Original Research Article

Prophylaxis Antibiotics For TRUS Biopsy: A Retrospective Analysis Comparing 2 Regimens

ABSTRACT

Background: Transrectal ultrasound guided prostate biopsy (TRUSBx) is a common urological procedure and quinolones has been widely used as a prophylactic antibiotic. However, controversies arise as there is increased incidence of quinolones resistance and side effect associated with it. Thus, this study will retrospectively review and compare the infectious outcome of Fosfomycin and ciprofloxacin as prophylaxis antibiotic regimens prior to TRUSBx.
Study design: Retrospective analysis
Place and Duration of Study: Urology Unit, Surgical Department, Hospital Raja Perempuan Zainab II, Kelantan from February 2020 to April 2021.
Methodology: Records of all patients who underwent TRUSBx in Hospital Raja Perempuan Zainab II, Kelantan from February 2020 to April 2021 reviewed. Patients were divided into 2 groups. In Group 1, patients received single-dose Fosfomycin (3 g, orally) the night before TRUSBx. In Group 2, patients received oral ciprofloxacin 500mg bd 1 day before TRUSBx and continued this twice daily to complete the total dose for 3 days. Short term outcomes in terms of infectious complications were compared.
Results: Study includes 188 patients (Group 1: 70 patients received single-dose oral Fosfomycin 3 g and Group 2: 118 patients received oral ciprofloxacin 500mg bd for 3 days). There was no significant mean difference in age, PSA, and prostate size between groups (P>.05). Only 2 patients from Group 1 and 4 patients from Group 2 developed afebrile UTI and successfully treated with oral antibiotic. Post-biopsy complicated UTI was observed in 1 patient (1.4%) in group 1 and 2 patients in group 2 (1.7%). There was no association between factors (types of prophylactic antibiotic given) and infectious complication rate (P>.05).
Conclusion: Non-invasive independent predictors for screening esophageal varices may decrease medical as well as financial burden, hence improving the management of cirrhotic patients. These predictors, however, need further work to validate reliability.

Keywords: Prostate, Biopsy, TRUS biopsy, antibiotic prophylaxis

1. INTRODUCTION

Prostate cancer is the second most common cancer diagnosed in men. An autopsy study reported that prostate cancer prevalence almost reaching 60% by the age of 80 years old [1].

Transrectal ultrasound guided prostate biopsy (TRUSBx) has been an accepted technique of getting tissue biopsy in diagnosing prostate cancer. However, this method is well known to have several complications. Post TRUSBx infection is the most feared complication and it ranges from asymptomatic bacteriuria, symptomatic UTI and severe sepsis. Studies have shown that prophylactic antibiotic have significantly reduce the infectious complications post TRUSBx [2]. Currently, there are controversies in choosing the optimal regimens of antibiotic prophylaxis.

Traditionally, Fluoroquinolones have been used as the prophylactic antibiotics of choice because of their excellent prostatic penetrance. Nevertheless, the rate of infection complication post TRUSBx has been rising in recent years due to dramatic increase in ciprofloxacin resistant organisms in patients undergoing TRUSBx has been reported [3,4]. Recent studies found that pre-biopsy screening for fluoroquinolone-resistant E. Coli is as high as 41.7% [4].

The rise of quinolones resistance has led to the search for an alternative prophylactic antibiotic prior to TRUSBx. Multiple studies have been done abroad to evaluate the use of alternative antibiotic such as Fosfomycin, cephalosporin and aminoglycoside [2]. Fosfomycin has been used in our hospital as an alternative prophylactic antibiotic as it has a better resistance rate, elevated activity against multidrug-resistant (MDR) Gram-negative bacteria and single oral dose usage [5-7].

Herein, we retrospectively review and compare local data on the infectious outcome of two different types of prophylaxis antibiotic regimens [time] prior to TRUSBx.

2. MATERIAL AND METHODS

After ethical approval, a list of patients who underwent TRUSBx in Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan from 1st February 2020 to 30th April 2021 will be obtained from the procedure record book. Indications for TRUSBx were raised PSA and nodular prostate on digital rectal examination (DRE). The demographic data of patients including the history, PSA, DRE findings will be obtained by a retrospective study of patient's medical records.

2.1 Antibiotic prophylaxis protocol

Patients who underwent TRUSBx from 1st February 2020 to 30th April 2021 were given either: Group 1, received single-dose Oral Fosfomycin 3g the night before the procedure day; and Group 2 received routine empirical prophylaxis in the form of oral ciprofloxacin 500mg bd, starting 1 day before TRUSBx and it will be continued twice daily to complete total dosage for 3 days. The type of prophylactic antibiotic given to the patient are based on the surgeon’s preference.

