Local Anesthesia by Topical Application of Lidocaine After Stratum Corneum Ablation with an Er:YAG Laser

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Citation

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Abstract

Background and Objectives: The stratum corneum, the outermost layer of skin, is the principle barrier to permeation of any drug through the skin, including local anesthetics. Removal of the stratum corneum using a pulse of infrared radiant energy could conceivably allow for rapid penetration of topically applied local anesthetic solutions. The purpose of this study was to provide preliminary information on the effectiveness of local anesthesia produced by topically applied lidocaine after ablation of the stratum corneum by an Er:YAG laser.
Methods: 50 adult volunteers were enrolled into the study. Participants were divided into two groups (4% lidocaine or 10% lidocaine) and had a site irradiated on the forearm of each arm with a 2.94 micrometer Er:YAG laser. The appropriate concentration of lidocaine was applied for 5 minutes on one arm and 10 minutes on the other. Pinpricks using a 25 gauge 1/2 mm lancet were performed and participants rated the pain using a 0 - 10 scale.
Results: The results of our study suggest that the transdermal administration of topically applied lidocaine is enhanced and topical anesthesia is produced at the site of stratum corneum ablation within 5 minutes. No anesthesia was found in areas tested outside of the ablation site. The ablation of the stratum corneum with the 2.94 micron wavelength radiant energy produced by an Er:YAG laser produced minimal discomfort and resulted in no immediate adverse effects.
Conclusions: Results suggest application of topical lidocaine after removal of the stratum corneum using the radiant energy produced by an Er:YAG laser produces rapid local anesthesia at the ablation site.

INTRODUCTION

The pain associated with needle-sticks is, at best, a brief and minor discomfort, and at worst, painful and traumatizing. Routine needle-stick procedures, such as blood sampling, placement of intravenous (i.v.) catheters, and immunizations, have often been discounted as being unimportant pain stimuli. The increasing interest in pain management in the medical community has facilitated growing recognition of the impact these procedure can have on patients and the potential benefit of interventions that decrease the pain and distress associated with the needle-sticks. Topical or local anesthesia is one method that has been widely used to decrease the pain associated with needle-stick procedures.

The stratum corneum, the outermost layer of skin, is the principle barrier to permeation of any drug through the skin, including local anesthetics. This barrier must be bypassed or altered in some manner to produce topical or local anesthesia. For instance, it has been shown that removal of the stratum corneum of human skin by tape stripping increases the flux of topically applied lidocaine by a factor of 7.9±8.1, as compared to intact skin.[1]

The most consistent clinical method of bypassing the stratum corneum is to use a needle to puncture the skin and infiltrate local anesthetic below the barrier. However, the discomfort associated with the anesthetic needle-stick and injection of the local anesthetic can be as painful or distressing as the subsequent procedure. Other considerations, beyond the potential patient benefit, include the disposal of the used needle and the risk to health care providers in the handling of the potentially infectious sharp.

A number of studies have focused on the use of a eutectic mixture of local anesthetics (EMLA), which is formulated to allow effective permeation across the stratum corneum.[2,3] The interest and broad acceptance of this topical anesthetic are evidence of the perceived need for needle-less topical anesthesia. EMLA has been shown to be quite effective at reducing the discomfort associated with such procedures as venipuncture or vaccination, as well as other superficial procedures.[4,5,6,7,8,9] One drawback of EMLA, however, is it must be in place for at least one hour to provide adequate

anesthesia. Regardless of the inconvenience associated with the required duration of application, EMLA has become popular worldwide in decreasing the pain associated with needle-sticks in children.

Another method of increasing the delivery of topically applied local anesthetic across the stratum corneum is by iontophoresis.[10,11,12] In this method of drug delivery, charged molecules are pulled across the stratum corneum and through the underlying tissue by an electromotive force. This force is produced by a current in the range of a few milliamps that is applied between the surface of the skin and subepidermal tissue for a period of 5 to 30 minutes. Iontophoresis devices are commercially available on the market for delivery of local anesthetics. Most devices take approximately 10 minutes to provide adequate anesthesia and the electrical current may cause a sensation that is described as uncomfortable by some patients.[11] However, results from two recent studies in children indicate that lidocaine iontophoresis produces effective topical anesthesia for IV placement without signs of dermal toxicity.[13,14]

