



ORIGINAL ARTICLE

Comparative Effectiveness of Single-Dose of Fosfomycin vs. Cefoxitin Plus Ciprofloxacin as A Prophylaxis to Prevent Transrectal Prostate Biopsy Complications

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Abstract

Objective: The antibiotic prophylaxis for prostate biopsy is not well established, usually is based on fluoroquinolones, but there is an increase of resistance. We explore the efficacy of Fosfomycin trometamol in comparison with ciprofloxacin plus cefoxitin as prophylaxis of this procedure.

Methods: A total of 432 transrectal ultrasound guided prostate biopsies were performed: 241 patients received prophylaxis with cefoxitin 2 g i.v. 1 hour before the procedure combined with ciprofloxacin 750 mg p.o. 1 hour before and 8 hours after the procedure A total of 184 patients received prophylaxis with single dose of fosfomycin trometamol 3 g oral the night before the procedure Adverse events in the 30 days following the procedure were analyzed.

Results: Related to overall complications of prostate biopsy, no significant differences were found between prophylactic regimens. No significant differences were found between groups in percentage of both infectious (2.9 vs. 2.2, p 0.64) and non-infectious complications (6.6 vs. 4.9, p 0.24). Percentage of prostatitis (2.2 vs. 2.9, p 0.64), sepsis (0 vs. 1.66, p 0.14) and hospital admissions (1.09 vs. 1.66 p 0.7) in fosfomycin group was lower than in cefoxitin plus ciprofloxacin group without reaching statistically significant differences.

Conclusions: The cohort that received fosfomycin trometamol in our study did not show a higher rate of infectious complications compared with the cohort that received cefoxitin plus ciprofloxacin. Fosfomycin-thrometamol is a safe and effective prophylactic alternative for use in transrectal ultrasound prostate biopsies.

Introduction

Prostate cancer is the most common malignant solid tumor in men > 70 years and the second cause of death due to cancer [1]. Clinical suspicion is based on an abnormal digital rectal examination (DRE) or persistently elevated prostate-specific antigen (PSA) levels. The main risk factors are: Family history of prostate cancer, advanced age, race, and PSA kinetics [2].

The standard diagnostic procedure is ultrasound-guided needle prostate biopsy, mainly by transrectal approach. It is recommended to take 10-12 core biopsies, bilaterally, from the base to apex of the peripheral zone of the prostate gland, with additional cores from suspicious areas [3].

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Transrectal ultrasound-guided (TRUS) prostate biopsy is typically a well tolerated procedure with low morbidity rate. The most frequent complications include hematospermia, hematuria, rectal bleeding and infections [3].

Increased bacterial resistance to antibiotics and the great variability between different geographical regions difficult the establishment of an antibiotic standardized prophylaxis protocol. In recent years, the increase of resistance to fluoroquinolones (FQ) in *E. coli* and the turn up of ESBL-producing *Enterobacteriaceae* have raised the question of the appropriateness of using FQ monotherapy as antibiotic prophylaxis for TRUS procedures [2-5]. Fosfomycin trometamol (FT) it is being proposed as a valid prophylactic option for TRUS prostate biopsy [6-9], since it is an oral antibiotic that can be taken as a single dose, so facilitating patient compliance, and also helps reducing the use of broad-spectrum antibiotics [1,10-13]. Before 2007 we used to perform antibiotic prophylaxis with ciprofloxacin. Due to increased antibiotic resistance we moved to cefoxitin plus ciprofloxacin protocol in 2007. In 2015, forced by an intermittent shortage of cefoxitin in our hospital we had to change our antibiotic profilaxies. We decided to switch to single-dose FT.

The aim of the present study is to compare the efficacy of antibiotic prophylaxis for TRUS prostate biopsy in a cohort receiving a single oral dose of FT and

a cohort receiving intravenous cefoxitin prophylaxis combined with ciprofloxacin orally.

Methods

A retrospective observational cohort study was carried out between January 2014 and September 2016 at the Hospital del Mar, Barcelona, a 420-bed university hospital that performs approximately 200 TRUS prostate biopsy procedures per year. The study involved the collaboration of medical professionals from the Urology, Radiology, Infectious Diseases and Pharmacy departments.

