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Morbidity and risk factors of transrectal prostate biopsy

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ABSTRACT

Objectives: To evaluate the incidence of minor complications that rarely need treatment (haematuria, hematospermia and rectal bleeding) and major complications (fever and shock) in patients undergoing transrectal biopsy of the prostate and to identify risk factors.

Material and methods: We present an analitic and prospective study where we evaluated 146 patients subjected to transrectal biopsy of the prostate from December 2007 to September 2008. Signs and symptoms experienced by the patients as well as the variables age, prostate volume, outcome, and whether it was a first biopsy or a subsequent one are analyzed.

Results: Eight patients (5.5%) suffered fever and seven (4.8%) of them were admitted. One of the patients (0.7%) suffered shock. The median of time between biopsy and fever was 3.5 days (1–10 days). Haematuria and hematospermia were more frequent in patients younger than 65 years ($p<0.05$) and fever and sepsis were more frequent in patients with prostate volume smaller than 55mL ($p<0.05$).

Conclusions: The complications of the transrectal biopsy of the prostate are frequent, autolimited and they rarely suppose a health hazard for the patients. The most frequent are haematuria and hematospermia, specially in younger patients, whereas infectious complications are rarer and in our study are more frequent in patients with smaller prostates.

We must take into account that the information to the patient is very important after a prostate biopsy, so we can avoid useless consultations (for example with haematuria) and it will enable the identification of important signs like fever earlier.

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Morbilidad y factores de riesgo de la biopsia transrectal prostática

R E S U M E N

Palabras clave:

Biopsia
Próstata
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Profilaxis
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Objetivos: Analizar la incidencia de complicaciones menores que no requirieron tratamiento médico (hematuria, hematospermia y rectorragia) y mayores (fiebre y sepsis) en los pacientes sometidos a biopsia transrectal prostática (BTRP) e identificar posibles factores de riesgo.

Material y métodos: Presentamos un estudio analítico, consecutivo, descriptivo, de una cohorte de 146 pacientes sometidos a BTRP desde diciembre de 2007-septiembre de 2008. Se analizaron los signos y síntomas que sufrieron y las variables edad, volumen prostático, resultado y el hecho de ser la primera biopsia o una sucesiva.

Resultados: En ese periodo 8 (5,5%) de los pacientes sufrieron fiebre, 7 (4,8%) de los cuales requirieron ingreso, con una mediana de estancia hospitalaria de 3 días. Un paciente (0,7%) presentó shock séptico. La mediana del tiempo de latencia, entre la BTRP y la aparición de fiebre, fue de 3,5 días (rango de 1-10 días). La hematuria y la hematospermia fueron más frecuentes en menores de 65 años ($p < 0,05$) y la fiebre en los pacientes con volúmenes prostáticos menores de 55 mL ($p < 0,05$).

Conclusiones: Las complicaciones de la biopsia transrectal prostática son frecuentes, auto-limitadas y muy raramente ponen en peligro la vida del paciente. Las más frecuentes son la hematuria y la hematospermia, dándose en pacientes de menor edad, mientras que las complicaciones infecciosas son más raras y en nuestra muestra son más frecuentes en pacientes con volúmenes prostáticos menores.

Consideramos de gran importancia informar al paciente de las complicaciones que pueden aparecer tras la BTRP, evitando así consultas innecesarias en los servicios de urgencias por los síntomas menores y permitiendo controlar precozmente el desarrollo de infecciones graves.

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Introduction

Transrectal prostate biopsy (TRPB) and the measurement of prostate-specific antigen (PSA) are unquestionably the two major tools used by urologists for the early diagnosis of prostate cancer; they permit treatment with curative intent. However, TRPB is an invasive test not exempt from severe (albeit infrequent) side effects^{1,2}; therefore, the procedure should be performed according to established urological guidelines.

The objectives of our study were to analyze the incidence of minor complications that do not usually require medical treatment (hematuria, hematospermia, and rectal bleeding) and major complications (fever and sepsis) among patients undergoing TRPB at our hospital, and to analyze the variables that may affect the development of those signs and symptoms.