Lasers which produce pulsed radiant energy in the ultraviolet or infrared region of the electromagnetic spectrum can be used to precisely remove the stratum corneum of skin in vitro, resulting in increased skin permeation of topically applied pharmaceuticals.[15] In these earlier studies, there was no histological evidence of damage to the underlying skin when the laser was used to remove the stratum corneum. Removal of the stratum corneum, using a pulse of infrared radiant energy produced by, for example an Er:YAG laser, could conceivably allow for rapid penetration of topically applied local anesthetic solutions.[16]

Therefore, the purpose of this study was to provide preliminary information on the effectiveness of local anesthesia produced by topically applied lidocaine (4% versus 10%) after ablation of the stratum corneum by an Er:YAG laser. Lateral spread of the anesthesia as well as any complications related to the laser ablation were also evaluated.

METHODS

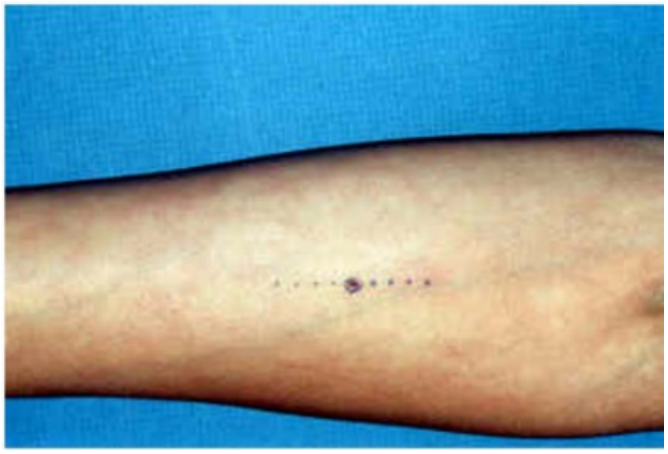
After obtaining Human Research Advisory Committee approval, 50 adult volunteers were enrolled into the study. All participants signed an informed consent form prior to any study procedures being performed. A numerical scale [0 = no pain; 10 = worst pain] used for reporting the pain associated with the study procedures was explained to the participants at this time.

Participants were divided into two groups. The first group of 25 had a LidoKain® patch (4% lidocaine; LidoKain®, Henley HealthCare, Houston, TX) applied to two test sites, one on each forearm. The LidoKain® was packaged as a single dose patch, and was applied as such over the laser treated sites for this group. The second group of 25 had liquid lidocaine applied to two test sites. For this group, 4 actuations of the metered dose valve (total dose 40 mg lidocaine) of 10% Lidocaine oral aerosol (10% lidocaine; Xylocaine®, Astra, Westborough, MA) was sprayed onto a Hill Top Chamber (Hill Top Research, Cincinnati , OH), saturating the gauze which was then placed over the treated sites. The Hill Top Chamber consists of a circular piece of gauze positioned within a semi-spherical soft plastic chamber that is open on one side. The gauze is held in contact with the skin surface, and the Chamber is held in place on the skin with dermatologic adhesive tape. Randomization determined whether the right or left arm was tested first.

The 2.94 micron wavelength pulsed radiant energy output of the Norwood Abbey Er:YAG laser was verified with a calibrated energy meter to be 275 25 millijoules (mJ) prior to each ablation. The radiant energy, in the form of a single 300 microsecond long pulse, was focused to produce an oval area of treated skin with dimensions of 1.5 mm x 4 mm. A clean, disposable tip was used on the end of the laser to collect any ablated material. The resulting laser beam intensity, 58.4 mJ/mm^2, causes little or no sensation when used to irradiate the skin. With the participant comfortably seated, one site was irradiated on the forearm of the randomized arm with the laser. This step took less than 1 minute to complete. Any comments about sensations noted at the time of the laser pulse were recorded. The irradiated site was circled with a black felt pen.(Figure 1) A control site, which was not irradiated, was identified and marked on the same forearm at least 3 cm away from the irradiated site. The irradiated site then had either the 4% lidocaine patch or the 10% lidocaine solution applied (depending on the study group).

