INFECTION COMPLICATIONS AFTER TRANSRECTAL ULTRASOUND-GUIDED PROSTATIC BIOPSY. ANALYSIS OF OUR EXPERIENCE

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Summary.- OBJECTIVES: To establish the rate of infectious complications derived from the use of transrectal ultrasound-guided prostate biopsy (TRUS), identify its microbiological profile and related risk factors.

METHODS: We designed a prospective non-randomized study in which we enrolled 220 patients undergoing TRUS biopsy at our centre between April and September 2008. The inclusion criteria were: suspicious digital rectal examination, PSA >10 ng/ml, and free/total ratio of PSA is assessed in patients with PSA 4-10 ng/ml. The exclusion criteria were: having an indwelling urinary catheter, the administration of antibiotic treatment in the week before the needle biopsy, manipulation of the urinary tract in the month prior to the needle biopsy, allergy to quinolones and risk of endocarditis, failure to comply with the antibiotic prophylaxis regimen and loss to follow-up.

We analyzed the relationship between diabetes, immunodepression, previous UTI or prostatitis and positive prebiopsy urine culture with the appearance of fever, dysuria or bacteriuria following needle biopsy.

RESULTS: Mean age was 69.5 years (+/-7.9), mean total PSA 12.7 ng/ml (+/-28.7), mean prostate volume 50.6 cc (+/-29.6) and mean number of cores obtained by needle biopsy 13.5 (+/-1.7). 25% of the patients had dysuria following needle biopsy, 3.2% fever and 4.5% bacteriuria. E.coli was the pathogen most frequently found in pre- and post-biopsy urine cultures.

No statistically significant relationship was found between the appearance of dysuria and fever and being diabetic, having immunosuppression, previous UTI or prostatitis, prostate volume and number of cores obtained in the biopsy.

Only the existence of a positive pre-biopsy urine culture and biopsy with more than 14 cores proved to have a statistically significant association with the existence of bacteriuria following biopsy, p=0.007 and p= 0.018, respectively.

CONCLUSIONS: Our rate of infectious complications was similar to that described in other series. The existence of a positive prebiopsy urine culture and obtaining more than 14 cores per biopsy was related, with statistical significance, to the existence of bacteriuria following the biopsy. E.coli was the most frequently isolated pathogen.
INTRODUCTION

Since the introduction of the prostate specific antigen (PSA) in the nineteen-eighties, and its use in screening campaigns, the detection of prostate cancer has increased considerably, particularly in earlier and potentially curable stages.

The transrectal ultrasound-guided prostate biopsy (TRUS) is a safe and regular procedure in the urologist’s daily practice, albeit not free of complications (1,2). A review of the literature shows that although the American Urological Association, in 2008, recommended, with a Ib level of evidence, the use of fluoroquinolones as the most suitable antibiotic prophylaxis for the prevention of TRUS-derived infectious complications, many groups continue to use their own prophylactic regimen. Similarly, we also observed divergences regarding the most suitable pre-biopsy analgesic and intestinal preparation protocols (3).

The objectives of this study are:

1. To establish our rate of TRUS-derived infectious complications.
2. To identify the risk factors associated with the development of infectious complications.
3. To identify the microbiological profile of post-prostate biopsy infections.

MATERIAL AND METHODS

We designed a prospective non-randomised study enrolling patients undergoing an ambulatory TRUS at our centre (Hospital Universitario 12 de Octubre, Madrid) between April and September 2008. In our department all patients with suspicious digital rectal examination, PSA >10 ng/ml are currently indicated for biopsy, and free/total ratio of PSA is assessed in patients with PSA 4-10 ng/ml.

The exclusion criteria were: being a urinary catheter carrier, administration of antibiotic treatment in the week before the biopsy, manipulation of the urinary tract in the month prior to the needle biopsy, allergy to quinolones and risk of endocarditis, inability to follow our regular antibiotic regimen, failure to comply with the antibiotic prophylaxis regimen and loss to follow-up.
Our usual pre-biopsy clinical procedure consists of intestinal preparation by means of conventional enema, anxiolytic medication (Bromazepam 1.5 mg) and antibiotic prophylaxis (Ciprofloxacin 500 mg) on the morning of the exploration.

Following the biopsy, two tablets of Ciprofloxacin 500 mg are given 12 and 24 hours after the first tablet.

For the study, a spontaneous sample was taken for urine culture prior to the TRUS (pre-biopsy urine culture) and a second urine sample on the seventh day post-biopsy (post-biopsy urine culture).

With the patient in the lithotomy position and with local anaesthesia (1% Mepivacain). Between 6 and 8 cores were taken from each prostate lobe and a further two from hypoechoic areas or suspicious nodes.

The urologist performing the needle biopsy collects data of interest for the study: number of previous biopsies, possible risk factors predisposing to infection (diabetes mellitus, immunodepression, history of prostatitis or urinary infection (UTI) and the existence of exclusion criteria.

A telephone survey on the seventh day after the biopsy was used to identify possible complications related to infection (dysuria and fever), and the patient was questioned on the conditions in which the post-biopsy urine culture was taken and whether the sample was taken at the same time as the infection symptoms (fever or dysuria), with the administration of antibiotic treatment, or if the patient had to go to the emergency room for this reason.

