Comparison of the Effectiveness of Pre-urodynamic Single-dose Levofloxacin with Post-urodynamic Levofloxacin for Three Days Related to the Incidence of Urinary Tract Infection: A Randomized Controlled Trial

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Purpose: The current study aims to compare the effectiveness of pre-urodynamic single-dose levofloxacin and post-urodynamic levofloxacin for three days related to the incidence of urinary tract infections post-urodynamic examination.

Materials and Methods: This is a single-blind randomized clinical trial conducted in three outpatient urology centers in Jakarta: Cipto Mangunkusumo General Hospital, Siloam Asri Hospital, and Persahabatan General Hospital using a consecutive sampling method between July 2019 - February 2022. The outcome of the study is the incidence of urinary tract infections in both treatment groups. Urinary tract infection was defined as a patient with one or more clinical symptoms of lower urinary tract infection and one or more urinalysis parameters positive for urinary tract infections.

Results: A total of 126 patients (63 patients in each arm) were included in the evaluation and analysis. Overall, urinary tract infections were detected in 25 cases (19.8%), 12 patients from the pre-urodynamic antibiotic group (9.5%), and 13 patients from the post-urodynamic antibiotic group (10.3%) (P = .823). E.coli was the most common bacteria found in the urine culture.

Conclusion: There is no significant difference between a single dose of 500 mg of Levofloxacin administered one hour before the urodynamic study and a once-daily dose of 500 mg of Levofloxacin for three days following the urodynamic study related to urinary tract infections prevention post-urodynamic examination.

Keywords: antibiotic; levofloxacin; prophylaxis; randomized trial; urinary tract infection; urodynamic study

INTRODUCTION

The urodynamic study (UDS) is an essential examination in the field of urology. Using UDS, the lower urinary tract function can be assessed, and the underlying diagnosis causing the lower urinary tract symptoms can be determined. However, given the invasive nature of the procedure, the risk of the patient contracting a urinary tract infection (UTI) after the study is high. The incidence of acquired UTI (asymptomatic or symptomatic) following UDS varies widely; however, literature report rates range from 1.5 to 36%.[1-3] For this particular reason, prophylactic antibiotics are given to avoid post-urodynamic infections. This statement is also supported by the results of a 2016 study by Rahardjo, et al. in which the administration of prophylactic antibiotics for 3 days after urodynamics was able to reduce the rate of UTI by 55% compared to a placebo.[4] Moreover, considering the increasing number of urodynamic examinations[5], the incidence of infection and the cost of administrating prophylactic antibiotics after urodynamics has become burdens on health services.[2-3] In previous studies, researchers have identified that administering levofloxacin for three days after UDS has high efficacy in preventing UTIs after UDS.[1] Moreover, several additional studies have also shown that single-dose prophylactic antibiotics have satisfactory efficacy in preventing UTIs after UDS.[6-9] The administration of single-dose antibiotics in preventing infection after certain invasive procedures have proven not only to have good efficacy but also to have better cost-efficiency.[10-14] This study aims to determine whether a single dose of levofloxacin 1 hour before the procedure may show equal, or even better efficacy than a daily dose for three days after UDS. An equal or better efficacy may indicate lower usage of antibiotics, leading to better cost-efficiency and better compliance from patients.[15]

MATERIALS AND METHODS

Study Population

This is an experimental study with a single-blinded randomized clinical trial design to compare the number of UTIs in a group of patients who received a single dose of 500 mg of levofloxacin one hour before the urodynamic study and patients who received levofloxacin 500 mg QD for three days after urodynamic study. The study was conducted in three outpatient urology centers in Jakarta: Cipto Mangunkusumo General Hospital, Siloam Asri Hospital, and Persahabatan General Hospital, be-

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ReceivedMay 2022 & Accepted September 2022

