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Efficacy and safety of a combined anesthetic technique for transrectal prostate biopsy: a single center, prospective, randomized study

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Introduction A transrectal ultrasound-guided (TRUS) biopsy is the gold standard for diagnosis of prostatic neoplasia. This exam is associated with pain and discomfort, and numerous methods of analgesia during this procedure have been described. There is still no consensus among urologists about the pain control technique that should be performed, even though the periprostatic basal nerve block is the most studied technique. The main objective of this study is to evaluate the benefit of adding local periapical prostatic anesthesia to the traditional periprostatic basal nerve block during TRUS biopsy.

Material and methods A total of 70 patients with indication for TRUS biopsy were enrolled in this study. Patients were randomized into 2 groups. Group 1 received a periprostatic basal nerve block. Group 2 received both periapical prostatic and periprostatic basal nerve blocks . The pain experienced during different moments of the procedure (introduction of the probe, anesthesia administration, removal of cores and 30 minutes after biopsy) was assessed using visual analog scales of one to ten. The rate of complications at 30 days post-biopsy was also assessed.

Results The difference in pain during the distinct moments of the TRUS biopsy was not significant between the two groups. There were no significant differences concerning age, level of total prostate-specific antigen (PSA) and prostate volume in both groups. There were also no statistically significant differences between the groups regarding the occurrence of complications and pathological findings.

Conclusions The administration of concurent periprostatic basal and periapical nerve blocks has no significant benefits as compared to a periprostatic basal nerve block alone.

Key Words: analgesia ‹› anesthesia ‹› rectal ‹› nerve block anesthesia ‹› prostate biopsy

INTRODUCTION

A transrectal ultrasound-guided (TRUS) prostate biopsy is the gold standard procedure for prostate cancer diagnosis since it allows for the pathological analysis of this organ's tissue with minimal invasiveness and consequences. However, it is a somewhat painful and uncomfortable procedure for most patients and, consequently, efforts must be made to minimize the pain and discomfort [1–6]. This is particularly important in patients that require a repeat biopsy and may deny it because of the experience they had during the first procedure.

Many analgesic and anesthetic methods have been used and described in the literature, namely the periprostatic basal nerve block, the intra-rectal administration of analgesic gel, sedation with anesthetic agents, administration of non-steroidal anti-inflammatory drugs and the intraprostatic anesthetic administration [2, 3, 7]. From all these methods,

the periprostatic basal nerve block has been the most extensively studied and is the most widespread [8–12]. Many authors have conducted various studies to understand which is the best location to administer anesthetic drugs. The periprostatic basal nerve block was described for the first time by Nash et al., as an administration of an anesthetic drug between the prostate and seminal vesicles. Another technique, the periapical nerve block, targets the sensitive somatic nerves at the apex of the prostate. Some studies have compared these two techniques, however with conflicting results. Currently, it is still unknown which is the best place to administer the anesthetic drug during TRUS prostate biopsy, although the periprostatic basal nerve block is the most studied technique.

Therefore, the objectives of this study are to compare the periprostatic basal nerve block alone with the periapical nerve block plus periprostatic basal nerve block in terms of anesthetic efficacy and safety.

MATERIAL AND METHODS

A prospective study was designed and performed after obtaining the Research Ethics Board approval. From July to December 2017, we included patients who had an indication for TRUS biopsy according to the EAU guidelines and who accepted being included in this study after having been informed about its nature and objectives. We excluded patients with chronic pain syndromes, inflammatory bowel disease, proctological disease, patients taking analgesic medication, patients allergic to lidocaine, patients submitted to saturation biopsies and patients taking antiplatelet or anticoagulant medications.

One week before the biopsy, every patient was handed an informative brochure, explaining the procedure, the preparation needed and the most frequent complications. On the day of the biopsy, the patients signed an informed consent form and were asked for their approval to be included in the study. All patients were administered a rectal enema on the day before the biopsy and all patients received antibiotic prophylaxis with ciprofloxacin.

The ultrasound machine used was the ALOKA® Prosound SSD-3500SV with a 13.5 MHz transrectal probe. A 22G 20 cm Chiba needle was used for lidocaine injection and a 18G co-axial biopsy needle was used for cores collection.

All biopsies were performed by the same urologist. The patient was positioned in the lateral decubitus position with knee and hip flexion and, 5 minutes before probe introduction, a 2% lidocaine and chlorhexidine gel was introduced in the patient's rectum.

