

Lidocaine suppository for transrectal ultrasound-guided biopsy of the prostate: a prospective, double-blind, randomized study

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Objective: To investigate analgesia using lidocaine suppository for prostate biopsy.

Material and methods: From 2007 to 2009, 160 patients underwent the trans-rectal ultrasound guided prostate biopsy at the Department of Urology, KBC Zagreb. Eighty patients received 60 mg lidocaine suppository intra-rectally at different time points from 15 to 120 minutes before biopsy and 80 patients received glycerine suppository as placebo. We also collected data about patient age, prostate specific antigen levels, prostate volume and pathohistological findings after the biopsy. The pain level was evaluated using a visual analogue scale (VAS).

Results: There were no statistically significant differences between the groups i.e. they were similar regarding the patients' age, prostate specific antigen levels, prostate volume and the incidence of diagnosis of malignancy on biopsy. The mean pain score in the lidocaine group (3 ± 1) was significantly lower than the mean pain score in the glycerine group (4.1 ± 1.3) [$p < 0.001$]. A noticeable trend towards lower pain scores in the lidocaine group was observed with more time elapsed from placing the suppository till the biopsy and the optimal time for performing the biopsy starts approximately one hour after placing the suppository.

Conclusion: Lidocaine suppository is an easy to use, self applicable (by the patient) and cheap method of local analgesia, with acceptable results. Possible complications related to this procedure are insignificant.

Key words: lidocaine suppository, prostate biopsy, analgesia, VAS score

Introduction

Prostate biopsy is a standard method for establishing the diagnosis of prostate cancer and therefore one of the most commonly performed urological procedures. Although in the past this was considered to be a relatively well tolerated procedure and thus no analgesia was applied in the great majority of cases, patient-reported data have shown that 65%-90% of patients suffered discomfort during prostate biopsy and 30% of them had significant pain.^(1,2) It has also been shown that almost 19% of patients would refuse a repeated biopsy without some form of analgesia.⁽³⁾ Different methods of analgesia for prostate biopsy have been investigated and among them periprostatic nerve block (PPNB) is considered as a gold standard. Recent meta-analyses have confirmed that PPNB is effective and safe in reducing pain caused by trans-rectal biopsy⁽⁴⁾ but many urologists still did not perform it, probably because they are not comfortable with this procedure.

In this study our objective was to investigate the analgesia effect of lidocaine suppository compared to glycerine suppository as placebo and optimal time of lidocaine application prior to biopsy.

Material and methods

From October 2007 to January 2009, 160 patients with abnormal digital rectal exam (DRE) or elevated prostate-specific antigen (PSA) values, or both, underwent transrectal ultrasound (TRUS) - guided biopsy at Department of Urology, KBC Zagreb, Croatia. The study was approved by the Institutional Review Board and each patient signed the informed consent. Exclusion criteria were: allergy to local anaesthetic, rectoanal pathology, chronic prostatitis, chronic pelvic pain, urge urinary symptoms, hemorrhagic diathesis, anticoagulation therapy, renal and hepatic insufficiency. We also excluded patients with a history of daily analgesic use which could influence their pain perception. This was a double blind study and patients were randomized in two groups. Group L (80 patients) received 60 mg lidocaine suppository (Lido-posterine suppositories, Dr. Kade Pharm, Berlin, Germany) intra-rectally at different time points from 15 to 120 minutes before biopsy, while group G

(80 patients) received glycerine suppository in the same way. All patients received intra-rectal lubricant jelly before DRE and probe insertion. Prophylaxis was carried out by the oral administration of 500 mg of ciprofloxacin a few hours before the biopsy and followed twice a day for five days in total. A cleaning enema was self-administered on the morning of the biopsy. The biopsy was taken with the patient in the prone (jack-knife) position by urologists experienced in undertaking of this procedure. The biopsy was taken under TRUS guidance using a 7.5 MHz trans-rectal probe (Sonoline X, Siemens, Berlin, Germany). Before the procedure, the prostate gland volume was determined and in all cases 12 core biopsy samples were taken, using automatic spring-loaded biopsy gun (Magnum, Bard, New Jersey, USA) with 18 gauge, 25 cm needle. A self-administrated 10-point visual analogue scale (VAS) was used to measure the pain scores before and immediately after the biopsy.

