

Between a Short-term and a Long-term Antimicrobial Prophylaxis in Prostate Biopsy: The Applicability in a Low-resource Setting

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Abstract

Background: Transrectal needle biopsy of the prostate (TNBP) is a common urological procedure with some attendant infective complications. Although most urological surgeons give antibiotic prophylaxis, there is, however, no consensus on the duration. This study compares the outcome of a three-day and seven-day antibiotic prophylaxis in TNBP. **Materials and Methods:** One hundred and twenty men who met the inclusion criteria were recruited and randomized into two equal groups. The patients in Group I received oral ciprofloxacin and metronidazole for three days and Group II received the same drugs for seven days. The antibiotics were commenced 2 h before the biopsy. Urine samples were taken for microscopy, culture, and sensitivity before the biopsy in all patients. For patients in group I, urine microscopy, culture and sensitivity were done on days 5 and 10 after biopsy, and on days 10 and 14 after biopsy for group II patients. Infective complications were determined by the presence of fever and positive urine cultures post-biopsy. **Results:** This comparative prospective study was done between June 2016 and November 2017. Groups I and II had comparable infective complication rates (11.70% for Group I and 3.30% for Group II) ($P = 0.212$). However, diabetics did better on a seven-day regimen ($P < 0.001$). *Escherichia coli* was the most common organism isolated (63.2%). Cephalosporins were the most effective antibiotics in post-biopsy infections in this study. **Conclusion:** Three-day oral ciprofloxacin and metronidazole are effective for prophylaxis in TNBP. However, a seven-day regimen is better in diabetics before a prostate biopsy. The cephalosporins are a good option in the management of post-biopsy infections caused by quinolone-resistant organisms.

Keywords: Antibiotics prophylaxis, complications, prostate biopsy, prostate carcinoma, prostate-specific antigen

INTRODUCTION

Prostate cancer is the second most common cause of cancer death after lung cancer.^[1] The incidence is higher among the black race.^[2] A hospital prevalence of 127–182.5 per 100,000 has been reported by many urologists in sub-Saharan Africa.^[3,4] Transrectal needle biopsy of the prostate (TNBP) is the established mode of obtaining tissue for histological diagnosis in men who are suspected to harbor the disease.^[5,6]

Although infective complications after TNBP are infrequent, most investigators suggest the use of prophylactic antibiotics.^[7,8] While some prospective studies recommend short-term (one–three days) antibiotic prophylaxis,^[9,10] others favor long-term (four–seven days) antibiotic prophylaxis.^[11,12] Recent reviews have shown that fluoroquinolones are a good choice for prophylaxis as most of the frequently found organisms following TNBP are

susceptible to these groups of antibiotics.^[9,13] Metronidazole is often added to the fluoroquinolones to cover for both coliforms and anaerobes which are likely to cause infections after TNBP.^[14,15] McArdle *et al.*^[16] noted that the use of ciprofloxacin and metronidazole during colorectal surgery significantly decreased surgical site infections.

Several works on antibiotics prophylaxis in TNBP have demonstrated that the time of initiation of prophylactic antibiotics

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plays an important role in infective complications associated with prostate biopsy.^[17-20] In this era of antibiotic resistance and the high cost of antibiotic agents, an effective short-course regimen for prophylaxis in TNBP would be of benefit to both patients and surgeons. This study aims to compare the outcome of a three-day and seven-day antibiotic prophylaxis in TNBP.

MATERIALS AND METHODS

This is a prospective hospital-based comparative study. Patients with prostate-specific antigen (PSA) of above 4 ng/ml, who had suspicious digital rectal examination (DRE) findings, or prostate ultrasound findings suggestive of prostate cancer were enrolled in the study. All participants had pre-biopsy urine culture done. Men with positive pre-biopsy urine culture were excluded from the study. They were, however, treated with antibiotics in accordance with the sensitivity pattern.

The recruited patients were randomly allocated to two groups using a computer-generated table of random numbers.^[21] Patients in Group I received oral ciprofloxacin (500 mg) 12 hourly and oral metronidazole (400 mg) 8 hourly for three days, starting two hour before the biopsy. Patients in Group II received the same antibiotics for seven days, also starting two hours before the biopsy.

