Perianal and intrarectal anaesthesia for transrectal biopsy of the prostate: a prospective randomized study comparing lidocaine–prilocaine cream and placebo

MARCO RABER, VINCENZO SCATTONI, MARCO ROSCIGNO, PATRIZIO RIGATTI and FRANCESCO MONTORSI
Istituto Scientifico Ospedale San Raffaele, Urology, Milan, Italy

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OBJECTIVES

To assess the effectiveness of perianal and intrarectal lidocaine-prilocaine cream for prostate biopsy.

PATIENTS AND METHODS

In a prospective, randomized, double-blind, placebo-controlled study, 200 consecutive patients were randomized to receive 5 mL lidocaine-prilocaine cream or 5 mL placebo peri-anally and transrectally before transrectal ultrasonography (TRUS)-guided prostate needle biopsy (mean number of cores, 12). The men were asked to grade the pain when the TRUS probe was inserted and during the biopsy procedure using a 10-point linear visual analogue pain scale.

RESULTS

At probe insertion, men in the anaesthetic group reported a significantly lower mean pain level than men in the placebo group (0.3 vs 1.6, $P < 0.001$). Men who had anaesthetic also reported less pain during biopsy punctures (1.8 vs 3.2, $P < 0.001$). Stratifying results by age, younger men (<67 years) benefited more from anaesthesia during probe insertion (0.9 vs 1.7; $P = 0.04$) and biopsy (1.8 vs 4.0, $P < 0.001$) than older men (1.0 vs 1.1, $P = 0.7$ and 1.9 vs 2.4, $P = 0.3$, respectively). There were only minor complications, and these were not significantly different between the groups.

CONCLUSION

Topical anaesthesia with prilocaine-lidocaine cream significantly reduced pain at transrectal probe insertion and during the biopsy procedure.

KEYWORDS

prostate cancer, biopsy, local anaesthesia

INTRODUCTION

Local anaesthetics are commonly used for TRUS-guided prostate biopsy [1–10]. Topical anaesthesia with lidocaine gel in the rectum has been reported to have controversial results vs placebo [11–15] and, in some studies, topical anaesthesia was reported to be inferior to periprostatic lidocaine injection [16–20]. The anaesthetic gel, usually 10–20 mL of lidocaine (1–2%), is applied in the rectal ampulla 10–20 min before introducing the TRUS probe and biopsy sampling [11–15]. However, the best anaesthesia for prostate biopsy has yet to be defined. Our objective was to determine whether pain is controlled better by a different local anaesthetic (EMLA®, Astrazeneca Co., Macclesfield, UK) with better pharmacological characteristics and a different site of application. The formulation is a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine, giving a high concentration (≈ 80%) of active substance. The efficient anaesthetic effect of lidocaine-prilocaine cream was first reported in 1982 by Ehrenstrom and Reiz [21]; they found a highly significant reduction in the pain after venous cannulation when the cream was used, compared with placebo. Various studies confirmed the effectiveness of topical anaesthetics in percutaneous and surgical procedures of the skin, and surgical procedures of the buccal and genital mucosa [22–25]. Topical application of lidocaine-prilocaine cream to the anus and anal canal has also proved effective in patients with acute anal fissures [26]. In the present study, we evaluated whether lidocaine-prilocaine cream, applied to the anal canal, anal ring, and rectal ampulla, is effective for controlling pain during TRUS probe insertion (somatic pain) and during biopsy puncture.

PATIENTS AND METHODS

From January to September 2003, 200 consecutive men with abnormally high PSA levels and/or suspicious DRE results underwent TRUS-guided prostate needle biopsy by one operator (M.Ra.); all provided informed consent. A cleaning enema was administered on the morning of the biopsy. The men were randomized, by a computer program, to receive 5 mL of lidocaine-prilocaine cream (EMLA, Astrazeneca) or placebo. Another operator (V.S.) administered local anaesthesia 30 min before TRUS and biopsy. A 5-mL syringe without a needle was filled with gel or anaesthetic cream: ≈ 1 mL of the cream is applied topically to the anal ring before the tip of the syringe enters the anal canal, and the rest is delivered into the anal canal and rectum. During the subsequent DRE, cream is 'massaged' along the anal ring, anal canal and anterior rectal wall. TRUS was performed using a 6.5-MHz end-fire probe (Hitachi Medical Co., Tokyo, Japan). The prostate size was determined according to standardized three-dimensional measurements computed by the ultrasound machine. Prophylaxis was by oral administration of ciprofloxacin 250 mg, one tablet every 12 h starting the evening before sampling, until 4 days after. Biopsies were taken with the patient in left lateral decubitus position, using an 18-G Tru-cut needle powered by a biopsy gun (Manan Pro-Mag 2.2; Manan Medical Products, Northbrook, IL, USA). In all cases, 12-core biopsy samples were taken. In a random