Table 1. Subject Characteristics

	Receiving single dose 500 mg Levofloxacin 1 hour prior to UDS (n = 63)	Receiving daily dose 500 mg Levofloxacin for 3 days after UDS (n = 63)
Age, year; mean ± SD (range)	52.75 ± 16.36 (18-84)	53.78 ± 17.17 (18-84)
Sex, n (%)		
- Male	33 (26.2)	38 (30.2)
- Female	30 (23.8)	25 (19.8)
Clinical diagnosis for performing UDS, n		
- LUTS	39	41
- OAB	16	18
- Stress Urinary Incontinence	4	1
- History of Urinary Retention	3	2
- Enuresis	1	0
- Neurogenic Bladder	0	1

UDS = urodynamic study; LUTS = lower urinary tract symptom; OAB = overactive bladder

tween July 2019 - February 2022, and it was registered with Clinical-Trials.gov number NCT05219877.

Calculation of the sample is made based on the calculation of proportions for two independent groups from previous literature. Considering the possibility of drop-out, it is decided that the number of samples taken is at least 100 patients. The balanced blocked randomization technique (block size of 4) was used to determine the sample treatment group for the study. Allocation concealment was performed in this study. The subject and physician who performed the UDS study were aware of which treatment protocol the patient received. However, the investigators (the doctor who examines and assesses if clinical UTI was present in the patients after antibiotic administration, the urodynamic nurses, and also the laboratory worker) were not aware of which drug regimen was administered to the research subjects. The main outcome of the study was to assess whether the administration of a single dose of 500 mg levofloxacin is more effective than a once-daily dose of 500 mg levofloxacin for three days in preventing UTI as an adverse event of urodynamic study. While the secondary outcomes were microorganism data in urine culture that cause UTIs in our population, clinical diagnoses for performing UDS, and sex difference correlation to the incidence of UTI post-UDS.

The Ethical Clearance number for the study KET-542/UN2.F1/ETIK/PPM.00.02/2019 was approved and issued by the Faculty of Medicine, Universitas Indonesia Ethics Committee. The research was conducted in ac-