All the patients underwent TNBP. An 18G Tru-Cut biopsy needle was used and 12 cores of tissue were taken according to the unit protocol. No form of bowel preparation was done. The patients were allowed home after an hour of observation. Patients in Group I were requested to attend for follow-up on the fifth and 10th days after the biopsy and those in Group II on the 10th and 14th day after the biopsy. All patients were told to return to the hospital in case of any complication(s). They were provided with telephone numbers to call in case of an emergency and an easy-to-use digital clinical thermometer for a twice-daily recording of their body temperature for the first 14 days after the procedure. All patients were questioned concerning symptoms of infective complications. Mid-stream urine samples were obtained for microscopy, culture, and sensitivity (m/c/s) during follow-up visits on days five and 10 for Group I and at days 10 and 14 for Group II. A structured pro forma was used to record relevant information for all patients.

Positive culture ($\geq 10^5$ colony forming units per ml) indicated urinary tract infection, irrespective of symptoms.^[13] Fever was defined as any temperature $>38^\circ\text{C}$ recorded in the first 14 days after the biopsy.^[22] Blood culture was obtained only in patients who reported back to the hospital on account of post-biopsy fever. This was after a history and physical examination had been carried out to rule out other causes of fever. Post-biopsy fever and positive urine cultures were regarded as indicators of infection after the biopsy.

All patients signed informed consent before taking part in this study. The Ethics Committee of Irrua Specialist Teaching Hospital gave approval for the study (Approval No: ISTH/HREC/2016/MARCH/27).

RESULTS

One hundred and twenty patients took part in this study. They were randomized into two groups of 60 patients each. The majority of the patients ($n = 92$ [76.7%]) were in their seventh and eighth decades of life [Figure 1]. The mean age of the participants was 69.8 ± 9.1 years. There was no statistically significant difference between the ages of patients in both groups ($P = 0.381$).

The mean PSA level was 36.6 ± 45.2 ng/ml (range: 5.7–310.2). The mean prostate size was 101.4 ± 91.4 g. There was no statistically significant difference between patients in Groups I and II in terms of means of PSA level ($P = 0.218$) and prostate size ($P = 0.233$). The risk factors for infective complications were similar in both groups [Table 1].

Indications for prostate biopsy in this study were elevated PSA and abnormal DRE findings in 67 (55.8%), elevated PSA only in 47 (39.2%), and abnormal DRE findings only in six (5.0%).

All non-infective complications were self-limiting. There was, however, no statistically significant difference between Group I and Group II in terms of haematuria ($P = 0.512$), perineal pain ($P = 0.306$), rectal bleeding ($P = 0.125$), acute urinary retention ($P = 0.679$), and haemospermia ($P = 0.619$) [Figure 2].

A total of 19 (15.8%) patients had a positive urine culture. Of these, 13 were in Group I, while six were in Group II. The organisms cultured are shown in Figure 3.

Twelve (10%) patients out of the 120 had a post-biopsy fever. Of these, nine (75%) were in Group I, while three (25%) were in Group II. There was no statistically significant difference between the two groups in terms of fever ($P = 0.165$). Five (41.7%) patients reported back to the hospital and had a blood culture done in addition to the urine culture. Of these five who had blood culture done, 4 had no growth, while one grew *Escherichia coli*. Four patients (all in Group II) required treatment with oral antibiotics. The patient (in Group I), whose blood culture grew *Escherichia coli*, was admitted and

