Comparative Efficacy and Patient Preference of Topical Anaesthetics in Dermatological Laser Treatments and Skin Microneedling

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ABSTRACT

Background: Topical anaesthetics are effective for patients undergoing superficial dermatological and laser procedures. Our objective was to compare the efficacy and patient preference of three commonly used topical anaesthetics: (2.5% lidocaine/2.5% prilocaine cream (EMLA®), 4% tetracaine gel (Ametop™) and 4% liposomal lidocaine gel (LMX4®)) in patients undergoing laser procedures and skin microneedling. **Settings and Design:** This was a prospective, double-blind study of patients undergoing laser and skin microneedling procedures at a laser unit in a tertiary referral dermatology centre. **Materials and Methods:** All 29 patients had three topical anaesthetics applied under occlusion for 1 hour prior to the procedure, at different treatment sites within the same anatomical zone. A self-assessment numerical pain rating scale was given to each patient to rate the pain during the procedure and each patient was asked to specify their preferred choice of topical anaesthetic at the end of the procedure. **Statistical Analysis:** Parametric data (mean pain scores and frequency of topical anaesthetic agent of choice) were compared using the paired samples t-test. A *P*-value of ≤0.05 was considered as statistically significant. **Results and Conclusions:** Patients reported a mean (±SD; 95% confidence interval) pain score of 5 (±2.58; 3.66-6.46) with Ametop™, 4.38 (±2.53; 2.64-4.89) with EMLA® and 3.91 (±1.95; 2.65-4.76) with LMX4®. There was no statistically significant difference in pain scores between the different topical anaesthetics. The majority of patients preferred LMX4® as their choice of topical anaesthetic for dermatological laser and skin microneedling procedures.

KEYWORDS: Topical anaesthetics, 2.5% lidocaine/2.5% prilocaine cream, tetracaine gel, liposomal lidocaine gel, Laser, skin microneedling

INTRODUCTION

Topical anaesthetics have been valuable for providing effective, non-invasive anaesthesia for superficial cosmetic and laser procedures. Their role in reducing discomfort has been proven in vascular, pigmented and epilation laser treatments, as well as for cosmetic injectables.[1]

Topical anaesthetics work by binding to the voltage-gated sodium channels, blocking sodium influx, thereby inhibiting nerve cell depolarisation and impulse conduction.[2] Increasing numbers of topical anaesthetics have become available in recent years. Factors influencing the choice of topical anaesthetics include efficacy, patient preference and cost considerations.[1,2]

In this prospective double-blind study, we aimed to compare the efficacy and patient preference of three commonly used topical anaesthetics: (2.5% lidocaine/2.5% prilocaine cream (EMLA®), 4% tetracaine gel (Ametop™) and 4% liposomal lidocaine gel (LMX4®)

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for laser and skin microneedling procedures. We also reviewed the available literature comparing these three topical anaesthetics.

MATERIALS AND METHODS

Twenty-nine patients undergoing a total of 30 laser or skin microneedling procedures over a 3-month period were included in the study. One patient had two procedures done at two different anatomical sites. All patients had the three topical anaesthetics (Ametop™, EMLA®, LMX4®) applied under occlusion at different treatment sites within the same anatomical zone by a trained nurse. Anatomical zones were divided into upper, middle and bottom treatment sites. One hour prior to the indicated procedure, Ametop™, EMLA® and LMX4® were applied in random order under occlusion to each treatment site. The duration of 1 hour was chosen to provide consistency among all the three topical anaesthetics. An even layer of Ametop™, EMLA® or LMX4® (approximately 1 g/10 cm^2) completely covering each treatment site was applied by the same trained nurse in a standardised approach. Using a numerical pain rating scale (0-10 numeric pain rating scale: 0 = no pain; 10 = worst possible pain), each patient was asked to self-report the pain intensity during the procedure. The operating clinician was blinded to the order of application of the anaesthetic agent. At the end of the procedure, each patient was asked to rate their most preferred topical anaesthetic agent based on their experience.

Statistical analysis

Parametric data (mean pain scores and frequency of topical anaesthetic agent of choice) were compared using the paired samples t-test. All data are presented as mean ± SD; 95% confidence interval. A *P* value of ≤0.05 was considered as statistically significant.

RESULTS

Informed consent was obtained from all 29 patients (M:F = 1:4) who were included in this study. The mean age was 31.26 (range 14-52 years). The procedures performed were skin microneedling (*n* = 12, 40%), carbon dioxide laser (*n* = 11, 36.7%), pulsed-dye laser (*n* = 4, 13.3%), and Q-switched Alexendrite laser (*n* = 3, 10%). The indications for treatment were post-acne scarring (*n* = 14, 46.7%), pigmentation (*n* = 3, 10%), port wine stains (*n* = 3, 10%), dermatosis papulosis nigra (*n* = 3, 10%), syringomata (*n* = 2, 6.7%), and individual cases (*n* = 1 each) of trichoepitheliomata, cafe-au-lait macules, fibrofolliculomas, telangiectasia and milia. The treated sites were face (*n* = 23, 76.7%), neck (*n* = 2, 6.7%), trunk (*n* = 3, 10%) and limb (*n* = 2, 6.7%). The mean pain score on the trunk and limbs (*n* = 5) for EMLA® was 5.8 (±2.4; 3.4-8.2), while that for Ametop™ was 7.2 (±3.43; 3.78-10.63) and LMX4® was 1 (±0.71; 0.29-1.71). As for the face and neck (*n* = 25), the mean pain score for EMLA® was 4.1 (±2.44; 1.61-6.49), Ametop™ was 4.5 (±1.97; 2.51-6.44) and LMX4® was 4.5 (±1.50; 3.02-6.03).

