EFFICACY OF SINGLE DOSE CIPROFLOXACIN VERSUS CEFTRIAXONE IN THE PREVENTION OF PROSTATE BIOPSY RELATED INFECTION

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Abstract

Background: *Prostate cancer is a major health concern world over, being the second most common neoplasm in men and the sixth commonest cause of cancer related death in the entire world. Trans-rectal ultrasound guided prostate biopsy is the gold standard technique for prostate cancer diagnosis. Prostate biopsy is associated with risk of urinary tract infection.*

Objective: *This study aims to compare efficacy of ciprofloxacin with that of ceftriaxone in reducing post-prostate biopsy infection.*

Methods: *This was a prospective comparative study done at Alex-Ekwueme Federal University Teaching Hospital Abakaliki. Fifty-six patients made up the study population, 28 in each group. Those in group I received intravenous ciprofloxacin while those in group 2 received intravenous ceftriaxone. The patients underwent digitally guided trans-rectal prostate biopsy. Patients were given easy to use thermometer to check temperature morning and evening for three days following the procedure. Blood and urine samples were taken for full blood count and urine culture respectively 3 days after biopsy. Statistical analysis was done using SPSS version 21.0.*

Results: *Five (17.86%) patients had fever in group 1 and one (3.57%) in group 2. Bacteriuria was recorded in 10 (35.71%) patients in group 1 and in 9 (32.14%) patients in group 2. Urinary tract infection was recorded in 3 (10.71%) patients in group 1 and in 2 (7.14%) patients in group 2. Sepsis occurred in 5 (17.86%) patients in group 1 and in one (3.57%) patient in group 2.*

Conclusion: *There was no statistically significant difference between ceftriaxone and ciprofloxacin in preventing post prostate biopsy infective complications. Key words: prostate biopsy, antibiotic, post-biopsy infection.*

Cite this article as: C. Odo, E.N Afogu, E.S.I Ugwuidu, T.U Mbaeri, E.A Obiesie, U.U Ogbobe, U.U Nnadozie, O.V Onyebum. Efficacy of Single Dose Ciprofloxacin Versus Ceftriaxone In The Prevention Of Prostate Biopsy Related Infection. Afrimedic Journal 2021; 7(1): 18-27

INTRODUCTION:

Prostate cancer is a major health concern world over, being the second most common neoplasm in men and the sixth commonest cause of cancer related death in the entire world.[1] It is the most common non-cutaneous cancer detected among men.[2] In Nigeria earlier study put the hospital incidence and annual death rate at 127/100,000 and 20,000 respectively.[3] A population based

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study however, placed the incidence at 19.1/100,000.[4]

Transrectal ultrasound (TRUS) guided prostate biopsy is the gold standard technique for prostate cancer diagnosis. However in our environment digitally guided prostate biopsy is still widely practiced due to the non-availability of rectal ultrasound probes. Prostate biopsy is indicated in men with raised serum level of prostate specific antigen (PSA), an abnormal digital rectal examination (DRE) findings or a combination of the two.[2] Complications are common following transrectal prostate biopsy occurring in 2 to 79% of patients undergoing this procedure.[5,6]

These complications could be traumatic (haematuria, haematochezia, haematospermia) or infective (fever, urinary tract infection or septiceamia). Earlier studies had noted infective complications to occur in 3.8 to 19% of cases.[7-10] Antibiotic prophylaxis is recommended for all patients going for prostate biopsy in a bid to reduce infective complications.[11] This is based on the fact that 16 to 100% of cases of biopsy with no antibiotic prophylaxis presented with either asymptomatic bacteriuria or transient bacteremia, increasing the risk for complications such as urinary tract infections, sepsis, and Fournier's gangrene.[11] The antibiotics for prophylaxis must have activity for bacteria from the flora of the skin, rectum and genitourinary tract. Aerobic and anaerobic organisms are commonly introduced into the prostatic tissue and blood when performing trans-rectal biopsies. Therefore, drugs used for prophylaxis must have activity against both aerobic and anaerobic organisms. The most common organisms are the gut commensals *Escherichia coli*, *Streptococcus faecalis* and Bacteriodes species.[12] The American Urological Association (AUA) best practice policy statement on urologic surgery antimicrobial prophylaxis recommends fluoroquinolones or first through third generation cephalosporins as the prophylactic antimicrobial of choice preceding prostate needle biopsy.[13] Escherichia coli (E. coli) is the commonest pathogen implicated in postTRUS biopsy sepsis, accounting for 75-90% infective complications in published series.[14]