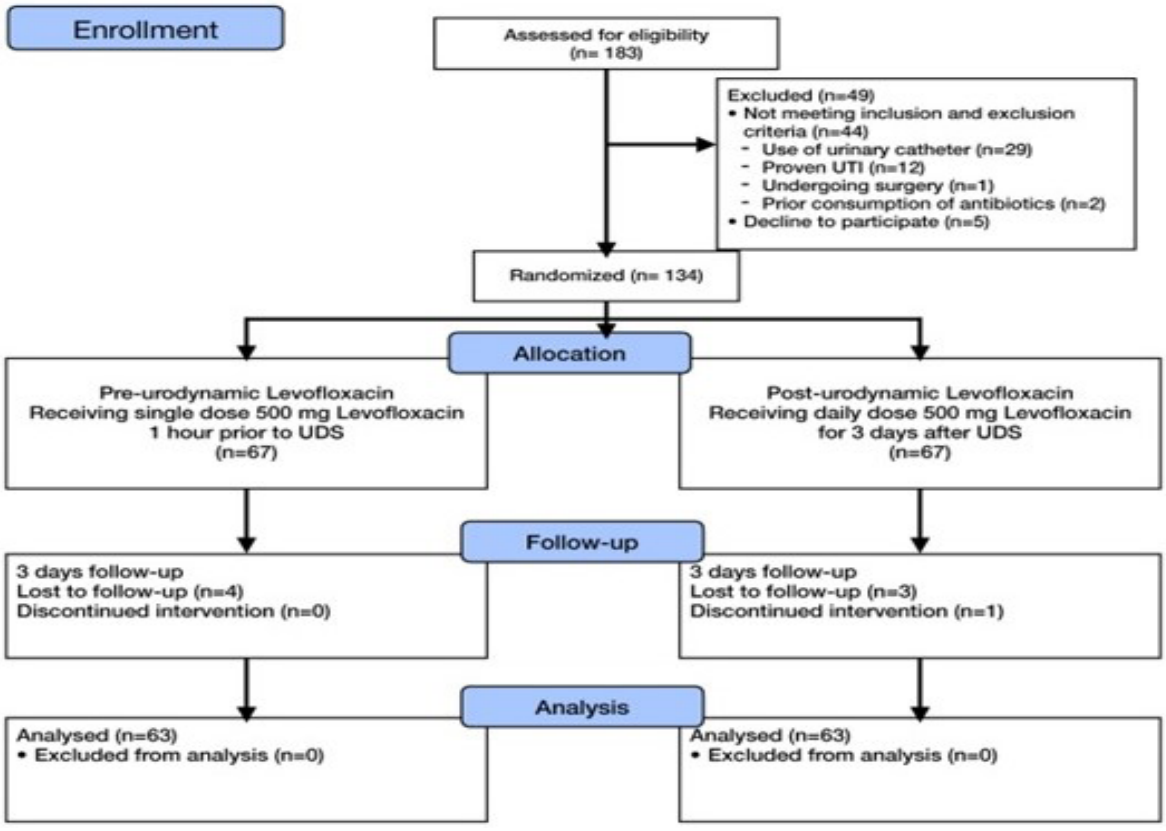

Figure 1. Diagram of the randomized trial of pre-urodynamic single-dose levofloxacin and post-urodynamic levofloxacin for three days related to the incidence of UTIs

Table 2. Patients' characteristics.

	Receiving single-dose 500mg Levofloxacin 1 hour prior to UDS (n = 63)	Receiving daily dose 500mg Levofloxacin for 3 days after UDS (n = 63)	RR (95% CI)	*P*-value
Number of UTI Cases post-UDS, n (%)	12 (19)	13 (20.6)	.92 (.45-1.86)	.823
UTI by Gender				
Male (n=71), n	5	10	.58 (.22-1.51)	.263
Female (n=55), n	7	3	1.94 (.57-6.75)	.294
Symptomatic UTIs, n (%)	6 (9.5)	8 (12.7)	.75 (.28-2.04)	.571
Positive urine culture, n (%)	6 (9.5)	4 (6.3)	1.5 (.44-5.06)	.510
Type of bacteria found in urine culture, n				
- E. Coli	2	3		
- K. Pneumoniae	3	1		
- S. epidermidis	1	0		
- No growth	4	6		
- No urine culture data	2	3		

UDS = urodynamic study; UTIs = urinary tract infections

cordance with the Declaration of Helsinki. All patients provided written informed consent before the start of the trial.

Inclusion and exclusion criteria

The data were collected using a consecutive sampling method until the required number of subjects was reached. The inclusion criteria were men and women above the age of 18 who underwent UDS and were willing to participate in the study. Patients who had at least one of the following exclusion criteria were not included in the study: allergy to levofloxacin, history of antibiotics consumption in 1 month before the study, pregnancy, uncontrolled and untreated diabetes mellitus, use of a urinary catheter, UTI confirmed by urinalysis before the study, or refusal to participate. Before UDS, patients were required to undergo urinalysis to confirm whether the patients suffering from a UTI or not. If a UTI was confirmed, the patient was excluded from the study.

Procedures

Patients who were willing to participate and did not meet any of the exclusion criteria were randomly divided into two groups: those receiving a single dose of 500 mg levofloxacin 1 hour before UDS, and those receiving a once-daily dose of 500 mg levofloxacin for three consecutive days after UDS. According to the standard UDS procedure, those eligible for the UDS underwent the procedure. Four days after UDS, the patients were followed up using urinalysis and checked for clinical symptoms related to UTI. After the urinalysis results were obtained and clinical symptoms assessed, patients who had confirmed UTIs were required to undergo urine culture and antibiotics sensitivity testing. A urinary tract infection is defined based on the results of urinalysis in which one of the following conditions is present: leukocyturia (found > 5 leukocytes/per field view), a positive result of bacteria, nitrite, and/or leukocyte esterase.

