

Study of Onset and Duration of Action of Local Anesthetic Eutectic Mixture in New Zealand White Rabbits

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Abstract

The present study was designed to investigate the local anesthetic activity of EMLA cream on intact skin of hind limbs of New Zealand white rabbits by employing a novel method "Pedaling reflex in rabbits". Five different doses of drug ranging from 0.5 to 2.5 mg was selected and applied to the ventral surface of the hind feet of both limbs. Uniform pressure was applied on anesthetized patches with help of a blunted probe. Six pricks were applied at different points on anesthetized patches and loss of pedaling reflex (leg retraction) followed by application of stimulus was considered as sign of anesthesia. A significant reduction in onset of anesthesia and a dose dependent increase in duration of anesthesia were recorded in the present study. The onset and duration of action for local anesthetic EMLA cream depends on dosage and contact time of drug on intact skin.

Keywords: White rabbit, EMLA cream

Introduction

Local anaesthetics are the drugs, which produce reversible loss of sensory perception especially pain in a restricted area of the body. Recent advances in medicinal chemistry lead to the development of newer local anaesthetics which are longer acting and suitable for using in multiple purposes. But these drugs are not effective when applied on intact skin. A variety of animal experiments are conducted to investigate the efficacy of local anaesthetics in animals and one among these experiments is infiltration anaesthesia conducted on guinea pigs (Vogel., 2002). Based on this reference, Activity of eutectic mixture of local anaesthetic (EMLA cream) on intact skin.

An attempt was made to develop a novel method, testing of leg retraction reflex (pedaling reflex) in New Zealand white rabbits to study the topical anaesthetic

Material and methods

New Zealand white rabbits were used in this study. All the animals were housed in animal house of Mamatha medical college with free access to food and water. The detailed study protocol was submitted to the institutional animal ethics committee and an approval was obtained before performing the study.

Inclusion criteria: only rabbits were selected.

- Both male and female rabbits were included.
- Rabbits weighing 2.5-3kg were included.
- All the rabbits were disease free.
- Animals exhibiting pedaling reflex of feet less than 4 seconds are included in this study.

Exclusion criteria: Drugs and chemicals- 5% prilox cream (eutectic mixture containing Lidocaine and prilocaine).

Methods

New Zealand white rabbits of either sex were selected for the study and they were divided in to five groups. Each group consists of six rabbits. These rabbits are kept in recumbent position, so that the fore limbs and hind limbs are exposed out. Remove hair on both the ventral surface of the hind feet and mark 2sqcm

Circles in the center with marker so that the skin will be exposed out clearly. Test the retraction of limbs by probing with a blunt probe. Weigh the drug in five doses of 0.5mg, 1mg, 1.5mg, 2mg and 2.5mg.

Apply the first dose 0.5mg to the first group, second dose 1mg to the second group, third dose 1.5mg to third group, fourth dose 2.0mg to fourth group and fifth dose 2.5mg to the fifth group. The drug is applied to the patches with help of a spatula. Then occlude the patch for 5 minutes with the help of stickers provided with the medicament. After five minutes remove the stickers with help of forceps and test the retraction reflex by probing.

Pedaling reflex (Vogel 2002): The rabbit retracts the leg immediately when we apply pressure by probing the area with the help of a blunted probe. Six pricks are made on the anesthetized patches at different points. Loss of leg retraction (pedaling reflex) is considered as sign of complete anesthesia. The procedure was repeated after 5 min and for every 10 minutes until the leg retraction reappears.

Statistics: Results of the present study was analyzed by employing student Kruskal wall is test and p value less than 0.001 was considered as statistically significant

Results

The time taken for the onset and duration of anesthesia was recorded in all the EMLA treated groups. A significant reduction in onset of anesthesia was recorded in all the EMLA treated groups. Treatment with low dose of 0.5 mg, the mean onset of anesthesia for right leg is 10.84min and for left leg is 13.33min (Figure.1 & Figure.2). However, treatment with high doses of 1.5mg, 2.0mg and 2.5mg, the mean onset of action in both right and left leg remains constant i.e. 5min. A dose dependent and significant increase in duration of anesthesia was recorded in all the drug treated groups (Figure.1 & Figure.3).

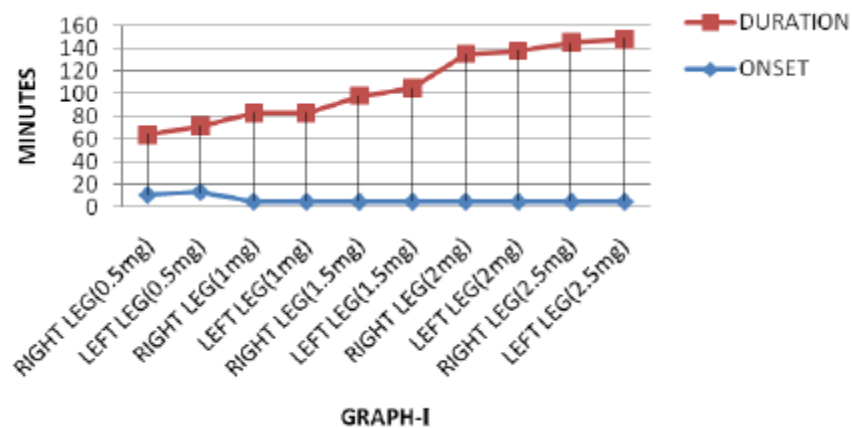


Figure. 1. Onset & Duration of different doses of eutectic mixture.

