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Comparison of the prophylactic effect of cefazolin injection versus oral levofloxacin as prophylactic antibiotic in TURP surgery: a randomized clinical trial

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Abstract

Introduction Use of antibiotic prophylaxis before transurethral resection of the prostate (TURP) is highly recommended. However, there is no agreement on the use of a single antibiotic for this purpose. This study aimed to compare the prophylactic effect of cefazolin injection with oral levofloxacin on postoperative complications in TURP surgery.

Trial design Body temperature and urine culture results were obtained two and five days after surgery. Drugs' side effects as well as surgery and catheterization time were also recorded.

Methods In an analytical-comparative trial, the participants were randomly divided into two groups to receive cefazolin or levofloxacin before the surgery.

Results The duration of surgery (min) and catheterization (days) were 41.5 ± 11.7 and 4.7 ± 1.8 for levofloxacin-treated group and 43.9 ± 11.9 and 4.7 ± 1.8 for cefazolin-treated group, respectively. The number of positive urine cultures, 2 and 5 days post-surgery were 12 and 14 for levofloxacin-treated group and 9 and 12 for cefazolin-treated group, respectively. Furthermore, both groups reported one fever two days after surgery and had no fever after 5 days. In total, no significant difference was observed between the two groups. Additionally, no correlation was observed between the demographic data (i.e. age, BMI and prostate volume) and the postoperative complications (i.e. fever and urinary culture tests), except between age and urinary culture 2 days after the surgery.

Conclusion Considering the lack of significant differences between the two groups, the use of oral levofloxacin is suggested as an easy to take and cost-effective alternative to injection of cefazolin before TURP surgery.

Trial registration Iranian registry of clinical trials, IRCT registration number IRCT20160514027893N4, available through www.irct.ir, Registration date: 2024-03-13 (Retrospectively registered).

Keywords Benign prostatic hyperplasia, Cefazolin, Levofloxacin, Prophylaxis, TURP

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Introduction

Benign prostatic hyperplasia (BPH) is a common age-related disease in men. Transurethral resection of the prostate (TURP) is a common method to manage BPH in moderate to severe stages, where indicated [1]. TURP is a clean and low-risk surgery. However, some complications may be observed after TURP, including bacteriuria and urinary tract infection (UTI). Risk factors for such complications include prolonged operation duration (i.e. more than 60 min), preoperative UTI, bacteriuria and other urinary system disorders [2, 3]. Therefore, prophylaxis is recommended before TURP to reduce the complications.

Reviewing the literature, quinolones and 3rd generation cephalosporins have been proposed as suitable antibiotics for prophylaxis against side effects of TURP [3]. A suitable antibiotic should not induce drug resistance, be effective against Gram-positive and Gram-negative bacteria in the urogenital area and have suitable tissue penetration. Therefore, trimethoprim-sulfamethoxazole and levofloxacin could be appropriate candidates for this purpose [4, 5]. Levofloxacin, a third-generation and broad-spectrum fluoroquinolone, acts against Gram-positive and Gram-negative bacteria, atypical bacteria and penicillin-resistant streptococci with appropriate tissue penetration [5]. Its oral form is effective in simple UTIs. Additionally, complications such as nausea and vomiting, photosensitivity and hepatotoxicity are less common with this medicine compared with other fluoroquinolones [6]. A previous study has shown the efficacy and safety of a single dose of levofloxacin 500 mg before prostate surgery [7]. Cefazolin, another effective antibiotic against Gram-positive and Gram-negative microorganisms, is also used as a prophylaxis in various urological surgeries [8]. Cefazolin is commonly used as prophylaxis in TURP [9] and its safety has been documented [9].

Although the need for prophylactic antibiotics is inevitable, evaluating different available guidelines for prophylaxis in urological surgeries, reveals controversy and lack of a conclusion, especially in duration of the prophylaxis [10]. Currently, the drug of choice as well as its duration of administration is still under debate [11, 12] and no USA or Europe guideline is available for this purpose [13]. Therefore, more detailed and extensive studies are required for this purpose. For instance, the prophylactic efficacy of intravenous (IV) cefazolin has been compared with single-dose oral ciprofloxacin in patients undergoing endourologic surgery. Ciprofloxacin indicated similar efficacy with substantially lower cost [14]. Single- and multiple-dose cefazolin have also been tried as prophylaxis for TURP. From the findings, in patients without presurgical pyuria or bacteriuria, single dose cefazolin is sufficient as prophylaxis [13]. Present study was conducted to compare the preventive effect of cefazolin (injection) with levofloxacin (oral) on postoperative complications in patients undergoing TURP.