During this period, a total of 432 TRUS guided prostate biopsies were performed: 241 patients received antibiotic prophylaxis with cefoxitin 2 g i.v. 1 hour before the procedure combined with ciprofloxacin 750 mg p.o. 1 hour before and 8 hours after the procedure (Group A). On the other hand, 184 patients received antibiotic prophylaxis with single dose of FT 3 g oral the night before the procedure (Group B) (Figure 1).

Description of the protocol: Before the procedure, all patients were tested using the urine dipstick test. If leukocytes were present in the urine, a urine culture was performed and targeted antibiotic treatment administered. The procedure was rescheduled after a negative urine culture was obtained. A rectal enema was given in all cases (139 mg/mL sodium dihydrogen phosphate anhydrous and 32 mg/mL disodium hydrogen

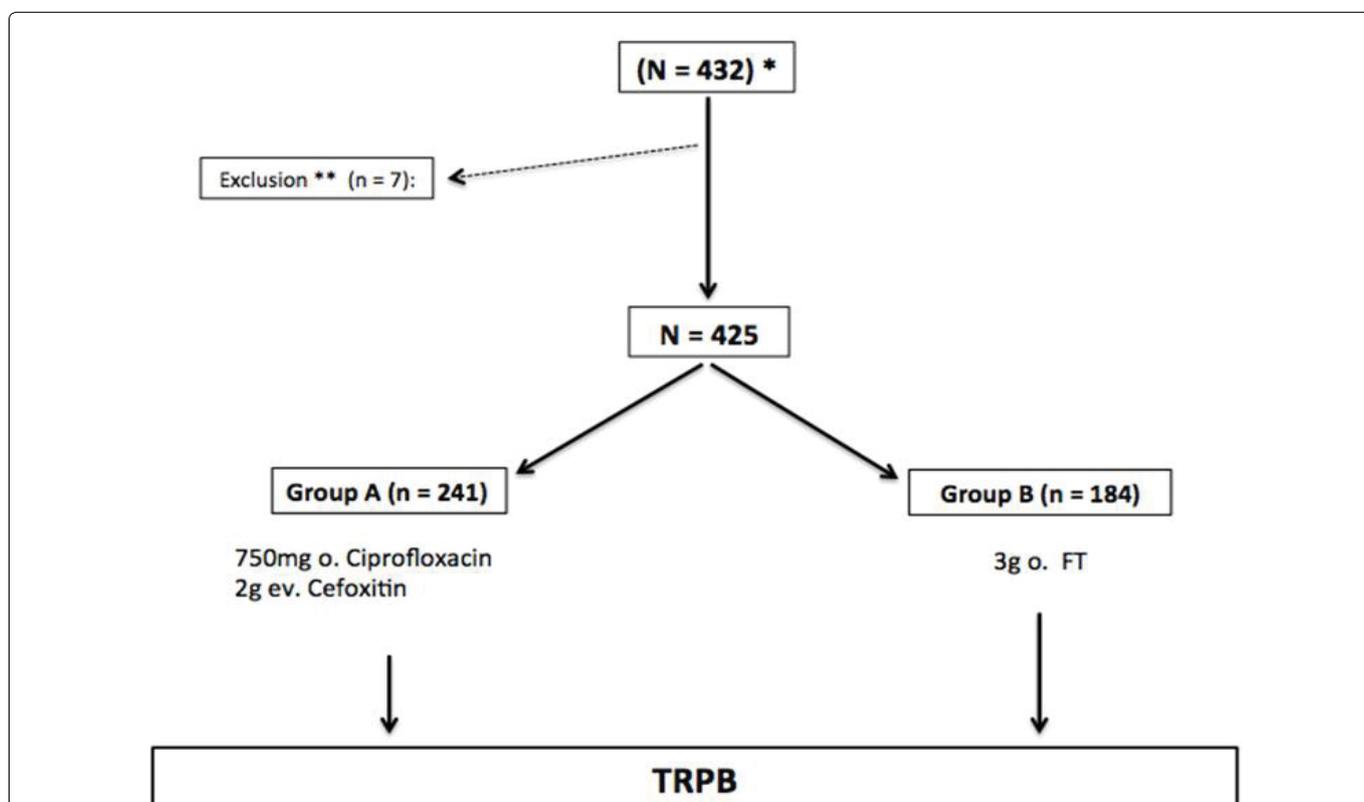


Figure 1: Flow diagram.

