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DIRECT COMPARISON OF CREAM AND CREAMY-GEL TOPICAL ANESTHETICS: A STUDY OF THE ELECTROFULGURATION-INDUCED PAIN

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ABSTRAK

Telah dilakukan uji klinis acak, buta ganda, komparatif-paralel, intra-individual membandingkan efikasi Eutectic mixture of local anesthetics (EMLA) dalam formulasi berbentuk krim dan creamy-gel *untuk mengontrol nyeri akibat elektrofulgurasi pada 34 relawan. Pada punggung mereka digambar 2 kolom dengan 8 lajur dengan pengaturan oklusi selama 10, 20, 30, 45, 60, 90 dan 120 menit. Lajur teratas digunakan untuk control nyeri tanpa aplikasi EMLA. Sensasi nyeri yang ditimbulkan tindakan elektrofulgurasi pada masing-masing lokasi dinilai menggunakan metode* Numerical Rating Scale *(NRS).*

Perbedaan nilai NRS kedua kelompok tidak bermakna mulai menit ke 10 (p=0,158), 20 (p=0,689), 30 (p=0,667), 45 (p=0,652), 60 (p=0,860), 90 (p=0,565) sampai menit ke 120 (p=0,642). Kedua kelompok menunjukkkan adanya korelasi negative yang sangat kuat antara lamanya oklusi dan nilai NRS dan keduanya mencapai keaaan analgesia kutan adekuat pada menit ke 45.

Dapat disimpulkan bahwa formulasi EMLA dalam vehikulum berbentuk creamy-gel *memiliki efikasi yang setara dengan vehikulum krim*
(MDVI 2007;34/4:156-158)

Kata kunci: *EMLA, sediaan* creamy-gel, *elektrofulgurasi.*

ABSTRACT

A randomized, double blind clinical trial to compare the efficacy of Eutectic Mixture of Local Anesthetics (EMLA) in a cream versus a creamy-gel vehicle formulation, in pain control for electrofulguration procedures.The back of each subject was used as an intervention unit, either for cream or creamy-gel group. Both drugs were applied randomly, in an occlusive dressing, in two rows of eight circular patches randomly. Pain intensity was recorded for both groups over time from minute 0, 10, 20, 30, 45, 60, 90 and 120. A second of 20 mA electrofulguration induced the pain, while Numerical Rating Scale (NRS) measured the pain intensity.

No significant NRS difference was found between two groups from minute 10 (p=0.158), 20 (p=0.689), 30 (p=0.667), 45 (p=0.652), 60 (p=0.860), 90 (p=0.565) and 120 (p=0.642). Adequate cutaneous analgesia was achieved in minute 45 for both groups with pain reduction of 86.8 % and 88.0% for the creamy-gel and cream group, respectively. There was a negative and strong correlation (R=-0.914; p=0.000) between pain sensation as measured by NRS and the duration of occlusion for both groups.

It is concluded that EMLA in a creamy-gel vehicle formulation has equal efficacy compared to the previously well-established EMLA which is in a cream vehicle.
(MDVI 2007;34/4:156-158)

Keywords: *EMLA, creamy-gel vehicle, electrofulguration*

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INTRODUCTION

Topical anesthetic drugs have a slow onset of action due to limited percutaneous absorption through an intact epidermis. To enhance penetration, EMLA, a formula based on oil-water emulsion cream containing 5% of lidocaine and prilocaine, which melts at a lower temperature than any of its components, was composed. The formulation enhances the ability of anesthetic drugs to penetrate the epidermis and accelerate the onset of cutaneous analgesia.[1,2] However, achieving an adequate cutaneous analgesia using an occlusive dressing still required at least 60 minutes[3-6]- which is too long for medical intervention.

Vehicle formulation in topical therapy is capable to influence percutaneous absorption and therefore the success of topical therapy.[7] A gel vehicle is a semi solid emulsion in alcohol base, it has a higher potency, lower hydration ability and higher irritation risk compared to a cream vehicle.[7,8] The efficacy of occlusive EMLA in a gel vehicle is better compared to its cream vehicle formulation, but it has a lower efficacy when administered in a non-occlusive application.[9,10] However, the efficacy of EMLA in a creamy-gel vehicle is still unclear. Therefore, the objective of this study is to compare the efficacy of EMLA in a cream versus in a creamy-gel vehicle formulation, in pain control for electro fulguration procedures.