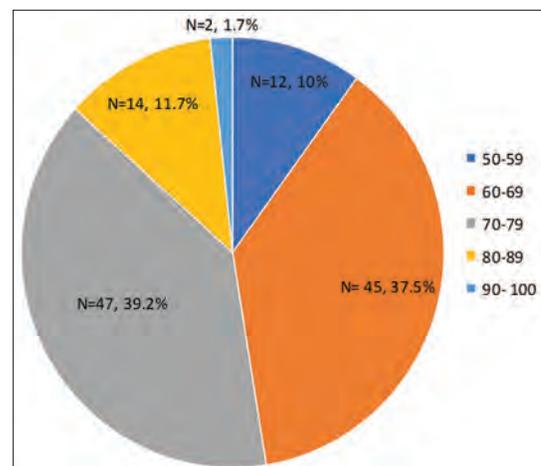


Figure 1: Age distribution of patients in decades

Table 1: Risk factors for infective complications in Group I and II

Risk factors	Prophylaxis group, frequency (%)		Statistics (χ^2 , df, <i>P</i>)
	Group I	Group II	
Diabetes mellitus			
Yes	6 (37.5)	10 (62.5)	1.154, 1, 0.283
No	54 (51.9)	50 (48.1)	
Antibiotics use within the last 14 days			
Yes	17 (60.7)	11 (29.3)	1.677, 1, 0.195
No	43 (46.7)	49 (53.3)	
Hospitalization within the last 14 days			
Yes	4 (66.7)	2 (33.3)	0.702, 1, 0.679 [†]
No	56 (49.1)	58 (50.9)	
Hypertension			
Yes	14 (40.0)	21 (60.0)	1.976, 1, 0.160
No	46 (54.1)	39 (45.9)	
Prolonged steroid use			
Yes	1 (100.0)	0	1.008, 1, 0.000 [†]
No	59 (49.6)	60 (50.4)	
Presence of indwelling catheter			
Yes	28 (47.5)	31 (52.5)	0.300, 1, 0.584
No	32 (52.5)	29 (47.5)	

[†]Fisher's exact. χ^2 : Pearson Chi-square

Table 2: Sensitivity pattern of postbiopsy cultured organisms

Drugs*	Group, frequency	
	Group I (n=13)	Group II (n=6)
Nitrofurantoin	4	1
Ceftazidime	4	2
Meropenem	3	1
Gentamicin	3	2
Ceftriaxone	2	2
Augmentin	2	-
Multidrug resistance	2	-

*Multiple sensitivities applied. *P*=0.192

treated for septicemia with parenteral antibiotics. There was no statistically significant difference between the sensitivity pattern of Group I and Group II (*P* = 0.192) [Table 2].

A significantly higher proportion of diabetic patients had infective complications in Group I ($X^2 = 18.330$, *df* = 1, *P* < 0.001). Similarly, a greater percentage of patients who were hospitalized within 14 days before biopsy had infective complications in Group I and this was significant ($X^2 = 4.404$, *df* = 1, *P* = 0.035) [Tables 3 and 4].

Of the 120 men, 78 (65%) had adenocarcinoma of the prostate, 35 (29.20%) had benign prostatic hyperplasia, four (3.3%) had prostatic intraepithelial neoplasia, and in three (2.50%), the prostate tissues were not enough for histological examination. The mean Gleason's score of the patients with prostatic adenocarcinoma was 7.0 (± 1.5). The majority of these patients (64 out of the 78) had Gleason's score >6.

DISCUSSION

There is no general agreement among urological surgeons on antimicrobial prophylaxis for prostate biopsy. The type and duration of the antibiotics used are still a subject of debate.^[11-13] There is also a controversy about which organisms play a major role in post-biopsy infections. Even the timing of antibiotics administration differs in various works. All these factors make direct comparisons among different studies difficult.^[6-9]

Age remains the strongest risk factor for carcinoma of the prostate.^[2] The peak age range in this study was 70–79 years. This was similar to what was reported by Badmus *et al.*^[4] and Eke^[23] among African patients. However, workers in Europe and the United States have reported a peak age range of 60–69 years.^[5,8,10] This difference may be because patients usually present late in our environment.^[4]

Indications for TNBP include elevated PSA, abnormal DRE, and transrectal ultrasound scan findings. In consonance with reports by Sieber *et al.*^[7] and Bootsma *et al.*,^[8] the most common indication for prostate biopsy in this study was elevated PSA (92.5%). The mean PSA level of 36.6 (± 45.2) ng/ml is high when compared to similar works that showed PSA ranges from 11.23 \pm 6.8 ng/ml to 18.6 \pm 22.4 ng/ml.^[19,24] This high PSA level may mean that our patients present at the advanced stage of the disease like has been variously reported in previous studies in our environment where there are no screening protocols.^[4,19,24] This finding buttresses the need for more public enlightenment and health education to ensure the early detection and management of this disease.