Figure 1

Figure 1: Right Forearm with Ablation and Tested Peripheral Sites Marked

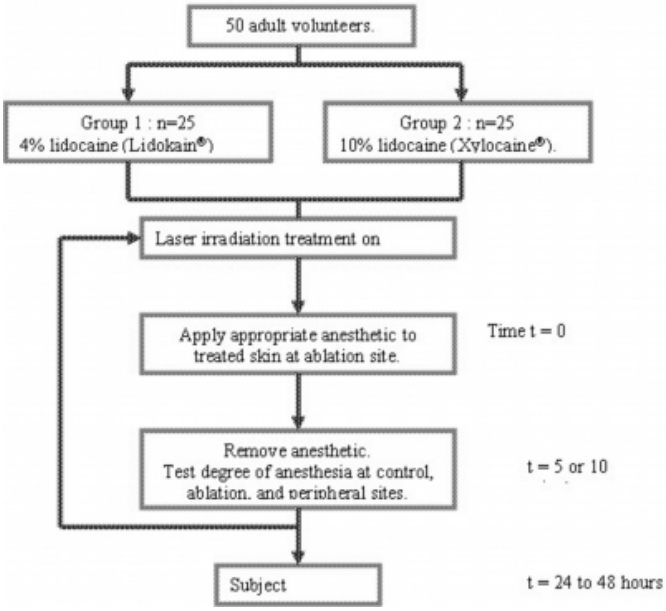


After 5 minutes of application, the 4% lidocaine patch or the 10% lidocaine solution was removed from the test site and the skin gently wiped with a sterile gauze. With the participant's vision averted, two pinpricks using a 25 gauge 1/2 mm lancet were performed at the control site on the forearm. Care was taken to use the same application pressure during all pinpricks. The participant was asked to rate the pain felt after each pinprick using the 0 - 10 scale. A series of pinpricks was then performed at the test site, starting in the center of the site, then 0.5 cm, 1 cm, 1.5 cm. and 2 cm from the center of the minor axis of the oval shaped irradiated site, in a single direction, toward the wrist.(Figure 1) Each participant was asked to rate the pain felt after each pinprick using the same 0 - 10 scale. Sensation was then tested using the same lancet at 0.5 cm, 1 cm, 1.5 cm, and 2 cm from the center, 180 degrees from the original direction, towards the elbow. Again, the participant was asked to rate the pain felt after each pinprick using the 0 - 10 scale.

After completion of all procedures for the first test site, a second test site was irradiated on the opposite forearm. The appropriate test solution or patch was applied. After 10 minutes of application, the same testing procedures were followed as outlined for the 5 minute site. After both sites were tested, Aquaphor Healing Ointment® (petrolatum) and a Band-Aid® were applied over each site. All participants were interviewed by telephone or in person within 48 hours after the needle-sticks to score any edema or erythema (on a 5 point scale of “none”, “mild”, “moderate”, “severe” and “extremely severe”) and to verify the absence of any other unforeseen complications. (Figure 2)

Figure 2

Figure 2: Flowchart of Procedures



RESULTS

The majority (86%) of the participants described the sensation of the laser ablation as non painful (i.e., “puff of air”, “no sensation”). Fourteen percent described the sensation as a “pinch”, “poke” or “sting”. Statistical analyses using Student's t-test showed no differences ($p<0.05$) in pain scores based on the concentration of the lidocaine (4% vs. 10%) or the duration it was on the skin (5 minutes vs. 10 minutes). A multiple comparison of the average pain scores was done, in each of the four treatment groups of the study, using a Kruskal-Wallis Z-value test.(Table 1) It was determined that there were significantly ($p<0.05$) lower pain scores between the ablation sites and the average of the control sites.

