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Original Research Article

A randomised controlled trial on effect of topical anaesthetics on injection pain during immunization in infants of 6 weeks to 6 months of age with pentavac vaccine

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ABSTRACT

Background: Pain is a both a sensory and an emotional experience when untreated and unrecognized, it extracts a significant physiological, biochemical and psychological toll on both the children and family members. Vaccine injections are considered to be the most common cause of iatrogenic pain in childhood. Positive experience during vaccine injection like reducing injection pain with local anaesthetics can avoid pre procedural anxiety in future, needle phobias, healthcare avoidance behaviors and maintain trust in healthcare providers.
Methods: This randomized controlled trial was done at immunization clinic of Rajah Muthiah Medical College Hospital over a period of 2 years.100 infants of age group 6 weeks to 6 months brought for Pentavac (DPT-Hib-Hepatitis B) combination vaccine were taken for study and allocated into control, intervention group (receiving local anaesthetic cream/lidocaine spray) and pain score was compared using modified behavioral pain score (MBPS).
Results: Among the three groups studied, the mean pain scores after vaccine injection were minimum in group A (infants with topical occlusive EMLA cream), followed by group B (infants with topical LA spray), whereas control group of infants who did not receive any local anaesthesia exhibited higher pain scores values.
Conclusions: Our study showing that topical occlusive EMLA cream significantly decreases injection pain in infants has applicability in clinical practice, where it can be routinely used in infants before administering intramuscular vaccine injections in settings where resources are not a constraint.

Keywords: Vaccine injection, EMLA cream, Pain score, Modified behavioral pain score

INTRODUCTION

Pain is defined by international association for the study of pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".[1] Pain is a dynamic experience often beneficial by warning of impending or actual injury, thereby preventing or restricting tissue damage. Barring this aspect, pain has only damaged effects in terms of metabolic and behavioural responses induced by it.

Vaccine injections are considered to be the most common source of iatrogenic pain in childhood, which are repeatedly administered to all children throughout infancy, childhood and adolescence. Vaccine injection pain can cause pre-procedural anxiety in the future, needle phobias and healthcare avoidance behaviours. Positive experiences during vaccine injections would promote and maintain trust in healthcare providers.

Factors affecting injection pain during immunization in infants can be modifiable or non-modifiable factors. Age,

gender, temperament, previous painful experience and cultural background are factors that cannot be modified. Pre-procedural preparation, injection site selection, needle selection, injectate properties, temperature, type of diluents and injectate formulation are pre procedural measures that can be modified. During injection, parental behaviour, securing the child, distraction, use of sucrose, topical anaesthetics, injection techniques, site pressure, and sequence of injections are factors which determine pain experienced by the child.

Studies which have addressed the use of topical anaesthetics for preventing immunisation pain in children are scanty. The data from our study shall determine the effect of local anaesthetics delivered by various modes for reduction of vaccination related injection pain in infants and compare them. With need for multiple vaccinations and risk of vaccine refusal due to injection pain with repeated vaccination, there is an urgent felt need for such a study.

The objective of this study is to compare the effect of topical anaesthetics (eutectic mixture of local anaesthetics (EMLA) cream, topical local anaesthetics (LA) spray) with that of control group for reduction of injection pain during immunization with Pentavac vaccine in infants of 6 weeks to 6 months using an objective pain assessment scale.

METHODS

The study is a randomized controlled trial conducted at the immunization clinic of Rajah Muthiah Medical College Hospital during the period of December 2020 to October 2022 after approved by institutional ethical committee board. The study population includes infants of age 6 weeks to 6 months reported to immunization clinic for immunisation with Pentavac vaccine (DPT-Hib-hepatitis B combination vaccine).

Sample size

100 infants, 34 in group A, 33 in group B and 33 in group C (control) were included.

Inclusion criteria

All healthy infants from 6 weeks to 6 months of age brought for immunization with Pentavac (DPT-Hib-hepatitis B) combination vaccine were a part of the study.