Before the procedure, all patients were instructed by the physician to score their level of pain from 0 (no pain) to 10 (most severe pain ever experienced) on the VAS. Patients with a baseline VAS score greater than 0 were excluded from the study. After the biopsy, the patients were informed about possible complications, such as fever, urinary retention, rectal bleeding, gross haematuria or hypotension. All patients were observed for an hour after the procedure to rule out possible early complications and then discharged when ready and stable.

Statistical analysis: the Kolmogorov-Smirnov test was used to describe data distribution. According to the distribution, appropriate nonparametric tests were used in the following analysis. Differences in quantitative variables between the lidocaine and the glycerol group were analyzed with the Mann-Whitney U test. Qualitative and categorical data were analyzed with the X² test. The ROC curve analysis was performed to assess the optimal time for inserting the lidocaine suppository. All P values <0.05 are considered significant. StatSoft, Inc. (2008) STATISTICA (data analysis software system), version 8.0. (www.statsoft.com) was used for all statistical procedures except the ROC curve analysis (MedCalc for Windows, v 11.01, www.medcalc.be).

Results

Of the 160 men, 80 were randomly selected to receive the lidocaine suppository intrarectally (group L) and 80 were randomly selected to receive placebo (glycerine suppository (group G). Table 1 shows the baseline characteristics of these two groups. There were no statistically significant differences between groups, i.e. they were similar regarding the patients' age, PSA level, prostate volume and the incidence of diagnosis of malignancy on biopsy. The median (interquartile range) pain score in the L group: 3.0 (2.2 - 3.8) was significantly lower than the median pain score in the G group: 4.0 (3.2 - 4.8), $p < 0.001$ (Fig.1). Both groups were divided into three different subgroups according to the time elapsed from suppository insertion till the biopsy. The first subgroup's time category was 15-45 minutes, the second 45-90 minutes, and the third >90 minutes. A noticeable trend towards lower pain scores in the L group was observed with more time elapsed from suppository insertion till the biopsy (Fig. 2). This was not found in the G group (Fig. 3).

Analyzing the data we found that the optimal time for performing the biopsy starts approximately one hour after the placement of suppository. There were no significant differences between the groups in minor complications, like mild rectal bleeding, mild haematuria and haemospermia. Five patients in the glycerine group and 3 patients in the lidocaine group had septic complications which resolved after treatment with IV antibiotics. No local or general adverse effects which could be related to the application of the anaesthetic have been observed.

Discussion

Lidocaine is widely used for different forms of local analgesia. For prostate biopsies the most commonly used form is gel, alone or in combination with other methods of analgesia. Trans-rectal application of lidocaine suppository for pain caused by anorectal pathology is common. Rectal mucosa has a high vascularisation with large absorption capacity and therefore rectal route can be suitable for delivering different drugs, including analgesic and local anaesthetics

Lidocaine suppositories are rarely used for prostate biopsies. In fact, to the best of our knowledge only three studies using lidocaine suppositories for trans-rectal ultrasound guided biopsy have been published up till now and all of them are confirming the analgesic effect of lidocaine suppositories in prostate biopsy alone or in combination with PPNB which is considered as a gold standard.^(5,6,7) In this study we have investigated the use of lidocaine suppository for prostate biopsy compared to glycerine suppository as placebo. Although previous studies used fixed time points (1h vs. 2h)^(5,6,7) we were using different time points for the biopsy after administering lidocaine suppositories (from 15 min. to 2 hours) in order to see if we can get better results using wider time frame. We have shown that the optimal time for performing a prostate biopsy starts approximately one hour after placing the lidocaine suppository, with better results being achieved the longer the suppository is in place prior to the biopsy. Similar findings have been shown in other studies, where better results have been achieved when biopsy was performed 2 hour after placing the suppository comparing to 1 hour.^(5,6)

