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Effect of Shorter Antimicrobial Prophylaxis and Pre-Intervention Measures on Infections Developing After Transrectal Prostate Biopsies

Transrektal Prostat Biyopsilerinden Sonra Gelişen Enfeksiyonlara Daha Kısa Antimikrobiyal Profilaksi ve İşlem Öncesi Uygulamaların Etkisi

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Abstract

Introduction: Transrectal prostate biopsy (TPB) is currently a commonly used invasive procedure for the diagnosis of prostatic diseases. Due to increasing infectious complications after TPBs in our institute, it was decided to change antimicrobial prophylaxis regimens and pre-intervention measures. The aim of this study was to evaluate the effects of shorter antimicrobial prophylaxis, intestinal cleansing and single use sterile gels on infections developing after TPBs in our tertiary-care educational hospital.
Materials and Methods: Infections developing in the last six months after TPB were evaluated retrospectively by using records of microbiology, radiology and urology departments. Sterilization and disinfection, antimicrobial prophylaxis regimens, intestinal decontamination procedures and routine biopsy procedures were reevaluated in cooperation with the corresponding clinics. Afterwards, it was decided to implement three changes in the TPB practice: 1) Shortening the antimicrobial prophylaxis, 2) Intestinal cleansing one day before the intervention by using enema, and 3) Using sterile gel (single patient use only) during biopsy. Patients were diagnosed as clinical or microbiologically confirmed healthcare-associated infection according to the 'Centers for Disease Control and Prevention' criteria. The preintervention period was 2007 July-December and the intervention period was 2008 January-July.
Results: Overall infection/infectious complication rate (10.5% vs. 3.8%; p=0.007), overall clinically defined infection rate (4.8% vs. 1.1%; p=0.028) and overall microbiologically defined infection rate (5.8% vs. 2.7%; p=0.002) decreased significantly in the post intervention period.
Conclusions: Our findings suggest that shorter antimicrobial prophylaxis regimens, using sterile gels and intestinal cleansing may be useful in the control of infections developing after TPB.
Keywords: Antibiotic prophylaxis, postoperative complication, prevention, quinolones, esbl

Öz

Giriş: Transrektal prostat biyopsisi (TPB) prostat hastalıklarının tanısında sıklıkla kullanılan temel invaziv girişimdir. Merkezimizde prostat biyopsileri sonrası enfeksiyon oranlarının artması nedeniyle antibiyotik profilaksi rejimlerinin ve kontrol önlemlerinin değiştirilmesine karar verilmiştir. Bu çalışmanın amacı TPB'den sonra gelişen enfeksiyonlara, kısa süreli antimikrobiyal profilaksi ile birlikte barsak temizliği ve steril jel kullanımı etkisinin değerlendirilmesidir.
Gereç ve Yöntem: Retrospektif olarak son altı ay içinde gelişen enfeksiyonlar radyoloji, mikrobiyoloji, üroloji kayıtları incelenerek belirlenmiştir. İlgili kliniklerle gerekli işbirliği yapılarak sterilizasyon dezenfeksiyon, profilaksi rejimi, barsak temizliği uygulamaları ve biyopsi sırasındaki işlemler

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yeniden değerlendirilerek üç noktada değişiklik yapılmasına karar verilmiş; 1) Antimikrobiyal profilaksi süresinin kısaltılması, 2) Barsak temizliğinin, müdahaleden bir gün önce lavman kullanılarak uygulanması, 3) Biyopsi sırasında tek kullanımlık steril jel uygulanması şeklinde planlanmıştır. Olgular 'Centers for Disease Control and Prevention' kriterlerine göre klinik veya mikrobiyolojik kanıtlı sağlıkla ilişkili enfeksiyon olarak tanımlanmıştır. Çalışmamızda izlem dönemi 2007 yılı Temmuz-Aralık ayları arasında gerçekleştirilmiş olup, 2008 yılı Ocak-Temmuz ayları arasında ilgili uygulamalar hayata geçirilmiştir.

Bulgular: Genel enfeksiyon/enfeksiyon komplikasyon oranı (%10,5 vs. %3,8; p=0,007), klinik olarak tanımlanmış enfeksiyon (%4,8 vs. %1,1; p=0,028) ve mikrobiyolojik olarak tanımlanmış enfeksiyon oranı (%5,8 vs. %2,7; p=0,002) ilgili düzenlemelerin uygulandığı dönemde anlamlı olarak azalmıştır.