Exclusion criteria

Patients with any coexisting acute or chronic painful condition, CNS disorder, birth asphyxia, hypoxic ischemic encephalopathy, infants on any medication (analgesics, sedatives and anti-epileptic drugs), and any known sensitivity to the topical anaesthetic or known history of G6PD deficiency were excluded.

The enrolled subjects were allocated into: intervention group which included group A (infants applied with topical occlusive EMLA cream (lidocaine and prilocaine) 60 minutes before injection, kept covered in occlusive dressing, and group B (infants applied with topical lidocaine spray, sprayed 10 seconds before injection), and the control group (group C) (infants not received any local anaesthesia). Sterile water at room temperature was sprayed 10 seconds before injection over the injection site.

Parents/guardians of the participants will be explained in prior about the study and informed consent will be obtained. Randomization was done using simple randomization by computer generated sequence. Vaccine was given intramuscularly into the anterolateral aspect of thigh by a trained nurse using 25 Gauge, 1 inch length needle inserted at 90-degree angle after standard skin preparation. Breast fed 1 hour before injection. Injection was given with infant lying on mother's lap. Primary data was recorded by the doctor posted in the clinic and blinded for study outcome. Distraction of the child by parents during vaccination was neither encouraged nor discouraged. Distraction of the child by the nurse delivering the vaccine during vaccination was discouraged. Pain score was measured by modified behavioural pain score (Table 1). Statistical analysis of data was done using statistical package for the social sciences (SPSS) 17 software.

Table 1: Modified behavioural pain scale in infants.

Parameter and findings	Points
Facial expression	
Definite positive expression	0
Neutral expression	1
Slightly negative expression, e.g., grimace*	2
Definite negative expression i.e., furrowed brows, eyes closed tightly**	3
Cry	
Laughing or giggling	0
Not crying	1
Moaning, quiet vocalizing, gentle or whimpering cry	2
Full lunged cry or sobbing	3
Full lunged cry, more than baseline cry	4
Movements	
Usual movements/activity or resting/relaxed	0
Partial movement or attempt to avoid pain by withdrawing the limb where puncture is done	2
Agitation with complex movements involving the head, torso or the other limbs, or rigidity	3

*Slightly negative expressions include brow bulging and naso-labial furrow; **definitely negative expressions include brow bulging naso-labial furrow eyes closed tight open lips with or without a reddened face; in MBPS sum of points for all 3 parameters are interpreted as, minimum score: 0, maximum score: 10

RESULTS

Out of 100 participants, 34 (34%) were categorized into group A, 33 (33%) were categorized into group B, and 33 (33%) were categorized into group C (Table 2). The age and gender distribution among the groups are given in Tables 3 and 4).

Table 2: Distribution of participants as per groups.

Group	Frequency	Percentage
Group A	34	34.0
Group B	33	33.0
Group C	33	33.0
Total	100	100.0

Table 3: Comparison of age categories between groups.

Age category	Group A	Group B	Group C	Total	P value
6 week to <10 week (%)	13 (38.2)	13 (39.4)	14 (42.4)	40 (40.0)	0.652
10 week to <14 week (%)	10 (29.4)	5 (15.2)	6 (18.2)	21 (21.0)	
≥14 weeks (%)	11 (32.4)	15 (45.5)	13 (39.4)	39 (39.0)	
Mean±SD in days	83.47±34.74	89.73±38.83	81.85±35.91	85.00±36.30	
Median (IQR) in days	82.50 (47.00–108.75)	90 (48–120)	76 (45–106)	113.0 (90–120)	
Minimum age in days	45	45	45	45	
Maximum age in days	180	180	180	180	
Total (%)	34 (100.0)	33 (100.0)	33 (100.0)	100 (100.0)	

P value based on one way ANOVA, SD – standard deviation

Table 4: Comparison of gender between groups.

Gender	Group A (%)	Group B (%)	Group C (%)	Total (%)	P value
Male	17 (50)	21 (63.6)	19 (57.6)	57 (57)	0.528
Female	17 (50)	12 (36.4)	18 (42.4)	43 (43)	
Total	34 (100.0)	33 (100.0)	33 (100.0)	100 (100.0)	

P value based on one way ANOVA

Table 5: Comparison of median pain score between groups.