2.2 TRUSBx technique and protocol

All TRUSBx was performed in an outpatient clinic setting. Bisacodyl Suppositories (10mg on night) were given as bowel preparation before the procedure. BK5000 ultrasound machine with an 8-MHz side-firing probe was used for TRUSBx. The patient was put in the left decubital position and biopsies were taken using BARD automated biopsy gun with a disposable 18-G biopsy needle. A standardized TRUSBx was taken through a systematic approach (according to Vienna Nomogram with a minimum 12-core biopsy taken from the base, mid-gland, apex of the right and left sides).

The urine analysis and urine cultures were conducted within 1 week before the TRUSBx as a standard operating procedure in all patients. Patients with symptomatic UTI will be treated and the procedure will be postponed. Whereas, patients with no UTI or asymptomatic bacteriuria will proceed with TRUSBx after taking the prophylactic antibiotic according to prescription. After the procedure, the patient was reminded to come back if there is any UTI symptoms or other serious complications. Phone calls will be made by the staff nurse in charge within 5-7 days post procedure to ask about the post TRUSBx complications. Patients with symptomatic UTI were admitted and treated accordingly. For those who are asymptomatic, follow up will be made at 1 month and post procedure complications were asked and documented as a standard protocol.

2.3 Outcome evaluation

The primary outcome was the incidence of post-TRUSBx afebrile UTI and complicated UTI. Afebrile UTI was defined as the presence of at least 2 lower urinary tract symptoms (dysuria, frequency, urgency and etc.) without fever

associated with evidence of bacteriuria. Whereas, complicated UTI was defined as febrile UTI with bacteriuria and evidence of sepsis necessitating hospital admission.

2.4 Statistical Analysis

The data will be analysed using Statistical Package for the Social Sciences (SPSS) software version 27. Descriptive data will be expressed as mean ± standard deviation (SD) for the numerical data or median and interquartile range (IQR) if the values were not normally distributed and then compared using t test or Mann–Whitney U test. The frequency and percentage will be used to compare the express the categorical data. Pearson's Chi-Square or Fisher exact test will be used to identify the association between the infectious complication and type of antibiotic received as prophylactic antibiotic. A P-value of less than 0.05 is considered statistically significant.

3. RESULTS

This study included 188 patients and they were divided into 2 groups (Group 1:70 patients and Group 2:118 patients). There was no significant mean difference in age, PSA, and prostate size between groups (P>0.05) (Table 1). The mean (SD) of age in group 1 was 67.6(6.03) years old and 67.1(6.01) years old in group 2. The median (IQR) of PSA was higher in group 1 with 17.70(8.2 – 57.8) compared to group 2 with 14.05(8.5 – 36.05). The median prostate size in groups 1 and 2 were 55.85cm3 and 72.50cm3, respectively. There was no association between the diabetic and complicated UTI or catheter and complicated UTI (P>0.05).

Table 1: Patients' demographic data

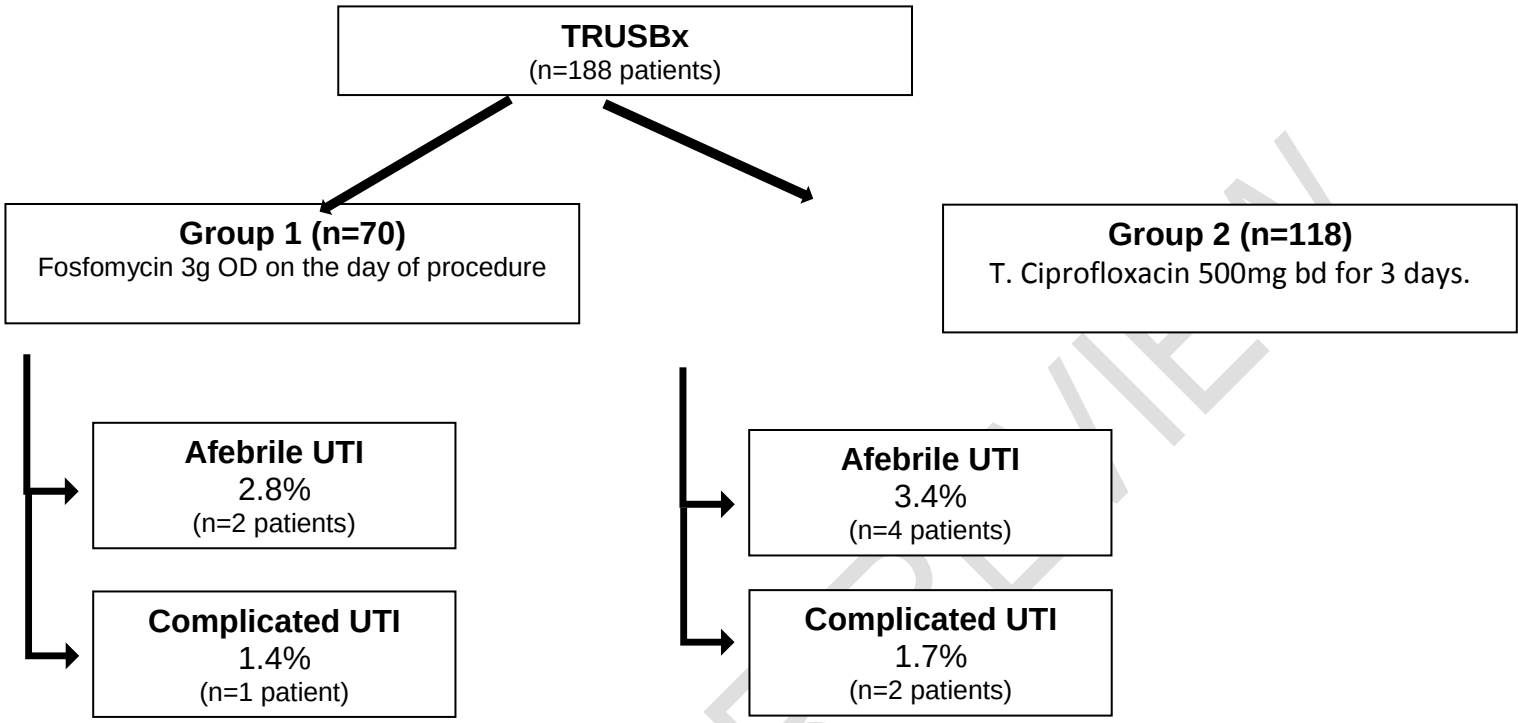
CHARACTER	GROUP 1 (n=70)	GROUP 2 (n=118)	P value
Age in years: mean (SD)	67.6 (6.03)	67.1 (6.01)	0.59 [a]
PSA (ng/ml): median (IQR)	17.7 (8.2-57.8)	14.05 (8.5-36.05)	0.44 [b]
Prostate size (CC): Median (IQR)	55.85 (40-88.3)	72.5 (49-96)	0.09 [a]