*Abnormal digital rectal examination and/or elevated PSA > 10 ng/ml, persistently elevated PSA > 4 ng/ml associated with low free; total PSA ratio (< 20%), control biopsy in patients being closely monitored for low-risk prostate cancer; **Allergy or intolerance to antibiotics administered in the study or under a different prophylactic regimen.

phosphate anhydrous in rectal solution) approximately 3 hours before the procedure. Anticoagulant and antiplatelet drugs (excluding acetylsalicylic acid 100 mg) were withdrawn 2-7 days before the procedure and re-introduced 2-5 days after, based on clinical criteria and comorbidities. During this period, anticoagulant therapy was replaced by low molecular-weight heparin at prophylactic doses, and antiplatelet therapy by 100 mg acetylsalicylic acid depending on criteria of hematology department.

All patients were provided with information about the procedure and possible post-biopsy complications and signed the specific informed consent for the performance of TRUS prostate biopsy. A transrectal transducer (EC9-4) with a biopsy needle guide (Sterile transvaginal needle guide, CIVCCO®) was used to develop the procedure.

The patient was informed of the need to consult the emergency department of the hospital if complications developed, such as hematuria, fever and/or local symptoms. A control visit was made in the first 30 days to assess any adverse effects associated with the TRUS prostate biopsy.

The inclusion criteria were: Abnormal digital rectal examination and/or elevated PSA > 10 ng/ml, persistently elevated PSA > 4 ng/ml associated with low free total PSA ratio (< 20%), or control biopsy in patients being in active surveillance protocol for prostate cancer.

The exclusion criteria were: Urinary tract infection, allergies or intolerance to the prophylactic antibiotics included in the study (n = 7). A total of 425 patients were included in our study.

The baseline variables were: Age, body mass index (BMI), diabetes mellitus, anticoagulant therapy, antiplatelet therapy (100 mg acetylsalicylic therapy was not considered a risk for bleeding), previous symptoms of lower urinary tract infection (LUTI) and type of biopsy (first or repeat).

The variables analyzed were all expected complications in the 30 days following the procedure: a) non-infectious: Bleeding lasting 3 days or more (hematuria, hematospermia, rectal bleeding), acute urinary retention (AUR) and perineal pain lasting 3 days or more; b) infectious: Prostatitis, orchiepididymitis and sepsis (defined as: Heart rate > 90 per minute, axillary temperature > 38 °C or < 36 °C, leukocyte count > 12,000 uL or < 4,000 uL, normal leukocyte count but with > 10% of immature cell forms present and/or respiratory rate > 20 rpm pCO₂ < 32 mmHg); c) number of hospital admissions and d) death.

All recruitment and research protocol were approved by the ethics committee, CEIC- Parc de Salut Mar, Barcelona, Spain.

The Mann-Whitney U test was used for quantitative variables and the Chi-squared test for comparison of qualitative variables. For multivariate analysis, a logistic regression model was performed (adjusted odds ratios). The STATA statistical software package, version 15 (STATA Corp., Texas, USA) was used for statistical analysis, with p < 0.05 being considered statistically significant.