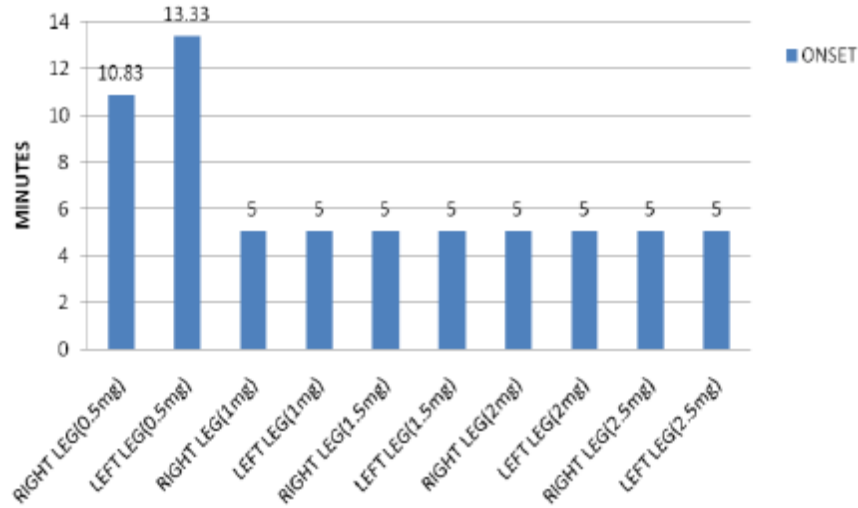


Figure. 2. Onset of eutectic mixture with different doses. (P value < 0.001)

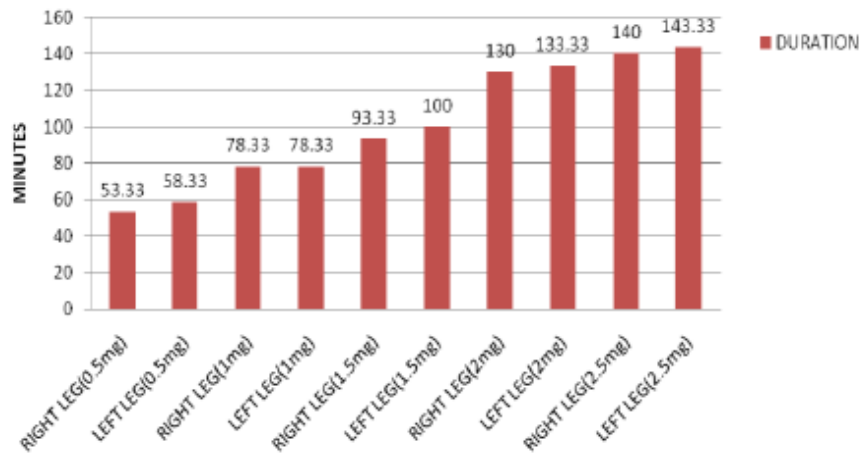


Figure. 3. Duration of eutectic mixture with different doses. (P-value < 0.001)

Discussion

Several topical anesthetic preparations are available such as sprays (Xylocaine spray, Astra pharmaceuticals) and gels (xylocaine gel) are not effective in producing the topical anesthesia when applied to the intact skin of animals and they are highly effective when applied to mucus membranes. However, subcutaneous administration of local anesthetics produces anesthesia, but the procedure itself is painful. Brodin et al., (1984) and Evers et al., (1985) demonstrated the use of eutectic mixture (25mg/ml of lignocaine & 25mg/ml of prilocaine) together with an emulsifier, enables preparation of an oil and water emulsion with high base content in the emulsion with a low anesthetic concentration. This cream is commercially available as EMLA cream (Astra Pharmaceuticals., Ltd) and has gained wide acceptance in human medical practice for producing topical anesthesia on intact skin when applied under occlusive dressing. EMLA cream is highly effective in anesthetizing intact skin for performing pain free venipuncture in children (Ehrenstorm Reiz and Reiz., 1982; Hallen and Uppfeldt., 1982; Wahlstedz et al., 1984; Hopkins et al., 1988) and adults (Hallen et al., 1985). Young et al., (1987) and Price (1988) reported EMLA as an effective anesthetic for performing lumbar puncture in children. It is also proved to be effective as local anesthetic for performing superficial surgeries (Juhlin et al., 1980). In humans, the EMLA cream must be covered with an occlusive dressing and left in contact with skin for about 30 to 60 min (Hallen et al., 1984; Hopkins et al., 1988). A similar duration of treatment might be necessary for

testing the topical anesthetic activity in animals. Based on the above reports, an attempt was made to study the onset and duration of topical anesthesia produced by EMLA cream in rabbits by employing a novel method “pedaling reflex in rabbits”. Treatment with low dose of EMLA (0.5 mg), the onset of action was longer. However, the onset of action observed with doses ranging from 1mg to 2.5mg remains constant i.e. 5min. A dose dependent increase in duration of anesthesia was observed with various doses of EMLA cream. This is an indicative of saturation of the drug after a particular dose in eliciting the action but duration of action continued to increase with proportionate increase of the dose. This will add to the existing knowledge.

Conclusion

The onset and duration of surface anesthetic EMLA cream not only depends up on the contact time but also on the dose of the eutectic mixture.

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