The reported incidence of complications after TNBP ranges from 2% to 79%.^[5,7,9,25] These complications are grouped into infective

Table 3: Association between postbiopsy infective complications and risk factors for infective complications in group I

Risk factors	Infective complications, frequency (%)		Statistics (χ^2 , df, P)
	Yes	No	
Diabetes mellitus			
Yes	6 (100.0)	0	18.330, 1, <0.001
No	10 (18.5)	44 (81.5)	
Antibiotics use within the last 14 days			
Yes	5 (29.4)	12 (70.6)	0.091, 1, 0.762
No	11 (25.6)	32 (74.4)	
Hospitalization within the last 14 days			
Yes	3 (75.0)	1 (25.0)	5.120, 1, 0.054 [†]
No	13 (23.2)	43 (76.8)	
Hypertension			
Yes	5 (35.7)	9 (64.3)	0.764, 1, 0.382
No	11 (23.9)	35 (76.1)	
Prolonged steroid use			
Yes	0	1 (100.0)	0.370, 1, 1.000 [†]
No	16 (27.1)	43 (72.9)	

[†]Fisher's exact. χ^2 : Pearson Chi-square

Table 4: Association between postbiopsy infective complications and risk factors for infective complications in Group II

Risk factors	Infective complications, frequency (%)		Statistics (χ^2 , df, P)
	Yes	No	
Diabetes mellitus			
Yes	2 (20.0)	8 (80.0)	0.809, 1, 0.330 [†]
No	5 (10.0)	45 (90.0)	
Antibiotics use within the last 14 days			
Yes	2 (18.2)	9 (81.8)	0.555, 1, 0.602 [†]
No	5 (10.2)	44 (89.8)	
Hospitalization within the last 14 days			
Yes	0	2 (100.0)	0.273, 1, 1.000 [†]
No	7 (12.1)	51 (87.9)	
Hypertension			
Yes	5 (23.8)	16 (76.2)	4.622, 1, 0.045 [†]
No	2 (5.1)	37 (94.9)	
Prolonged steroid use			
Yes	7 (11.7)	53 (88.3)	χ^2 : uniform cells
No	7 (11.7)	53 (88.3)	

[†]Fisher's exact. χ^2 : Pearson Chi-square

and non-infective complications. Although prophylactic antibiotics minimize the infective complications following TNBP, it does not eliminate them. Overall, the complication rate in this work was 54.21%. Most of these complications were inconsequential and self-limiting. Shittu and Kamara^[25] in Ibadan documented a lower complication rate (26%) using a three-day antibiotics prophylaxis. In his work, 3–6 core tissues were taken which may account for the difference in the complication rates. The non-infective complication rate observed in this study was 43.3%. This was similar to those seen in other studies.^[7,25] Haemorrhagic complications consisting of haematuria, rectal bleeding, and haemospermia predominated accounting for 40.8% of the non-infective complications.

The effectiveness of antibiotic prophylaxis in reducing infective complications in TNBP was first reported by Crawford *et al.*^[26]

in 1982. In a work by Aron *et al.*,^[15] ciprofloxacin and tinidazole combination was shown to be sufficient in preventing infective complications following TNBP in selected persons. In this study, post-biopsy fever and positive urine cultures were regarded as indicators of infection, as in other studies.^[6,8,9,26] Post-procedure fever was noted in 10% of patients. Prior publications had noted fever ranging from 1.7% to 6.3%.^[27-30] 15.8% positive urine cultures documented in this study were higher than the rates documented in some series.^[27,28,30]

Quoted figures for hospitalization following TNBP range from 0.3% to 0.6%.^[27,29] Urosepsis occurred in one (0.8%) patient in this study and required admission and treatment with parenteral antibiotics. This was the only serious infective complication observed in this study. This hospitalization rate of 0.8% is in keeping with the rates following TNBP seen in other

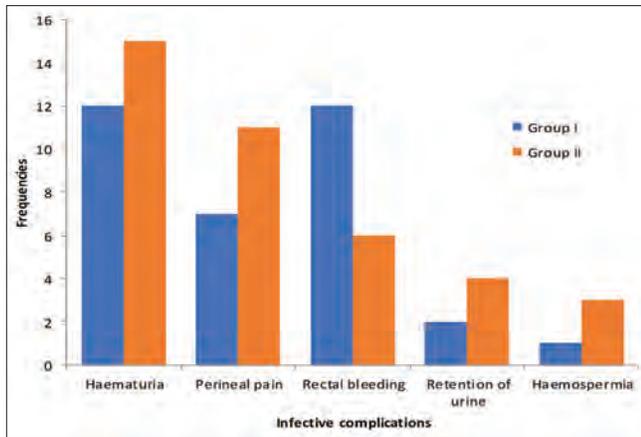


Figure 2: Distribution of noninfective complications

studies.^[27-29] This sepsis rate of 0.8% may reflect a relatively low rate of fluoroquinolone resistance in our environment. This is in contrast to a work done in North America that showed an increased rate of post-biopsy sepsis probably due to a rising bacterial resistance.^[5] Complications such as acute prostatitis, epididymo-orchitis, and prostatic and ischioanal abscesses reported in the literature^[19,31] were absent in this study. These complications may be regarded as rare even in the presence of risk factors for infective complications.