The overall mean (±SD; 95% confidence interval) pain score with Ametop™ was 5.00 (±2.58; 3.66-6.46), with one urticarial reaction observed. The mean pain score for EMLA® was 4.38 (±2.53; 2.64-4.89); whilst that for LMX4® was 3.91 (±1.95; 2.65-4.76) [Figure 1]. The differences in mean pain scores between the different topical anaesthetics for all procedures were not statistically significant (Ametop™ vs. EMLA®, *P* = 0.057; Ametop™ vs. LMX4®, *P* = 0.124, EMLA® vs. LMX4®, *P* = 0.675). There were also no significant differences when laser and microneedling procedures were considered in isolation.

Overall, LMX4® (*n* = 13, 55.6%) was the most preferred topical anaesthetic for dermatological laser and skin microneedling, followed by EMLA® (*n* = 11, 37%), and Ametop (*n* = 3, 11%) [Figure 2]. Two patients were unsure of their most preferred topical anaesthetics. When considered laser and skin microneedling in isolation, LMX4® was also the most preferred topical anaesthetic (*n* = 7, 43.8%, for laser, *n* = 7, 50% for skin microneedling).

In terms of adverse effects, only one urticarial reaction was observed with Ametop™ and no reactions were observed with the other topical anaesthetics.

DISCUSSION

Our observation concludes that while there is no statistically significant difference among the three

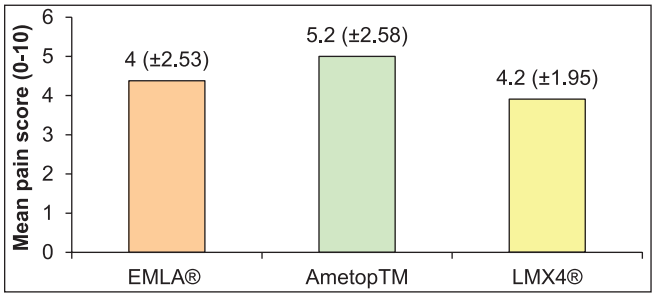

Figure 1: Mean pain score of three topical anaesthetics

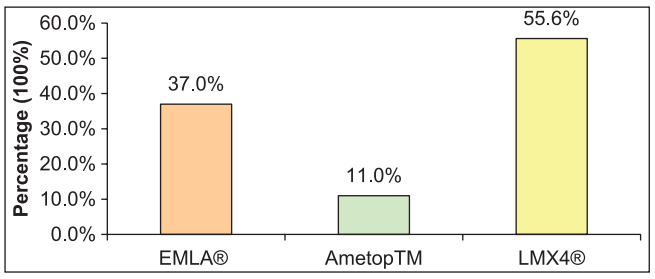

Figure 2: Patient preferred choice of topical anaesthetics

topical anaesthetic agents in terms of mean pain score, the Ametop™ sites had the highest mean pain score and LMX4® had the lowest mean pain score. This was reflected in the choice of topical anaesthetic by patients undergoing laser and skin microneedling procedures with LMX4® being the most preferred topical anaesthetic and Ametop™ the least preferred.

EMLA® (Eutectic Mixture of Local Anaesthetics) consists of two amide group local anaesthetics: 2.5% lidocaine and 2.5% prilocaine. It was the first commercially available topical anaesthetic that provides effective analgesia. Many studies have shown that analgesia is achieved after 60 minutes of application of EMLA®, with an initial blanching effect due to peripheral vasoconstriction followed by redness due to vasodilatation.[3-5] Even with the vasoconstrictive effect, EMLA has been shown to produce safe and effective results in pulsed dye laser treatments and to reduce laser-induced pain stimuli in Q-switched Nd:YAG laser.[3,6,7] It is recommended that EMLA should be applied for 1 hour under occlusion prior to laser treatment.[6] This facilitates the accumulation of the anaesthetic agent in the stratum corneum during occlusion, which continues to diffuse to the sensory nerves in the dermis after its removal.[8] In general, the anaesthetic effect of EMLA lasts between 1 and 3 hours.[9] The development of methaemoglobinaemia is a rare but known complication of prilocaine, and it should be used in caution in neonates (especially premature infants), those with glucose-6-phosphate deficiency or with medication known to exacerbate methaemoglobinaemia and congenital methaemoglobinaemia.[3]

