

Topical Anesthetic Effect of EMLA and Iranian Products in Preventing Pain During Intravenous Blood Sampling Procedures: A Double-Blind Randomized Clinical Trial

Fariba Jaffary¹; Mohammad Ali Nilforoushzadeh^{1,2,*}; Parviz Toossi³; Hajar Zarkoob²; Foroud Shahbazi⁴

¹Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

²Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran

³Skin Research Center, Shahid-Beheshti University of Medical Sciences, Tehran, Iran

⁴School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

*Corresponding author: Mohammad Ali Nilforoushzadeh, Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-9133137166, Fax: +98-2122201710, E-mail: sdllrc@mui.ac.ir

Received: November 22, 2013; **Revised:** December 23, 2013; **Accepted:** April 5, 2014

Background: The patients' concerns about injection pain can cause some unwanted adverse reactions such as hypotension, vasovagal shock, syncope, and unconsciousness. Therefore, using a skin anesthetic can facilitate performing many medical procedures.

Objectives: This double-blind randomized clinical trial was designed to compare the anesthetic effect of topical EMLA 5% cream with Iranian lidocaine 5% and benzocaine 5% creams.

Patients and Methods: Sixty-four healthy volunteers were randomly allocated into two groups. In each individual, EMLA cream and one of Iranian topical anesthetic products, namely lidocaine 5% and benzocaine 5%, were tested. One hour before blood sampling, a predetermined amount of A or B cream was used on the right cubital fossa and the same amount of C or D cream on the left cubital fossa. Blood sampling was done via cubital fossa veins with a 2 cc syringe. The pain of blood sampling was recorded using visual analogue scale (VAS). Data were analyzed by student t-test and ANOVA using SPSS version 11.

Results: At the end of study, the EMLA products (A and B) caused a significant decrease in pain ($P < 0.05$) in comparison with the products C (lidocaine) and D (benzocaine) while there was no differences between benzocaine and lidocaine. In this study, no significant side effect was observed.

Conclusions: Although the results of this study showed superiority of application of EMLA cream as a topical anesthetic for pain relief of blood sampling, both lidocaine 5% and benzocaine 5% offer considerable efficacy in pain relief of venipuncture.

Keywords: Pain Management; EMLA; Anesthetics, Topical

1. Background

Pain management facilitates accomplishment of many medical procedures like blood sampling and injections particularly for children vaccination and laser hair removal. Fixing intravenous catheters in patients causes anxiety and leads to some reactions like hypotension, vasovagal shock, syncope, and unconsciousness. Patient anxiety and fear of injection lead to some problems for nurses; therefore, pain reduction is very important to them. If the pain of venous blood sampling reduces, success rate will be greater, the blood vessels will be damaged less frequently, and access to other vessels will be more possible. Various treatment methods and strategies have been suggested for pain reduction including injection treatments, topical treatments, and iontophoresis

among which the topical treatment is a more tolerable one (1, 2). EMLA 5% cream (1:1 mixture of benzocaine and lidocaine) is a eutectic mixture; it means that melting point of the two agents reduces when mix with each other. Consequently, they will form a eutectic liquid at the temperatures higher than 16-17°C. This makes a concentration gradient on the skin that facilitates the absorption. EMLA cream is widely used for painful processes like curettage, laser therapy of vascular lesions, skin biopsy, phimosis, shock wave lithotripsy (SWL), and cryotherapy of oral ulcers (3-6). In Iran, lidocaine is usually used for topical anesthesia.

2. Objectives

The aim of this study was to compare the efficacy and

Implication for health policy/practice/research/medical education:

The fear and stress caused by injection, particularly intralesional injection that is an effective treatment method in most skin diseases, is still one of the challenges of this method. It seems that using topical EMLA 5% cream before injection can be an effective product for reducing injection pain in contrast to the other products.

Copyright; Skin and Stem Cell Research Center, published by Kowsar Corp. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

side effects of two Iranian topical anesthetic products, namely lidocaine 5% and benzocaine 5%, with EMLA 5% cream as the standard product in prevention of the pain during venous blood sampling.

