Original Article

Randomized, double-blind controlled topical anesthesia induced by iontophoresis of lidocaine

Authors:
Juliano Vilaverde Schmitt[1]
Hélio Amante Miot[2]

[1]Specialist - Dermatologist - Fundação Pró-Hansen
[2]Doctor - Assistant Professor - Department of Dermatology at FMB-Unesp

Correspondence to:
Juliano Vilaverde Schmitt
Rua Fernando Amaro, 1116
Bairro Cristo Rei Curitiba - PR
CEP 80050-020

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ABSTRACT

Introduction: Needle infiltration of local anesthetic is a painful procedure, thus, a topical anesthetic is a comfortable alternative. However, it is difficult to deliver transcutaneous polar drugs. Iontophoresis is a noninvasive technique that uses electrical current for releasing electrically charged drugs through biological membranes. **Objective:** To evaluate the anesthesia induced by iontophoresis of lidocaine for a standardized painful stimulus. **Material and methods:** Randomized, controlled, double-blind study, involving 10 volunteers under the anesthetic effects of topical application of lidocaine gel 2% and noradrenaline 1:50.000, with or without iontophoresis of 1.85 milliamps for 13 minutes. Pain sensitivity was evaluated by the prick of a 21G needle in the arms posterior region, using a visual numerical scale. **Results:** Patients mean age was 50.8 ± 11.4 years. Nine of them were women. All had previously received infiltrative anesthesia. Iontophoresis was well tolerated by volunteers. The median pain scores were 0 and 3 for the arm that received the iontophoresis and for the one that did not receive, respectively ($p < 0.01$). **Conclusion:** The anesthetic effect in the region subjected to iontophoresis suggests an efficient and comfortable method for promoting local anesthesia in the surgical approach of pediatric, hyperalgic, or needle-phobic patients.

Keywords: anesthesia, lidocaine, ambulatory surgery, iontophoresis.

INTRODUCTION

Application of local anesthetic is often painful, with topical anesthetic being a painless option. EMLA (eutectic mixture of local anesthetics) is the topical anesthetic most studied and effective in relieving pain in superficial procedures.[1-7]

Unfortunately, EMLA should be applied at least one hour before the procedure to cause effective anesthesia.[8,9] This occurs because the cutaneous administration of charged drugs, such as local anesthetics, is particularly difficult.[10]

Under normal conditions, the transdermal penetration of drugs is limited to a few molecules, which should be powerful, small and slightly lipophilic.

Iontophoresis is a noninvasive technique, based on the application of an electric current of low intensity to facilitate the release of a variety of drugs, charged or not, through biological membranes (Figure 1).[11]

This study aimed to compare the anesthetic effect of topical lidocaine gel with and without the addition of a controlled electric current.

MATERIAL AND METHODS

The study was designed according to the premises of a randomized, controlled, double-blind trial involving 10 patients of both genders, eligible among patients referred for ambulatory surgical procedures at the Fundação Pro-Hansen, located in Curitiba, which serves patients in general dermatology and leprosy from the public health system.

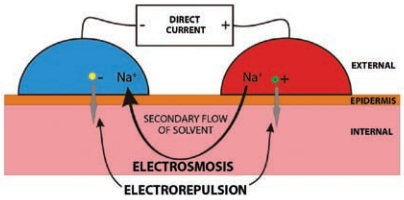

Figure 1 – Basic principles of iontophoresis. . Iontophoresis is processed by two main principles: electrorepulsion and electrosmosis.

Patients excluded from the sample were those with pacemakers, who reported allergy to any component of the gel used, or presented sensitivity changes, or any dermatosis on the posterior region of the arms (Figure 2).

The electric current was applied by means of non-commercial devices developed for this purpose, which produces controlled electric current of approximately 1.85 mA (Figure 3).

The electrodes were filled with hydrophilic gel formulated by adding 0.75% of carboxymethylcellulose to a solution of 2% lidocaine and noradrenaline 1:50.000, and fixed on the back of the arms. One arm received the gel with the electric current and the other only the gel. Randomization of the arms that receive the electrical current was performed by a software random number generator.

For statistical analysis of pain scores, we used the nonparametric Wilcoxon test, considering significant $p < 0.05$.

Participants underwent a painful stimulus applied by a blind investigator through a prick of a 21G needle, after performing the above procedure. Immediately after, patients were asked about the intensity of pain using a Visual Numerical Scale (VNS), internationally validated, ranging from zero (no pain) to 10 (worst imaginable pain).[12]

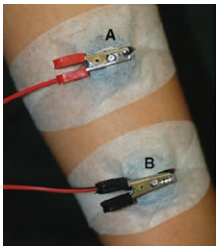

Figure 2 – Iontophoresis of lidocaine. Standardization of electrode placement for the experiment: a) positive electrode, b) negative electrode.