Material and methods

Between December 2007 and September 2008, 181 TRPBs were performed at our hospital. A telephone survey was used to ask about signs and symptoms experienced by patients over

the 6 months following the biopsy. Of the 181 patients, 146 were considered valid; the rest were excluded due to inability to make telephone contact (29 patients) or inadequate data collection (6 patients). A prospective analysis of the post-TRPB complications was conducted. Fever (temperature above 37.8°C) was considered a major complication, and gross hematuria, rectal bleeding (any amount of blood in urine or stool), and hematospermia (darker semen or blood in the ejaculate) were considered minor complications (not requiring medical treatment). The duration (in days) of these signs was recorded. In all patients, the indication for the biopsy was a PSA above 4 ng/mL. The median age of the sample was 66 years (range: 44-81). The median PSA of the sample was 7.8 ng/dL (range: 4.02-51.20). Patients agreed to the procedure and the potential side effects of the TRPB by signing an informed consent form approved by the hospital's ethics committee. The antibiotic therapy employed in all patients was that recommended by our service's protocol, which consists of ciprofloxacin 500 mg PO 12 hours before the procedure and every 12 hours for 10 days thereafter. Bowel preparation with two cleansing enemas was indicated: on the night before and one hour before the biopsy. Patients on anticoagulant treatment with acenocoumarol were instructed to discontinue the medication at least 5 days before the TRPB;

the medication was replaced with enoxaparin administered up to 12 h prior to the procedure.

TRPBs are ultrasound-guided and performed with an ATL C9-5 probe covered with two echo-sleeves and an attached endocavity needle guide (Civco Medical Instruments®). A digital rectal exam was done before introducing the ultrasound device. Per protocol, approximately 5 mL of local anesthetic (2% mepivacaine) were injected in each notch between the prostate and the seminal vesicles, which are easily identified as hyperechoic areas known as the "Mount Everest sign". Then, during the latency period of the local anesthetic, the prostate volume was measured. The median prostate volume of patients in our sample was 55 mL (range: 12-135 mL). An automatic instrument (Pro-MagTM Ultra®) was used to obtain a median of 10 cylinders/patient (range: 4-13). The number depended on the attending urologist's judgment. The needle employed was a single-use Pro-MagTM® that obtains 18G specimens measuring 20 mm in length. After completing the procedure, the patients were given an information sheet explaining that gross hematuria, hematospermia, and rectal bleeding may be normal, as is an increase in body temperature up to 38°C; patients were advised to visit the hospital if they had a higher fever.

A statistical analysis was done to assess the association between the above mentioned complications (fever, hematuria, rectal bleeding, and hematospermia) and the variables age, prostate volume, biopsy result (positive or negative for prostate cancer), and whether this was the first or subsequent biopsy. The Chi squared test was used for qualitative variables, and $p < 0.05$ was the level of statistical significance. The SPSS 15.0 package was used to perform the statistical analysis.

Results

The incidence of major complications (fever-sepsis) was 5.5%, and the overall incidence of minor complications was 65% (table 1).

Of the 146 patients, eight (5.5%) presented with fever, seven of whom (4.8%) were hospitalized for a median of three days (range: 1-9 days). The anamnesis, physical examination, chest X-ray, and basic urine test revealed that the cause of the fever lay in the genitourinary tract. One patient presented with septic shock of urinary origin that required admission in the ICU and the administration of vasoactive drugs and mechanical ventilation; his progress was good, and he was released on the 9th day. All patients received, as first line, a third generation cephalosporin (ceftriaxone) monotherapy, except for the patient with septic shock, who also received an aminoglycoside (amikacin). The following are the results of the urine cultures done on these patients: 2 (25%) were contaminated, 2 (25%) were negative, and 4 (50%) were positive for E. Coli. The antibiogram of the four positive cultures was similar, showing resistance to ampicillin, cotrimoxazole, and ciprofloxacin; there was evidence of sensitivity to amoxicillin clavulanic acid, and to second and third generation cephalosporins.