A descriptive analysis of the series was performed and contingency tables (Chi-square test) was used to assess the combination between possible risk factors and complications found, considering p<0.05 as the level of statistical significance.

RESULTS

A total of 260 patients were enrolled, 220 of whom fulfilled the inclusion criteria, and 40 were excluded.

Mean age was 69.5 years (+/-7.9), total mean PSA 12.7ng/ml (+/-28.7), mean prostate volume 50.6 cc (+/-29.6) and mean number of cores obtained by needle biopsy 13.5 (+/-1.7)(Table I).

In 76.8% patients the biopsy was performed for the first time, 17.7% had already had one and in 5% it was the third time they were undergoing the procedure (Table I).

With regard to the pathological anatomy of the biopsy, we found 57.5% without evidence of malignancy or with foci of prostatitis, 38.2% were diagnosed with acinar adenocarcinoma and 4.1% of patients had atypias or high-grade PIN (Table I).

The 17.3% of patients had some kind of risk factor for infection: 13.2% diabetics, 1.4% on immunosuppressive treatment and 3.6% with a history of prostatitis or previous UTI (Table I).

82.7% patients collected the pre-biopsy urine culture and 90.5% collected the post-biopsy urine culture. Of the former, 91.2% of the samples were sterile, 3.8% were contaminated and 4.9% were positive (2% E.coli, 0.9% E. faecalis, 0.5% Klebsiella, 1.5% others). Of the post-biopsy urine cultures, 89.9% were sterile, 8.5% were positive (4.6% E.coli, 1.9% Enterococci, 0.9% Pseudomonas, 1.1% other) and 1.4% were contaminated (Table I). Of the patients that delivered the sample on the seventh day after the procedure, 7.8% presented symptoms at the time the sample was taken.

75% of the patients did not present voiding symptoms when they were polled. Mild dysuria was present in 24.1% of patients and 0.9% presented intense dysuria that required treatment. We found 4.5% of symptom-free bacteriuria. 94.5% of the patients polled were fever-free over the first week after the procedure, although 3.2% patients had to go to the emergency room for fever. We only identified one case of hospitalisation for a serious procedure-derived infectious complication (0.5%) (Table I).

The existence of fever during the first week after the procedure was not statistically significantly associated with: diabetes (p=0.36), immunodepression (p=0.88), history of UTI or prostatitis (p=0.73), number of cores biopsied (p=0.27), prostate size (p=0.08) and previous positive urine culture (p=0.9) (Table II).

Neither was the presence of dysuria during the first week post-procedure related in a statistically significant way to the existence of a previous positive urine culture (p=0.21), the number of cores biopsied (p=0.93), prostate volume (p=0.36), diabetes (p=0.76), immunodepression (p=0.92) and history of UTI or prostatitis (p=0.64) (Table II).

A positive post-biopsy urine culture was not related to diabetes (p=0.06), immunodepression (p=0.7), UTI or previous prostatitis (p=0.53) or with...
<table>
<thead>
<tr>
<th><strong>Number of patients</strong></th>
<th>220</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>69,5 (7,9)*</td>
</tr>
<tr>
<td><strong>PSA (ng/ml)</strong></td>
<td>12,7 (28,7)*</td>
</tr>
<tr>
<td><strong>Number of cores</strong></td>
<td>13,5 (1,7)*</td>
</tr>
<tr>
<td><strong>Prostatic volume (cc)</strong></td>
<td>50,6 (29,6)*</td>
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**Number of biopsies:**
- First biopsy: 169 (76,8%)
- Second biopsy: 39 (17,7%)
- Third biopsy: 11 (5%)
- Fourth biopsy: 1 (0,5%)

**Histopathology:**
- NEM or Prostatitis: 127 (57,5%)
- Adenocarcinoma: 84 (38,2%)
- PIN o Atypias: 9 (4,1%)

**Prebiopsy urine culture:**
- Sterile: 166 (91,2%)
- Positive: 9 (4,9%)
- Contaminated: 7 (3,8%)

**Postbiopsy urine culture:**
- Sterile: 179 (89,9%)
- Positive: 17 (8,5%)
- Contaminated: 3 (1,4%)

**Microorganisms:**
- **Prebiopsy urine culture:**
  - _E. coli_: 2%
  - _E. faecalis_: 0,9%
  - _Klebsiella_: 0,5%
  - Others: 1,5%
- **Postbiopsy urine culture:**
  - _E. coli_: 4,6%
  - _Enterococcus_: 1,9%
  - _Pseudomonas_: 0,9%
  - Others: 1,1%

**Risk factors:**
- Diabetes mellitus: 29 (13,2%)
- Immunodepression: 3 (1,4%)
- Prostatitis o previous UTI: 8 (3,6%)

**Complications related with infection:**
- Disuria: 53 (24,1%)
- Fever: 7 (3,2%)
- Bacteriuria postbiopsy: 9 (4,5%)
- Hospitalisation: 1 (0,5%)

*mean (Standard desviation)  PSA = Prostate Specific Antigen  NEM = No Evidence of Malignancy  PIN = Prostatic Intraepithelial Neoplasia  UTI = Urinary Tract Infection*
prostate volume (p=0.31). However, the existence of a positive pre-biopsy urine culture and biopsy with more than 14 cores proved to have a statistically significant association with the existence of bacteriuria following the biopsy, p=0.007 and p=0.018, respectively (Table II).

