mortality. It is commonly caused by gram negative coliform bacteria of fecal origin. fluoroquinolones are the most commonly preferred antibiotic used as empirical prophylaxis agent. Despite empiric prophylaxis, the incidence of complication following TRUS is 2.2%, out of which 22% are due to fluroquinolone resistant organism. So a prior rectal swab culture and targeted culture specific agent will reduce the incidence of infectious complication.

Aims and objectives

To ascertain the prevalence of fluoroquinolone resistant organisms in men undergoing TRUS guided prostate biopsy and to assess the efficacy of targeted antimicrobial prophylaxis based on rectal swab cultures in reducing the rate of infectious complications

Results

A total of 255 patients underwent rectal swab culture sensitivity before TRUS biopsy. Ciprofloxacin sensitive (CS) rectal flora was found in 215(84.3%) and Ciprofloxacin resistant (CR) in 40(15.7%) of cases. Univariate analysis demonstrated that patients with CS and CR rectal flora were similar except that a history of urinary tract infection was more common in CR patients (p = 0.004).Only 5 patients (1.9%) developed uncomplicated UTI following culture directed antibiotic therapy. These were managed by augmenting with second antibiotic with no sequel.

Conclusion

Culture directed targeted antimicrobial prophylaxis achieved a low rate of infectious complications in patients with CS or CR rectal flora, limited morbidity and no sequelae. These results suggest that this individualized method of prophylaxis may be widely applied to all patients undergoing TRUS guided prosta biopsy

Keywords: Prostate biopsy,Culture specific antibiotics,Infectious complications.

Introduction

Transrectal ultrasound (TRUS) guided prostate biopsy is still the gold standard method of diagnosis of prostate cancer. More than two million transrectal ultrasound guidedprostate biopsies (TRUSP) are performed in the US and Europe annually [1, 2]. Infectious complications range from uncomplicated urinary tract infections (UTIs) to prostatitis to sepsis and death [3]. Empiric antimicrobial prophylaxis reduced the risk of infectious complications [4] but, with increasing resistance, infections after biopsy have risen [1, 5–9] and are most commonly CR-GNB[10]. Two primary prophylaxis strategies have emerged to prevent post biopsy infections, a targeted or an empiric approach [7, 11–13]. The targeted approach involves obtaining a pre-

biopsy rectal swab culture and choosing an antimicrobial agent based on culture results. TRUS guided prostate biopsy carries the risks of hematuria, hematospermia, and infectious complications,like prostatitis, epididymo-orchitis, bacteremia, and sepsis.The proposed mechanism of infection involves the biopsy needle passing through the rectal mucosa with fecal contamination seeding the bladder and vasculature, rather than the bladder being the origin.[31]]However, antimicrobial prophylaxis before transrectal biopsy reduces the risks of infectious complications as compared with placebo (8% versus 25%).[31] American urology association best practice policy on urologic surgery recommends fluroquinolones as the first line antibiotic prophylaxis before doing a prostate biopsy. The infectious complications despite antibiotic prophylaxis in prostate biopsy have been described upto 11% of cases[32,33,34,35,36] , including sepsis in 2.2% cases.[34,35,38] The most common flora causing infection after transrectal prostate biopsy are coliforms and the organisms identified include Escherichia coli, Enterobacter, Proteus and Klebsiella.[32]

Aims and objectives

To ascertain the prevalence of fluoroquinolone resistant organisms in men undergoing TRUS guided prostate biopsy and to assess the efficacy of targeted antimicrobial prophylaxis based on rectal swab cultures in reducing the rate of infectious complications

Material & Methods

A Prospective study was carried out at urology department, SCB Medical college, Cuttack from November 2015 to November 2017. Patients undergoing TRUS guided prostate biopsy with prior rectal swab culture were included in the study. Exclusion criteria were finger guided prostate biopsy, no rectal swab culture prior to TRUS biopsy, abnormal coagulation profile, severe immunosuppression, acute prostatitis and painful anorectal conditions like fissure or hemorrhoids .Prophylactic antimicrobial agents were selected using a pre-determined protocol. Patients with CS-GNR received ciprofloxacin 500 mg orally 2 h before TRUS biopsy and continued for 5 days thereafter. Subjects harboring CR-GNB received an antimicrobial agent based on the culture sensitivity report. A standard 12 core TRUS biopsy was performed in all patients by a single urologist. Patients were then followed up for evidence of UTI i.e dysuria, fever, urgency, pyuria, if any.

Results

Clinical characteristics;

255 patients were included in the analysis .Patient demographics and clinical characteristics of the 255 patients stratified by ciprofloxacin susceptibility status are listed in Table 1. 215 (84.3%) had CS-GNB and 40 (15.7%) had CR-GNB on rectal swab culture. Univariate analysis demonstrated that patients with CS and CR rectal flora were similar except that a history of urinary tract infection was more common in CR patients ($p = 0.004$).

