

Impact of fecal carriage of extended-spectrum beta-lactamase producing *Enterobacteriaceae* on the outcomes of transrectal needle biopsies of the prostate

Geniş spektrumlu beta laktamaz üreten *Enterobacteriaceae* taşıyıcılığının prostatın transrectal iğne biyopsisi sonuçlarına etkisi

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ABSTRACT

Objective: This study aimed to address the prevalence, the risk factors and the results of fecal carriage of extended-spectrum beta-lactamase producing *Enterobacteriaceae* (ESBL-PE) in patients who had undergone transrectal needle biopsy of the prostate (TRNBP).

Patients and Methods: A total of 143 patients who had undergone TRNBP were included. Of these, 33(23%) had fecal carriage of ESBL-PE. The mean age of the patients was 62 ± 7.5 (43-81) years.

Results: A univariate analysis showed that quinolone or other antibiotic use within the last 2 months, prostatitis, and diabetes mellitus (DM) were significantly associated with the presence of ESBL-PE. A multivariate analysis showed that quinolone use within the past 2 months (OR: 4.865; CI: 1.45-16.1), and DM (OR: 4.04; CI: 1.64-10) were found to be significant. Development of dysuria ($p<0.001$), fever ($p=0.046$) and chills ($p=0.002$) after TRNBP were shown to be related to the presence of ESBL-PE. There was no asymptomatic bacteriuria and sepsis, the rate of symptomatic urinary tract infection was 19%.

Conclusion: This study showed that pre-biopsy risk factors for the presence of ESBL-PE were quinolone or other antibiotic use within the last 2 months and presence of DM. Changing prophylactic regimens should not be recommended due to the low rate of severe complications.

Key words: Extended-spectrum beta-lactamases, Transrectal needle biopsy of the prostate, Fecal carriage, Infection

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ÖZET

Amaç: Bu çalışmada, transrektal prostat biyopsisi (TRPB) öncesi, hastalarda dışkıda geniş spektrumlu beta-laktamaz üreten *Enterobacteriaceae* (GSBL-ÜE) taşıyıcılığı oranları, risk faktörleri ve sonuçları gösterilmesi amaçlanmıştır.

Hastalar ve Yöntem: Toplam 143 TRPB yapılan hasta çalışmaya alınmıştır. Bunların 33(%23)'ünde GSBL-ÜE taşıyıcılığı bulunmuştur. Ortalama hasta yaşı $62 \pm 7,5$ (43-81)dir.

Bulgular: Tek değişkenli analizle son 2 ayda kinolon veya başka bir antibiyotik kullanımı, prostatit ve diabetes mellitus (DM) GSBL-ÜE taşıyıcılığı ile ilişkili bulunmuştur. Çok değişkenli analiz, son 2 ayda kinolon kullanımı (OR: 4,865; CI: 1,45-16,1), ve DM (OR: 4,04; CI: 1,64-10) varlığını önemli faktörler olarak göstermiştir. TRPB sonrası disüri ($p<0,001$), ateş ($p=0,046$) ve üşüme-titreme ($p=0,002$) gelişmesi GSBL-ÜE taşıyıcılığı ile ilişkili bulunmuştur. Asemptomatik bakteriyüri ve sepsis saptanmamıştır. Semptomatik üriner sistem infeksiyon oranı %19'dur.

Sonuç: Bu çalışma GSBL-ÜE taşıyıcılığı için biyopsi öncesi risk faktörlerinin son 2 ayda kinolon veya diğer antibiyotik kullanımı ve DM varlığı olduğunu göstermiştir. Ciddi infeksiyonların düşük oranda olması nedeniyle profilaksi rejimlerinin değiştirilmesi önerilmemektedir.

Anahtar kelimeler: Geniş spektrumlu beta-laktamaz, Transrektal prostat iğne biyopsisi, Fekal taşıyıcılık, Enfeksiyon

Introduction

Extended-spectrum beta-lactamase producing *Enterobacteriaceae* (ESBL-PE) carriage is increasing in the community, especially in elderly males in all over the world [1,2]. Intestinal colonization is a major factor for transmission in the community [3]. Valverde et al. have pointed out that the prevalence of ESBL-PE infections has increased dramatically during the last decade in Spain [2]. Moreover, an increase in the fecal carriage of E.coli that produce ESBL from 0.1% in 2002 to 1.7% in 2005 has been noted in the USA [4]. The incidence of fecal carriage of ESBL-PE in Turkey was 15.2% in a recent study [5].

Transrectal ultrasound guided needle biopsy of the prostate (TRNBP) is used by urologists to diagnose and

stage prostate cancers. Even though it is accepted as a safe procedure, complications such as bleeding and infection can occur. TRNBP performed without prophylactic antibiotic administration is related to subclinical temporary bacteremia in 73-100% of patients and to symptomatic urinary tract infections (UTIs) in up to 87% of patients [6]. In a Swedish study, the rates of symptomatic UTI and sepsis were reported as 0.9% and 0.001% respectively among patients using single dose fluoroquinolone prophylaxis [7]. Major risk factors for development of UTI after prostate biopsies were defined as use of corticosteroids, presence of urinary catheters, diabetes mellitus (DM) and prostatitis [8]. We investigated the prevalence of fecal carriage of ESBL-PE in patients undergoing TRNBP, analyzed the risk factors for ESBL before biopsy and described the outcome of the patients.

