

Comparison of Ciprofloxacin with a Combination of Cefixime-Clavulanic Acid Treatment in the Prophylaxis of Transrectal Prostate Biopsy

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Transrektal Prostat Biyopsisi Profleksisinde Siprofloksasin ile Sefiksime-Klavulonik Asit Tedavisinin Karşılaştırılması

ABSTRACT

Introduction: In this study, we aimed to compare retrospectively the efficacy of 500 mg ciprofloxacin with a combination of 400 mg cefixim and 125 mg clavulanic acid to prevent potential infections and complications after TRUS-PB.

Method: We evaluated 276 patients who underwent prostate biopsy with the aim to diagnose prostate cancer between March 2014 and January 2016. First group of patients were given ciprofloxacin twice daily and the second group of patients a combination of 400 mg cefixim and 125 mg clavulanic acid once a day both for two days before the procedure and these drugs were continued 3 days after the procedure. In both groups urinalysis and urine culture were performed one day before and 10 days after procedure. Both groups were compared in terms of postoperative infections and complications.

Results: Mean age of the patients was 62.5 years in Group 1, and 63.4 years in Group 2. Mean PSA level was 12.3 ng/dL, 11.4 ng/dL in group 2. Mean prostate volume was 45.3 cm³ in Group 1, 48.5 cm³ in Group 2. Urine culture positivity was observed in 12 patients in Group 1 and in 10 patients of in Group 2. High fever with urine culture positivity was observed in 1 patient in Group 1 and in 2 patients in Group 2. There was no statistically difference between groups in terms of postoperative infections and complications.

Conclusion: Ciprofloxacin and combination of cefixime-clavulonic acid are effective regimens for the prevention of postoperative infectious complications after TRUS-PB. Increasing antibiotic resistance in recent years will determine the choice.

Keywords: prostate biopsy, prophylaxis, urinary tract infection

ÖZ

Amaç: Bu çalışmada, TRUS-PB sonrası oluşabilecek enfeksiyöz oluşumu önlemede, oral kullanılan 500 mg siprofloksasin ile 400 mg sefiksime-125 mg klavulonik asit kombinasyonunun etkinliğini retrospektif olarak karşılaştırmayı amaçladık.

Gereç: Mart 2014 ve Ocak 2016 tarihleri arasında prostat kanseri teşhisi amaçlı 12 kor TRUS-PB uygulanan 276 hasta değerlendirmeye alındı. Birinci gruptaki hastalara işlemden 2 gün öncesinden 500 mgr siprofloksasin günde iki doz, ikinci gruba işlemden 2 gün önceden 400 mgr sefiksime, 125 mgr klavulonik asit kombinasyonu günde tek doz olarak oral başlandı ve işlemden 3 gün sonrasına kadar devam edildi. Her iki gruba da işlemden 1 gün öncesi ve işlem sonrası 10. günde tam idrar incelemesi ve idrar kültürü analizi yapıldı. Her iki grup işlem sonrası gelişen enfeksiyon ve komplikasyonlar açısından karşılaştırıldı.

Bulgular: Birinci gruptaki hastaların ortalama yaşı 62.5, ikinci grupta 63.4 olarak izlendi. Ortalama PSA seviyesi 1. grupta 12.3 ng/dl, 2. grupta 11.4 olarak izlendi. Ortalama prostat hacmi 1. grupta 45.3 ml, 2. grupta 48,5 ml olarak izlendi. Birinci gruptaki hastalardan 12'sinde idrar yolu enfeksiyonu gelişirken, 2. grupta 10 hastada izlendi. İkinci grupta 1 hastada yüksek ateş gelişirken. 2. grupta 2 hastada gelişti. Her iki grupta da işlem sonrası enfeksiyon ve komplikasyon gelişimi açısından istatistiksel fark gözlenmedi.

Sonuç: TRUS-PB sonrası enfeksiyöz komplikasyonları önlemede kullanılan siprofloksasin ve sefiksime-klavulonik asit kombinasyonu etkin rejimlerdir. Son yıllarda artan antibiyotik direnci seçimin belirleyicisi olacaktır.

Anahtar kelimeler: prostat biyopsi, profilaksi, üriner sistem enfeksiyonu

Alındığı tarih: 06.12.2018

Kabul tarihi: 15.01.2019

Yayın tarihi: 31.01.2019

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INTRODUCTION

Transrectal ultrasound-guided prostate biopsy (TRUS-PB) is an invasive procedure used as a standard technique in the diagnosis of prostate cancer ⁽¹⁾. Infectious complications are frequently observed when using the transrectal route ⁽²⁾. A standard prophylactic regimen has not yet been established regarding the prevention of more severe infectious complications, despite the fact that prostate biopsy is a frequently used procedure. Several oral and intravenous prophylactic antibiotic regimens have been attempted and proposed ⁽³⁾. Numerous publications are available regarding the antibiotic prophylaxis before TRUS-PB to reduce infectious complications ^(4,5). However, recent studies have shown an increase in infection rates after TRUS-PB ^(6,7). The cause of this increase is resistance to TRUS-PB prophylaxis using oral trimethoprim-sulfamethoxazole (TMP-SMX) and fluoroquinolones which are recommended in the American and European urology guidelines ^(7,8).