Figure 3

Table 1: Mean (Stand Deviation) Pain Reports

		4% Lidocaine (Lidokain®) Patch		10% Lidocaine (Xylocaine®)	
		5 minutes	10 minutes	5 minutes	10 minutes
(toward wrist)	2.0 cm	5.1 (2.9)	4.8 (2.9)	5.8 (2.6)	5.1 (2.6)
	1.5 cm	4.9 (3.0)	4.6 (2.5)	5.4 (2.9)	5.0 (2.7)
	1.0 cm	4.6 (2.7)	5.0 (3.2)	5.0 (2.8)	4.4 (2.4)
	0.5 cm	4.2 (2.7)	3.9 (2.5)	3.8 (2.7)	4.0 (2.3)
	Ablation	1.7 (2.1)	1.3 (1.9)	1.8 (2.4)	2.1 (2.4)
(toward elbow)	0.5 cm	4.8 (3.0)	4.0 (2.8)	4.7 (2.6)	4.9 (3.1)
	1.0 cm	5.5 (2.9)	4.7 (2.7)	4.9 (2.8)	4.5 (2.6)
	1.5 cm	5.4 (2.9)	5.4 (2.7)	5.0 (2.7)	4.9 (2.8)
	2.0 cm	5.5 (3.1)	4.7 (2.7)	5.5 (2.7)	5.1 (3.0)
	Control	4.2 (2.9)	4.3 (3.2)	4.8 (3.0)	3.9 (3.0)

This study does not provide any evidence of a clinically useful amount of lidocaine diffusing laterally from the ablation site.

Only one participant reported mild edema at the ablation site at 48 hours. This resolved without complication. No other problems were noted at the ablation site.

DISCUSSION

There has been a considerable amount of effort expended over the past several years to identify methods of decreasing the pain associated with superficial procedures, including needle-sticks. Currently used techniques include superficial injection of local anesthetic, use of iontophoresis to facilitate absorption across the skin, and application of EMLA cream. All can be quite effective, but the use may be limited by such issues as duration of application required, pain of injection, or discomfort associated with electrical stimulation. In addition, disposal of sharps continues to carry significant infection risk. In light of these issues, there remains a need for a needle-less method to provide effective topical anesthesia with a quick onset and without associated discomfort.

Previous studies have shown that removal or alteration of the stratum corneum can increase the absorption of local anesthetics into the skin.[15,17] The use of the Er:YAG laser to ablate the stratum corneum is one method that may prove very useful. Early studies have suggested that the laser can ablate the stratum corneum without permanent damage to the skin.[18,19] The results of our study suggest that the transdermal administration of topically applied lidocaine is enhanced and topical anesthesia is produced at the site of stratum corneum ablation within 5 minutes. The ablation of the stratum corneum with the 2.94 micron wavelength radiant energy produced by an Er:YAG laser was associated with minimal discomfort and resulted in no immediate adverse effects.

As with many pain related investigations, it was somewhat difficult to determine the influence of personal experience on the pain report in our study. For instance, one participant reported almost every pain stimulus as being a 10. Although the participants were instructed in the use of the 0 –10 scale prior to the study procedures, the meaning of a 10 seemed to be absolute for some subjects and relative for others.

Another limitation of the study may have been the manner in which the control was handled and the lack of blinding. All participants knew they would have pin-pricks at both a site they had local anesthetic applied and at an untreated site. The control site was not disguised in any way and was tested first. This may have led to a certain amount of anticipatory influence on pain ratings. There could also be concern about whether the ablation itself produces some anesthetic effect. The decision to not test an “ablation only” site was based on early experience of the laser developers that suggested certain preparations of lidocaine (e.g. 2% in a wax base) applied to the ablation site produced no significant anesthetic effect. From this information, we extrapolated that ablation of the stratum corneum likely produces no significant anesthetic effect and we felt that an ablation only site would not have added information to this preliminary study. Finally, there may have been some gender bias since the majority of the subjects were female. No effort was made to equalize the number of males vs. females in this study.

The intention of this study was to test the concept of producing rapid, local anesthesia by topically applying lidocaine to skin where the stratum corneum has been ablated by the radiant energy produced by an Er:YAG laser. Although the concept seems to be feasible, no dramatic conclusions can be drawn as of yet. There are likely other formulations of local anesthetics that will be much more effective with this form of administration than the preparations used in this study. In addition, other stimuli (IV placement, IM injection) will need to be tested to assess the effectiveness of this method of producing topical anesthesia in other clinical situations. Nonetheless, this study has shown that it is possible to obtain rapid local anesthesia with topical lidocaine after treating the skin with the radiant energy produced by an Er:YAG laser. Given the documented desire of patients for relieving the pain associated with needle-sticks, further investigations should be performed to determine the clinical utility of this technique

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