Methods

Study population

During April 2019 to April 2020, adult patients, 58 to 89 years old, undergoing TURP at Imam Hassan hospital (Bojnurd, Iran), were taken for the randomized study. A sample size of 100 patients (50 in each group) was used for a two-sided Z-test of difference between the proportions, with 80% power and a 5% significance level. The 17.6% difference represents the difference between a 3.4% bacteriuria rate in the cefazolin group [2] and a 21% rate in levofloxacin group [15]. In a prospective design, patients were randomly divided into two groups of 50. An online random allocation software (www.random.com) was employed for the randomization. One group received 1 g IV cefazolin, one hour before surgery, while the second group was given 500 mg oral levofloxacin, two hours before TURP surgery. The statistical analyst was blinded during the analysis period. Enrolment of the participants and assignment to the intervention groups were performed by the prinicipal investigator. The trial was ended when the required sample size was achieved.

The demographic and clinical data were documented for all patients. The data included age, prostate volume, body mass index (BMI), underlying disease(s), pathology results of the removed tissue, duration of surgery, duration of catheterization, results of urine culture tests (2 and 5 days after surgery), body temperature (2 and 5 days after surgery) and drugs' side effects.

Inclusion and exclusion criteria

The inclusion criterion was negative urine culture before surgery. The non-inclusion criteria included a history of immunodeficiency diseases or cancer as well as receiving corticosteroids, endocarditis prophylaxis or any other antibiotic for the past two weeks, a history of surgery or manipulation in the urinary tract, hypersensitivity to cefazolin or levofloxacin or the use of drugs interacting with flouroquinolones. The exclusion criteria were patients who sustained urethral injury during surgery, cases where the relevant tissue was not entirely removed during the resection procedure, excessive bleeding (requiring open surgical or medical intervention) and the diagnosis of a tumor or malignancy in patients who had not been previously diagnosed. All patients that met the inclusion/exclusion criteria, provided consent and were enrolled in the study. It is worth noting that none of the planned exclusion criteria were encountered during the study.

The surgery was performed in all cases under epidural anesthesia lithotomy position. Patients were undergone cystoscopy, followed by TURP while strictly maintaining

the sterile technique. All surgeries were performed by a single surgeon. The operation time was 20 to 55 min, followed by placement of a size 24 three-way Foley catheter for irrigation (with normal saline) and production of traction for 45 min. Urinary culture test, as the primary outcome measure, was performed 2 days and 5 days after the surgery. Figure 1 represents the study design.