CHARACTER	GROUP 1 (n=70)	GROUP 2 (n=118)	P value
Diabetes: N (%)	15 (21.4)	21 (17.8)	0.57 [c]
On catheter: N (%)	16 (22.8)	30 (25.4)	0.85 [d]

Prostate cancer was detected in 47 patients (25%). The overall incidence of asymptomatic bacteriuria prior to TRUSBx was 44 patients (23.4%) in which 13 patients were given Fosfomycin and 31 patients were ciprofloxacin as prophylactic antibiotics respectively. 56% of asymptomatic bacteriuria patients were on catheter and 22% of them are diabetic.

There was no association between the type of antibiotic used as prophylactic antibiotic and infectious complication rate (afebrile UTI and complicated UTI) (p>.05). A total of 4 patients (3.4%) had afebrile UTI and 2 patients (1.7%) with complicated UTI in Group 2. Meanwhile, 2 patients (2.9%) had afebrile UTI, and 1 patient (1.4%) had complicated UTI in Group 1. All afebrile UTI patients were successfully treated with oral antibiotics as outpatients. Complicated UTI developed within 48 h after TRUSBx, and E. coli was detected from blood culture in 2 patients. Antibiotic sensitivity showed resistance to ciprofloxacin in these two patients. All complicated UTI cases were successfully managed with intravenous antibiotics and no patient requires ICU admission.

Figure 1: Study design algorithm and infectious complication



TRUSBx: trans rectal ultrasound guided prostate biopsy, OD: once daily, UTI: urinary tract infection

4. DISCUSSION

TRUSBx is a common procedure done by urologists to establish the histological diagnosis of prostate cancer. However, this procedure is not without complication. The infectious complication is the most common cause of hospitalization following TRUSBx ranging from 0.1–6.3% [8-10]. Infection-related complications following prostate biopsy include asymptomatic bacteriuria, symptomatic urinary tract infection, complicated UTI and sepsis. The overall incidence of infectious complications including afebrile UTI and complicated UTI in this study was 4.8%. The incidence of complicated UTI which requires hospital admission 1.6% in the present study was within the published reports [8-10].

Many reports have shown that the use of prophylaxis antibiotics has reduced the incidence of infectious complications. However, there is no consensus on the type of antibiotics, optimal time starting and duration of antibiotic to start prior to TRUSBx. To our knowledge, the use of quinolones as prophylaxis antibiotics have been widely used worldwide. Nevertheless, Quinolone resistance rates have risen steeply in recent years. In many parts of the United States, 10%–30% of community-associated Enterobacteriaceae are quinolone resistant and more than 50% of quinolone resistant Enterobacteriaceae are seen in other parts of the world especially Asia [11,12]. From our internal audit in Hospital Raja Perempuan Zainab II in 2013 and 2020, the rates of quinolones resistant E. Coli obtain from the urine were as high as 30% and 28% respectively. Moreover, the use of quinolones has recently been restricted by European Medicines Agency due to the rise of quinolone resistant organisms and the risk of potentially permanent adverse events.