There was no statistically significant difference between Group I and Group II in terms of post-procedure fever and positive urine culture ($P = 0.068$ for fever and $P = 0.166$ for positive urine culture). A similar study done to determine the difference in infective outcome between a single and a five-day course of prulifloxacin showed no significant difference between the two groups of patients studied (0.95% and 0.90%).^[7] This may mean that the availability of antibiotics in the bloodstream and the prostate during a prostate biopsy is more important than the duration of antimicrobial prophylaxis in determining post-biopsy infective complications.

Some workers have identified both patient and procedural factors that may predispose patients to infective complications.^[32-34] Patient-specific risk factors identified include diabetes mellitus, prolonged steroid use, preexisting urinary tract infections, and recent hospitalization.^[35,36] Prolong indwelling urethral catheter has also been noted as a risk factor for post-biopsy infective complications.^[37] Low infection rates have been observed in patients with risk factors for infective complications who had long-term antibiotic prophylaxis following prostate biopsy compared to their counterparts who had short-term antibiotic prophylaxis.^[13] Aus *et al.*^[13] reported an infection rate of 4.9% in patients who received 400 mg norfloxacin twice daily for one week and 11% in patients who received 400 mg norfloxacin twice daily for one day. In their study, they included patients with diabetes, UTI, and indwelling urethral catheters. The most pronounced effect of the one-week regimen was noted in patients with risk factors for infection.

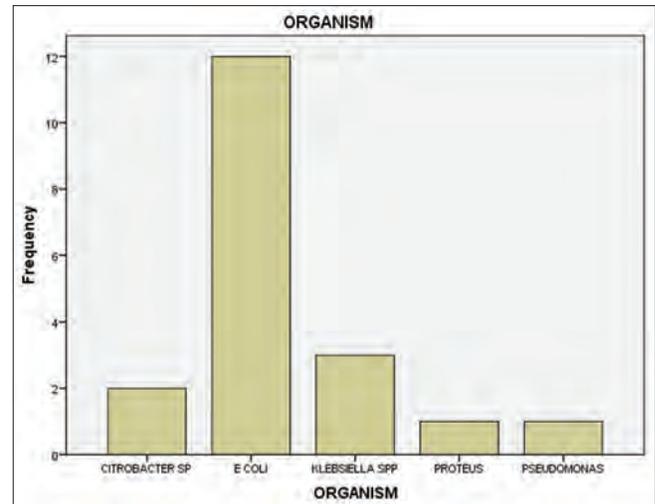


Figure 3: Distribution of postbiopsy culture

In this study, diabetics were noted to have a statistically significant higher risk of infective complications following three-day antibiotic prophylaxis. On the other hand, their counterparts who had seven-day antibiotic prophylaxis did not have a higher occurrence of infective complications [Tables 3 and 4]. Patients with hypertension, presence of a urethral catheter, antibiotics use within 14 days before biopsy, hospitalization within 14 days before TNBP, or prolonged steroid use did not have a high risk of infective complications following prostate biopsy. This suggests that patients who are diabetics may fare better, in terms of infective complications, when placed on a seven-day antibiotics regimen.

E coli was the most common organism isolated in this study, with a good sensitivity to the cephalosporins. This observation is in consonance with findings from similar works.^[6,9,11] This suggests that cephalosporins can be used in the treatment of infective complications developing after prostate biopsy.

CONCLUSION

TNBP has a low incidence of major complications. A three-day prophylactic oral ciprofloxacin and metronidazole regimen is effective for prophylaxis in TNBP. A seven-day regimen is, however, recommended in patients who are diabetics before TNBP. Quinolone-resistant *E. coli* was the most common microorganism in infections occurring after TNBP under quinolone–metronidazole prophylaxis. The most effective antibiotic in infections caused by quinolone-resistant organisms was cephalosporin.

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Conflicts of interest

There are no conflicts of interest.

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