Another study has shown that the rate of fluoroquinolone resistant E. coli in post-biopsy blood stream infections was 62%.[15] Consequently, the use of fluoroquinolone antimicrobial as prophylaxis prior to prostate biopsy is a significant risk factor for subsequent E.coli infection.[16,17.] Again, the wide spread use of fluoroquinolones to treat urinary tract infections has increased the rate of fluoroquinolone resistant *Escherichia coli*.[18] It was reported that the causative pathogen in urinary tract infection after transrectal prostate biopsy was mainly *Escherichia coli* with high resistance

rate to fluoroquinolones.[18] In view of this rising resistance of *Escherichia coli* to fluoroquinolones, there is need to try other antibiotics with good activity against expected bacteria flora encountered during prostate biopsy. For this reason, this study aims to compare efficacy of ciprofloxacin with that of ceftriaxone in reducing infective complication following prostate biopsy.

METHODOLOGY This was a comparative cross sectional study done at the Urology unit of our institution, over 13 months (April 2019-April 2020). Sample size of 56 was determined using Fisher's formula.[19] Inclusion criteria were elevated prostate specific antigen (PSA) level greater than 4ng/ml, abnormal digital rectal examination (DRE) findings or elevated PSA and abnormal DRE. Abnormalities on DRE include hard or nodular prostate, obliteration of the median sulcus and winging of the lateral lobe. Excluded from the study were patients with symptomatic urinary tract infection or suspected prostatitis, diabetics with poor glycemic control, those with acquired immunodeficiency syndrome, those with hypersensitivity to ciprofloxacin or ceftriaxone and patients on urethral catheter. Ethical approval (FETHA/REC/Vol 2/2018/059) was obtained from the ethics committee of our institution and a written informed consent was obtained from each patient. The patients were randomly assigned to two groups. Those in group I (28) received intravenous ciprofloxacin (Juhel) 400mg at induction of anaesthesia while those in group 2 (28) received intravenous ceftriaxone (Rocephin) 1g at induction of anaesthesia. Patients in both groups received bisacodyl (dulcolax) rectal suppositories 20mg nocte starting 2 nights before the procedure as well as intravenous metronidazole (Juhel) at induction of anaesthesia. All patients included in the study had pre-biopsy negative urine culture result. The patients underwent digitally guided 10-core trans-rectal prostate biopsy on an out-patient basis. The procedures were performed by a single Urologist with patient in left lateral position under low dose saddle block as described Obi and colleague[20]. Patients were provided with easy to use thermometer with which to check their temperature morning and evening for three days following the procedure. Blood and urine samples were taken for full blood count and urine culture respectively 3 days after biopsy. During outpatient visit on the third day after biopsy, a clean catch mid-stream urine sample was collected and sent to the microbiology laboratory within 30 minutes. Patients were classified as positive for infective complications if there was leukocytosis (total white cell count > 12000/mm^3 on full blood count), positive urine culture (≥105colony forming units per ml) with or without symptoms (urinary frequency, dysuria, perineal pain or supra-pubic pain), systemic inflammatory

response syndrome with positive urine culture (sepsis). Data analysis was done with statistical package for social sciences (SPSS) version 21. The mean differences between continuous variables were compared using independent Students t-test or Mann-Whitney test depending on whether variables are normally distributed or not. Associations between categorical variables were tested using Fischer's exact test. The level of significance was set at p< 0.05. RESULTS The mean age of the participants was 71.78±8.94 years with a range of 52-89 years. The age distribution of the participants is as shown in figure 1. The peak age distribution was 70- 79 accounting for 24(42.86%) of the total patients.