Sonuç: Çalışmamızdaki bulgular kısa antimikrobiyal profilaksi rejimi, tek kullanımlık steril jel ve barsak temizliği uygulamasının prostat biyopsisi sonrası gelişebilecek enfeksiyonların kontrolünde faydalı olabileceğini göstermektedir.

Anahtar Kelimeler: Antibiyotik profilaksisi, postoperatif komplikasyon, önleme, kinolonlar, esbl

Introduction

Transrectal ultrasound-guided prostate biopsy (TPB) is currently a commonly used and essential procedure for the diagnosis of prostatic diseases[1]. Transrectal ultrasound-guided prostate biopsy is usually an uncomplicated and well-tolerated procedure under appropriate antibiotic prophylaxis[2]. However, an increasing risk of complications following TPB has been observed recently in several centers. These complications include bleeding, urinary obstruction, tumor seeding, bacteremia, and urinary tract infection (UTI)[3,4]. Urinary tract infection is the most common infectious complication of prostate biopsy and develops approximately in 5% of patients after the procedure[1]. Antibiotic prophylaxis before the biopsy decreases UTI rate, but patients with urethral catheter and diabetes mellitus are still at risk for serious infectious complications, such as sepsis or bacteremia, despite adequate prophylaxis[5]. Major infectious complications such as sepsis, Fournier's gangrene, and UTI requiring hospital admission have been reported in patients who did not receive prophylactic antibiotics[6]. Therefore, it is necessary to use the most appropriate antibiotic in the appropriate period in patients who are planned to have prostate biopsy in order to prevent both infectious complications and anti-bacterial resistance.

Due to increasing infectious complications after transrectal prostate biopsies in our institute in 2007, we decided to change antimicrobial prophylaxis regimens and some pre-intervention measures by working in harmony with the hospital infection control committee and urology department. In this study, we aimed to evaluate the effects of shorter antimicrobial prophylaxis and intestinal cleansing and use of sterile gels (single patient use only) on infections developing after transrectal prostate biopsies in our tertiary-care educational hospital.

Materials and Methods

After observing an increase in infections developing after TPBs at the end of 2007, biopsies were stopped and procedures before and during the biopsies were evaluated extensively. Infections developing in the last six months were evaluated retrospectively by using records of microbiology, radiology and urology departments. Sterilization and disinfection, antimicrobial prophylaxis regimens, intestinal decontamination procedures and routine biopsy procedures were reevaluated in cooperation with the corresponding clinics.

It was seen that the biopsies were performed in the same operating room by the same staff in both periods. Before the intervention, local anesthetic was injected into both prostate lobes. Four samples were taken from each prostate lobe. Hence, 10 interventions occurred through the prostate and the colon.

No outbreak was detected during the study period. Infections did not cumulate in one surgeon or another. Afterwards, it was decided to implement three changes in the TPB practice:

1) Five-day antimicrobial prophylaxis (oral ciprofloxacin 500 mg q12h+ornidazole 1 g q12h started two days before the biopsy and lasted until the third day and amikacin 500 mg once during the biopsy) was changed to single-day prophylaxis (oral ciprofloxacin 500 mg q12h + ornidazole 1 g q12h given 2 h before the biopsy)[7,8].

2) We started to practice intestinal cleansing one day before the intervention by using enema [Fleet enema adult enema, Kozmed, Turkey, implemented twice on the day (8 h apart) before the biopsy].

3) We started using sterile lubricant gels during biopsy instead of multiple use gels. The enema and the gel did not have antimicrobial content. All consecutive patients, who were planned to have biopsy due to suspicion of prostate malignancy in our tertiary-care educational hospital, were included for this interventional study. A total of 480 biopsies were evaluated during the study period.

The patients were diagnosed as clinically defined nosocomial infection or microbiologically confirmed nosocomial infection according to the CDC criteria[9]. The pre-intervention period was 2007 July-December and intervention period was 2008 January-July.

Blood cultures were performed on Bact-Alert (Bio Merioux, France). Urine cultures and bacterial identification were performed by conventional methods. Susceptibility to ciprofloxacin was determined and interpreted according to the Clinical and Laboratory Standards Institute criteria by means of disk diffusion susceptibility tests on Mueller-Hinton agar (Oxoid Ltd., Basingstoke, UK). Extended spectrum beta-lactamase (ESBL) detection was performed by the double-disk synergy test (Oxoid Ltd., UK)[10]. The data were recorded and evaluated using the Microsoft Office Excel program. SPSS version 20.0 was used for the statistical analysis. In the analysis of the data, descriptive statistical methods, the Student's t-test and chi-square test were used for comparison and a p value <0.05 was considered to be statistically significant.