The patients were systematically and randomly assigned to one of two groups. Group 1 was administered 10 ml of 1% lidocaine divided in two injections in each of the angles between the prostate and the seminal vesicles (periprostatic basal injection). Group 2 was administered 10 ml of 1% lidocaine divided in four injections: two 3 ml injections in each of the angles between the prostate and the seminal vesicles and two 2 ml injections lateral to the prostatic apex (periprostatic basal and periapical injections). Five minutes after the lidocaine injections, 12 systematic random cores were taken.

After the biopsy, a Pain Visual Analog Scale (Pain VAS) from 0 to 10 was used. The patient had to give a pain score for each of the biopsy steps: probe introduction, anaesthetic injection, core taking and pain 30 minutes after biopsy.

Other variables collected were: age, prostate size (calculated during TRUS), complications in the first 30 days and biopsy result.

Data processing and statistical analysis was performed using Microsoft Excel 2010, IBM SPSS IBM SPSS® version 24. To test for normality of distribution of variables, Kolmogorov-Smirnov test and histogram visual analysis were used. To compare categorical to parametric continuous variables we used the t-student test. To compare categorical to non-parametric continuous variables, the Mann-Whitney U was used. The Chi-square test ($\chi 2$) was used to compare two categorical variables. Tests were considered statistically significant for p value <0.05.

RESULTS

After applying the exclusion criteria to all of the patients submitted to a TRUS prostate biopsy between July and December 2017, 70 patients were included in this study. The mean age was 67.8 ±7.91 years, the mean mean prostate-specific antigen (PSA) was 8.94 ±6.26 ng/mL and the mean prostate volume was 53 ±23 mL.

There was no statistically significant difference between the two groups, concerning age, total PSA and prostate volume (Table 1).

There were no statistically significant differences between the two groups concerning the pain felt during the four recorded moments. Although the periapical anesthesia led to a lower mean pain intensity during anesthesia injection and core retrieval, this difference did not reach statistical significance ($p = 0.443$ and $p = 0.618$ respectively) (Table 2).

The most painful step was the introduction of the ultrasound probe, which can't be prevented by the injection of lidocaine and, as such, did not differ between groups. The least painful stage was 30 minutes after the biopsy and there were also no differences between both groups.

Table 1. *Patient characteristics*

	Group 1	Group 2	p
Age	67.46 ±7.24	68.14 ±8.62	0.678
Total PSA	7.51 ±4.85	10.37 ±7.20	0.126
Prostatic volume (ml)	48.45 ±14.21	57.83 ±28.79	0.098

PSA – prostate-specific antigen

Table 2. *Analysis of pain scores between groups*

	Group 1	Group 2	p
Probe Introduction	4.08 ±2.26	3.51 ±1.96	0.269
Anesthesia injection	1.92 ±1.51	1.63 ±1.51	0.185
Core retrieval	2.16 ±1.90	1.95 ±1.46	0.124
30 minutes after	0.67 ±0.79	0.81 ±0.95	0.160

Table 3. *Analysis of complication rates between groups*

		Group 1	Group 2	p
Complications	Yes	7 (20%)	5 (14.3%)	0.076
	No	28 (80%)	30 (85.7%)	

Using a Pearson correlation we found that pain scores in the four stages for a single individual were found to be related to one another. This means that patients who feel more pain in the introduction of the probe will feel more pain during the rest of the biopsy.
When analyzing the effect of age, prostate volume and findings of malignant disease in pain scores, we verified some interesting results. Age was positively related to pain during the introduction of the probe ($p = .02$) and that prostate volume was positively associated with pain felt 30 minutes after the biopsy.
There were no differences between groups regarding complications after biopsy ($p = 0.752$). (Table 3). Finally, there were no differences between both groups concerning the findings of malignant disease in the biopsy cores ($p = 0.811$).