Although different agents have been proposed to start before the prostate biopsy, ciprofloxacin, the most widely used, is considered to be sufficient in terms of cost and benefit ⁽⁹⁾.

In this study, we compared the efficacy of the cefixime-clavulanic acid prophylactic regimens in preventing infectious complications, considering the progressive resistance to fluoroquinolones.

MATERIAL and METHODS

After approval by the ethics committee (KA EK/2018.4.8), a total of 276 patients who underwent 12 core transrectal prostate biopsies between March 2014 and January 2016 for the purpose of diagnosing prostate cancer were retrospectively evaluated. Prostate biopsy indications include serum prostate specific antigen (PSA) levels greater than 4.0 ng/ml and/or an abnormal digital rectal examination. Patients were divided into two groups. In Group 1, 132 patients were given 500 mg cipro-

floxacin twice a day 2 days prior to the procedure and continued for 3 days after the procedure. In Group 2 of 144 patients, a combination of 400 mg cefixime and 125 mg clavulanic acid was started once a day for 2 days before the procedure and continued for 3 days after the procedure at the same dose. Then, 125 ml of enema was applied for bowel preparation in the morning, and the anal and perianal area was cleaned with povidone-iodine solution. Logiq 200 G.E. Pro Series ultrasonography device and biplanar 6.5 MHz intracavity ultrasonic probe were used for ultrasonographic examination. All procedures were performed with the patient in the lateral decubitus position. After inserting the ultrasound probe into the rectum, 2 ml of 2% prilocaine hydrochloride solution was injected into the peri-prostatic area as local anesthesia. Prostate sizes were calculated in millilitres using the formula length × height × width × 0.52 in three dimensions. The 18 G disposable Geotec TRUS Biopsy Kit was used for biopsy. All patients underwent 12 core biopsies. Before the procedure, urine analysis and urine cultures were done for all patients. Patients with a urinary tract infection (UTI) were not included in this study. All patients were informed about the possible complications and were called for control on the 10th day after the procedure for performing urine analysis and urine culture.

SPSS 20.0 program was used for statistical evaluation. For the comparison of measurable values, Student's t-test was used, and chi-square test and Fisher's exact test were used for the comparison of numerical values. P<0.05 was considered to be statistically significant.

RESULTS

In Group 1, the mean age of the 132 patients was 62.5±8.7 years, the mean serum PSA value was 12.3±11.96 ng/ml and the mean prostate volume was 54±14.43 ml. In Group 2, the mean age of the 144 patients was 63.4±8.3 years, the mean serum PSA level was 11.4±11.78 ng/ml and the mean pros-

Table 1. Demographic data and clinical findings.

	Group 1 (n=132)	Group 2 (n=144)	p
Age (years)	62.5±8.7	63.4±8.3	0.128
PSA (ng/ml)	12.3±11.96	11.4±11.78	0.685
Prostate volume (ml)	54±14.43	51.99±14.8	0.12

Table 2. Infectious and non-infectious complications in the two groups.

	Group 1 (n=132)		Group 2 (n=144)		p
	No.	Rate	No.	Rate	
Urine culture positive	12	9.09%	10	6.4%	0.511
Fever	1	0.7%	2	1.3%	0.613
Haematuria	14	10.6%	12	8.3%	0.518
Haematospermia	8	6%	8	5.5%	0.858
Rectal bleeding	5	3.7%	6	4.1%	0.872

tate volume was 51.99±14.8 ml. No significant difference was observed between the groups in terms of age, PSA levels and prostate volumes ($p>0.05$) (Table 1).

All patients were called for the control on the 10th postoperative day and evaluated for infectious complications by performing urinalysis and urine culture. In the first group, a positive urine culture was observed in 12 (9.09%) patients and 1 (0.7%) patient was hospitalised due to fever and treated. Non-infectious complications in Group 1 patients were hematuria in 14 (10.6%), hematospermia in 8 (6.0%) and rectal bleeding in 5 (3.7%) patients. In Group 2, 10 (6.4%) patients were found to have UTI, and 2 (1.3%) patients were hospitalised due to fever and treated with intravenous antibiotics. Non-infectious complications in the second group were hematuria in 12 (8.3%), hematospermia in 12 (5.5%) and rectal bleeding in 6 (4.1%) patients. No urinary retention was observed in both groups; the complications observed in the groups are shown in Table 2. No statistically significant differences were observed in infectious and non-infectious complications between the two groups ($p>0.05$).

DISCUSSION

Prostate cancer is one of the most common cancers in men and the second most common cause of death after lung cancer ⁽¹⁰⁾. Due to the increased frequency of measuring the PSA level, there has been an increase in the number of prostate biopsies ⁽¹¹⁾. The upper limit of normal serum PSA level is accepted as 4.0 ng/ml. However, in approximately 20% of the patients diagnosed with prostate cancer, the serum PSA level was less than 4.0 ng/ml, and it is common to note that the threshold is now reduced to 2.5 ng/ml ⁽¹²⁾.