3. Patients and Methods

In this double-blind randomized clinical trial, 64 healthy volunteers were recruited and randomly assigned to receive either A or B topical creams on their right cubital fossa. Moreover, they were randomly assigned to receive either C or D creams on their left cubital fossa; therefore, there were two groups each comprised 32 individuals. One centimeter of assigned cream was applied on the cubital fossa. In order to prevent differences and variations in the results, all the blood sampling were taken by one nurse from the cubital fossa veins with 2 cc syringe and blue needles (SUPA Inc, Iran). The pain intensity was recorded by the patients using visual analogue scale (VAS) method. In this scale, the scores of zero and ten stand for painless state and the most painful feeling, respectively (1). Products encoding was done by the administrator and the person who took the samples and the volunteers were not aware of the type of applied products. Any local skin reaction like erythema, edema, or irritation were recorded. The data analysis was performed employing SPSS version 11 (SPSS Inc., Chicago, Illinois, USA) using student's t test and ANOVA. After decoding the study medications, it was revealed that A and B creams were EMLA cream while C and D were lidocaine and benzocaine creams, respectively.

4. Results

Sex distribution and mean age indicated that 46 males and 18 females with the mean age of 35.7 ± 17.2 years old participated in this study. In this study, EMLA 5% cream was applied on right cubital fossa of 64 volunteers and lidocaine 5% and benzocaine 5% creams each were applied on the left cubital fossa of 32 participants before blood sampling. The comparison of pain intensity differences in the three groups was based on the 10-unit observational pain scale. It indicated that pain intensity after using EMLA 5% cream was significantly less than after using the two other products (Table 1). No significant difference was observed between pain intensity between lidocaine 5% and benzocaine 5% creams ($P = 0.66$). In addition,

there was no hypersensitivity reactions or any other side effects after using these products on the injection area.

5. Discussion

The fear and stress caused by injection particularly intralesional injection, which is an effective treatment method in most skin diseases, is still one of the challenges of this method (1). In this research, applying topical EMLA 5% cream before injection resulted in significantly more pain reduction in comparison to lidocaine 5% and benzocaine 5% creams. There was no difference between pain intensity after applying topical lidocaine 5% and benzocaine 5% creams. Although most of the studies indicate a significant pain management after using EMLA 5% cream in contrast to placebo, study results of applying EMLA cream in comparison with other anesthetic creams were contradictory. EMLA cream had more, less, or equal effects on the pain relief in comparison with lidocaine cream; in cases in which topical liposomal lidocaine was applied, lidocaine showed more analgesic effects than EMLA cream (7). It seems that particle size has a determinant role in effectiveness of this topical cream. EMLA cream showed significant effects in pain reduction before dentistry interventions (8). EMLA cream had also made a significant reduction in the intensity of prostate biopsy pain in comparison with lidocaine cream and placebo (9). Using EMLA cream to reduce the pain caused by intralesional injection for alopecia areata (30, 45, and 60 min before injection) showed a significant effect in 85% of the cases in comparison with injection in lesions without using EMLA. It seemed that delayed injection would be more effective during EMLA cream application (10). However, the results of the mentioned study might need some considerations due to small sample size (27 cases). Time is an important constrain in achieving anesthetic effect of EMLA. The patients usually gain the advantages of EMLA 60 min after application; however, 90-minute interval is required for the maximum effectiveness (5, 6, 11). On the other hand, the analgesic effect was seen after 5 min (1). Moreover, the results of a meta-analysis showed that EMLA cream had a significant effect in pain reduction caused by venipuncture in comparison with placebo. It seems that 85% of individuals who used this product before venipuncture enjoyed its benefits. The other advantage of this drug that might be exclusive and unique among other topical anesthetic drugs is its safety

Table 1. Comparison of Pain Intensity in the Three Treatment Groups ^a

	Number of Patients	Pain Intensity	95% Confidence Interval	P Value
EMLA 5%	64	1.7 ± 1.62	1.18-2.06	< 0.05
Lidocaine 5%	32	2.26 ± 1.57	1.67-2.85	
Benzocaine 5%	32	2.5 ± 1.74	1.89-3.10	

^a Data are presented in Mean ± SD.