Results

A total of 425 patients were included in the study. The

Table 1: Baseline characteristics by prophylactic group.

| | Group A (IV Cefoxitin + pocipro) | Group B (Oral FT) | Total | p |
|--------------------------------------|--|----------------------|------------|-------|
| Age (m ± SD) | 66.69 ± 8.6 | 68.95 ± 9.1 | | 0.02 |
| Obesity (n, %) | 38 (21.8) | 34 (24.3) | 72 (16.9) | 0.61 |
| Diabetes Mellitus (n, %) | 31 (12.9) | 43 (23.5) | 74 (17.4) | 0.005 |
| Previous SLUTI ¹ (n, %) | | | | |
| No previous SLUTI | 166 (70) | 166 (64.1) | 282 (66.3) | 0.20 |
| a-blockers ² (n, %) | 58 (24.5) | 44 (24.3) | 102 (24) | 1.00 |
| 5-ARI ³ (n, %) | 10 (4.2) | 16 (8.8) | 26 (6.1) | 0.07 |
| Urinary Catheter ⁴ (n, %) | 3 (1.3) | 5 (2.8) | 8 (1.8) | 0.30 |
| Repeat Biopsies ⁵ (n, %) | 52 (21.6) | 28 (15.2) | 80 (18.8) | 0.09 |
| ACO/AAS ⁶ (n, %) | 36 (15) | 18 (9.8) | 54 (12.7) | 0.11 |
| PSA (m ± SD) | 26.4 ± 151.2 | 43.21 ± 171.95 | | 0.23 |
| Prostate Vol. ⁷ (m ± SD) | 51.10 ± 29.2 | 56.27 ± 31.5 | | 0.12 |
| Cores ⁸ (m ± SD) | 11.8 ± 5.5 | 11.97 ± 2.4 | | 0.09 |

¹Symptoms of lower urinary tract infection before the TRUS; ²Alpha-blockers +/- anticholinergics / beta-3 agonists.

³5-ARIS, 5α-reductase inhibitors, +/- anticholinergics /beta-3-agonists; ⁴Those wearing urinary catheter at the time of the TRUS;

⁵Repeat biopsies: 1 or more previous biopsies; ⁶Long-term anticoagulation or antiplatelet therapy; ⁷Prostate volume measured by transrectal ultrasound; ⁸Overall number of core biopsies taken during the TRUS procedure.

baseline characteristics are compared in Table 1. Patients in group B were older and presented higher prevalence of diabetes than patients in group A. Related to overall complications of TRPB prostate biopsy (Table 2), no significant differences were found between prophylactic regimens. Likewise, no significant differences were found between groups in both infectious and non-infectious complications. Nevertheless, it is worth to notice that percentage of prostatitis, sepsis and hospital admissions in the FT group (group B) was lower than in the cefoxitin plus ciprofloxacin group (group A) but not reaching significant differences. No deaths were related to performing TRUS prostate biopsy during the study.

The presence of complications of any kind 30 days after the TRUS procedure by prophylactic group is shown in Table 2.

There were 7 the cases of prostatitis in group A, 5 of them with *E. coli* one of them beta-lactamase AmpC plasmid producer. One case due to susceptible *Klebsiella pneumoniae* and the last one with negative urine culture. Three of the *E. coli* were resistant to cephalosporins and fluoroquinolones In group B, 4 cases of prostatitis were detected: 2 urine cultures were negative and in the other two *E. coli* was isolated, one of them resistant to cephalosporins and FQ. It should be noted that all the microorganisms isolated in the cultures of the overall cohort were sensitive to FT.

Four cases of sepsis occurred, all in the cefoxitin + ciprofloxacin group. Blood cultures were performed in all cases of sepsis, of which 2 were negative and in the remaining 2, *E. coli* AmpC plasmid producer and multisensible *K. pneumoniae* were isolated with the same antibiogram as in urine cultures. It should be noted that the *E. coli* AmpC plasmid producer isolated, only was sensitive to carbapenems and FT, and the patient was treated with FT 50 mg every 8 hours per 30 days with resolution of sepsis and subsequently negative urine culture.

The hospital admissions in group B (2 patients), were due to non-infectious complications (severe hematuria), while all the admissions of group A (4 patients) were due to urinary sepsis secondary to TRUS procedure.