Microbiological characteristics; of the 40 patients with CR-GNB, 37 (92.5%) harbored Escherichia coli, 1 (2.5%) Pseudomonas aeruginosa, 1 (2.5%) Citrobacter freundii and 1 (2.5%) Klebsiella pneumoniae. The antimicrobial susceptibility profiles of the CR- E.coli isolates are shown in table 2. of patients with CRflora (40 patients), sensitivity pattern with other antibiotic was cefuroxime (1.94%), cotrimoxazole (25.2%), amoxicillin /clavulanic acid (26%), cefixime (27.2%), ceftazadime (50.5%) and piperacillin/tazobactum (85.4%) (Table 2).

Infectious complications- 250 patients (98.2%) did not develop infections, while 5 (1.8%) had clinical infections and 3 (1.2%) of these were culture-proven .The infection outcomes stratified by CS or CR status are shown in Table 3. The characteristics of the 5 patients who developed infectious complications are shown in Table 4. All infections occurred in patients who received single drug targeted prophylaxis. Infectious complications occurred in

3 (66.7%) patients within 7 days and in 2 (33.3%) patients at 8, 11 days, respectively. The 2 patients with uncomplicated UTIs were managed as outpatients, 2 with antimicrobial therapy; those with complicated UTIs or sepsis were managed with antimicrobial therapy as inpatients for 1–5 days. All patients recovered without sequelae. Two (40%) of the 5 patients with infections were culture negative. Of the 3 patients with positive cultures, 2 (1 ciprofloxacin and 1 amikacin) were prophylaxis failures, i.e. the infecting bacteria were susceptible to the prophylactic drug they received.

Discussion

Rectal swab cultures can determine the population of CR-GNB in the rectal flora. Puig et al [38]studied infectious complications in 1018 patients, who underwent TRUS prostate biopsy, first 614 patients were biopsied without antibiotic prophylaxis and next 404 patients were biopsied with antibiotic prophylaxis. They revealed that rate of infectious complications were significantly higher in patients without prophylaxis as compared with patients who received prophylaxis (10.3% vs3.7%, p=0.0001) with more than three fourth of major complications occurring in patient not receiving prophylaxis. Taylor A, Murphy A et al [14]; evaluated targeted antimicrobial prophylaxis in men undergoing TRUS guided prostate biopsy based on rectal swab culture results. A total of 457 men underwent transrectal ultrasound guided prostate biopsy, and of these men 112 (24.5%) had rectal swab obtained while 345 (75.5%) did not. Among those who received targeted prophylaxis 22 (19.6%) men had fluoroquinolone resistant organisms. There were no infectious complications in the 112 men who received targeted antimicrobial prophylaxis, while there were 9 cases (including 1 of sepsis) among the 345 on empirical therapy (p = 0.12). Fluoroquinolone resistant organisms caused 7 of these infections.

In this study, the CR rate was 15.7%. We agree with Van Besien et al. [25]**;** Who stated that the benefit of targeted prophylaxis depends on local CR prevalence rates. A randomized, blinded trial would subject the approximately 20% of patients who harbor CR flora and receive FQ prophylaxis to the known 5-fold higher risk of infectious complications [25]. Similarly, empiric augmented prophylaxis could also subject patients to ineffective antimicrobial prophylaxis. In our study infection rate after targeted prophylaxis is 1.8%(5) which is as per litreture. Patients having CR organism is 15.7% (40) of which 2(8%) patients have infection episode. Indeed, of the 5 patients identified, 3 had negative cultures before antimicrobial therapy was initiated and 1 was negative at 7 days but positive within 30 days. More importantly, only 2 (0.8%) had significant clinical infections and only 1 was culture-proven, febrile UTI (0.2%) and sepsis (0.2%).Of the 5 patients with infections, only 3 had prior exposure to fluoroquinolones, a rate similar to those who did not become infected. Of the 3 patients with positive cultures, 2 were prophylaxis failures, i.e. the infecting bacteria was susceptible to the prophylactic drug given, (ciprofloxacin 1, and amikacin 1). Of the 3 culture-proven infections, the bacteria were multidrug resistant in 3, and of these, 1 were ESBLs. Limitations are It was a single institution study and, for ethical reasons, was not blinded or controlled.Other complications like Erectile dysfunction, a potential complication of TRUS prostate biopsy was not evaluated, but it may occur as a result of inflammation induced by infection [30].

Conclusion

Culture directed targeted antimicrobial prophylaxis achieved a low rate of infectious complications in patients with CS or CR- GNB rectal flora, limited morbidity and no sequelae. These results suggest that this individualized method of prophylaxis may be widely applied. . Further

studies are needed to explore reasons for targeted prophylaxis failure and to determine comparative efficacy of non-ciprofloxacin-containing targeted prophylaxis regimens.