Diclofenac can be used for prostate biopsy in the form of suppository as well. The advantage of diclofenac use is attributed to its locally and systematically antiinflammatory effect which can also reduce post-procedural pain.^(8,9) It is also important to mention that there is a higher risk of thrombocyte dysfunction and related prolonged time of bleeding (rectal bleeding and haematuria) with the use of non-steroid antiinflammatory drugs (NSAID).^(8,9) On the other hand, according to a number of papers cited in a recent review by Cassuti et al. local anaesthetics also possess a wide range of anti-inflammatory actions which can be superior to traditional anti-inflammatory agents of the NSAID and steroid groups with fewer side-effects.⁽¹⁰⁾ It has also been shown that local anaesthetics have antimicrobial activity as well.⁽¹¹⁾ Some of them like lidocaine and bupivacaine exhibited higher degrees of antimicrobial activity which can be an important advantage for procedures such as prostate biopsy. According to the majority of papers and recently published meta-analyses the best analgesia for prostate biopsy can be achieved by using the periprostatic nerve block (PPNB).⁽⁴⁾ Although many centres have accepted this form of analgesia, there is still a significant number of urologist who are not using this procedure in their daily praxis.⁽¹²⁾ Reasons for this vary, but it is likely that some of them are not familiar with the procedure itself, while others cite discomfort of patients

due to puncture with the needle. Also, although one study has shown a significantly higher rate of bacteriuria in the PPNB patients, ⁽¹³⁾ the recent paper published by Turgut et al. which included 200 patients, showed that PPNB is not associated with increased risk of local and systemic infection.⁽¹⁴⁾ In some patients PPNB does not completely eliminate pain, especially related to insertion of ultrasound probe in the rectum. In fact, it may cause a stinging sensation and can be even more painful than the prostate biopsy itself.⁽¹⁵⁾

Research has shown that a combination of topical anesthesia before inserting the transrectal probe and PPNB achieved better analgesia during the entire procedure than application of a PPNB alone ^(7, 16). The most likely reason for this are two origins of pain, one of the placing the transrectal probe and another because of multiple punctures of anterior wall of the prostatic capsule. ⁽¹⁶⁾ The lack of our study is that we did not evaluate the pain scores separately for different parts of the procedure (for the biopsy itself and for placing the ultrasound probe). Some patients reported even more pain from placing the ultrasound probe in the rectum than from the biopsy itself. This finding has also been reported by other authors ⁽¹⁷⁾ Szlauer R et al. showed in their last paper that addition of lidocaine suppositories to PPNB improving analgesia in comparison to PPNB alone.⁽⁷⁾ Our study did not include comparison with PPNB since it is not routinely performed at our institution.

One of the most effective topical anesthetics is a eutectic mixture of lidocaine and prilocaine which applied perianally-intrarectally can be used for prostate biopsy. ^(18,19) In comparison with PPNB alone, combining the EMLA cream with PPNB is more effective in reducing pain during all phases of the prostate biopsy.⁽¹⁶⁾ But EMLA demands a relatively long time from cream application till the probe insertion and biopsy and requires the involvement of medical personnel in the procedure itself, not to mention the cost of the cream which is not insignificant.⁽¹⁶⁾

We have shown that with the application of lidocaine suppositories acceptable analgesic results can be achieved without any risk. Moreover, this is a simple and cheap form of analgesia which can be performed by the patient himself. The procedure can also be used alone or in combination with other methods of analgesia.

We have also shown that the optimal time for performing a biopsy starts approximately one hour after the placement of the suppository. No statistically significant influence of different variables (patient age, PSA value and patohistological findings) which are important for patients going on prostate biopsy on VAS score have been found.

Based on previous research, a combination of topical anesthetics and PPNB gives the best result, but for institution where PPNB is not routinely performed and the application of prilocain-lidocain cream is expensive and requires additional engagement of medical staff, lidocaine suppository may be acceptable form of analgesia. Lidocaine suppository is an easy to use, self applicable and cheap method of local analgesia with acceptable results. Possible complications related with this procedure are insignificant.

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Table 1. Baseline patient characteristics in the lidocaine and glycerol groups.

Figure 1. Median pain level of the lidocaine and glycerol groups.