Discussion

Antibiotic prophylaxis in TRUS prostate biopsy significantly reduces bacteriuria and urinary infections and consequently hospitalization rates [1,2,14,15]. Although the procedure carries a low incidence of complications, in some cases may lead to severe sepsis and even death [14-17]. In our series, we detected low rate of life threatening complications requiring hospital admission: 4 patients due to urinary sepsis (0.9%). Likewise, the implementation of prophylactic protocol based on FT has been shown to be effective, with low infectious complication rates (2.2%) and no case of urinary sepsis, although without showing statistically significant differences compared to the previous prophylactic regimen, based on ciprofloxacin plus cefoxitin.

In 2007, we introduced a new antibiotic prophylaxis protocol for TRUS prostate biopsy procedures based on cefoxitin 2 g iv + 2 doses of 750 mg ciprofloxacin po, promoted by the increase in *Enterobacteriaceae* resistant to fluoroquinolones and ESBL-producing bacteria in our environment, similar to the percentage estimated in Spain between 2013 and 2016 by the EARS Net 2016 (31-35%) [18]. The 2007 protocol was based on the microbiological characteristics of bacteria isolated from urine cultures, including those with ESBL-producer *Enterobacteriaceae* [19]. Urinary sepsis due to ESBL-producing *Enterobacteriaceae* (mainly ESBL-producing *E. coli*) is a well known problem and the continued use of FQ as prophylaxis for TRUS procedures helped increase antimicrobial resistance. For this reason, and also because of the problem of shortage of cefoxitin in our hospital, the antibiotic prophylaxis protocol for TRUS was reconsidered, switching to FT in monodose.

Table 2: Complications after TRUSBP according to prophylactic group.

| | Group A (IV Cefoxitin + pocipro) | Group B (Oral FT) | p < 0.05 |
|------------------------------|---|------------------------------------|--------------------|
| Infectious, n (%) | 7 (2.9) | 4 (2.2) | 0.64 |
| Prostatitis | 7 (2.9) | 4 (2.2) | 0.64 |
| Orchiepididymitis | 0 | 0 | 1.00 |
| Sepsis | 4 (1.66) | 0 | 0.14 |
| Non-Infectious, n (%) | 16 (6.6) | 9 (4.9) | 0.24 |
| Hematuria | 7 (2.9) | 2 (1.09) | 0.31 |
| Rectal bleeding | 0 | 1 (0.54) | 0.43 |
| Perineal pain | 1 (0.41) | 1 (0.54) | 1.00 |
| Acute urinary retention | 3 (1.24) | 5 (2.72) | 0.30 |
| Hematospermia | 1 (0.41) | 0 | 1.00 |
| Hospitalization | 4 (1.66) | 2 (1.09) | 0.70 |

FT is a bactericidal phosphonic acid derivative that acts on the cell wall inhibiting peptidoglycan synthesis. It is mainly excreted by the kidneys. After a 3 g oral dose, urinary drug concentrations remain higher than 100 micro g/ml for 30-48 hours [20,21], thus ensuring high penetration into the prostate tissue [12,15,20]. The fact that urinary levels of the drug remain high for more than 24 hours, together with its excellent safety profile [20], means that it can be administered the night before the procedure, so facilitating patient compliance. FT exhibits very high activity among *Enterobacteriaceae*, including beta-lactamase producers, and at the same time reduces antimicrobial resistance in these pathogens to broad-spectrum antibiotics [20]. Its pharmacokinetic characteristics, easy of patient compliance and susceptibility of *Enterobacteriaceae* make FT an effective alternative for TRUS.

There is some literature supporting the use of FT in prophylaxis for TRUS prostate biopsy. Lista, et al. [22] conducted a randomized prospective study including 312 patients who were treated with ciprofloxacin and 359 with single-dose FT, and Ongün, et al. [10] carried out a retrospective descriptive study of 620 patients, comparing single-dose oral FT with single-dose ciprofloxacin or levofloxacin [23]. Both studies concluded that FT was a valid alternative in prophylaxis for TRUS prostate biopsy, since no statistically significant differences between groups were found. In our study, an almost 50% drop in cases of post-TRUS procedure prostatitis was observed among patients receiving prophylaxis with FT versus those receiving cefoxitin + ciprofloxacin, which represented a considerable reduction in post-biopsy sepsis and hospital admission in this group, although the differences were not statistically significant.