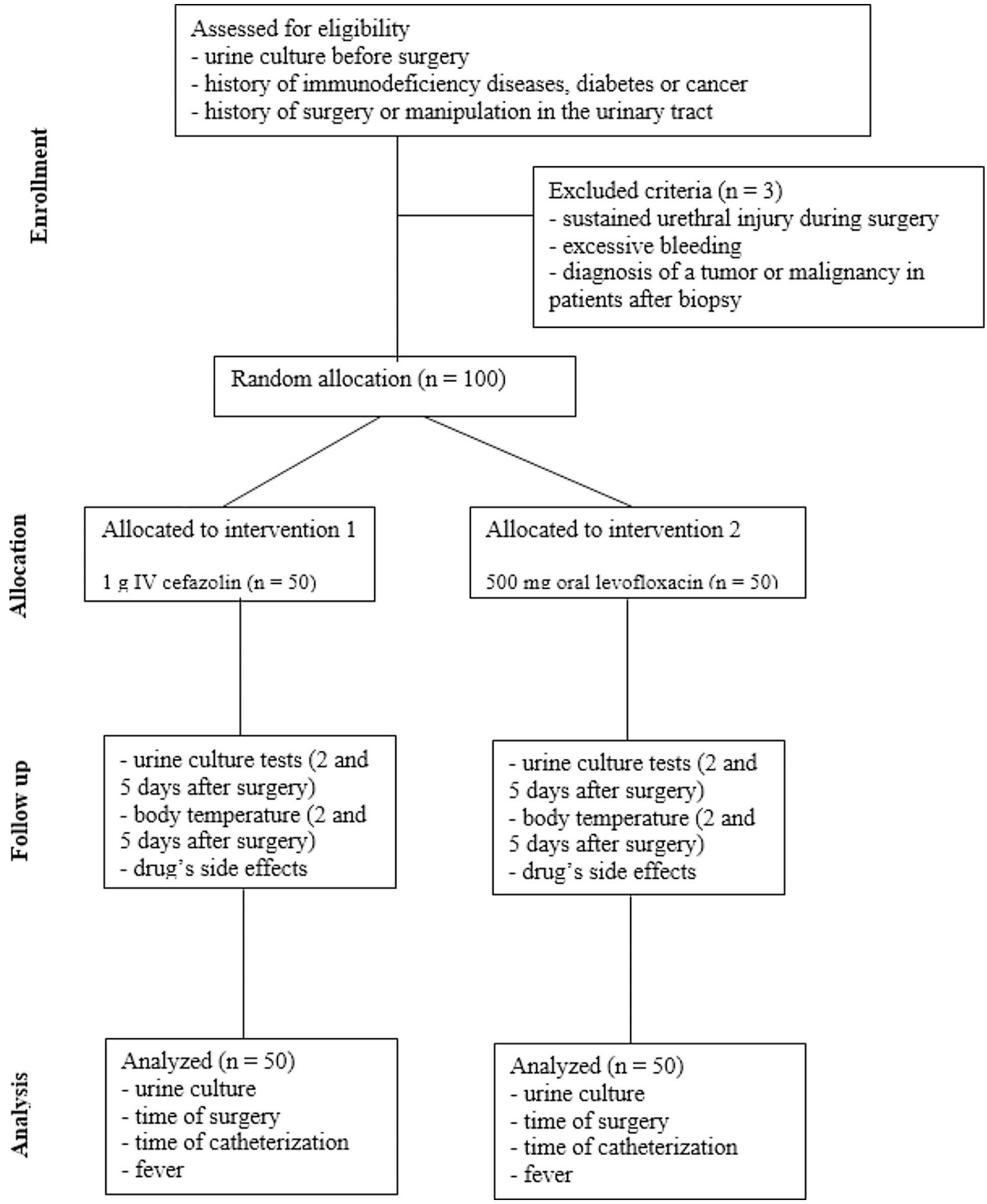

Fig. 1 Flow of participants through each stage of the study

Ethics

This study was approved by the Ethics Committee of North Khorasan University of Medical Sciences (ethics code IR.NKUMS.REC.1399.011). Written consent was obtained from all patients before being enrolled in the studies. The patients were free to leave the study at any time, which was clearly stated in the written consent form. All participants were assured that all their information remained confidential.

Statistical analysis

Data were analyzed using SPSS statistical software version 26, and *p*-value less than 0.05 was considered as significant. For comparison between the two groups, the independent *t*-test or chi-square tests were used as given below.

Results

The main complaint of the patients was lower urinary tract symptoms (89%) and urinary retention (11%). The underlying diseases in the patients included hypertension (14%), diabetes mellitus (13%) and ischemic heart disease (10%). The prostate volume was determined as 35 to 105 g, using sonography.

Characteristics of the study population have been summarized in Table 1. From the details, using in-dependent *t*-test, there was no significant difference between the two groups in age, BMI or prostate volume (p-value > 0.05).

Catheter blockage was observed in 4 of the cefazolin-treated patients and 5 of the levofloxacin-treated patients which was replaced with a new one. Two to seven days post-surgery, the catheter was removed (see Table 2). Table 2 briefs the time of surgery as well as postoperative complications, as observed in this study. The findings indicate no significant difference in either of time of surgery, time of catheterization, fever (>38 °C) after 2 and 5 days as well as urine culture tests after 2 and 5 days. Furthermore, no adverse effect was reported in either of groups.

To further analyze the correlations between the variables in this study, the effect of age, BMI and prostate volume was analyzed on catheterization time as well as fever and urinary culture results, 2 days and 5 days after the surgery (see Table 3). The details show a correlation between age and positive urine culture two days after surgery. Furthermore, age and prostate volume had significant correlation with catheterization time.

Table 1 The characteristics of the study population in levofloxacin and cefazolin groups

Characteristics	Levofloxacin	Cefazolin
Age (years)	70.8 ± 7.1	71.7 ± 7.3
BMI	24.7 ± 1.7	24.80 ± 2.1
Prostate volume (g)	68.8 ± 15.8	69.2 ± 16.7

Table 2 Comparison of time of surgery and postoperative complications between levofloxacin- and cefazolin-treated groups

Characteristics	Levofloxacin	Cefazolin	Statistical test	*p*-value
Time of surgery (min)	41.5 ± 11.7	43.9 ± 11.9	*t*-test	>0.05
Duration of catheterization (days)	4.7 ± 1.8	4.7 ± 1.8	*t*-test	>0.05
Number of patients with fever, 2 days after the surgery	1	1	--	--
Number of patients with fever, 5 days after the surgery	0	0	--	--
Number of positive urine cultures, 2 days after surgery	12	9	Chi-square	>0.05
Number of positive urine cultures, 5 days after surgery	14	12	Chi-square	>0.05
Adverse reaction(s)	Not observed	Not observed	--	--

Table 3 *p*-value obtained for correlation between demographics and postoperative complications and catheterization time

