

*Original Article***Comparative Study on Clinical Efficacy of Topical Anesthetic Dermal Products in Iran and its Foreign Standard Cream, EMLA 5%, in Pain Management of Intravenous Blood Sampling on Healthy Volunteers**

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Abstract

Background: Using a skin anesthetic can facilitate doing many medical procedures. In this double-blind randomized clinical trial, the anesthetic effect of EMLA cream was evaluated in comparison with lidocaine 5% and benzocaine 5%.

Methods: Sixty four healthy volunteers were randomly divided into four groups. One hour before blood sampling, a certain amount of A or B cream was used on the right cubital area and the same amount of C or D cream on the left cubital area. Blood sampling was done via cubital vein with a 2 cc syringe. The pain of blood sampling was recorded using Visual Analogue Scale (VAS).

Results: At the end of study, after opening the codes, 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 the current study, no special side effect was observed.

Conclusion: The results showed that using EMLA cream as a local anesthetic is superior to lidocaine 5% and benzocaine 5% for pain relief of healthy people blood sampling.

Key words: Pain management, Intravenous blood sampling, EMLA, Topical local anesthetic.

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Pain management facilitates accomplishment of many medical measures like blood sampling and injections, particularly for pediatric vaccination and unwanted 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 for them. If the pain of venous blood sampling reduces, it will have a greater success

rate, 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 like injection treatments, topical treatments and iontophoresis among which the topical treatment is a more tolerable one for the patients.^{1,2} One of the mentioned strategies EMLA cream 5% (1:1 mixture of benzocaine and lidocaine) is an eutectic mixture; it means that melting point of the two agents reduces when mix with each other. Consequently, they will form

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an eutectic liquid at a temperature higher than 16 to 17°C. This makes a concentration gradient on the skin that can facilitate the absorption. EMLA cream is widely used for painful processes like curettage, laser therapy of vascular ulcers, skin biopsy and cryotherapy of oral ulcers.^{3,4} In Iran, lidocaine is usually used for local anesthesia. In current study, it was decided to compare the efficacy and side effects of these two local domestically manufactured anesthetic products (lidocaine 5% and benzocaine 5%) with EMLA cream 5%, as a standard product, in removing the pain of venous blood sampling.

Methods

In this double-blind randomized clinical trial 64 healthy volunteers were recruited. Randomly, one hour before blood sampling, cream A or B was rubbed on the right cubital area and C or D on the left cubital area. The amount of the used material of all four mentioned products was similar. In order to prevent differences and variations in the results, all the blood sampling were done by one person and was taken from the cubital vein with 2 cc syringe and blue needles made by SUPA Company. The pain intensity was recorded by the patients using Visual Analogue Scale (VAS) method. In this scale, zero stands for painless state and score 10 for the most painful feeling.¹ Products encoding was done by the administrator; and the person who took the samples and the volunteers did not know anything about the type of products. Any local skin reaction like erythema, edema or irritation was also recorded. The analysis of data was done by SPSS 11 software using Student's t-test and ANOVA for comparison of products. After decoding the data, it was revealed that A and B were EMLA while C was

lidocaine and D was benzocaine.

Results

In this study, EMLA 5% was used on right hand in 64 volunteer before blood sampling, lidocaine 5% on left hands of 30 person and benzocaine 5% on left hand of 34 volunteers. Sex distribution and mean age indicated that 46 male and 18 female with the mean age and standard deviation of 35.7 ± 17.2 years participated in this study. The comparison of pain intensity changes in the 3 groups based on the 10-unit observational pain scale indicated that pain intensity after using EMLA cream 5% was significantly less than that after using the two other products (Table 1, $P < 0.05$).

No significant difference was observed between pain intensities in users of lidocaine 5% and benzocaine 5% ($P = 0.66$). Also, in this study, no side effects, sensitivity and erythematic reactions were observed after using these products on the injection area.

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, the comparisons of pain intensity changes following the application of three local anesthetics, EMLA, lidocaine 5% and benzocaine 5% (domestically manufactured products) showed that using EMLA cream 5% before injection resulted in significantly more pain reduction compared to other two products. There was no difference between pain intensity after using lidocaine 5% and benzocaine 5% creams. Although most of the accomplished researches indicated a significant pain management

Table 1. Comparison of pain intensity changes in the 3 groups.

Groups	Number of Patients	Pain Intensity Mean \pm SD	95% Confidence Interval	P value
EMLA 5%	64	1.7 ± 1.62	1.18 - 2.06	
Lidocaine 5%	30	2.26 ± 1.57	1.67 - 2.85	< 0.05
Benzocaine 5%	34	2.5 ± 1.74	1.89 - 3.10	

after using EMLA cream compared to placebo, study results of using EMLA cream in comparison with other anesthetic creams were not aligned. EMLA cream had more, less or equivalent effects on the pain relief in comparison with lidocaine cream.⁵ In cases in which liposomal lidocaine was used, lidocaine showed more analgesic effects than EMLA.⁵ It seems particle size has a determinant role in effectiveness of this drug. Using EMLA cream in reduction of the pain showed its significant effects before dentistry interventions.⁶ EMLA cream also had made a significant reduction in prostate biopsy pain intensity in comparison with lidocaine cream and placebo.⁷ In a research, using EMLA cream in reduction of the pain caused by intralesional injection for alopecia areata (30, 45 and 60 minutes before injection) showed a significant effect in 85% of the cases in comparison with injection in lesions without using EMLA. It seems delayed injection had been more effective during EMLA cream application.⁸ However, the results of this study may need some considerations due to small sample size i.e (27 cases). Time is an important constrain in achieving anesthetic effect of EMLA. The patients usually gain the advantages of EMLA 60 minutes after application, but for the maximum effectiveness, 90-minute interval is required.⁹ although the analgesic effect was also seen after 5 minutes.¹ The results of meta-analysis also showed that EMLA cream had a significant effect in pain reduction caused by blood sampling and cannulation in comparison with placebo. It seems 85% of individuals who use this product before blood sampling, enjoy its benefits. The other advantage of this drug which may be exclusive

and unique among other local anesthetic drugs, is that EMLA is safe for using in children, even in premature infants.^{4,9} Rosa et al. had a parallel result with the current study about using lidocaine and benzocaine compared with placebo in relief of injection pain.¹⁰ 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. Although methemoglobinemia is a potential concern of using this drug and met-hemoglobin level of the serum in EMLA users was higher than that in placebo users (approximately 5% to 6%), there was no sign of met-hemoglobinemia in this concentration range. Also methemoglobinemia is not common and usually does not occur in low doses and short term use.¹¹ In the current study no special side-effect was seen. Based on this research, it seems EMLA can be suggested as an effective product for reducing injection pain much better than other two products. Producing domestic products similar to EMLA and comparison of its efficacy with EMLA cream is advocated. Moreover, cost-effectiveness of EMLA should be compared with lidocaine and benzocaine creams in order to make the correct decision.

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