Use of targeted antimicrobial prophylaxis based on pre-biopsy screening of rectal cultures to identify *Enterobacteriaceae* was recently suggested as a possibility [20,21,24-26]. Kisa, et al. [25] analyzed the risk factors for infectious complications and FQ and FT resistance in *Enterobacteriaceae* isolated in rectal swab cultures obtained 3-7 days before TRUS biopsy. Patients without risk factors received ciprofloxacin or FT prophylaxis regardless of the results of the rectal culture, while those with risk factors received targeted antibiotic prophylaxis using ciprofloxacin or FT. Of the 110 patients included in the study, FQ resistance was detected in 60.9% of pre-biopsy swabs, and FT resistance in only 2.7%. There were no statistically significant differences between groups with respect to infectious complications. The authors concluded that ciprofloxacin prophylaxis should be given or not depending on the presence of risk factors and then targeted according to the results of the rectal culture, while the use of FT as antibiotic prophylaxis was completely independent of these two factors. We did not analyze the resistance patterns of the causative uropathogens of post-TRUS

infections in our study due to the low incidence of adverse events, although the number of patients with infectious complications was higher in the group with FQ prophylaxis than in the one treated with FT prophylaxis. The two groups were comparable in terms of risk factors. According to commented findings, new studies should be focused on analyzing the risk factors for infectious complications post-TRUS prostate biopsy. This would allow the physician detect the subjects with the highest risk and therefore provide antibiotic prophylaxis based on rectal swab.

The main limitation of our study is the low rate of infectious complications after TRUS prostate biopsy, that could be the meaning of not seeing statistical differences between groups and didn't allow us to analyze the resistance patterns of the causative uropathogens. Obviously, its retrospective nature and the small cohort of patients that is used also could reduce the impact of the study.

Conclusions

In conclusion, it can be state that the use of FT in antibiotic prophylaxis for TRUS biopsies could be a valid alternative, since those patients who received it as prophylaxis in our study did not show a higher rate of infectious complications compared with the previous prophylactic regimen. This observation, together with the fact that FT is easy to administer and reduces the appearance of resistance to broad-spectrum antibiotics, leads us to consider that single dose FT is a safe and effective prophylactic alternative for use in TRUS biopsies.

References

1. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, et al. (2013) Systematic review of complications of prostate biopsy. *Eur Urol* 64: 876-892.
2. Zani EL, Clark OAC, Netto NR (2011) Antibiotic prophylaxis for transrectal prostate biopsy. *Cochrane Database Syst Rev*.
3. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, et al. (2017) EAU-ESTRO-SIOG Guidelines on prostate cancer. Part 1: Screening, diagnosis, and local treatment with curative intent. *Eur Urol* 71: 618-629.
4. (2015) European Association of Urology Guidelines on urological infections.
5. (2017) Prostate cancer. NCCN clinical practice guidelines in oncology.
6. Yang L, Gao L, Chen Y, Tang Z, Liu L, et al. (2015) Prophylactic antibiotics in prostate biopsy: A meta-analysis based on randomized controlled trials. *Surgical Infect* 16: 733-747.
7. Jones JS (2015) Optimal antibiotic use to prevent post-prostate biopsy infection. *J Urol* 194: 282-283.
8. Bosquet Sanz M, Argente VG, Guzmán SA, García MAB, Villa MT, et al. (2006) Comparative study between tobramycin and tobramycin plus ciprofloxacin in transrectal prostate biopsy prophylaxis. *Actas Urol Esp* 30: 866-870.