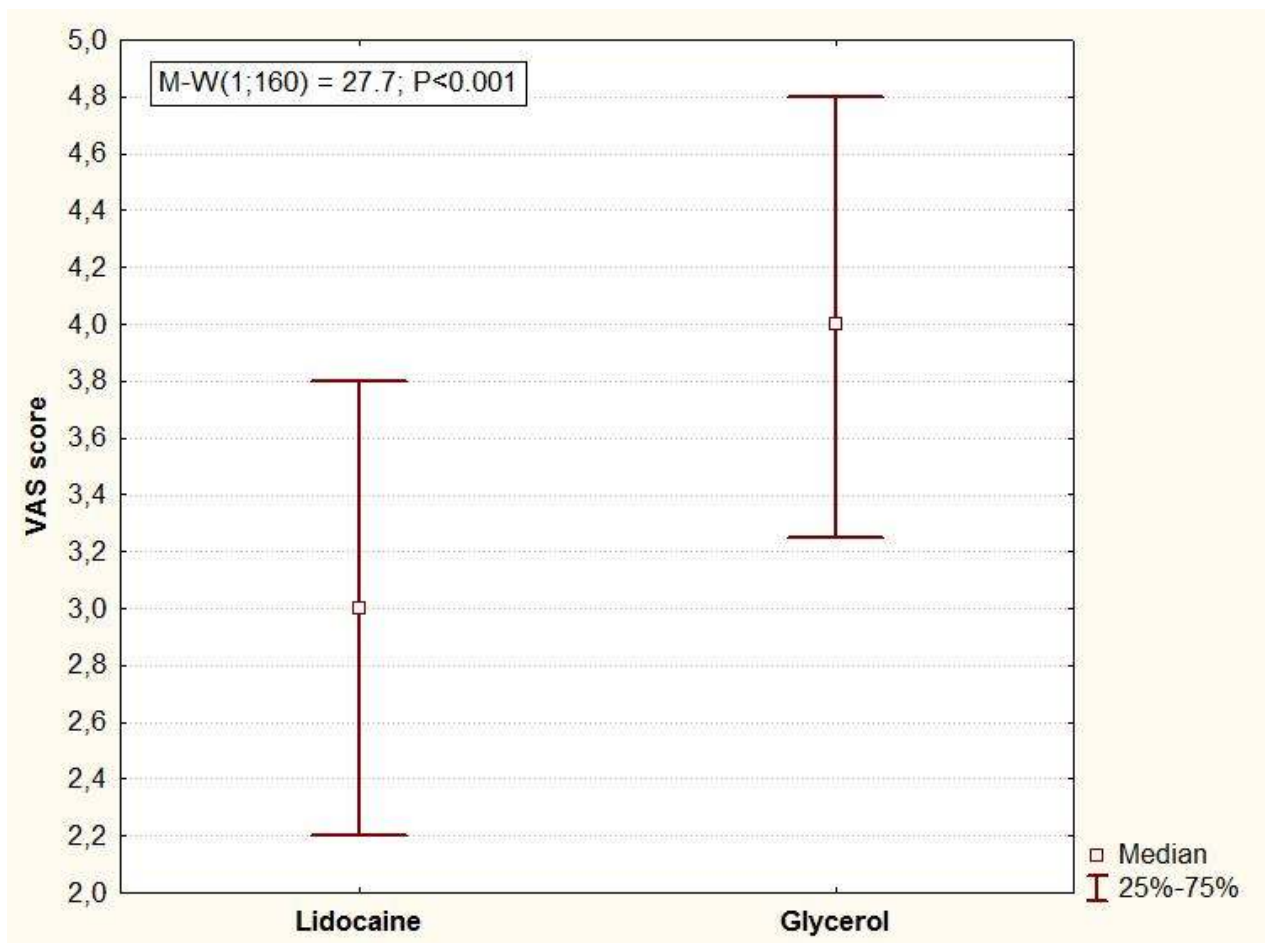


Figure 2. VAS score depending on the time of the placement of the suppository before the procedure in the lidocaine group, with the VAS score decreasing as more time elapses from the placement of the suppository till the biopsy.

