ORIGINAL PAPER

URINARY TRACT INFECTIONS

Fluoroquinolone-resistant Escherichia coli in intestinal flora of patients undergoing transrectal ultrasound-guided prostate biopsy – possible shift in biopsy prophylaxis

Przemysław Adamczyk[1], Kajetan Juszczak[2], Małgorzata Prondzinska[3], Anna Kędzierska[1], Hanna Szwajkert-Sobiecka[3], Tomasz Drewa[1,4]

[1]Department of General and Oncologic Urology, Nicolaus Copernicus Hospital, Toruń, Poland
[2]Department of Urology, Memorial Rydygier Hospital, Cracow, Poland
[3]Department of Microbiology, Nicolaus Copernicus Hospital, Toruń, Poland
[4]Department of General and Oncologic Urology, Nicolaus Copernicus University, Bydgoszcz, Poland

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Corresponding author
Przemysław Adamczyk
Nicolaus Copernicus City Hospital
Department of General and Oncologic Urology
17/19, Batorego Street
87–100 Toruń, Poland
phone: +48 606 184 840
przemekad@poczta.onet.pl

Introduction Infection of prostate gland following biopsy is common complication. Most common pathogen is E.coli. Since fluorochinolones are commonly prescribed as prophylaxis, infection caused by E.coli leads to complicated infections, especially due to fluoroquinolone-resistant species.
The aim of this study was to evaluate the incidence of fluoroquinolone-resistant E.coli species in rectal swabs of patients undergoing prostate biopsy and to define appropriate antimicrobial agent as prostate biopsy prophylaxis.
Material and methods Rectal swabs were collected in 159 patients undergoing prostate biopsy. The identification of E.coli was performed using the BBL Crystal E/NF identification (ID) System.
Results In the rectal swab of 112/159 patients E.coli was found. In 47/159 cases after incubation, the microbiological evaluation showed no E.coli in these swabs. Defining the specific resistance to microbiological agents, we obtained that E.coli resistant to ciprofloxacin was found in 40 out of 112 patients (50.9%). Resistance to I and II generation of cephalosporin were found in 7%, and 5%, respectively. In 40 out of 112 (35.7%) E.coli resistant to trimetoprim/sulfametoksazol was reported. E.coli resistant to amoxicillin with clavulonian acid and ampicillin was found in 16 out of 112 (14.28%), and in 67 out of 112 patients (59.8%), respectively.
Conclusions In all cases with fluoroquinolone-resistant E.coli species positive rectal swabs I generation of cephalosporin seems to be a best choice for prostate biopsy prophylaxis. Moreover, II generation of cephalosporin should be considered for treatment of the eventual subsequent infection. The evaluation of rectal swabs before prostate biopsy is crucial in determining targeted antimicrobial prophylaxis.

Key Words: prostate biopsy ‹› fluoroquinolone-resistant E.coli

INTRODUCTION

The main method of prostate cancer diagnosis is a transrectal ultrasound (TRUS) – guided prostate biopsy. It allows not only to obtain histological material necessary for correct diagnosis, but also to visualize prostate and to locate lesions suspected to be cancerous. It is done under local anesthesia in outpatients departments [1,2]. Although generally prostate biopsy is considered as not difficult procedure, it harbors risk of complications, reported in some series up to 50%. The most common complications are as follow: pain, hematuria, hematospermia, urine retention, and urinary tract infection, etc. [3]. Several complications related to infection can be diagnosed after transrectal prostate biopsy, as follow:

asymptomatic bacteruria, urinary tract infection, acute prostatitis, bacteremia, and sepsis. The incidence of urinary tract infection after transrectal ultrasound-guided biopsy ranges between 2% and 6%, with even half of patients developing bacteriemia, which can be followed with sepsis, with incidence of 0.1–2.2% [4]. Escherichia coli is one of the most common pathogen affecting urinary tract. The typical localization for this pathogen remains fecal, but usually affects urinary tract, accounting for approximately 75–90% pathogens of infectious complications [5, 6, 7]. In general urinary tract infections are often treated with quinolones (especially fluoroquinolones generation) in daily practice. Quinolones are known to be delivered in high concentrations into the prostate gland, therefore a concept of antibiotic prophylaxis with this drug emerged. Many studies demonstrated big benefit of antibiotic prophylaxis before transrectal ultrasound-guided prostate biopsy. Kappor et al. [8] demonstrated in a randomized, double-blind controlled study, that the use of ciprofloxacin lowers the incidence of urinary tract infection, and the number of unnecessary hospitalizations, compared with placebo group. Moreover, Aron et al. [9] reported that infectious complications rates decreased 3-fold when fluoroquinolones were used as prophylaxis, compared with placebo (8% *vs.* 25%). Therefore fluoroquinolones were included into prostate biopsy prophylaxis. Although, the choice of regimen, and type of antimicrobial agent is still debatable [10]. Additionally, in 1998, Sieber et al. [11] reported first two cases of urinary tract infections caused by Escherichia coli resistant to fluoroquinolones, in a series of 4439 transrectal ultrasound-guided prostate biopsy with fluoroquinolones prophylaxis. On the other hand, recent studies have shown that infections with fluoroquinolone-resistant Escherichia coli after prostate biopsy are increasingly being noted [12, 13, 14].

The aim of this study was to evaluate the incidence of fluoroquinolone-resistant Escherichia coli species in rectal swabs of patients undergoing transrectal ultrasound-guided prostate biopsy and to define appropriate antimicrobial agent as prostate biopsy prophylaxis.

MATERIAL AND METHODS

This prospective study was performed with 159 consecutive patients (mean age: 55–80 years) qualified to transrectal prostate biopsy due to prostate cancer suspicion on the basis of elevated PSA level (cut-off value was set at 4 ng/ml), changes found on digital rectal exam (DRE), and/or the presence of changes in the transrectal ultrasound (TRUS) image. Acetylsalicylic acid and oral anticoagulants were discontinued 7 days before prostate biopsy. Biopsies were performed with a spring loaded biopsy gun and 18-gauge Tru-Cut needle. All patients had antibiotic prophylaxis with ciprofloxacin which was administrated orally (500 mg) after biopsy, and prescribed for 5 following days (500 mg twice a day).

Rectal swab and microbiological culture with antibiogram were performed in all patients before transrectal prostate biopsy. Most commonly used antibiotics in urinary tract infections were analyzed: ampicillin, amoxicillin with clavulonian acid, cefalexin, cefuroxim, trimetoprim/sulfametoksazol, and ciprofloxacin. The identification of genus and species of bacteria strains was performed using a conventional method. The identification of Escherichia coli species was performed using the BBL Crystal E/NF identification (ID) System (Becton Dickinson). This system is a miniaturized identification method employing modified conventional and chromogenic substrates. It is intended for the identification of aerobic gram-negative bacteria that belong to the family Enterobacteriaceae, as well as some of the more frequently isolated glucose fermenting and nonfermenting gram-negative bacilli.

Only Escherichia coli microorganisms were identified. Susceptibility to antimicrobial agents was tested by disk diffusion method according to the recommendations of the National Reference Centre for Antimicrobial Susceptibility Testing (KORLD). The quality control was used strain of Escherichia coli ATCC 25922. Interpretation of results was based on existing guidelines European Committee on Antibacterial Suscepibility Testing (EUCAST version 4.0.). The resistance-mechanism related to production of extended-spectrum β-lactamases (ESBLs) was not evaluated in current microbiological protocol.

RESULTS

In this prospective study 159 consecutive patients were included. In the rectal swab of 112 patients Escherichia coli was found, and in 47 after incubation this pathogen was not found. Escherichia coli resistant to ciprofloxacin was found in 57 out of 112 patients (50.9%). In 40 out of 112 (35.7%). Our results showed Escherichia coli strains susceptibility for ampicilin, trimetoprom/sulfometoksazol and ciprofloxacin, as follow: approximately 40%, 64%, and 48%, respectively. The bacterial strain susceptibility determines the borderline antimicrobial therapy efficacy (Table 1).