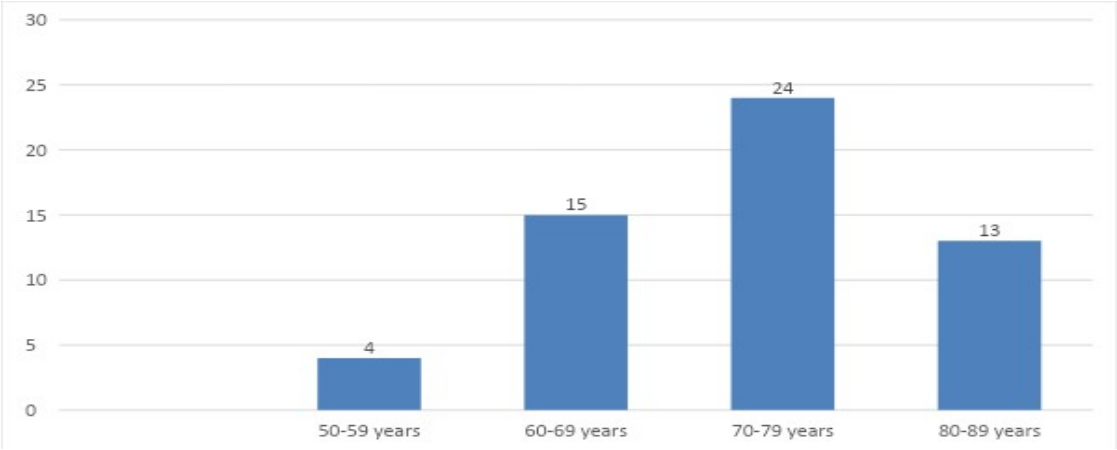

Figure one: Bar chart showing the distribution of age groups among study participants (n=56).

Comparison of mean for age, median for prostate volume and PSA between the two groups showed no statistically significant difference (table 1).

Table I: showing the comparison of mean for age, median for prostate volumes and serum PSA between the two groups.

Variable	Group I (n=28) Mean ±SD	Group 11 (n=28) Mean ±SD	t-value	P-value
Age (years)	70.32± 9.02	73.25± 8.79	-1.230	0.224
Variable	Group I*(n=28)* (Mean rank)	GroupII*(n=28)* (Mean rank)	z-value	p-value
PSA (ng/ml)	27.36	29.64	-0.524	0.600

Prostate Volume (mls)	31.66	25.34	-1.450	0.147

Table II: Fischer exact test analysis showing the level of association in the presence of post biopsy infection between group 1 and group II

Variable	Group (%)		χ^2-value	p-value	Clavlien-Dindo class	Intervention offered	Outcome
	Group I (n=28)	GROUP II (n=28)					
Fever							
No (n=50)	23 (46)	27 (54)	2.986	0.193	2		
Yes (n=6)	5 (83.33)	1 (16.7)					
Bacteriuria							
No (n=37)	18 (48.65)	19 (51.35)	0.079	1.000	1		
Yes (n=19)	10 (52.63)	9 (47.37)				None	Full recovery
UTI							
No (n=51)	25 (49.02)	26 (50.98)	0.219	1.000	2		
Yes (n=5)	3 (60)	2 (40)				Antibiotics	Full recovery
Sepsis							
No (n=50)	23(46)	27(54)	2.986	0.193	2	Antibiotics	Full recovery
Yes(n=6)	5(83.33)	1(16.67)					
Overall Infection rate							
No (n=26)	10 (38.46)	16 (61.54)	2.584	0.180			
Yes (n=30)	18 (60)	12 (40)					

The table above shows the infective complications following prostate biopsy in the two groups and the Clavien-Dindo classification. Five patients had fever in group 1 while one had fever in group 2. Bacteriuria was recorded in 10 patients in group 1 and in 9 patients in group 2. Urinary tract infection (UTI) was recorded in 3 patients in group 1 and in 2 patients in group 2. Finally sepsis occurred in 5 patients in group 1 and in only one patient in group 2. An important observation is the fact that fever occurred only in patients that had sepsis. The table also showed that only those with UTI and sepsis received antibiotics and that all the treated patients made full recovery.