Results

All subjects were male with suspected prostate malignancy. There was no difference in terms of age between pre-intervention and intervention periods (54.5±4.6 vs. 55±-3.1; p>0.05).

Overall infection/infectious complication rate, overall clinically defined infection rate and overall microbiologically defined infection rate decreased significantly in the post intervention period (Table 1). However, the decrease in overall bacteremia, UTI, *E. coli* infection, *Enterococcus* spp. infection and ESBL-producer *E. coli* infection was not significant (Table 1).

Discussion

Transrectal ultrasound-guided prostate biopsy is a commonly used invasive intervention for the diagnosis of prostate cancer. However, various life-threatening complications such as bacteremia, septicemia, meningitis or UTI, which extend the length of hospital stay and cause morbidity and mortality, may develop following TPB[11]. Bootsma et al.[12] reviewed six randomized controlled studies on antibiotic prophylaxis in TPB. They stated that antibiotic prophylaxis significantly reduced the risk of bacteriuria compared with placebo. Besides, clinical guidelines which were published after 2008 recommend antibiotic prophylaxis, typically with oral fluoroquinolone or 1st/2nd/3rd generation cephalosporin, aminoglycoside + metronidazole or clindamycin, and aztreonam + metronidazole or clindamycin prior to TPB, and recommend that prophylaxis should be started within one hour before procedure, two hours for intravenous fluoroquinolines and discontinued within 24 hours[7,8].

Selection of prophylactic antibiotic and duration of administration in patients undergoing prostate biopsy are important in preventing infection and antibacterial resistance. Aron et al.[13] randomized 231 TPB patients into three groups; group 1 received placebo, group 2 was given a single dose of ciprofloxacin (500 mg) and tinidazole (600 mg), while those in group 3 were given the same combination q12h for three days. They reported that urinary infection rate was higher, if no antibiotics were used. However, continuing the antibiotic prophylaxis for three days offered no benefit over single-dose prophylaxis. Sabbagh et al.[14] enrolled 363 TPB patients prospectively in their randomized-controlled study. The patients were divided into two groups to receive either single day or three days of fluoroquinolone antibiotic prophylaxis. The prophylaxis was given at least one hour prior to biopsy. Two of the 363 patients, one in each group, had an episode of sepsis. They concluded that there was no significant difference between single day and three day antibiotic prophylaxis in TPB[14]. Briffaux et al.[15] compared single day vs. three day ciprofloxacin prophylaxis in TBP cases in a prospective randomized study including 288 men. The patients were randomized to receive either one preoperative dose ciprofloxacin 1000 mg 2 h before prostate biopsy, or three days of ciprofloxacin treatment. Six cases in each group developed asymptomatic bacteriuria, and one case in each group developed prostatitis. As in the previously

Table 1. Effect of the interventions on the infectious complications

	2007 July-December Total biopsy: 294	2008 January-July Total biopsy: 186	p
Overall infectious complications	31 (10.5%)	7 (3.8%)	0.007
Overall clinically defined UTI	14 (4.8%)	2 (1.1%)	0.028
Overall microbiologically defined infection	17 (5.8%)	5 (2.7%)	0.002
Bacteremia	10 (3.4%)	4 (2.1%)	0.42
UTI	7 (2.38%)	1 (0.5%)	0.18
Bacteremia + UTI	4 (1.3%)	1 (0.5%)	0.38
E. coli UTI and/or bacteremia	16 (94.1%)	5 (100%)	0.15
ESBL*-producer *E. coli* UTI and/or bacteremia	6 (37.5%)	1 (20%)	0.18
Enterococcus spp. UTI	1 (5.8%)	0 (0%)	0.31

*ESBL: Extended-spectrum beta-lactamase, *E. coli: Escherichia coli,* UTI: Urinary tract infection

mentioned studies, there was no significant difference between one or three day ciprofloxacin prophylaxis. In our study, five day antibiotic regimen was changed to one day regimen with pre-interventions. It was found that there was no superiority of five day antibiotic regimen to one day regimen while the rate of infectious complications was reduced in one day regimen (clinically defined infection: 4.8% vs. 1.1%; p=0.028; microbiologically defined infection: 5.8% vs. 2.7%; p=0.002).