Table 1 – Association between complications and the variables analyzed

Incidence (%)	n (%)	Age (years)		Prostate volume (cc)			Result		First or subsequent biopsy				
		>66	<66	p	<55	>55	p	Positive	Negative	p	1st	Subsequent	p
Fever	8 (5.5%)	3 (2.2%)	5 (3.6%)	0.187	8 (6.1%)	0	0.022	1 (0.7%)	7 (4.8%)	0.156	8 (5.5%)	0	0.233
Hematuria	57 (49%)	25 (18%)	31 (22.3%)	0.003	34 (26%)	17 (13.0%)	0.363	20 (13.8%)	37 (25.5%)	0.876	47 (32.2%)	10 (6.8%)	0.384
Rectal bleeding	26 (18.8%)	11 (7.9%)	13 (9.4%)	0.127	16 (12.2%)	8 (6.1%)	0.590	9 (6.2%)	17 (11.7%)	0.884	23 (15.8%)	3 (2.1%)	0.648
Hematospermia	33 (21.9%)	11 (8%)	21 (15.2%)	0.001	20 (15.4%)	12 (9.2%)	0.979	8 (5.5%)	24 (16.6%)	0.147	20 (13.8%)	12 (8.3%)	0.000
Statistical analysis per Chi-squared test.													
Statistical significance: p<0.05.													

Statistical analysis per Chi-squared test.
Statistical significance: $p < 0.05$.

The median time between the TRPB and the development of fever was 3.5 days (range: 1-10); the 10-day antibiotic prophylaxis regimen was completed in two (25%) of the eight patients.

Regarding minor complications, 57 patients (49%) had gross hematuria with a median duration of 3 days (range: 1-32); 26 patients (18.8%) had rectal bleeding for a median 3 days (range: 1-28); and 33 patients (21.9%) had hematospermia with a median 6.41 bloody ejaculations (range: 1-25 ejaculations). No patient required medical care for the minor complications.

The results of the statistical analysis of the variables are shown in table 1, and described below:

Age

The sample was divided in two groups according to the median age: one group under the age of 66 years, and one group over that age. The incidence of the four symptoms studied was compared, and statistically significant differences were found only for hematuria and hematospermia (a higher incidence in the group under 66 years old).

Prostate volume

The sample was divided in two groups according to prostate volume larger or smaller than the median (55 mL). When the incidence of the four symptoms was compared between the two groups, statistically significant results were found only for fever, with a higher incidence in patients with a prostate smaller than 55 mL; in fact, all the cases of fever occurred in patients with a prostate volume under 55 cc.

Result of the prostate biopsy

Patients with a positive biopsy for prostate cancer were compared with those with a negative result. No statistically significant differences between the two groups were found when the symptoms (fever, hematuria, rectal bleeding, and hematospermia) were compared.

First vs. subsequent biopsy

The sample was divided in two groups according to whether the biopsy was the first or subsequent; the symptoms were compared. A statistically significant difference was found only for hematospermia, with a higher incidence among those for whom the biopsy was their first.

Discussion

The complications of transrectal prostate biopsy can be classified as minor (usually not requiring treatment) such as hematuria, hematospermia, rectal bleeding, dysuria, and pain, and major (life-threatening) complications such as fever or sepsis. The latter may require hospitalization³. A literature review reveals that there is a wide range of incidences of these complications: gross hematuria (84-13%); hematospermia

(84-9%); rectal bleeding (100-2.8%); symptomatic infection (0.75-11%)¹⁻¹³. The incidence of hematospermia may be underestimated if the issue of whether or not patients ejaculate in the study period after the biopsy is not considered. Raaijmakers et al and Kakehi et al considered that detail, and reported that hematospermia is the most common symptom after rectal prostate biopsy in patients who ejaculate during the months following the procedure^{1,2}. Gross hematuria is the hemorrhage most commonly assessed, and is considered by numerous authors to be the most common sign^{5,6,11}. The latency time between the biopsy and the development of fever in our study was similar to that reported by other authors¹⁴.