Variable	Age	BMI	Prostate volume
Fever, 2 days after the surgery	>0.05	>0.05	>0.05
Fever, 5 days after the surgery	--	--	--
Urinary culture, 2 days after the surgery	0.01	>0.05	>0.05
Urinary culture, 5 days after the surgery	>0.05	>0.05	>0.05
Catheterization time	0.035	>0.05	0.001

Discussion

Administering appropriate antibiotics for a certain period before surgery is named antibiotic prophylaxis. The antibiotic prophylaxis helps decrease the risk of bacterial/fungal infections after the surgery. The selection antibiotic type and dosage is affected by the type of surgery, the overall health conditions of the patient, as well as the realted guidelines. It is worth noticing that the antibiotic prophylaxis should not be abused or extended beyond what is necessary [16]. A single-dose antibiotic prophylaxis is currently recommended for class II/ clean-contaminated genitourinary procedures under controlled conditions, including all procedures for benign prostatic hyperplasia treatment [17]. This study aimed to compare the prophylactic efficacy of levofloxacin with cefazolin. Both antibiotics are inexpensive, have long biological life and do not generally cause allergic reactions. While levofloxacin can be safely used in patients with beta-lactam allergy, fluoroquinolones, including levofloxacin, may be associated with risk of tendinitis and tendon rupture. Consequently, use of fluoroquinolones has been suggested to be limited

to the conditions that are caused by bacteria. However, fluoroquinolones are still frequently used in urologic procedures [18]. Subsequent to a TURP procedure, the probability of bacteriuria is between 6 and 43%. Therefore, the use of a prophylactic agent is recommended (5). This study was conducted to compare the effectiveness of cefazolin injection with oral levofloxacin on postoperative complications of TURP. Levofloxacin is a fluoroquinolone with good bioavailability in prostate which is active against most of bacteria causing UTI [19]. Levofloxacin has shown adequate prophylaxis in transrectal prostate biopsy. A single 500 mg dose of oral levofloxacin 30 to 60 min before procedure managed to prevent UTI in 376 out of 377 patients at low risk (10).

Results indicated no significant difference between the two groups in postoperative complications, including positive urine culture and fever. In line with our results, a study evaluating the efficacy of prophylactic ciprofloxacin in TURP showed significant improvement; while no UTI was observed in the group receiving oral ciprofloxacin, 11.6% UTI was reported in the group receiving routine antibiotic prophylaxis (14). Another study compared the efficacy of 500 mg levofloxacin with 1920 mg trimethoprim-sulfamethoxazole in 400 patients on TURP. Results highlighted the duration of operation and catheterization as the risk factors for bacteriuria. The bacteriuria rate was 28% and 21% for levofloxacin at days 3 to 5 and 5 to 7, respectively, similar to that of trimethoprim-sulfamethoxazole (26% and 20% at days 3 to 5 and 5 to 7, respectively) (4). A multi-center prospective randomized study was performed to evaluate the prophylactic effect of oral tosufloxacin against intravenous cefotiam. Fever and UTI was checked following the TURP. The study condluded no significant difference between the outcomes of the two antibiotics, suggesting use of oral antibiotics due to its lower medication cost [20].

Analyzing the correlations between demographics and postoperative complications in our study indicated a significant relation between age and positive urinary culture, two days after the operation: Our findings show that higher age has higher risk of positive urethral culture results. This finding has been reported previously [21, 22]. The report showed that urine culture immediately after catheter removal had higher bacteriuria in older ages. Additionally, catheterization time was shown to be dependent on age and prostate volume. It is arguable that with increasing age and prostate volume, the time required for the prostate to be recovered after the surgery becomes longer, thus, the catheterization time is expected to be longer too. It is also worth noticing that due to nature of the administered dosage forms (i.e. injection versus oral), we were not able to blind the patient, which is an important limitation of the study.

Conclusion

To sum-up, the present study showed that use of cefazolin and levofloxacin have no significant difference in terms of their prophylactic efficacy before TURP. The medicines also showed no important side effect. Considering the facts that levofloxacin is cheaper for the patient and it does not require a trained person for injection, levofloxacin appears to be a drug of choice before TURP.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40360-024-00814-x.

Supplementary Material 1

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Data is available upon request from corresponding author.

Author contributions
RH: Study conception and design, data interpretation, manuscript draft. AK: Study design, data analysis. AR: Study concenption. DA: data collection. AA: data interpretation and discussion. All authors reviewed the results and approved the final version of the manuscript.

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Data availability
Data are available on request from authors.

Declarations

Ethics approval and consent to participate
Approval number from the Ethics Committee of North Khorasan University of Medical Sciences: IR.NKUMS.REC.1399.011. Written consent was obtained from all patients before being enrolled in the studies.

Consent for publication
All authors give their consent for the publication of the data/manuscript.

Competing interests
The authors declare no competing interests.

Consort statement
The study adheres to CONSORT guidelines.

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