MATERIALS AND METHODS

After obtaining approval from the Local Ethics Committee on Health and Medical Research, 34 healthy subjects who fulfilled inclusion and exclusion criteria were enrolled in each step of the study. The inclusion criteria were: 1) 17-50 year-old; 2) free from any skin diseases on the back; 3) no history of hypersensitive reaction against any topical medication or adhesive plaster; 4) completed and signed the informed consent form. The exclusion criteria were: 1) currently receiving medication which contain analgesic, sedatives, or alcohol; 2) using an implant electric support device such as heart-pace maker; and 3) pregnant or breastfeeding.

The study design used was a parallel-comparative, randomized, double-blind, intra-individual clinical trial using the skin on the back as an intervention unit. Two rows of eight circular patches each measuring 1.5 cm^2 were drawn on the back skin using indelible ink. A trained researcher used applicator to administer a dose of 0.1 gram/cm^2 EMLA in cream vehicle (*EMLA® AstraZeneca AB, Sodertalje, Sweden*) and EMLA in a creamy-gel vehicle (*Estesia® Pharmacore Labs., Jakarta, Indonesia*) to a test chamber (ûþ-*Chamber®, Dermato-Venereology Department, Gadjah Mada University, Yogyakarta, Indonesia*). All of the spots, with the exception of the one marked minute-0, were covered with the chambers for 10, 15, 20, 30, 45, 60, 90 and 120 minutes. Simple randomization was used to determine the position of each group; cream vehicle on the left side or the right side of the rows. The occlusive application was arranged in such a manner that each has experienced occlusion for the duration required when pain stimulation was given. The spot marked minute-0 served as a control spot hence received no treatment. All the application procedures were performed by two trained researchers in the application procedure room.

One second of 20mA electrofulguration *(Liarre® S.r.l.HFS 45 portable electro surgery unit, manufactured by Via G. Di Vittorios-40020 Calsfiumanere [BU]-Italy)* induced the pain sensation, while pain intensity was measured by the modified Numerical Rating Scale (NRS). The NRS uses a 0-10 pain score range (0 = no pain, 10 = pain intensity at control spot). Pain intensity was recorded for both groups in minute 0, 10, 20, 30, 45, 60, 90 and 120. Adequate analgesia is defined as e" 75% NRS pain score reduction compared to pain intensity at the control spot.

In order to obtain a double-blind measurement, the researchers who stimulated pain sensation and recorded pain intensity were different from those who conducted the application procedures and the application procedure were conducted in a different room from the pain stimulation procedure.

The analysis of pain differences registered in the two groups was made using Wilcoxon Signed-rank test. Power analysis indicates that 20 subjects are required to detect a difference of 2 points on a 0-10 rating score with a power of 0.8 and alpha of 0.05. Spearman's correlation coefficient was used in analyzing the correlation between duration of occlusion and NRS pain score. All analysis used SPSS-12.0 statistical software.

RESULTS

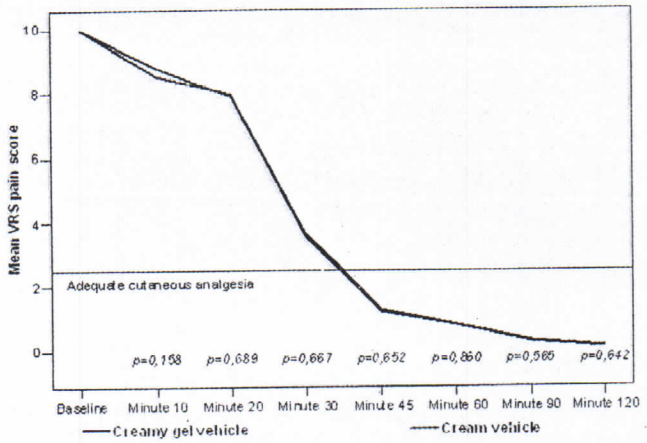
The study involved thirty-four healthy subjects (26.56 $\pm$ 4.53 year-old). Spearman's coefficient correlation as measured by NRS and the duration of occlusion were similar for both groups (*R=-0.914; p=0.000*). Comparison of NRS between two groups, in every observation spot, is shown in figure 1.

No adverse effects (stinging, burning sensation or blistering) were reported by all the subjects involved in this study.

