

Original Article

Comparing the pain ratings of two topical lidocaine preparations

Estudo comparativo entre escores de dor após uso de duas preparações de lidocaína tópica

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ABSTRACT

Introdução: The increase in the demand for cosmetic procedures has in turn stimulated the search for effective and safe analgesia. Topical anesthetics are an alternative to infiltrative anesthesia, and promote an appropriate analgesia without inducing adverse effects.

Objective: To compare the pain ratings of two topical lidocaine formulations in patients undergoing fractional CO₂ laser therapy.

Methods: Eight patients underwent a single fractional CO₂ laser session after applying a commercial formulation of 4% lidocaine on the right side of the face and a dispensed 30% lidocaine formulation combined with 7% tetracaine on the left side of the face. The intensity of the pain was assessed using the visual analogue pain intensity scale at the end of the procedure.

Results: No significant statistical differences were detected between the formulations.

Conclusions: Formulations with high concentrations of anesthetics are not more effective than commercial products in producing analgesia.

Keywords: anesthetics; anesthesia and analgesia; lasers.

RESUMO

Introdução: Os procedimentos cosmiátricos têm aumentado, e com eles, a busca de analgesia eficiente e segura. Os anestésicos tópicos são opção às anestésias infiltrativas, devendo promover analgesia adequada e atuar na pele íntegra, sem induzir efeitos adversos.

Objetivo: Comparar os escores de dor entre duas formulações tópicas de lidocaína, em pacientes submetidos à terapia com laser fracionado de CO₂.

Métodos: Oito pacientes foram submetidos a uma sessão de laser de CO₂ fracionado, após a aplicação de formulação industrializada de lidocaína 4% na hemiface direita e formulação magistral de lidocaína 30% associada à tetracaina 7% na hemiface esquerda. A intensidade da dor foi avaliada através da escala visual analógica de dor (EVA) no final do procedimento.

Resultados: Os anestésicos tópicos, nas formulações magistral e industrializada, não apresentaram diferença estatisticamente significativa na avaliação dos escores de dor. **Conclusões:** Os dados sugerem que fórmulas com grande concentração de anestésicos não são mais eficientes em produzir analgesia do que as formulações industrializadas.

Palavras-chave: anestesia; anestesia e analgesia; lasers.

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INTRODUCTION

The recent growth in demand for cosmetic and surgical procedures has stimulated the search for efficient, fast, safe and painless analgesia. In this context, topical anesthetics are increasingly considered an alternative to infiltrative anesthetics.^{1,2}

An ideal topical anesthetic promotes the appropriate amount of anesthesia in a short period of time, acting on healthy skin without inducing systemic or topical adverse effects or discomfort. These pharmacologic properties are partially achieved using commercially-available eutectic and liposomed preparations.³

On the other hand, the increased risk of side effects resulting from dispensed formulations containing high concentrations of anesthetics (from the ester and amide groups) is often underestimated; they are widely used in cosmetic procedures due to their greater anesthetic effect.¹

Therefore, these substances and their pharmaceutical preparations should be studied – their diffusion and percutaneous distribution capacity in particular – which is a challenge in the field of pharmaceuticals and an opportunity for achievement in dermatologic surgery.¹

The CO₂ laser's action mechanism is based on heat production, and its application is a painful procedure that generates discomfort for the patient. The objective of this study, which was conducted in compliance with the Declaration of Helsinki's ethical principles, was to evaluate the effects of two topical dispensed lidocaine preparations, comparing pain scores in patients who underwent treatment with fractional CO₂ laser.^{4,5}

METHODS

This pilot split study compared two formulations in eight patients with acne scars or photoaging from the Instituto Lauro de Souza Lima's Dermatology Department. The 7 women and 1 man, aged 20–70 (average 41.3 years), were treated with a single session of fractional CO₂ laser (Pixel CO₂®, Alma lasers, Caesarea, Israel). The energy level ranged from 16 to 27 watts, and 3 to 5

passes were applied. At least 30 minutes before the procedure, the patients received a commercial preparation of 4% lidocaine (Dermomax®, Aché laboratórios farmacêuticos, São Paulo, Brazil) on the right side of the face and a dispensed formulation of 30% lidocaine combined with 7% tetracaine on the left side of the face. In order to avoid bias, that information was not disclosed to the patients. Although the laser parameters used varied among patients according to their individual characteristics and proposed treatment, they were kept consistent for each patient. Patients rated pain intensity separately for each side of the face using the visual analogue pain intensity scale (VAS), from 0 (no pain) to 10 (maximum pain). The mean value and standard deviation were computed for the scores obtained with the patients treated with the commercial (A) and dispensed (B) formulations. The effects of the two treatments were compared using the Wilcoxon paired t-test ($p < 0.05$).

RESULTS

Statistical analyses demonstrated that the topical anesthetics, both the dispensed and commercial preparations, did not present significant differences on the pain induced by fractional CO₂ laser therapy on the right and left sides of the face, respectively (Table 1).