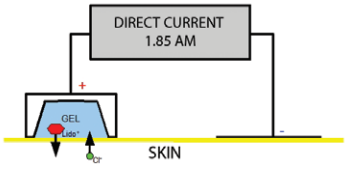

Figure 3 – Schematic diagram of ontophoresis device.

RESULTS

The average age of patients was 50.8 ± 11.4 years. Nine were women and one was man. All patients have received at least one infiltrative anesthesia. The median pain scores were 0 and 3 for the arm that received the electrical current and the arm that did not received it, respectively (Graph 1). The difference between the scores was considered significant ($p < 0.01$ - Wilcoxon).

Half of the patients reported mild burning, while 20% reported mild pruritus, both transitory. Even so, when asked about the convenience of the procedure, 40% patients considered it little uncomfortable, and 60% not at all uncomfortable.

There was no evidence of cutaneous changes resulting from the process.

DISCUSSION

The application of a weak electrical current to transfer charged substances through biological membranes, i.e., iontophoresis, is not a new technique. It was first described by Veratti in 1748, and has been modified over the years according to the needs and technological capacity.[13]

Iontophoresis of lidocaine facilitates the transport of these molecules into the skin under the influence of an electric current. It can promote topical anesthesia of intact skin in 5 to 15 minutes. This technique was effective in reducing pain associated with venous cannulation, curettage, biopsy by shaving or punch in children and adults, and it was better than EMLA in a comparative study. Another study that evaluated iontophoreis of lidocaine concluded that it was not a effective technique.[14-16] Similarly, lidocaine serum levels after the procedure were not significant, showing the local transport of the drug.[17]

It was also found that the combination of adrenaline at a concentration of 1:160,000, or more, with 2% lidocaine increased iontophoresis anesthetic efficacy.[18] In 2007, a patch with lidocaine and epinephrine for use with iontophoresis equipment was released by the Food and Drug Administration (FDA) in the U.S. for local treatment of pain.[19]

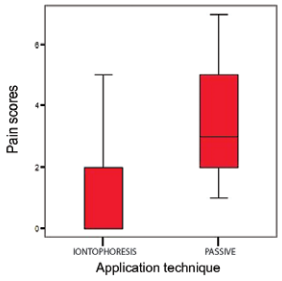

Gráfico 1 – Pain scores in arms undergoing iontophoresis or at off electrode (Wilcoxon, $p < 0.01$).

The present study demonstrated that the process of iontophoresis was well tolerated and produced effective anesthesia over a relatively short time, if compared with the time required for the action of other anesthetic skin creams available in our practice. Some patients reported mild burning or itching at the beginning of the process, which can be controlled by reducing the applied electrical current.

The main limitation of our study might be related to the small sample size. However, as the difference in scores had great magnitude, with high statistical significance, it is considered satisfactory for this study.

Due to the anesthetic efficacy demonstrated by the study, we conducted two punch biopsies followed by suture using only anesthesia by iontophoresis of lidocaine. The first patient underwent a biopsy of the right forearm, and the second, on the left leg, both of which required no additional infiltration of anesthesia.

Although this is not a new technique, the application of topical anesthesia by iontophoresis for dermatologic surgery is not widespread in our country, and we did not find similar studies in the indexed literature.

The anesthetic effect in the region subjected to iontophoresis suggests an efficient, safe, well tolerated, and comfortable way to promote local non-invasive anesthesia, supporting the surgical approach of pediatric, hyperalgic, needle-phobia patients.

The technique of iontophoresis may also be promising in the release of other medications of dermatological interest such as botulinum toxin, steroids, vitamin C, and lighteners in the treatment of melasma, or antifungal for the treatment of onychomycosis.[19-22]

Subsequent controlled trials should compare the effectiveness of topical anesthesia induced by iontophoresis with the standard forms infiltration, topical, cryoanesthesia and other modalities, such as sonophoresis induced by ultrasound.[23]

Further studies should be performed with greater samples, stratified by gender, age, topography, and dermatological indication, as well as different schemes of iontophoresis on the current intensity, application time, concentration and vehicle of different anesthetic drugs to understand the potential indications of topical anesthesia induced by iontophoresis in dermatological surgery.

CONCLUSION

An anesthetic effect was observed with the application of topical lidocaine gel with adrenaline induced by iontophoresis.

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