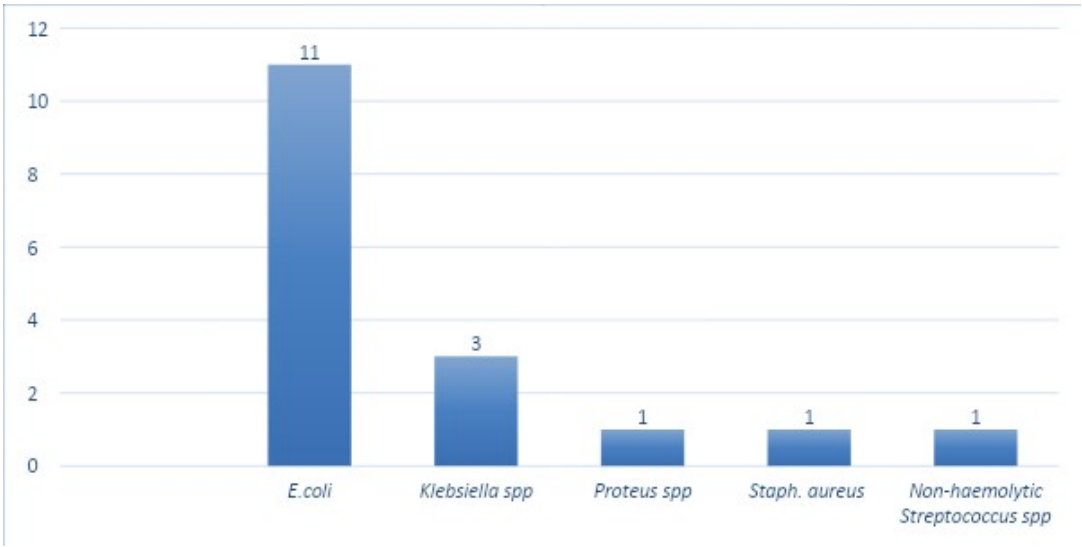

Figure two: Bar chart showing the distribution of bacterial isolates in the group 1

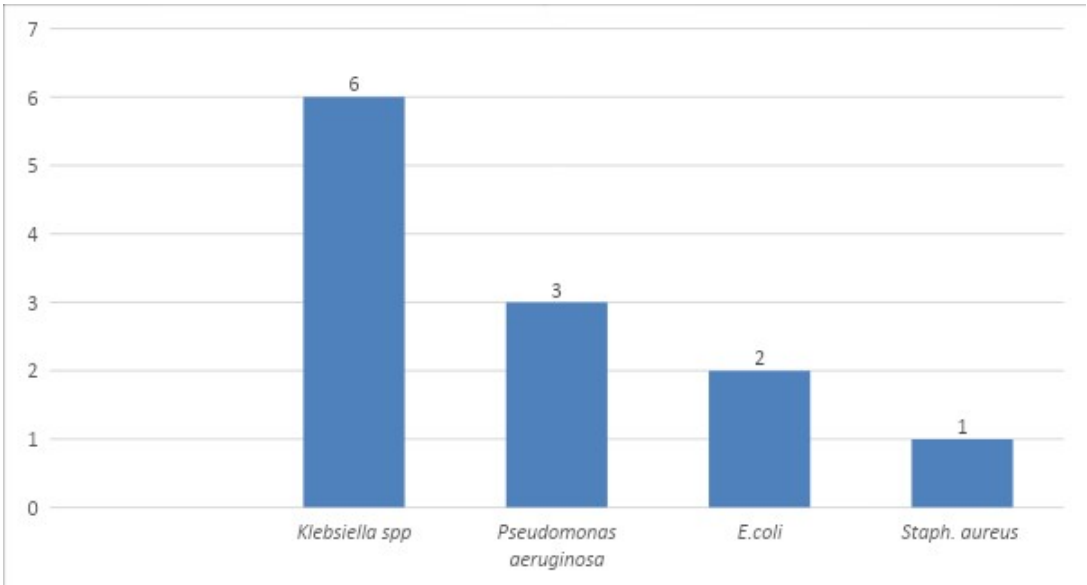

Figure three: Bar chart showing the distribution of bacterial isolates in the group 2