Table 1: clinical characteristics of the study population stratified by ciprofloxacin susceptibility status

	Ciprofloxacin-susceptible N = 215 (84.3%)	Ciprofloxacin-resistant N = 40 (15.7%)	All N = 255	P value
Demographics Age, mean±SD, (range), years	62.7 ± 9.1 (33-88)	61.6 ± 7.6 (42 – 77)	62.5 ± 8.9 (33 – 88)	0.323
Clinical characteristics Reason for biopsy, n (%)				0.745
Elevated PSA	178 (83.0)	33 (82.5)	211 (82.9)	
Abnormal DRE	15(6.7)	2 (5.0)	17 (6.5)	
Both	13 (6.3)	3 (7.5)	16 (6.3)	
Other	09 (4.0)	2 (5)	11 (4.3)	
Biopsy result n (%)				0.848
Negative	110 (50.9)	19 (47.5)	129 (50.4)	
Prostate cancer	83 (38.8)	17 (42.5)	100 (39.4)	
HGPIN	22 (10.2)	04 (10.0)	26 (10.2)	
History of urinary tract infection, n (%)				0.004
Yes	19 (9.1)	08 (20.0)	27 (10.8)	
No	191 (88.8)	36 (75.0)	227 (86.7)	
Unknown / missing	05 (2.1)	02 (5.0)	07 (2.5)	
History of urinary retention, n (%)				0.769
Yes	16 (7.7)	03 (7.5)	19 (7.6)	
No	177 (82.3)	32 (80.0)	209 (82.0)	
Unknown / missing	22 (10.0)	05 (12.5)	27 (10.4)	
Hospitalized in prior 1 year, n (%)				0.653
Yes	21 (9.8)	03 (7.5)	24 (9.4)	
No	187 (87.0)	36 (90)	223 (87.7)	
Unknown / missing	07 (3.3)	1 (2.5)	08 (2.9)	

Table 2: Demographic and microbiologic characteristics

Serial No	Variable	Number
1	Total patients	255
2	Mean age (in years)	62.7 (33-88)
3	Flora in rectal swab	255
	Escheriachia coli	251(98%)
	Klebsiella	1(0.5%)
	Pseudomonas	2 (1%)
	Citrobacter	1 (0.5%)
4	FQ sensitive	215(84%)
5	Total no of FQ resistant flora	40(15.7%)
6	Antibiogram of FQ resistant Organism	
	Piperacillin/tazobactum	35(86%)
	Ceftazadime	20(50%)
	Cefixime	11(27%)
	Amoxicillin/calvulanic acid	10(26 %)
	Cotrimoxazole	9(25%)
	Amikacin	10(26%)
	Cefuroxime	02(1.9%)

Table 3 Infectious outcomes of the intent to treat and per-protocol study populations stratified by ciprofloxacin susceptibility status

	Ciprofloxacin-susceptible	Ciprofloxacin-resistant	All	P value
	N (%) = 215 (84.3)	N (%) = 40 (15.7)	N (%) = 255	
Any infection n, (%), 95% CI	3 (1.4), 0.5–3.8	2 (5), 0.8–10.6	5 (1.8) 0.8–3.3	0.314
No/Yes (n/n; %/%)	212/3 (98.6/1.4)	38/2 (95/5)	250/5 (98.2/1.8)	
Type of infection; n (%)				0.277
None	212 (98.8)	38 (95)	250 (98.2)	
Uncomplicated UTI	1 (0.4)	1 (2.5)	2 (1.0)	
Complicated UTI	1 (0.4)	0 (0.0)	1 (0.2)	
Urosepsis	1 (0.4)	1 (2.5)	2 (0.6)	

Abbreviations: UTI urinary tract infection

Table 4 characteristics of patients with infections post – TRUS Prostate biopsy

Types of infection	Age	Cipro	Abxprophy	Days to infection	Positive culture? Culture site	Organism susceptible	Treatment	Hospitalised? If so, LOS	Resolved	Comments
Uncomplicated UTI	65	S	Cipro	1	No	NA	NA	NA	NA	Resolved
Uncomplicated UTI	62	R	Amikacin	8	Yes, Urine	E.Coli: S-amikacin; R amp, amp/sul, cipro, tmp/smx and ESBL	Unknown	No	Yes	Amikacin failure
Complicated UTI	71	S	Cipro	6	Yes, Urine	K.Pneumoniae; S –cipro, R amp, tmp/smx	Piperacilin, ceftriaxone, cefixime	No, 1 day observation	Yes	Cipro failure
Urosepsis	66	S	Cipro	11	Yes, Urine	E.Coli:S-cipro, R pip, tmp/smx	ceftriaxone, cefixime	Yes, 2 days	Yes	Clinical diagnosis
Urosepsis	62	R	Tmp/smx	6	No	NA	Piperacilin; meropenem, cefixime	Yes, 5 days	Yes	Clinical diagnosis

Abbreviations: Abxprophy – antibiotic prophylaxis, Amp Ampicilin, Cipro – Ciproflaxacin, ESBL – Extended spectrum beta lactamases, Infxn – Infection, Los – Length of stay, S – Sensitive, R – Resistant, tmp/smx – Trimethoprim/ Sulfamethoxazole, UTI – Urinary tract infections

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