DISCUSSION

The fractional CO₂ laser is an ablative laser type that is proven to be efficient in the treatment of acne scars and photoaging. Among the possible undesirable effects of the procedure, pain has always been a limiting factor. The decrease in pain associated with the advent of fractional technology allowed procedures that previously required infiltrative anesthesia, blockings and sedation to be carried out with topical anesthetics.^{4,5}

These agents act in dermal nerve endings to promote cutaneous analgesia, however their chemical features and the horny layer's structure limit the efficacy of topical anesthetics. Eutectic

Table 1: Evaluation of two topical lidocaine preparations by pain scores*, in the right (A) and left (B) sides of the face of patients after CO₂ laser therapy

Patients	Commercial formulation (A)	Dispensed formulation (B)
1	7	4
2	2	3
3	5	5
4	1	6
5	5	8
6	3	7
7	8	9
8	2	6
Mean	4.125	6.0
Standard deviation	2.532	2.0

* Visual analogue pain intensity scale ($p = 0.0781$)

blends were developed in order to minimize the factors that limit the penetration and effectiveness of topical anesthetics; anesthetic agents were incorporated into films, and the active principles were contained in liposomal membranes. Liposomes are synthetic biological membranes composed of lipidic layers of phosphatidylcholine, cholesterol and electrolytes that involve aqueous layers. These formulations facilitate the anesthetic's diffusion in the skin: they carry the encapsulated substance to the dermis, protect the anesthetic from metabolic degradation, promote its gradual liberation and extend the duration of their effects.^{1,6,7}

Analgesia results from the local anesthetic's interaction with the nerve endings' sodium channels, blocking its influx. This increases the excitation threshold, thus gradually reducing the activation of the action potential and transmission of the nervous pulse. In order for these events to take place, the local anesthetics must diffuse through the horny layer down to the interior of the nerve fibers. An anesthetic's diffusion capacity, potency, pharmacokinetic features and adverse events are intrinsically related its chemical structure and physiochemical properties.^{1,2}

Chemically, local anesthetic molecules are formed by an aromatic portion, an intermediate chain and a terminal amines functional group. The aromatic portion is responsible for liposolubility and tissular diffusion. The intermediate chain can be constituted by an ester group, which is biotransformed in the plasma by plasmatic esterases or by an amides group, biotransformed by microsomal hepatic enzymes. In the terminal portion of the chain there is an amines functional group that induces the blocking of the voltage-dependent sodium channels.^{1,2,8}

Adverse events depend mainly on the agents' chemical structure and concentration. Currently, it is known that local anesthetics can unchain allergic reactions of types I (immediate hypersensitivity) and IV (contact dermatitis). Anesthetics of the amida type (lidocaine and prilocaine, among others), rarely cause reactions, however they can unchain these two types of hypersensitivity.^{8,9} Those of the ester type (for instance procaine and tetracaine) cause allergic reactions more frequently, usually from type IV. Regarding the concentration, the majority of adverse events result from direct toxic reactions in the cardiovascular and central nervous system, caused by excessive injected doses or high concentrations applied on large areas of the body, fast systemic absorption or when accidentally administered inside a blood vessel. These reactions include unrest, paresthesias, metallic taste, nausea, vomiting, disorientation, tremors, unconsciousness, A-V block, bradycardia and convulsions, and can develop into respiratory depression, coma, arterial hypotension, cardiac failure and death.³

In this study we compared the effectiveness in the control of pain using an industrialized commercial formulation and a dispensed (higher concentration) formulation. Taking into consideration the scores' mean value and standard deviation, there was no significant difference between the pain on the right and left sides of the face, induced by laser therapy. This finding alone is sufficient to question the need for manipulated formulations containing high concentrations of anesthetics, which expose patients to greater risks of adverse effects.

On the other hand, when comparing pain scores in the same patient, it was observed that only one patient presented a lower score on the side of the face treated with dispensed lidocaine, while another presented a score similar to that obtained with the application of the commercial product, meaning that 6 out of 8 patients perceived the pain as more intense on the side of the face treated with the dispensed formulation. In this manner, while partial, these outcomes suggest that commercial pharmaceutical preparations are more effective in relieving pain. Due to the smaller concentration of the anesthetic in the commercial formulation, we can also assume there is a lower risk of adverse effects, especially when treating large areas of the body.

It is worth noting that the differences in the intensity of pain described by the patients are due to some factors such as the differences in the used power, the number of passes, and individual sensitivity. The results also point towards the need to increase the number of subjects in order to clarify the effectiveness of dispensed anesthetic agents and evaluate the costs, risks and benefits of these preparations. Controlled and randomized studies involving dispensed preparations are needed to validate good dispensing practices and inform the makers of the formulations.

CONCLUSION

The data suggest that dispensed formulations with great concentrations of anesthetics are not more efficient than commercial products in producing analgesia. ●

REFERÊNCIAS

1. Monteiro EO. Anestésicos tópicos. *Rev Bras Med.* 2008; 65(n. esp): 12-18.
2. Froes GC, Otoni FA, Gontijo G. Anestésicos Tópicos. *Surg Cosmet Dermatol.* 2010; 2(2) 111-16.
3. Carvalho JCA, Mathias RS. Anestésicos locais. In: Manica JT, 2 ed. *Anestesiologia. Princípios e técnicas.* Porto Alegre: Artmed; 1997. p.332-39.
4. Matić M, Lazetić B, Poljacki M, Duran V, Ivkov-Simić M. Low level laser irradiation and its effect on repair processes in the skin. *Med Pregl.* 2003;56(3-4):137-41.
5. Murison MS, Tucker SC. Providing pain relief for laser resurfacing: effectiveness of the CoolAnalgesia device. *J Plast Reconstr Aesthet Surg.* 2007;60(4):432-6.
6. Frankel E; Trumbore MW. Reduction in procedure-associated pain by treatment with a unique topical anesthetic foam containing 4% lidocaine. *J Clin Aesthet Dermatol.* 2009; 3(12):43-49.
7. Chorny M, Levy RJ. Site-specific analgesia with sustained release liposomes. *Proc Natl Acad Sci U S A.* 2009;106(17):6891-2.
8. Catterall W, Makie K. Local anaesthetics. In: Goodman & Gilman's Editors. *The pharmacological basis of therapeutics.* 10th. New York: McGraw-Hill; 2001. p. 367-84.
9. Friedman PM, Mafong EA, Friedman ES, Geronemus RG. Topical anesthetics : EMLA and beyond. *Dermatol Surg.* 2001;27(12):1019-26.