In the literature, we can find an increase in infection rates due to increased number of TRUS-PB procedures. A study reported that when antibiotics were not taken after prostate biopsy, approximately 18% of the patients had fever, 70% of them bacteremia and 21% of them bacteriuria ⁽¹³⁾. In another study investigating necessity of antibiotherapy after TRUS-PB, the rate of infectious complications was observed to be 10.3% in the untreated group and 3.7% in the treated group, with a significant difference between the groups. In addition, in the untreated group, sepsis was observed in three and Fournier's gangrene in one patient. The authors noted that the use of antibiotics after TRUS-PB decreased the risk of infection ⁽¹⁴⁾.

The infectious complications after the procedure are usually asymptomatic bacteriuria as well as UTI, fever and urosepsis. In a study comparing ciprofloxacin with placebo, UTI was identified in 5% of the patients in the placebo group and 3% of the patients received ciprofloxacin, while hospitalisation was reported in only 2% of the patients for urosepsis in the placebo group ⁽¹⁵⁾. In another study, a positive urine culture was observed in 4% of the patients in the ciprofloxacin group and in 2.8% of the patients in the TMP-SMX group. There was no significant difference in comparison of the two antibiotics ⁽¹⁶⁾. Although antibiotic treatment was given before and after transrectal prostate biopsy, *E. coli* meningitis has been reported in the literature, so it is necessary to perform the TRUS-PB procedure within a certain

discipline ⁽¹⁷⁾.

In another study comparing single-dose norfloxacin with one week of norfloxacin prophylaxis, no statistical difference was observed between the two regimens in preventing the complications of patients without a risk factor. A weekly regimen was observed to be more effective in patients with diabetes and urinary catheter and in patients with prior history of infection ⁽¹⁸⁾. Manecksha et al. also stated that the administration of prophylactic antibiotics 24 h before the procedure reduces the risk of infection after biopsy by 55% ⁽¹⁹⁾.

Despite the fact that initiation of prophylactic antibiotic is important to reduce infectious complications, intestinal cleansing is another important component in reducing infections. Intestinal cleansing improves the quality of the image. A study published on this subject reported that intestinal cleansing significantly reduced the infectious complications ⁽²⁰⁾. Rees et al. showed that povidone-iodine administration, which is a local antiseptic, reduced the risk of infection by 17% when compared to the non-treated group before TRUS-PB ⁽²¹⁾. In our study, povidone-iodine administration and intestinal cleansing were performed before the procedure, and we believe that this could reduce the risk of infection.

Various antibiotic regimens have been used and recommended to prevent infections after TRUS-PB. However, none of them have a complete effect on all infections, because the infections were due to several bacteria such as, *E. coli*, *Staphylococci*, *Enterococci* and *Proteus* obtained in the analysis ⁽²²⁾. Therefore, ciprofloxacin is the most preferred antibiotic because of its effect on both the intestinal flora and the urinary system ⁽²³⁾. Studies have shown that *E. coli* is the most frequently isolated bacterium in urine cultures and in our study only *E. coli* was observed in urine cultures.

Numerous studies have suggested antibiotic prophylaxis in terms of reducing infection rates after treat-

ment. In a review of these studies, it has been stated that fluoroquinolone groups are not superior to each other and a single standard type of antibiotic regimen is not suitable because the bacteria causing sepsis are mostly antibiotic resistant ⁽²⁴⁾.

Although fluoroquinolones are still effective in TRUS-PB prophylaxis, there is an increase in fluoroquinolone resistance. In any patient, 50% of infectious complications are caused by fluoroquinolone-resistant pathogens when biopsy-proven infective symptoms are present ⁽²⁵⁾. In a study on resistant pathogens leading to UTI, in 45.5% of the cases ciprofloxacin and in 44.8% of them TMP-SMX resistance was detected ⁽²⁶⁾. This situation should not be ignored when antibiotic prophylaxis is planned. In our study, ciprofloxacin resistance was observed in two patients who were hospitalised with fever and dysuria and treated with intravenous antibiotics. In a recent study, ciprofloxacin-resistant *E. coli* was detected in 53.5% of culture samples taken from rectal swabs before biopsy and resistant *E. coli* was observed in six of nine patients with high fever. Therefore, the authors stated that the antibiotic regimens should be amended ⁽²⁷⁾.

In this study, we discussed the comparison between the previously uninvestigated cefixime-clavulanic acid combination in the literature and the widely used ciprofloxacin both in the prophylaxis of TRUS-PB.

In conclusion, both antibiotic regimens were found to be effective and reliable methods to prevent infection after prostate biopsy. Although clinical experience is at the forefront of prophylactic antibiotic regimen planning, in the future, we believe that antibiotic resistance will affect the selection of antibiotics to be used in regimens of prophylaxis.

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