LMX4®, (previously known as ELA-Max) is another widely used topical anaesthetic, containing 4% lidocaine in a liposomal delivery system. Liposomes facilitate the penetration of encapsulated lidocaine to the dermis (using their lipid bilayered structure to easily penetrate through the hydrophobic stratum corneum) and prevent its degradation, thus providing sustained release. Studies have shown that LMX4® provides effective analgesia after 30 minutes of application and produces minimal skin changes, as compared to other topical anaesthetics such as EMLA® and Ametop™.[3,10] In general, the recommended application time for LMX4® is 60 minutes with no occlusion required.[3]

Ametop™ (previously known as amethocaine 4% gel) contains 4% tetracaine in a lecithin-gel base. It is a long-acting ester anaesthetic and has been shown to provide effective analgesia within 30-45 minutes of application lasting for 4-6 hours.[3,11] Transient local erythema is the most commonly reported adverse reaction.[11]

Our literature review revealed only a limited number of studies providing an overall comparison involving all three agents. A systematic review has shown that in 10 randomised controlled trials comparing EMLA® to other topical anaesthetics (topical lidocaine and topical tetracaine-based agents) in dermal instrumentation procedures (i.e., intravenous cannulation, arterial cannulation, venepuncture and insertion of spinal needles), comparable analgesic efficacy between EMLA® and LMX®, and greater analgesic efficacy in topical tetracaine-based agents was found. However, some of the studies included used a higher concentration (5%) of tetracaine.[12]

Friedmann *et al.* compared four topical anaesthetics including: EMLA®, LMX4®, Ametop™ and betacaine-LA using a Q-switched 1064 nm Nd:YAG laser as the pain inducer.[13] They found that EMLA® and LMX4® had higher levels of anaesthetic efficacy compared to Ametop™ and betacaine-LA.[13] A recent study comparing these three topical anaesthetics (EMLA®, LMX4®, Ametop™) using the tactile spatial resolution method as an objective measure of efficacy revealed that all three decreased tactile spatial discrimination thresholds significantly, but LMX4® and Ametop™ appeared to be faster acting than EMLA®.[14]

Similar to our results, a previous study of pain control for long-pulsed 1,064 nm Nd:YAG laser therapy showed comparable visual analogue scale (VAS) pain scores between EMLA (34.53 ±SD 23.264) and LMX4® (5% lidocaine, 35.73 ± SD 23.783), respectively.[15] Another randomised, double-blinded study also concluded comparable analgesic effect between LMX4® and EMLA® for electrodessication of dermatosis papulosa nigra. Similar to our study, the mean pain scores (scale 0 = none, 10 = very severe) was slightly lower with LMX4® (2.9 ± SD 2.0) than EMLA (3.3 ± SD 2.2), although there was no significant difference between the two.[16] Our mean pain scores with EMLA® (4.38 ± 2.53) and LMX4® (3.91 ± 1.95) were higher than these means, probably due to the more painful nature of our procedures. However, our study showed that LMX4® was the patients' anaesthetic agent of choice, probably due to the rapid-acting and sustained effect of LMX4® as compared to EMLA® and Ametop™.[3]

In contrast, a double-blinded study of 29 patients undergoing pulsed-dye laser treatment for port wine stains showed significant reduction of laser-associated pain with Ametop™ compared to EMLA.[17] Ametop™ provided satisfactory analgesia in all but one patient whereas EMLA provided satisfactory analgesia in only two-third of patients.[17]

The main limitation of this study is the small number of subjects, which may contribute to the statistically insignificant results. The study was underpowered

Table 1: Cost comparison of Ametop™, EMLA® and LMX4®

Topical anaesthetic agent	Cost per gram
EMLA®	£0.35
LMX4®	£0.60
Ametop™	£0.72

to evaluate the efficacy endpoints. The limitation was exacerbated by varied treatment procedures performed. The study only examined three relatively mild topical anaesthetics as these are the commonly available topical anaesthetics. Other available topical anaesthetics with stronger potency were not studied. There may also be a possible effect of one topical anaesthetic agent diffusing into the adjacent area covered by another topical anaesthetic agent. However, as the application of the topical anaesthetics to each treatment section was made in random order, this minimised the potential bias due to diffusion of any anaesthetic agent. The reasons behind patient's choice of topical anaesthetic were not elicited in the study. The total duration of anaesthesia achieved by each topical anaesthetic was not recorded; however, there were no reports of excessive post-procedural pain from the patients in this study.

Cost-analysis of the three topical anaesthetics using the British National Formulary reveals variation between these three agents. Ametop™ is the most expensive (£0.72/g; 1.5 g tube costs £1.08), followed by LMX4® (£0.60/g; 5 g tube costs £2.98), and EMLA® which is the cheapest (£0.35/g; 5-g tube of EMLA® costs £1.73) [Table 1].[18]

CONCLUSIONS

Our study did not show any significant difference in patient self-reported analgesia between Ametop™,[3-5] EMLA® and LMX4®; however, the trend suggests that patients tend to prefer LMX4® and EMLA® over Ametop™ for laser and skin microneedling procedures. Further studies of topical anaesthetics for dermatological laser and cosmetic procedures are necessary to confirm these preliminary findings in order to help physicians select the most appropriate topical anaesthetic agent for their patients.

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Conflicts of interest

There are no conflicts of interest.

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