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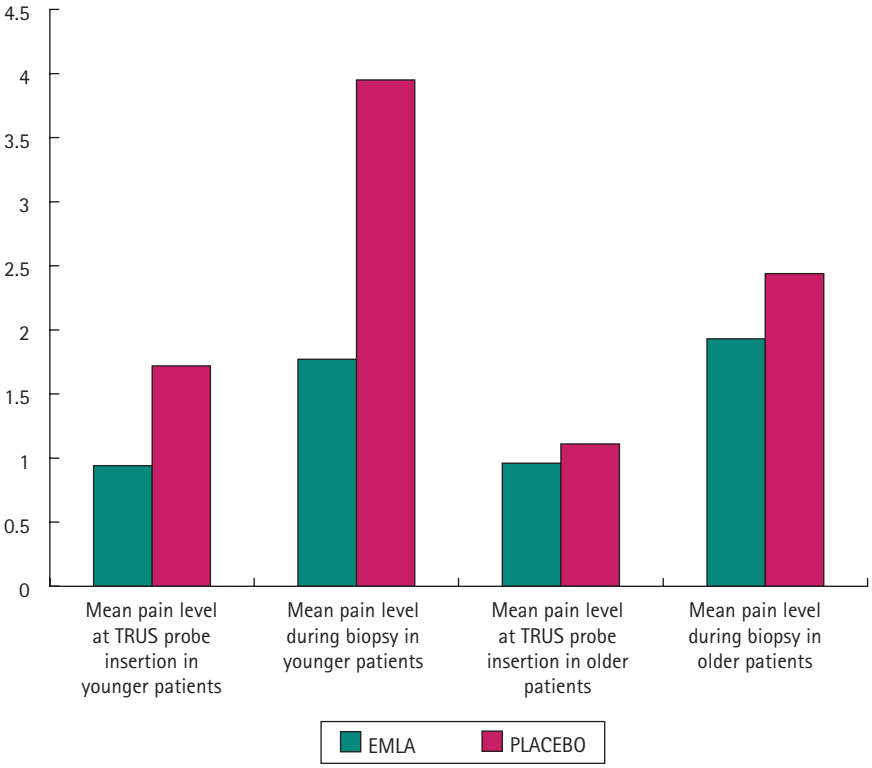
Variable	Anaesthetic	Placebo	P
Younger men			
N	48	49	
Mean (SD):			
Age, years	60.8 (3.9)	61.2 (3.5)	0.6
Pain at probe insertion	0.9 (1.4)	1.7 (2.3)	0.04
Pain during biopsy	1.8 (2.5)	4.0 (3.2)	<0.001
Older men			
N	52	51	
Mean (SD):			
Age, years	72.0 (4.4)	73.0 (5.0)	0.26
Pain at probe insertion	1.0 (0.7)	1.1 (2.5)	0.68
Pain during biopsy	1.9 (2.7)	2.4 (2.6)	0.33

TABLE 1
Pain levels in younger and older men

FIG. 1. Mean pain level in the anaesthetic and placebo groups in younger and older men at TRUS probe insertion and during biopsy.



fashion, two prostate cores were taken from each peripheral side, apical margin, and base, and ≈10 min after biopsy, another operator (M.Ro.) asked the men to complete a visual analogue scale questionnaire using a scale of 0 (no complaint) to 10 (maximal complaint) of pain both during probe insertion and biopsy punctures. Intermediate and major complications during and after the procedure (48 h), e.g. vasovagal hypotension, fever >38°C, gross haematuria, rectal bleeding, dysuria, and urinary retention, were recorded. We analysed the ordinate scales used to grade symptoms as continuous variables. Student's *t*-test was used to evaluate these and other continuous variables, and the chi-squared test for categorical data.