Statistical Analysis

A descriptive report was used to describe each subject, including their age, gender, and reason for undergoing UDS, whereas analytic studies were utilized to compare the event of UTI in the pre-urodynamic antibiotic group and the post-urodynamic antibiotic group. The Chi-square test was used to compare the association between UTIs and the treatment groups, if no expected cell count was less than 1 and at most 20% of the expected cell counts less than 5, otherwise Fisher's exact test was chosen. Relative risk (RR) and its 95% confidence interval (CI) were used to analyze the data. The statistical analysis was performed using IBM SPSS Statistics version 23. A p value < 0.05 was used to determine statistical significance.

RESULTS

One hundred eighty-three patients were assessed for eligibility. Forty-four patients were excluded due to the use of a urinary catheter (n = 29), having a documented UTI before the UDS study (n = 12), prior antibiotic use (n = 2), and undergoing surgery (n = 1). Five participants declined to take part in this study.

One hundred thirty-four patients who were willing to participate and had no exclusion criteria were divided into two groups randomly: 67 patients who received a single dose of 500 mg levofloxacin 1 hour before UDS, and 67 patients who received a once-daily dose of 500 mg levofloxacin for three days after UDS.

Four patients from the group who received antibiotics before UDS were lost to follow-up. Meanwhile, three patients from the group who received antibiotics after UDS were also lost to follow-up, and one had to discontinue the intervention due to hematuria experienced two days after UDS, requiring further evaluation and treatment. In total, 63 patients from each group were analyzed. Figure 1 presents a flow diagram of the randomized trial. The characteristics of the patients who underwent UDS in each group are presented in Table 1. The clinical diagnoses for performing UDS were Lower Urinary Tract Symptoms (LUTS) (n = 80 patients; 63,4%), overactive bladder (OAB) (n = 34 patients; 27%), stress urinary incontinence (SUI) (n = 5; 4%), history of urinary retention (n = 5; 4%), neurogenic bladder (n = 1; 0.8%), and enuresis (n = 1; 0.8%).

During the filling phase, 56 patients (44.4%) had small bladder capacity, 33 patients (26.2%) had detrusor overactivity, 17 patients (13.5%) had low bladder compliance, 8 patients (6.3%) had large bladder capacity, 3 patients (2.4%) had stress urodynamic incontinence, and 1 patient (0.8%) had detrusor overactivity incontinence. A patient could have more than one diagnosis during the filling phase. In the voiding phase, forty-eight patients (38.1%) had detrusor underactivity and 49 patients (38.9%) had a bladder outlet obstruction. During this phase, the patients could also receive multiple diagnoses. Normal urodynamic results were found in 12 patients (9.5%) in both the filling and voiding phases.

Overall, UTIs were found in 25 cases (19.8%) of the 126

post-UDS patients (12 of 63 patients from the pre-urodynamic antibiotic group (9.5%) and 13 of 63 patients from the post-urodynamic antibiotic group (10.3%); P = .823). Fifteen of them (five in pre-urodynamic antibiotic group and ten in post-urodynamic antibiotic group) were male patients. Six (9.5%) patients from the pre-urodynamic antibiotic group were symptomatic UTIs while 8 patients (12.7%) from the post-urodynamic antibiotic group had symptomatic UTIs. E.coli was the most common bacteria found in the urine culture followed by K.pneumonia and S.epidermidis. We also discovered ten patients with UTIs who had no bacterial growth in their urine culture/isolation. A comparison of the UTI cases in both groups is presented in **Table 2**.

DISCUSSION

The urodynamic study (UDS) is a widely used diagnostic tool in the evaluation of patients with voiding dysfunction, urinary incontinence, bladder outlet obstruction, and neurogenic bladder. Despite the aseptic procedure, patients still have a chance of developing urinary tract infections (UTIs) as one of the most common complications associated with UDS. Therefore, prophylactic antibiotics, which vary considerably in the choice of antimicrobial agents and routes of administration, are often used in several urologic invasive procedures to prevent UTIs afterward. However, previous studies regarding the use of prophylactic antibiotics post-UDS have revealed inconsistent results. There is no consensus in the literature regarding antibiotic prophylaxis for urodynamic investigation.