9. Briffaux R, Coloby P, Bruyere F, Ouaki F, Pires C, et al. (2009) One preoperative dose randomized against 3-day antibiotic prophylaxis for transrectal ultrasonography-guided prostate biopsy. *BJU Int* 103: 1069-1073.
10. Ongün S, Aslan G, Avkan-Oguz V (2012) Effectiveness of single-dose fosfomycin as antimicrobial prophylaxis for patients undergoing transrectal ultrasound-guided biopsy of the prostate. *Urol Int* 89: 439-444.
11. Ishizaka K, Kobayashi S, Machida T, Yoshida KI, et al. (2007) Randomized prospective comparison of fosfomycin and cefotiam for prevention of postoperative infection following urological surgery. *J Infect Chemother* 13: 324-331.
12. Rhodes NJ, Gardiner BJ, Neely MN, Grayson ML, Ellis AG, et al. (2015) Optimal timing of oral fosfomycin administration for pre-prostate biopsy prophylaxis. *J Antimicrob Chemoter* 70: 2068-2073.
13. Falagas ME, Giannopoulou KP, Kokolakis GN, Rafailidis PI, et al. (2008) Fosfomycin: Use beyond urinary tract and gastrointestinal infections. *Clin Infect Dis* 46: 1069-1077.
14. Womble PR, Linsell SM, Gao Y, Ye Z, Montie JE, et al. (2015) A Statewide intervention to reduce hospitalizations after prostate biopsy. *J Urol* 194: 403-409.
15. Muñoz D, Vicens AV, Moragues MO (2009) Antibiotic prophylaxis in transrectal prostate biopsy. *Actas Urol Esp* 33: 853-859.
16. Luong B, Danforth T, Visnjevac O, Suraf M, Duff M, et al. (2015) Reduction in hospital admissions with the addition of prophylactic intramuscular ceftriaxone before transrectal ultrasonography-guided prostate biopsies. *Urology* 85: 511-516.
17. Hayatzaki K, Menne S, Nielsen K (2014) Prophylactic antibiotics reduce sepsis after biopsy of the prostate. *Dan Med J* 61: A4963.
18. (2016) Antimicrobial resistance surveillance in Europe. Annual report of the European Antimicrobial Resistance and Surveillance Network (EARS-Net).
19. Horcajada JP, Busto M, Grau S, Sorlí L, Terradas R, et al. (2009) High prevalence of extended-spectrum beta-lactamase-producing Enterobacteriaceae in bacteremia after transrectal ultrasound-guided prostate biopsy: A need for changing preventive protocol. *Urology* 74: 1195-1199.
20. Taylor AK, Murphy AB (2015) Preprostate biopsy rectal culture and postbiopsy sepsis. *Urol Clin North Am* 42: 449-458.
21. Liss MA, Nakamura KK, Meuleners R, Kolla SB, Dash A, et al. (2013) Screening rectal culture to identify fluoroquinolone-resistant organisms before transrectal prostate biopsy: Do the culture results between office visit and biopsy correlate? *Urology* 82: 67-71.
22. Lista F, Redondo C, Meilán E, García-Tello A, Ramón de Fata F, et al. (2014) Efficacy and safety of fosfomycin-trometamol in the prophylaxis for transrectal prostate biopsy. Prospective randomized comparison with ciprofloxacin. *Actas Urol Esp* 38: 391-396.
23. Unnikrishnan R, El-Shafei A, Klein EA, Jones JS, Kartha G, et al. (2015) For single dosing, levofloxacin is superior to ciprofloxacin when combined with an aminoglycoside in preventing severe infections after prostate biopsy. *Urology* 85: 1241-1246.
24. Cussans A, Somani BK, Basarab A, Dudderidge TJ (2016) The role of targeted prophylactic antimicrobial therapy before transrectal ultrasonography-guided prostate biopsy in reducing infection rates: A systematic review. *BJU Int* 117: 725-731.
25. Kisa E, Altug MU, Gurbuz OA, Ozdemir H (2017) Fosfomycin: A good alternative drug for prostate biopsy prophylaxis: The results of a prospective, randomized trial with respect to risk factors. *Int Braz J Urol* 43: 1068-1074.
26. Steensels D, Slabbaert K, De Wever L, Vermeersch P, Poppel HV, et al. (2012) Fluoroquinolone-resistant E.coli in intestinal flora patients undergoing transrectal ultrasound-guided prostate biopsy-should we reassess our patients for antibiotic prophylaxis? *Clin Microbiol Infect* 18: 575-581.