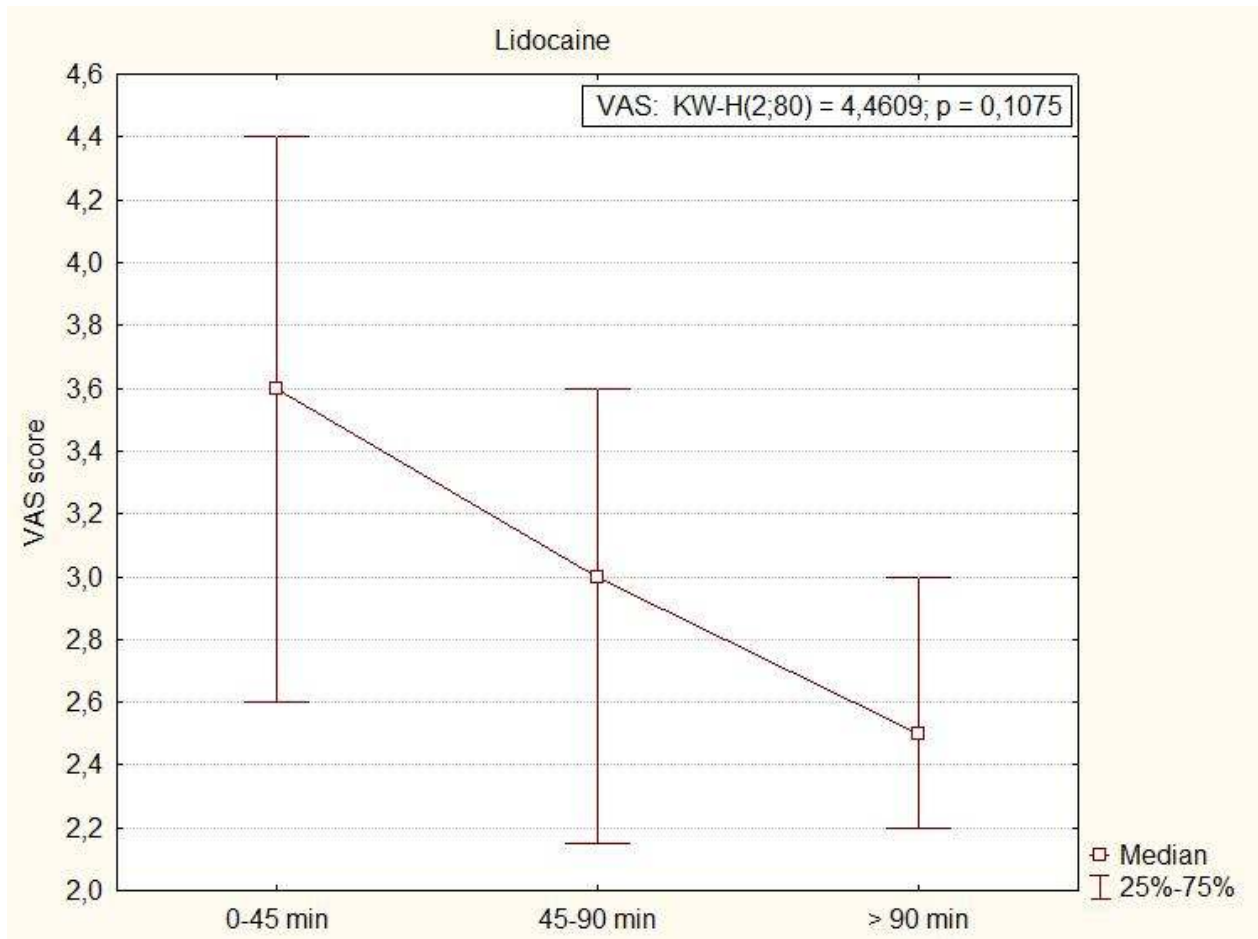


Figure 3. VAS score depending on the time of the placement of the suppository before the biopsy in the glycerol group, with no significant differences in VAS score being observed during the time elapsed from the placement of the suppository till the biopsy.