According to recent protocols, targeted antibiotics based on rectal swab cultures or augmented prophylaxis (combination of 2 different classes of antibiotics) are recommended [2,6]. Fosfomycin as an alternative prophylaxis antibiotic has been considered as it has a better resistance rate, elevated activity against multidrug-resistant (MDR) Gram-negative bacteria and single oral dose usage [6,7,13]. A systematic review and meta-analysis on Fosfomycin showed significantly lower septic complications in those who receive Fosfomycin prophylaxis in comparison with quinolone-based prophylaxis regimen [2,14]. In this study, we found that more patients in Group 2 (received routine empirical prophylaxis in the form of oral ciprofloxacin 500mg bd 1 day before TRUSBx and continued this twice daily to

complete total dosage for 3 days) developed afebrile UTI and complicated UTI as compared to Group 1 (received single-dose Fosfomycin 3 g, orally on the same day before TRUSBx). However, this difference was not statistically significant.

The antibiotic prophylaxis protocols comparing Fosfomycin versus Ciprofloxacin and incidence of infectious complication after TRUSBx in other reports are summarized in Table 2. The highest incidence of post-TRUSBx sepsis was observed in patients who received ciprofloxacin (12.9%) [16] while the lowest incidence was reported with Fosfomycin antibiotic prophylaxis according to rectal swab cultures (0%) [18].

Table 2: Antibiotic prophylaxis protocols and incidence of sepsis after TRUSBx

Reference	**No of patients**	**Antibiotic regimens**	**Infectious complication %**
Volkan Sen [5]	300	Gp 1: Fosfomycin single dose 3 g orally the night before the procedure Gp 2: Ciprofloxacin 500 mg orally 60 min before the procedure	Gp 1: 2% Gp 2: 7.3%
Fahmy AM [15]	412	Gp 1: Fosfomycin single-dose (3 g, orally) 1–2 h before TRUSBx Gp 2: Ciprofloxacin 500 mg orally + metronidazole 500 mg at least 1 h before TRUSBx and continued this twice daily for 3 days	Gp 1: 1.9% Gp 2: 8.5%
T Cai [16]	1109	Gp 1: Fosfomycin 3 g orally 3 h before and 24 h after the first administration Gp 2: Ciprofloxacin 500 mg orally twice daily for 5 days starting 1 day before the procedure	Gp 1: 1.6% Gp 2: 12.9%
F. Lista [17]	671	Gp 1: Ciprofloxacin 500 mg BD orally for 5 days Gp 2: Fosfomycin 3 g orally in two doses (24 h before and 24 h after biopsy).	Gp 1: 2.2% Gp 2: 2.5%
Kisa E, et al. [18]	110	Group A (without risk factors) Gp A1: Fosfomycin single dose the night before the biopsy Gp A2: Ciprofloxacin twice daily for 5 days Group B (with risk factors) Gp B1: Fosfomycin single dose (according to rectal swab result) Gp B2: Ciprofloxacin twice daily for 5 days (according to rectal swab result)	 Gp A1: 10% Gp A2: 6.3% Gp B1: 0% Gp B2: 6.7%
V Sen et al. [19]	300	Gp 1: Fosfomycin 3 g night before the procedure Gp 2: Ciprofloxacin 500 mg single dose 60 min before the procedure	Gp 1: 2% Gp 2: 7.3%
Present study	188	Gp1: Fosfomycin 3g OD on the day of procedure Gp 2: Ciprofloxacin 500mg bd 1 day before TRUSBx and continued BD to complete total dosage for 3 days	Gp 1: 4.3% Gp 2: 5.1%

We acknowledge that there are several limitations of this study. One of the limitations of this study is the retrospective nature of this study. There might be a selection bias in deciding the type of prophylactic antibiotic given to the patients. Another limitation is, there might be a recall bias. The patient might not be able to recall past histories of a post-TRUSBx infectious complication. It is possible that some patients might have gotten urinary tract infections and taken some medication or antibiotics over the counter but forgotten these past events. Therefore, these would underestimate the total number of patients with afebrile UTI. Finally, a relatively small sample size limiting us from critically evaluate the association of antibiotics with the incidence of post-TRUSBx infectious complications.

5. CONCLUSION

Oral Fosfomycin could be used as a reliable alternative to ciprofloxacin as it has a comparable infectious complication rate. At the same time, it has the advantage of a single oral dosage and a better resistance rate. On top of that, using Fosfomycin as a prophylactic antibiotic hopefully will reduce the incidence of quinolones resistance organism.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

TRUSBx : Transrectal ultrasound guided prostate biopsy
UTI : Urinary tract infection