for using in children even in premature infants (4, 11, 12). The results of the study by Rosa et al. was similar to the current study with regard to the lidocaine and benzocaine cream use in relieving injection pain in comparison with placebo (13). It seems that formation of eutectic liquid and consequently creating concentration gradients is the reason of faster effectiveness of EMLA in comparison with lidocaine and benzocaine topical creams. Although met-hemoglobinemia is a potential concern of using this cream and met-hemoglobin level of the serum in EMLA users was higher than in placebo users (approximately 5% to 6%), there was no sign of met-hemoglobinemia in this concentration range. In addition, met-hemoglobinemia is not common and usually does not occur in low doses and short-term use (14). In the current study, no special side effects were seen. Based on this research, it seems that EMLA cream can be recommended as an effective product in reducing venipuncture pain in comparison to the other two products. Producing domestic products similar to EMLA cream and comparison of their efficacy is advocated. Moreover, cost-effectiveness of EMLA should be compared with lidocaine and benzocaine creams in order to make the correct decision.

Acknowledgements

This article was the result of the research project no. P/T/M 811 approved by Skin Research Center of Shahid-Beheshti University of Medical Sciences, Tehran, Iran. We also appreciate the personnel of School of Pharmacy Dr Roya Derakhshan, Dr Nazli Ansari, and Dr Hossein Najafzadeh for their collaboration in accomplishing this project.

Authors' Contribution

All authors had participated equally in this study.

Financial Disclosure

There was no financial disclosure for the research.

Funding/Support

There was no funding support for the research.

References

1. Smith MS, Holder PG, Leonard K. Efficacy Of A Five-minute Application Of EMLA Cream For The Management Of Pain. *Int J Anesthesiol.* 2002;**6**(1).
2. Rogers TL, Ostrow CL. The use of EMLA cream to decrease venipuncture pain in children. *J Pediatr Nurs.* 2004;**19**(1):33-9.
3. Upadya M, Upadya GM. Anesthesia for dermatological surgery. *Indian J Dermatol Venereol Leprol.* 2005;**71**(3):145-54.
4. Anonymous.. *EMLA cream and patch monograph.* Mississauga: Astra Zeneca Canada INC; 2006.
5. Liu J, Zang YJ. Comparative study between three analgesic agents for the pain management during extracorporeal shock wave lithotripsy. *Urol J.* 2013;**10**(3):942-5.
6. Bach Ct, Zaman F, Kachrilas S, Kumar P, Buchholz N, Masood J. Drugs for Pain Management in Shock Wave Lithotripsy. *Pain Res Treat.* 2011.
7. Zempsky WT. Pharmacologic approaches for reducing venous access pain in children. *Pediatric.* 2008;**122**(Supplement 3):S140-53.
8. Lim S, Julliard K. Evaluating the efficacy of EMLA topical anesthetic in sealant placement with rubber dam. *Pediatr Dent.* 2004;**26**(6):497-500.
9. Galosi AB, Minardi D, Dell'atti L, Yehia M, Muzzonigro G. Tolerability of prostate transrectal biopsies using gel and local anesthetics: results of a randomized clinical trial. *J Endourol.* 2005;**19**(6):738-43.
10. Mosavi ZB. Iranian Journal of Dermatology. Effect of EMLA cream in reducing pain in intralesional corticosteroid alopecia. *Yeah Ata.* 1999;**3**:31-4.
11. Schechter NL, Zempsky WT, Cohen LL, McGrath PJ, McMurtry CM, Bright NS. Pain reduction during pediatric immunizations: evidence-based review and recommendations. *Pediatric.* 2007;**119**(5):e1184-98.
12. Ferrante P, Cuttini M, Zangardi T, Tomasello C, Messi G, Pirozzi N, et al. Pain management policies and practices in pediatric emergency care: a nationwide survey of Italian hospitals. *BMC Pediatr.* 2013;**13**:139.
13. Rosa AL, Sverzut CE, Xavier SP, Lavrador MA. Clinical effectiveness of lidocaine and benzocaine for topical anesthesia. *Anesth Prog.* 1999;**46**(3):97-9.
14. Weise KL, Nahata MC. EMLA for painful procedures in infants. *J Pediatr Health Care.* 2005;**19**(1):42-7.