Patients and Methods

One hundred and forty-three patients who applied for TRNBP at the Department of Infectious Diseases and Clinical Microbiology, School of Medicine, Marmara University between October 2008 and February 2010 were recruited. No restriction was applied for the use of prophylactic antibiotics, which were mainly quinolones, fosfomycin, aminoglycosides and cephalosporins. The rectal swabs containing fecal material were obtained before the biopsy and were spread onto two MacConkey agar plates, each supplemented with 1 µg/ml cefotaxime or 1 µg/ml ceftazidime. At least two colonies with distinct morphotype were selected for subsequent characterization. Combined disc method was used to verify the ESBL production according to the Clinical and Laboratory Standard Institute (CLSI) guidelines (CLSI, M100-S18, Wayne, PA, USA, 2008). Urine cultures were obtained before, 3 and 14 days after the biopsy. Symptomatic urinary tract infection was defined as a culture positive on the third day for any pathogen and any existing urinary tract symptoms. Patients with 38° C fever after TRNBP were identified as febrile. Blood cultures were obtained from the febrile patients.

Statistical Analysis

The relationship between the fecal carriage of ESBL-PE and post biopsy complications was analyzed using the software SPSS for Windows, version 15.0; (SPSS Inc, Chicago, Illinois, USA). Data obtained were presented as mean ± SD, controlled for normal distributions by the Kolmogorov-Smirnov test and compared by the unpaired Student's t-test when the distribution appeared normal. Categorical data between two or more groups were compared by the Pearson χ² test. The effect of ESBL on the clinical outcomes was assessed by a multivariate analysis model, where the dependent variable was kept constant while the independent variables changed according to the course of the follow up. A p value of <0.05 was accepted as statistically significant.

Results

Of the 143 patients enrolled, 33 (23%) had fecal carriage of ESBL-PE. The mean age of the patients enrolled in the study was 62 ± 7.5 (43-81) years. Follow-up urine cultures could be obtained from 103 (72 %) of the patients on the 3rd day and from 70 (49%) patients on the 14th day. Bacteriuria was detected in 16 (15.5 %) patients on the 3rd day, there were no growths in the urine cultures for the 14th day. Prophylaxis of patients before biopsy was not interfered. Eighty one (56.5%) of patients were given prophylactic fluoroquinolone, 62 (43.5%) of patients were given cefuroxime axetil.

In the univariate analysis, quinolone or other antibiotic use within the last 2 months, prostatitis, and DM were found to be significantly associated with the fecal carriage of the ESBL-PE (Table I). In the multivariate analysis, quinolone

Table I. Univariate analysis of the risk factors for ESBL producing *Enterobacteriaceae* carriage before biopsy

	ESBL (+)	ESBL (-)	p
Quinolone use within the last 2 months	15/33 (45%)	12/110 (11%)	<0.0001
Antibiotic use within the last 2 months	22/33 (67%)	31/110 (28%)	<0.0001
Prostatitis	9/33 (27%)	12/110 (11%)	0.020
Hospitalization within the past 3 months	2/33 (6%)	2/110 (2%)	0.195
Urethral catheterization within the past 2 months	1/33 (3%)	0/110	0.231
DM	8/33 (24%)	7/110 (6%)	0.003

use within the previous 2 months (OR: 4.865; CI: 1.45-16.1), and DM (OR: 4.04; CI: 1.64-10) was found to be significantly associated with the fecal carriage of ESBL-PE.

Development of dysuria (p<0.001), fever (p=0.046) and chills (p=0.002) after TRNBP were found to be related with ESBL the fecal carriage of ESBL-PE. Symptoms such as suprapubic tenderness, hesitancy and frequency were not found to be related with ESBL-PE.

Discussion

The increase in ESBL-PE infections after prostate biopsies has prompted us to elucidate the possible risk factors for such infections. Both an increase in infections and the fecal carriage of ESBL-PE has been reported in recent studies [2, 9]. Even though a significant number of epidemiological studies have questioned the fecal carriage of ESBL-PE in healthy individuals, not much information has been reported about the specific subset of patients who received the TRNBP procedure. In our study, the fecal carriage of ESBL-PE in this specific group of patients was investigated.

The incidence of fecal carriage of ESBL-PE (in 23 % of the patients) in our study was one of the highest among other recent studies. The rate of fecal carriage of ESBL-PE was reported as 7.3% in Tunisia, which is another Mediterranean country [10]. The prevalences were reported as relatively low in Spain (6%) [11]. However, several studies have reported higher than Tunisia but lower than our results (16.7%, 15.6%) [9, 12]. In a study from Turkey, the rate of fecal carriage of ESBL-PE was reported as 15.2% [5], whereas in our study this rate was found to be much higher.

We did not observe an increased rate of asymptomatic bacteriuria after the biopsy in patients with ESBL-PE carriage. In our study the symptomatic urinary tract infection rate was 19% with no sepsis after TRNBP. The rate of sepsis was shown to be between 0.5-2% in various studies from different countries [13]. Our results might be related with the limited number of patients in the study population.

Antibiotic prophylaxis for TRNBP should be given for reducing infectious complications, although the choice of antibiotic is not clear. Despite increasing numbers of reports suggesting an increase of urinary tract infections (UTIs) with ESBL producing *E.coli* after TRNBP, it is difficult to recommend a major change in the current prophylaxis practice, mainly a single dose fluoroquinolone to reduce the number of such infections since the number of severe infective complications is still low, as in our study.

Our results also demonstrate an independent correlation between the fecal carriage of ESBL-PE and the presence of DM as in previous reports [14,15]. This might be secondary to a high rate of hospitalizations or to antibiotic usage in diabetic patients [14]. Further large scale prospective studies in diabetics are needed to clarify this relation.

Conclusion

In conclusion, the fecal carriage of ESBL-PE was detected in 23 % of patients undergoing TRNBP, which is one of the highest rates in the literature. Pre-biopsy risk factors for the fecal carriage of ESBL-PE were quinolone or other antibiotic use within the last 2 months and the presence of DM. A change in prophylactic regimens cannot be recommended due to low rate of severe complications in our study.

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