DISCUSSION

The study showed that the achievement of adequate cutaneous analgesia for the cream vehicle group was in minute 45 and was considered to be faster than findings made

Figure 1 Mean NRS pain scores for cream and creamy-gel group over time, from minute 0 (at the control spot), 10, 20, 30, 45, 60, 90 and 120.



in an earlier study, which was realized in minute 90.[9] This finding may be due to the different EMLA cream used and different technique of pain stimulation. The previous study used an electrodessication which was known to be more invasive procedure compared to electrofulguration technique. The pain intensity reduction was similar in every point of observation over time, for both groups. In minute 45, the pain intensity reduction of cream vehicle group is better than creamy-gel group but the difference is not significant.

Based on figure 1, an observation can be made to the effect of occlusive dressing on the pain intensity scores. There was a negative and strong correlation between pain sensation as measured by NRS and the duration of occlusion, which was similar for both groups. Similar results were reported by Wirohadidjojo *et al.* (2001)[9] and Sulistiyono *et al.* (2003).[10] These findings may be primary due to the effect of occlusion. It is an established fact that occlusion will cause various skin physiologic alterations that resulting in decreased TEWL, such as increasing stratum corneum water content, swelling of corneocytes, altering intercellular lipid phase organization, and increasing skin surface temperature and superficial blood flows.[11,12] A decreasing TEWL is a reflection of decreased skin barrier function which will enhance percutaneous absorption of topical drug and accelerate the drug onset of action.[7,8]

It is concluded from our study that EMLA in a creamy-gel vehicle formulation has equal efficacy compared to the previously well-established EMLA, which is in a cream formulation.

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REFERENCES

1. Huang W, Vidimos A. Topical anesthetics in dermatology. *J Am Acad Dermatol* 2000; 43: 286-98.
2. Friedman PM, Mafong EA, Friedman ES, *et al.* Topical anesthetics update: EMLA and beyond. *Dermatol Surg* 2000; 127: 1019-6.
3. Friedman PM, Fogelman JP, Nouri K, *et al.* Comparative study of the efficacy of four topical anesthetics. *Dermatol Surg* 1999; 25: 950-4.
4. Eichenfield LF, Funk A, Fallon-Friedlander S, *et al.* A clinical study to evaluate the efficacy of ELA-Max (4% liposomal lidocaine) as compared with eutectic mixture of local anesthetics cream for pain reduction of venipuncture in children. *Pediatrics* 2002; 109: 1093-9.
5. Guardiano RA, Norwood CW. Direct comparison of EMLA versus lidocaine for pain control in Nd:Yag 1,064 nm laser hair removal. *Dermatol Surg* 2005; 31: 396-8.
6. Gupta AK, Sibbald RG. Eutectic lidocaine/prilocaine 5% cream and patch may provide satisfactory analgesia for excisional biopsy or curretage with electrosurgery of cutaneous lesion. *J Am Acad Dermatol* 1996; 35: 419-23.
7. Redelmeier TE, Schaefer H. Pharmacokinetics and topical applications of drugs. In: Freedberg IM, Eizen AZ, Wolff K, *et al.* editors. Fitzpatrick's *Dermatology in General Medicine*. 5th ed. New York: McGraw-Hill Co; 2003. p.2697-706.
8. Strober BE, Washenick K, Shupack JL. Principles of topical therapy. In: Freedberg IM, Eizen AZ, Wolff K, *et al.* editors. Fitzpatrick's *Dermatology in General Medicine*. 5th ed. New York: McGraw-Hill Co; 2003. p 2319-23.
9. Wirohadidjojo YW, Etnawati K, Sulistiyono T, *et al.* An efficacy comparison of occlusive lidocaine /prilocaine combination cream and gel. *MDVI* 2001; 28: 188-92.
10. Sulistiyono T. A comparison of 75% electrodessication pain reduction between gel and cream lidocaine/prilocaine combination on normal skin (thesis). Yogyakarta, Indonesia: Gadjah Mada Univ.; 2003.
11. Zhai H., Maibach HI. Occlusion vs Skin Barrier Function. *Skin Res and Technol* 2002; 8: 1-6.
12. Zhai H, Maibach HI. Skin occlusion and irritant and allergic contact dermatitis: an overview. *Contact Dermatitis* 2001; 44: 201-6.