RESULTS

The anaesthetic and placebo groups (100 men in each) were similar in age, prostate size, PSA levels, histological results, and operative duration; their median (range) age was 66.8 (46–87) years. During TRUS probe insertion, men who had anaesthetic reported a significantly lower mean pain level than those in the placebo group (0.3 vs 1.6; $P < 0.001$). During probe insertion, 12% of men who had anaesthetic reported some pain (any grade) vs 32% in the placebo group ($P < 0.001$). Men who had anaesthetic reported less pain during biopsy punctures (1.8 vs 3.2, $P < 0.001$), and the percentage of men who reported some pain was significantly lower in the anaesthetic group than in the placebo group ($P = 0.04$).

We stratified the results by age with a threshold of 67 years (median). In younger men, significantly less pain was reported by the anaesthetic group than by the placebo group during probe insertion (0.9 vs 1.7) and biopsy (1.8 vs 4.0), and there was no difference in older men during either probe insertion or biopsy (Table 1, Fig. 1). In the placebo group, younger men reported significantly more pain than older men (4.0 vs 2.4, $P = 0.01$).

No general or local adverse effects were associated with the anaesthetic. During and after biopsy, four men in the placebo group and two in the anaesthetic group had vasovagal symptoms; these resolved with administration of i.v. atropine. One man in each group had a septic complication that resolved after treatment with i.v. antibiotics. There were only minor complications, e.g. mild haematuria, mild rectal bleeding and haemospermia, with no differences between the groups.

DISCUSSION

Intrarectal lidocaine gel was the first local anaesthetic method described in an attempt to reduce the pain of transrectal biopsy. The results of previous studies have been equivocal, and the concentration, volume and timing of application have not been standardized. Some authors [11,12] reported significantly less pain with local anaesthesia than with placebo, but others did not [13–15]. In 2000, Soloway and Obek [1] described a novel effective anaesthetic method using periprostatic lidocaine infiltration. Significant pain reduction was confirmed by others both against placebo [2–10] and against topical anaesthesia using intrarectal lidocaine gel [17–19]. Consequently, periprostatic

infiltration is now considered the reference standard and is 'strongly' recommended before prostate biopsy [3].

Pain during prostate biopsy has two components, originating from TRUS probe insertion and the biopsy punctures. In previous experience of prostate biopsy without analgesia, Luscombe and Cooke [27] reported that, for 27% of men, the pain of probe insertion was as bad as or worse than pain from the needle biopsies. This was confirmed by the present study; 36% of the placebo group reported some pain during probe insertion and 15% had a pain score of ≥6. Stirling *et al.* [16] showed that men who had intrarectal lidocaine had significantly less pain at probe insertion but not at biopsy. Conversely, men who had periprostatic injections had significantly less pain at biopsy but not at probe insertion. The present study showed significant pain reduction in both parts of the biopsy procedure, and to our knowledge is the first to report using lidocaine-prilocaine cream. The efficacy of this might be due to the formulation; this eutectic mixture of lidocaine-prilocaine has a higher concentration (≈ 80%) of active substance than the commonly used lidocaine gel (≈ 20%) [21]. This leads to better drug penetration and better anaesthesia in the richly innervated soft tissue between the rectal wall and prostate capsule, as shown by Hollabaugh's anatomical studies [28]. The timing of application of anaesthetic (30 min before probe insertion) might be critical; in previous reports on intrarectal lidocaine gel, this time was always 10–20 min [11–15]. The site of application might also explain the better results; we think that anaesthetising a somatic innervated region of the anal canal (lower one-third) and ring, reduces the pain from probe insertion. To our knowledge, the present study is the first description of this method of application. The present method might be important for reducing pain during biopsy.

Younger men generally report a higher overall pain level than older men [29,30]. The present data confirm this; in the placebo group, younger men reported a higher pain level than older men. The application of peri-anal and intrarectal lidocaine-prilocaine cream significantly reduced pain during the procedure in men <67 years of age, but not in older men. Thus, we recommend this application especially for younger men, who have a higher level of sensitivity.

In conclusion, the present study shows that topical peri-anal, intra-anal and intrarectal administration of 5 mL of prilocaine-lidocaine cream reduced pain from the somatic nerves of the anal canal and sphincter when a TRUS probe was inserted, as well as during biopsy of the prostate. The anaesthetic seemed more effective in younger men, and reduced discomfort and pain during the entire TRUS biopsy procedure without adding complications.

CONFLICT OF INTEREST

None declared.

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Correspondence: Raber Marco, Istituto Scientifico Ospedale San Raffaele, Urology, Milan, Italy.
e-mail: raber.marco@hsr.it