DISCUSSION

Serum determination of PSA, digital rectal examination and TRUS are currently basic tools for the early detection of prostate cancer (4).

TRUS is a safe and regular procedure in the urologist’s daily practice, although it is not free of complications which, while mostly frequent and mild, may become very serious (1,2). The minor complications include: haematuria (10-74%), haemospermia (9-78%), rectal bleeding (1-40%) and dysuria. And as major complications: pain (9-30%), fever (0.6-4.2%), bacteremia (100%), bacteriuria (13-36%), symptomatic UTI (13-20%), AUR (0.4-6%) and hospitalisation (0-1.6%) (1-6).

A review of the literature shows that although the American Urological Association, in 2008, recommended, with a 1b level of evidence, the use of fluoroquinolones as the most suitable antibiotic prophylaxis for the prevention of TRUS-derived infectious complications, many groups continue to use their own prophylactic regimen. Similarly, we have also observed divergences in terms of the most suitable pre-biopsy analgesic and intestinal preparation protocols (3).

In many centres a local anaesthetic is not commonly used. In our Department we inject 10 ml of 1% mepivacaine into the vesicoprostatic angles to achieve peripheral nerve blockade, which is conducive to good tolerance of prostate biopsy (7).

There is insufficient scientific evidence on the use of enemas and disposable kits to support their role in infection prevention (3). In our centre the administration of a conventional enema and the use of disposable kits are routine practice.

There is scientific evidence that the use of antibiotic prophylaxis reduces the rates of bacteriuria, febrile genitourinary infection and post-TRUS sepsis to less than 5% (8). The choice of the antibiotic and its efficacy will depend fundamentally on its bioavailability and the sensitivity of the target microorganism.

The fluoroquinolones provide good coverage against urinary pathogens and reach high concentrations in urine and in prostate tissue. Single doses, more economical, and short oral regimens are preferred in patients without risk factors. Longer regimens (more than 4 days) might be justified in high-risk patients (diabetics, concomitant steroid consumption, immunodeficiency, pre-existing bacteriuria, history of prostatitis and prostates > 75 cc) (3). However, in our study we could not demonstrate that diabetes, immunosuppression, history of UTI or prostatitis and prostate volume are significantly related to a greater incidence of infection-related events. Only one statistically significant relationship was demonstrated between a positive pre-biopsy urine

<table>
<thead>
<tr>
<th>Complications after biopsy</th>
<th>Diabetes mellitus</th>
<th>Immuneplejion</th>
<th>UTI or previous prostatitis</th>
<th>Prostatic volume (&gt; 45cc)</th>
<th>Number of cores (&gt;14)</th>
<th>Positive prebiopsy urine culture</th>
</tr>
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<tbody>
<tr>
<td>Fever</td>
<td>p=0.36</td>
<td>p=0.88</td>
<td>p=0.73</td>
<td>p=0.08</td>
<td>p=0.27</td>
<td>p=0.9</td>
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<tr>
<td>Disuria</td>
<td>p=0.76</td>
<td>p=0.92</td>
<td>p=0.64</td>
<td>p=0.36</td>
<td>p=0.93</td>
<td>p=0.21</td>
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<tr>
<td>Positive postbiopsy urine culture</td>
<td>p=0.06</td>
<td>p=0.7</td>
<td>p=0.55</td>
<td>p=0.31</td>
<td>p=0.018</td>
<td>p=0.007</td>
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*Contingency table. UTI= Urinary Tract Infection
culture and obtaining more than 14 cores by needle biopsy with the existence of bacteriuria following the needle biopsy.

In our series, as occurs in the literature, the most frequently isolated pathogen is Escherichia coli, followed by gram-negative bacilli (Klebsiella, Pseudomonas) and enterococci (2,3).

Our rate of complications related to infectious processes is similar to that which has been described by other authors: dysuria 24.1%, asymptomatic bacteriuria 4.5%, fever 3.2% and hospitalisation for sepsis (0.5%). Therefore, and despite the fact that the percentage of resistances for quinolones in Spain is estimated at 40%, it seems that our clinical procedure and our short antibiotic prophylaxis regimen are sufficient to prevent infectious complications, although a comparative study with another antibiotic regimen would be necessary to determine superiority.

CONCLUSIONS

Our rate of infectious complications is within the ranges described in different series in the literature.

The existence of a positive pre-biopsy urine culture and obtaining more than 14 cores per biopsy was related, with statistical significance, to the existence of bacteriuria following the biopsy.

The microbiological profile of our series shows that infection by E. coli is the most frequent.

REFERENCES AND RECOMMENDED READINGS (*of special interest, **of outstanding interest)