The incidence of UTIs after UDS was found to be 19.8% in this study. The present finding was similar when compared to a prior study conducted in 2016.[4] Several studies have reported incidences of acquired UTIs (asymptomatic or symptomatic) after urodynamic examination ranging between 1.5 and 36%.(1,3,16-17) This large discrepancy may be due to the time of urine testing, catheterization technique, the difference in study populations in terms of age or underlying problems, the UDS performance method, and different definitions of urinary tract infections.[18-20]

Several studies do not support routine prophylaxis, as there is no significant improvement in the overall prevalence of UTIs after urodynamic investigation. Meanwhile, other studies suggest that prophylaxis is useful.[21-23]. Although the results of different studies are conflicting, two previous meta-analyses reported that the use of prophylactic antibiotics reduced the bacteriuria risk caused by urodynamic tests.[1,3] According to Rahardjo et al.[4], a three-day course of 500mg of levofloxacin daily could decrease the incidence of symptomatic UTIs from 28.6% to 12.7%. On the other hand, a single dose of antibiotics within an hour before UDS appears to be a suitable option for reducing the incidence of symptomatic UTIs in patients with neurogenic bladder and asymptomatic bacteriuria who undergo UDS.[24] To date, no clinical trial has been performed regarding the timing of prophylactic antibiotics, and to our knowledge, the present study is the first randomized trial to compare prophylactic antibiotics given pre-urodynamic study and post-urodynamic study concerning post-UDS UTIs.

This study shows that there is no significant difference in the group of patients who received a single dose of 500 mg levofloxacin one hour before the UDS and patients who received levofloxacin 500 mg QD for three days after the UDS in terms of UTI incidence. In the AUA Best Practice Policy for antibiotic prophylaxis, fluoroquinolones are designated as first-line prophylaxis. Alternative antimicrobials include cotrimoxazole, aminoglycoside, ampicillin, cephalosporin, and amoxicillin/clavulanate. However, when selecting a prophylactic antibiotic, local microorganisms, and their sensitivity-resistance data patterns, patient allergies, preceding urine cultures, and antibiotic cost should all be considered.[25] The provider's clinical judgment must always be taken into account.

Our study also found that there was no difference in the incidence of UTIs postprocedural between male and female patients, although 15 out of 25 were male patients. This finding contradicts the previous study that identified one of the important predictors of post-UDS UTIs including the male sex (P = .02).[26] The use of single-dose antibiotics as prophylaxis for infection has been studied throughout the decades.[27-29] The studies have shown that the efficacy of shorter single-dose antibiotic administration is comparable to longer regimens.[27-28,30] A shorter regimen also reduces cost and workload and improves patient comfort. Given the fact that in this study, the number of patients who suffered from UTIs post-UDS was similar between each group in a descriptive fashion, we can conclude that the efficacy of a single dose of 500 mg Levofloxacin one hour before UDS is similar to that of a QD administered for three days after UDS. This fact provides the patient and the healthcare provider with a choice of which antibiotic regimen suits the patient's needs and comfort.

CONCLUSIONS

The efficacy of a single dose of 500 mg of Levofloxacin administered one hour before UDS is comparable to that of a once-daily dose of 500 mg of Levofloxacin for three days following UDS. There is no significant difference between a single dose of 500 mg of Levofloxacin administered one hour before the urodynamic study and a once-daily dose of 500 mg of Levofloxacin for three days following the urodynamic study related to urinary tract infections prevention post-urodynamic examination. This information allows healthcare providers to choose which antibiotic regimen best matches the needs of their patients, taking into account cost, compliance, and the local microorganism sensitivity resistance data.

ACKNOWLEDGMENTS

This work was funded by the Operational Grant of Cipto Mangunkusumo General Hospital (HK.01.07/3.3/8470/2019), subjected to the first author.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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