However, fluoroquinolone resistance has increased worldwide, and fluoroquinolone-resistant organisms on rectal swab culture are predictors of infectious complications after prostate biopsy[16]. Tukenmez Tigen et al.[17] evaluated 400 men prospectively to determine the relationship between the prevalence of ESBL-producing *Enterobacteriaceae* fecal carriage and post-biopsy infections in patients who underwent prostate biopsy. They observed that ESBL carriage was associated with using quinolones or other antibiotics in the last two months and presence of diabetes mellitus which caused a high rate of post-biopsy symptomatic UTI[17]. Hence, alternative prophylactic regimens may be needed at centers where resistance rates are high. Adibi et al.[18] started an augmented regimen of three days of ciprofloxacin or trimethoprim sulfamethoxazole in addition to one dose of intramuscular gentamicin before biopsy because of increasing infectious complications. They found that the rate of hospitalization due to post-biopsy infections decreased from 3.8% to 0.6% in patients who received gentamicin. They identified that the rate of fluoroquinolone-resistant *E. coli* urinary infection and/or bacteremia was 73% in patients who received standard prophylaxis. Only 9% of patients had strains resistant to gentamicin. For this reason, each center should establish its own protocol for antibiotic prophylaxis in TPB, taking into account the national and local antibiotic resistance rates instead of standart prophylaxis regimens[19].

Rectal cleansing with enemas, suppositories, or iodine lavage are controversial in TPB. Zaytoun et al.[20] evaluated a total of 1438 TPB cases retrospectively. They found no statistically significant difference in the incidence of infection or sepsis between groups receiving enemas or not. In another study, Carey and Korman[21] retrospectively evaluated 448 patients. They have identified infectious complications in 10 (4.4%) of 225 patients who received enemas before biopsy and in 6 (3.2%) of 185 in the group without enema. They concluded that enema before biopsy had no clinically significant outcome advantage and increased patient cost in those who received appropriate antibiotic prophylaxis. In case of rectal cleansing, different implementations were used in some studies. Ghafoori et al.[22] divided 280 patients who were scheduled to undergo TPB, randomly into two equal groups. The case group received an intrarectal mixture of povidone-iodine and lidocaine gel before the biopsy and the other group received only lidocaine gel. They concluded that simple use of widely available povidone-iodine for rectal cleansing before TPB might reduce infection rate. Issa et al.[23] evaluated 1.642 consecutive TPB procedures in which formalin (10%) was used to disinfect the needle tip after each biopsy core and compared with a historical series of 990 procedures. They found that the overall rate of urinary infection and sepsis were lower (0.30% vs. 0.80%, p=0.13) with using formalin disinfection.

When performing TPB, administration of multiple-use ultrasound lubricant gel may cause infectious complications. Olshtain-Pops et al.[24] reported four patients infected with *Achromobacter xylosoxidans* during an outbreak after TPB due to multiple use of lubricant gel used in the procedure. In the present study, there were three concomitant interventions which caused a significant decrease in overall infection/infectious complication rate (10.5 vs. 3.8%, p=0.007). It is very probable that each of these interventions had positive effect to a certain degree on outcomes. However, it was not possible to analyze the effect of each intervention the effect of each single intervention.

The most important disadvantage of our study was the fact that it was an interventional study, therefore, it compared retrospective non-intervention cohort with the intervention cohort and it was not a randomized-controlled study. However, although the dataset was relatively old, it resulted in an important effect on outcomes and we believe that the interventions may be beneficial for settings with similar problems.

Conclusion

The presented interventions for biopsy procedure resulted in a significant decrease, more than 50% and p<0.05, in the post-biopsy infection rates. Our findings suggest that shorter antimicrobial prophylaxis regimens, using sterile gels and intestinal cleansing may be useful in the control of infections developing after TPB.

Ethics

Ethics Committee Approval: Since the study comprised interventions suggested in guidelines and investigated the effects of these interventions retrospectively, no ethics committee approval was required.

Informed Consent: A consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practice: A.Ş, E.K., S.T., C.Ö., Concept: B.A., S.U., E.K., Data Collection and Processing: B.A., H.A.E., O.R.S., H.S., Analysis and Interpretation: H.S., S.U., B.A., O.R.S., Literature Search: H.A.E., B.A., Writer: H.A.E., O.R.S., B.A.

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