Pain score	Median (IQR)			P value
	Group A	Group B	Group C	
Pain score before vaccination	2 (1–2)	2 (1–2)	1 (0–2)	0.233
Pain score after vaccination 15 seconds	4 (4–5)	7 (5–7)	7 (6.5–8)	0.001
Pain score after vaccination 60 seconds	3 (2–4)	3 (2–4)	4 (4–5)	0.001
Pain score after vaccination 5 minutes	2 (2–3)	3 (2–3)	4 (3–5)	0.001
Total	34	33	33	

P value based on Kruskal Wallis test, IQR – inter quartile range

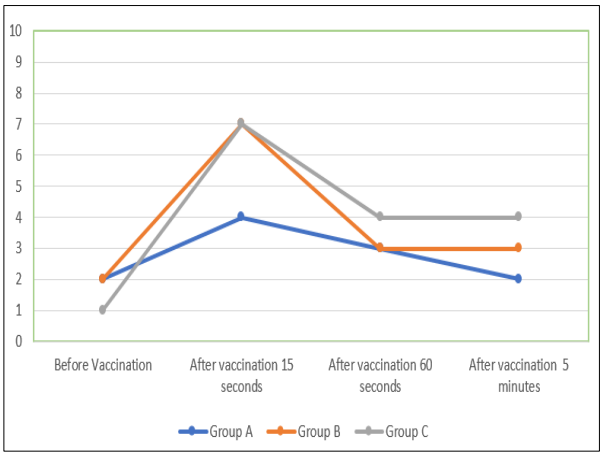

Figure 1: Line diagram showing median ain score between groups.

The median pain score before vaccination was equally distributed between three groups with the p value showing more than 0.05. The median pain score 15 seconds after vaccination was higher among group B and group C when compared to group A with the p value of less than 0.05. The median pain score 60 seconds after vaccination was higher among group C when compared to group A and group B with the p value of less than 0.05. The median pain score 60 seconds after vaccination was equally distributed between group A and group B with the p value of more than 0.05.

The median pain score 5 minutes after vaccination was higher among group C when compared to group A and group B with the p value of less than 0.05. The median pain score 5 minutes after vaccination was equally distributed between group A and group B with the p value of more than 0.05 (Table 5 and Figure 1).

DISCUSSION

Childhood immunization is a proven tool for eradicating and controlling infectious diseases. Many individuals refuse vaccination for their children because of pain from requisite needle puncture. Routine immunisation plays a key role in maintaining global public health. Several methods have been employed to reduce injection pain during immunization in children.

In our study, we used topical occlusive EMLA cream, topical lidocaine spray before Pentavac vaccination and compared their effects. Our study was a randomised controlled of 100 children in the age group of 6 weeks to 6 months. Among the three groups studied, we observed that the median pain scores after vaccine injection were minimum in group A (infants with topical occlusive EMLA cream), followed by group B (infants with topical lidocaine spray), whereas control group of infants who did not receive any local anaesthesia exhibited higher pain scores values.

Our findings of topical occlusive EMLA cream being the most effective in preventing injection pain are similar to various studies. Taddio et al studied EMLA cream to prevent injection pain associated with DPT vaccination in infants.[2] In their study, the mean difference in the pre and post injection pain score measured by modified behavioural pain scale was lower in the EMLA group as compared to placebo group (p=0.001).

Halperin et al studied the role of lidocaine-prilocaine patch (EMLA) in decreasing the pain associated with subcutaneous injection of MMR vaccine and noted that the pain score measured by modified behavioural pain scale (MBPS) was significantly lower in those who received the patch.[3] In another study conducted by Halperin et al noted that EMLA patch application was effective in reducing pain associated with intramuscular injection of DTaP-IPV-Hib and hepatitis B vaccines.[4] They also noted that it does not affect the antibody response to DTaP-IPV-Hib and hepatitis B vaccine as compared to placebo. Antibody response to diphtheria, pertussis, tetanus antigens, Hemophilus influenza type B and hepatitis B were measured by enzyme immunoassay and poliovirus 1, 2 and 3 by neutralization.