The efficacy of antibiotic prophylaxis in TRPB deserves little discussion nowadays. The studies conducted by Puig et al and Bonatti et al show statistically significant differences between the rate of infectious complications after TRPB with and without antibiotic prophylaxis^{9,10}. There is a moderate to high level evidence that the use of antibiotics reduces post-biopsy bacteriuria, but not so much evidence about a decrease in the rate of symptomatic infection¹⁵. The first-choice antibiotics continue to be fluorquinolones and TMP-SMX¹⁶; however, the latter is not recommended in our country due to its high resistance rate.

Current debates about antibiotic prophylaxis focus on duration. Several studies compared short prophylaxis regimens (24 h) to longer ones (3-10 days), and did not find statistically significant differences in the development of infectious complications^{3,4,17}. Along these lines, one of the pioneering studies was that conducted by Aus et al in 1996, which encouraged the use of longer treatment regimens; it compared 1-day regimens with 1-week regimens of antibiotic prophylaxis, and better outcomes were obtained with one-week prophylaxis; this improvement, however, is acknowledged to appear predominantly in patients with risk factors: carriers of a bladder catheter, prior urinary infections, and diabetes^{12,16,18}. We used a long prophylaxis regimen (10 days) and obtained similar rates of infectious complications as other reviews, if not higher (5.5% with fever). We believe that this difference may be attributed to our routine use of local anesthesia for prostate biopsies; however, Luján Marco et al did not report higher complication rates with local blockage compared to intravenous analgesia¹⁹. In most studies reviewed, the anesthesia used is not discussed, so we assume that it was not used.

The rate of quinolone-resistant *E. Coli* increases every year, and in many hospitals in Spain it exceeds 30%. Studies similar to this one have found that 75% of patients who presented with sepsis after a TRPB had a history of receiving quinolones⁸. Taking this into consideration, plus the fact that the antibiogram of patients with fever after a TRPB is quite similar even between studies in different countries^{1,7}, prophylaxis recommendations could be modified in the future to also consider second and third generation cephalosporins and the amoxicillin-clavulanic acid combination as first choice, since they are more sensitive antibiotics and have acceptable concentration levels in the prostate parenchyma. Thus, the anamnesis acquires more relevance when a biopsy

with prophylaxis is indicated, to avoid a recently used antibiotic family.

Other authors consider a larger prostate a risk factor for infection¹⁸⁻²⁰, but we found that all patients who experienced fever had a prostate smaller than 55 mL (median); this may be related to the fact that 10-12 specimens were obtained from all patients, regardless of volume. This might lead us to consider a relationship of "aggression-volume" that may increase the risk of bacteria entering the bloodstream and causing a systemic reaction. Whether the biopsy was the first or a subsequent one did not show differences in the incidence of fever, even though other authors consider that a prior TRPB in the same patient is a risk factor¹³.

There is currently no consensus regarding the use of pre-TRPB cleansing enemas²¹; some authors have shown that this procedure reduces the rate of bacteriuria and bacteremia after the manipulation²², but others judge that it does not significantly reduce potentially severe complications, and instead increase patient cost and discomfort²³.

Conclusion

This study shows that minor bleeding complications are common and self-limited, and that it is essential to educate patients about their development in subsequent weeks in order to avoid adding concerns about those symptoms to the uncertainty of awaiting the result of the biopsy. This information also teaches patients to visit the emergency service when they have fever, which prevents the arrival of patients with more severe conditions or in septic shock. We have acceptable rates of symptomatic infection after the use of antibiotic prophylaxis with ciprofloxacin (94.5% of patients do not present with fever) and the only remaining question is whether to shorten the duration in order to help slow down the rate of resistance to quinolones.

Conflict of interest

The authors state that they have no conflicts of interest.

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