DISCUSSION

Urologists have employed several approaches in an attempt to reduce prostate biopsy related infection. Key among these approaches is the use of prophylactic antibiotics which is a

standard recommendation for all patients going for prostate biopsy.[11]

This study compared the efficacy of ciprofloxacin with ceftriaxone in reducing infective complications post prostate biopsy.

The mean age of participants in this study was 71.78±8.94 and the peak age range was 70-79. This is not surprising since prostate cancer is a disease of the ageing male population. This distribution is similar to that reported by other studies in our sub-region.[9,21] There were no significant difference in the mean age between the two groups. Also there was no significant difference in the median of PSA and prostate volumes between the two groups.

The indicators of infective complications in this study were urosepsis (systemic inflammatory response syndrome with positive urine culture), urinary tract infection (positive urine culture with clinical symptoms of dysuria, urgency and suprapubic pain), bacteriuria (positive culture in the absence of symptoms). More patients in group 1 had infective complications compared to group 2 (18 versus 12). However, the difference in infection rate was not statistically significant (p =1 for bacteriuria, p = 1 for UTI, p = 0.193 for sepsis). These findings are similar to observations by Bianca Grassi De Miranda and colleagues[22] that demonstrated that ceftriaxone (infection rate 0.7%) was more effective compared to ciprofloxacin (infection rate 6.4%) in reducing infective complications following prostate biopsy. However, unlike the study by Bianca Grassi De Miranda et al the difference in infection rate between the 2 groups in this study when subjected to statistical analysis was not significant. This observation may be attributed to the fact this study had a small sample size of 56 in contrast to the study by Bianca Grassi De Miranda et al with a sample size of 744.

All patients that developed infective complications in this study belonged to either Clavien-Dindo grade 1 (bacteriuria) or 2 (sepsis and UTI). Those that developed UTI were effectively treated with oral antibiotics on an outpatient basis. Three out of the 6 patients that developed sepsis were admitted in the emergency department and received intravenous antibiotics and intravenous fluids while the rest were treated with oral antibiotics. All fully recovered, no mortality was recorded in this study. The overall admission rate due to infective complications in this study was 5.36% which is comparable to a rate of up to 3.1% reported by earlier studies.[23,24,25,26] Those that had asymptomatic bacteriuria were not treated. Post biopsy related infections such as acute prostatitis, prostatic abscess and epididymorchitis were not observed in this study. This may be attributed to the fact that patients with risk factors that can predispose to the above infections such as uncontrolled diabetes, urinary tract

infections and indwelling urethral catheters were excluded from this study.

Positive post biopsy urine cultures were identified in 17 patients in group 1(figure 2). The most common organism isolated was *Escherichia coli* in 11 (64.71%) cases. Others included Klebsiella species (3/17.65%), *Staphylococcus aureus* (1/5.88%), Proteus species (1/5.88%) and non-haemolytic streptococcus species (1/5.88%). These findings are similar to results in earlier studies by Agbugui et al[10] and Ugwumba and colleagues[27]. Positive post biopsy urine cultures were identified in 12 patients in group 2 (figure 3). In this group the most commonly isolated organism was klebsiella species (6/50%). Others included pseudomonas aeruginosa (3/25%), E. coli (2/16.67%), and staphylococcus aureus (1/8.33%). The cultured organisms were similar between the 2 groups, however, the prevalence of the offending organisms differs. This is most likely due to varying susceptibility of the cultured organisms to the different prophylactic antibiotics used in the respective groups.

CONCLUSION

There was no statistically significant difference between ceftriaxone and ciprofloxacin in preventing post prostate biopsy infective complications. This was probably due to the relatively small sample size in this study. Therefore, another study utilizing larger sample size may be needed to further validate this finding.

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