Escherichia coli resistant to trimetoprim/sulfametoksazol was reported. Escherichia coli resistant to cefuroxim was obtained in 6 patients (6/112 – 5.35%).

In 8 out of 112 (7.14%) Escherichia coli resistant to cefalexin was found. Escherichia coli resistant to amoxicillin with clavulonian acid and ampicillin was found in 16 out of 112 (14.28%), and in 67 out of 112 patients (59.8%), respectively. Other typical pathogens for urinary tract infection (e.g. Klebsiella, Proteus species, etc.) were not analyzed.

Follow up of 159 patients after transrectal ultrasound-guided prostate biopsy revealed that in only two cases acute prostatitis was diagnosed which required admission to the hospital. In these two cases blood culture was taken, and in both cases septicemia of Escherichia coli resistant to quinolones were discovered. Additionally the rectal swabs were also positive to Escherichia coli quinolones-resistant species. Both patients were successfully treated with cefuroxim, with resolution of infection within 3 days.

DISCUSSION

Transrectal ultrasound-guided prostate biopsy is one of most commonly performed urological procedure worldwide. Proper antimicrobial prophylaxis in patients qualified to prostate biopsy significantly reduces the fever, bacteruria, bacteriemia, urinary tract infection, epidydimitis, prostatitis, etc. Additionally, the need for hospitalization is also reduced [15]. Routine antimicrobial prophylaxis is strongly recommended in all patients before prostate biopsy. It is worth mentioning that the data from international survey revealed that approximately 98.2% of patient undergoing prostate biopsy received antimicrobial prophylaxis and the most commonly prescribed drugs were fluoroquinolones (92.5%) [16]. Despite prophylaxis the risk of infective complications after prostate biopsy still remains. Over the past decade, the infectious complications after prostate biopsy have become more complicated and clinical significant by the emergence of fluoroquinolone-resistant Escherichia coli strains. This fact results in big challenge appropriate selection of prophylactic and therapeutic antimicrobial agents [7]. Moreover, positive predictor for prostate infection after biopsy was defined, as occurrence of fluoroquinolone-resistant microorganisms in rectal swabs [17]. Williamson et al. [18] study revealed that Escherichia coli resistant to fluoroquinolones was reported in 62% bloodstream isolates after transrectal prostate biopsy compared with 14% bloodstream isolates from other males within the same population.

Possibility of fluoroquinolones resistance came probably from overuse of quinolones for every urinary tract infection by general practitioners. Ciprofloxacin demonstrates good ability to penetrate both urinary system, as well as prostate gland, so it seems to be the best solution for urologist to use. Recently, a shift in ciprofloxacin use has to be done, due to increasing pathogen non-sensitivity. The resistance to quinolones is presented by many papers, but so high level was generally not seen in community based prospective study [19]. Generally, susceptibility of less than 80% is considered as a borderline of safe antibiotic use [20]. In case of patients involved into a study, such level was not meet in case of ampicillin, trimetoprim/sulfometoksazol and ciprofloxacin (drugs commonly used in treatment of urinary tract infection). It is interesting to note that adding clavulonian acid to amoxicillin, raises level of susceptibility to 88%, what makes it possible to use in clinical setting.

According to the results of our study, the first choice of treatment of febrile urinary tract infection following prostate biopsy should be cephalosporins. Both first and second generations harbors almost the same susceptibility of 93% and 95%, respectively. Therefore it seems, that those antimicrobial agents can be used in clinical setting. It seems, that second generation of cephalosporin (cefuroxim) should remain a drug of choice in patients hospitalized with febrile urinary tract infection following prostate biopsy. First generation cephalosporin, like cefasolin, is affordable, and well penetrating to the prostate tissue, and therefore can be used as prophylactic agent in prostate biopsy as well.