DISCUSSION

There are essentially two factors responsible for the pain felt by patients during prostate biopsy: the introduction of the ultrasound probe into the patient's rectum and the perforation of the prostate capsule, which is densely innervated [2, 8, 9, 11]. Since the needle perforates the rectum above the pectinate line of the anus, there is not significant pain caused by the mucosal perforation, since it is innervated by visceral and not somatic nerves [3, 9]. The pain caused by the introduction of the probe can be minimized by the introduction of a lidocaine gel, as the one used in this study. However, only the pain caused by the core retrieval is hypothetically reduced by the periprostatic basal and periapical lidocaine injections, the techniques tested in this study.
The prostatic innervation originates from the sympathetic fibers from T10 to L2 and parasympathetic fibers from S2 to S4. These fibers merge to form the pelvic plexus from which the periprostatic plexus originates. The periprostatic plexus originates near the seminal vesicles' tip and runs between the prostate and the rectum, in the prostate's postero-lateral portion [11].
Schostak et al. [13] evaluated the differences between a periprostatic basal block, periapical block and the combination of both, concluding that the periapical nerve block was more effective. These findings were reinforced by Kuppusamy et al. [14].
However, other authors did not reach the same conclusion. Cevik et al. [15] concluded that there was no statistically significant difference between the pain perceived by patients who received the periprostatic basal nerve block and patients who received a combination of a periprostatic basal and a periapical nerve block. More studies were done to compare exclusively the periapical and periprostatic basal nerve blocks also reaching contradictory results [16, 17, 18].
In our study, we firstly verified that the addition of a periapical nerve block to the standard periprostatic basal injection did not cause more pain. This conclusion is contradictory to two studies existent in the literature that imply that the periapical injection is more painful [13, 19], although there is a study by Nguyen et al. that is in accordance with our results regarding this step [17].
The main objective of this study was to assess if the addition of periapical anesthesia was more effective in reducing the pain felt by patients during the core retrieval and after the prostatic biopsy. We based our hypothesis on the knowledge that prostate innervation is made up of two different nerve bundles, one that runs lateral to the postero-superior face of the prostate and one that perforates the apex of the gland [12]. Although the mean of the pain scores was lower on the group that received injections in both sites, it did not reach statistical significance and, as such, we can conclude that the addition of periapical lidocaine is not superior to a sole periprostatic basal injection. This conclusion had been already demonstrated in the papers by Cevik et al. and Schostak et al. [13, 15]. We think that a possible explanation for this is the fact that lidocaine injected basally infiltrates along the Denonvilliers fascia [18, 19] and, consequentially, there is no advantage in injecting lidocaine in other places. However, studies that compared isolated periapical

anesthesia with isolated periprostatic basal anesthesia, concluded that the periapical injection was superior [13, 14, 17, 18, 19].

We also concluded that the pain scores that an individual felt during the different steps of the biopsy were related to one another and that the pain felt during the introduction of the probe predicted the pain felt in the following steps.

When analyzing other factors, other authors suggested that age and prostatic volume could influence pain [2, 3, 15, 16, 19]. Our results suggest that age is related to the pain felt during probe introduction. This can be explained by a more fragile physical health and mental status as well as discomfort caused by the positioning in elderly patients. We also verified that larger prostate volumes were related to higher pain scores 30 minutes after the biopsy. A possible explanation for this fact is that the lidocaine does not infiltrate as effectively along the bigger capsule areas of larger prostates.

Finally, we analyzed if there were any differences in the complications' rates between both groups. Although the addition of two injections in group 2 could hypothetically increase the complications' rates, namely infectious complications, we did not verify that. Our results suggest that the addition of a periapical injection does not influence complications. As predicted, the anesthetic strategy did not influence malignant disease prediction.

There are some limitations in this study. Although it is a prospective study, pain is a subjective symptom and, as such, difficult to assess in a uniform way. However, the VAS is the most widely used tool for pain assessment and a more precise way to evaluate pain does not yet exist. The small size of the sample could have led to insufficient statistical power in some of the tests used. A sham injection of saline should have been administered to patients in Group 1, so that the patients could not guess which anesthesia they were receiving by the number of injections. Also, the doctor knew which kind of technique he was using, which could have influenced the way he performed the rest of the biopsy procedure. A double-blind study with sham injections would be ideal to eliminate these biases. Finally, a third group, subject to only periapical anesthesia should have been created, in order to fully understand which of the two nerve blocks is more effective.

For the future, we suggest a double-blind, sham-controlled study with a wider number of patients and with a third 'periapical only' group. Doing so might eliminate most biases and reach stronger and more meaningful conclusions.

CONCLUSIONS

This study appears to demonstrate that the addition of a periapical nerve block to a periprostatic basal nerve block does not result in significantly better pain control. However, further studies with more patients may clarify this, since the mean pain in some biopsy steps was lower in the group which received the additional periapical block. The rates of complications were similar between the two anesthetic strategies, which makes us conclude that the periapical block is safe and does not lead to increased complication rates.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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