O'Brein et al in their double blind, randomised, placebo-controlled trial using 4% amethocaine gel found that 4% amethocaine gel significantly reduces the pain of measles-mumps-rubella vaccination in infants when compared with placebo and does not interfere with subsequent development of protective antibody levels.[5] Pain score was measured by MBPS.

Chambers et al did a systematic review of psychological interventions for reducing pain and distress during routine childhood immunizations.[6] They reported that the evidence suggests that breathing exercises, child-directed distraction, nurse-led distraction, and combined cognitive-behavioral interventions are effective in reducing the pain and distress associated with routine childhood immunizations.

Shah et al did a systematic review and meta-analyses of effectiveness and tolerability of pharmacologic and combined interventions for reducing injection pain during routine childhood immunizations.[7] Authors concluded that topical local anesthetics, sweet-tasting solutions and combined analgesic interventions, including breastfeeding, were associated with reduced pain during childhood immunizations and should be recommended for use in clinical practice.

Uhari et al studied the use of eutectic mixture of lidocaine and prilocaine for alleviation of vaccination pain in infants.[8] The authors reported that the discomfort and pain caused by vaccination may prevent some parents from having their young children vaccinated.

Cassidy et al did a randomized double-blind, placebo-controlled trial of the EMLA patch for the reduction of pain associated with intramuscular injection in 4- to 6-year-old children.[9] Pain measurements included: children self-report on faces pain scale; facial action on the child facial coding system; the Children's Hospital of Eastern Ontario pain scale and parents and technician ratings on a visual analogue scale. Parents rated their own and their child's immunization-related anxiety on a visual analogue scale. Study reported that EMLA patch group had significantly less pain measures compared with the placebo group. Of the children in the placebo group, 43% had clinically significant pain, compared with 17% of children in the EMLA patch group. No severe adverse symptoms occurred as a result of either EMLA or placebo patch application.

Maikler studied the effects of a skin refrigerant/anaesthetic and age on the pain response of infants receiving immunization.[10] Authors revealed fewer distress behaviours following refrigerant spray and more complex, varied behavioural responses for older infants.

Page et al have demonstrated that topical vapocoolant spray such as ethyl chloride are effective in reducing the pain during emergent venous punctures.[11] The studies of the role of skin refrigeration with vapocoolant by Abbott et al, Cohen et al and Maikler et al have demonstrated its role in reducing the pain scores in children when given before the vaccination.[10,12,13]

The EMLA (lidocaine and prilocaine) in topical occlusive cream penetrates intact skin, causing dermal anaesthesia, and significantly reduces puncture pain.

The finding in our study showing that topical occlusive EMLA cream significantly decreases injection pain following immunisation in infants has applicability in clinical practice. If this finding is supported by large randomised controlled trials, topical occlusive EMLA

cream can be routinely used in infants before administering intramuscular vaccine injections in settings where resource is not a constraint.

The limitations of our study are, it was confined to studying only the effect of local anaesthetics (topical EMLA cream, lidocaine spray) in reducing injection pain during immunization in infants. Other potential confounding factors like injection formulation, injection site selection, needle length, vaccine temperature, distraction techniques, site pressure, injection technique and parental behaviour were not included in this study. This suggests a need for a large randomized controlled trial in Indian condition including all these factors.

CONCLUSION

In our randomised controlled study comparing the effect of topical occlusive EMLA cream, lidocaine spray and no local anaesthetic in reducing injection pain during immunization in infants, topical occlusive EMLA cream and topical lidocaine spray were effective in alleviating injection pain perceived by infants during vaccination and were found to be better than no topical anaesthetic. Use of topical occlusive EMLA cream led to lower pain scores than use of LA spray. Pain due to intramuscular injection of vaccines is distressing to both the infant and caregivers. Among the several measures proposed to relieve injection pain following vaccination, topical anaesthetics have been reported to be effective, but have not been extensively employed in clinical practice. Our study indicates that topical occlusive EMLA cream may be beneficial in reducing injection pain during immunization in infants, with potential for regular use in immunization clinics.

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