It is worth noting that final concentrations of the antimicrobial agents differ significantly. The final fluid concentration of cefazoline and tissue concentration of cefuroxim can achieve 10 μg/ml and 7.6-29.2 μg/g value, respectively. On the other hand final tissue concentration of ciprofloxacin was recorded at 0.6-4.18 μg/g level. Moreover, tissue level of levofloxacin is greater than corresponding plasma level [21]. Similarly, Steensels et al. [22] also recommend cephalosporins (especially third generation, e.g. ceftriaxone) as an alternative prophylaxis in patients with a high

Table 1. *Percentage of Escherichia coli sensitive strains*

Antibiotic	Percentage of sensitive strains of Escherichia coli
Ampicillin	40%
Amoxicillin with clavulonian acid	88%
I generation cephalosporin – Cephalexin	93%
II generation cephalosporin – Cefuroxim	95%
Trimetoprim/sulphametoxazole	64%
Ciprofloxacin	48%

risk of faecal carriage of fluoroquinolone-resistant strains before biopsy and/or infectious complications. Treatment of bacterial prostatitis is demanding due to the lack of active antimicrobial agents transmembrane transport, as well as poor tissue and fluid penetration especially in inflammated organs. Thus, proper prophylaxis is recommended. As far as concerned antimicrobial prophylaxis after transrectal ultrasound-guided prostate biopsy, the prostate gland antimicrobial agent penetration should be considered. In general with increasing pH gradient across the membrane between plasma and prostatic tissue the higher concentration of antimicrobial agents is observed. In case of inflammation the pH of prostatic fluid increases up to 7–8.3 in chronic prostatitis, as compared with physiological pH values set on 6.5–6.7. Moreover, antimicrobial agents which are unionized easily diffuses through cellular membranes [23, 24]. Winningham et al. [25] experimental study showed that most drugs are unable to cross the electrically charged lipid membrane of the prostate epithelium to reach therapeutic levels within the prostatic acini. ß-lactam drugs are characterized by poor lipid solubility and in consequence poorly penetrates into prostatic tissue and fluids. On the other hand some cephalosporins, which are weak acids with low lipid solubility, may achieve equal or even higher concentration, as compared with inhibitory concentration of antimicrobial agent. Fluoroquinolones present very good penetration into fluid and parenchyma of prostate gland [26].

In accordance with the results of Saade et al. [27] study the evaluation of the type of Escherichia coli strains in patients undergoing transrectal ultrasound-guided prostate biopsy seems to be very important to reduce the risk of complications development after prostate biopsy. It was concluded that patients after transrectal ultrasound-guided prostate biopsy, with co-existing risk factors for fluoroquinolones-resistant bacteruria are patients with higher risk for infection. Such factors are as follow: fluoroquinolone exposure (set at 27.5% of all cases), diabetes, prior hospitalization, and positive culture with Escherichia coli resistant to fluoroquinolones. Moreover, the authors reported a 5-fold increase in bacteruria and a 4-fold increase in bateriemia caused by Escherichia coli after prostate biopsy.

All above mentioned fact show that proper antimicrobial prophylaxis in patients undergoing transrectal ultrasound-guided prostate biopsy is crucial in prevention for infectious complications. In selected cases when the risk of fluoroquinolones-resistant Escherichia coli strains is at higher level, the shift in prostate biopsy prophylaxis (from fluoroquinolones to cephalosporins) should be considered.

CONCLUSIONS

In conclusion it can be stated that in all cases with fluoroquinolone-resistant Escherichia coli species positive rectal swabs first generation of cephalosporins seems to be a best choice for transrectal ultrasound-guided biopsy prophylaxis. Moreover, second generation of cephalosporins should be considered for treatment of the eventual subsequent infection. The evaluation of rectal swabs before prostate biopsy is crucial in determining targeted antimicrobial prophylaxis. However, further prospective studies are required evaluating the usefulness of cephalosporins in infections related to transrectal ultrasound-guided prostate biopsy.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

The manuscript was prepared according to scientific and ethical rules.

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