

Original Research Article

A study of effect of topical anaesthetics on injection pain during immunization in infants

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ABSTRACT

Background: Immunization is a necessary aspect of health care of children and injections are there for unavoidable. Many factors affect injection pain during immunization in infants. This study aims to see the effect of use of local anesthetics delivered by various modes for attenuation of vaccine related injection pain in infants and to compare them.

Methods: An Open Label Four-Arm Randomized Control Trial of 300 healthy infants of age group 6 weeks to 6 months reported to immunization clinic for immunization with DPT-HiB-Hepatitis B combination vaccine were taken for study. The enrolled subjects were allocated into control group and intervention group (who were applied some form of local anesthesia).

Results: Among the four groups of the patients studied we observed a statistical difference in the mean pain scores of the patients recorded at 15 second, 60 second and 5 min after vaccine injection (p value 0.0024 - 0.000). Group A (Infants with topical occlusive LA cream) showed minimum pain scores values at 15 second, 60 second and 5 min after vaccine injection, followed by Group C (Infants with topical LA spray with vapocoolant) whereas Control group (Infants not received any local anaesthesia) and Group B (Infants with topical LA spray without vapocoolant) exhibited the maximum pain scores.

Conclusions: Topical occlusive local anesthetic cream and topical LA spray with vapocoolant, were found to be better than topical LA spray without vapocoolant or no topical anesthetic. Use of topical occlusive LA cream led to a lowest pain score. There was no significant difference in the profile of side effects following injection in the four group.

Keywords: Immunization pain, Local anesthetics

INTRODUCTION

Immunization is a necessary aspect of health care of children and injections are therefore unavoidable. Pain due to intramuscular injection of vaccines is distressing to the infant and caregivers. Infants are reported to have pain memory and react more intensely if they have had experience with previous painful procedures. Many factors affect injection pain during immunization in

infants. During injection, parental behavior, securing the child, distraction, use of sucrose, topical anesthetics, injection techniques, site pressure, and sequence of injections, are factors which determine pain experienced by the child.¹

Topical anesthetics have been reported to be effective, but have not been extensively employed in clinical practice.² This study was an open label four- arm

randomized, controlled trial on the effect of topical anesthetics on injection pain during immunization in infants.

METHODS

The study was done at Immunization clinic of a tertiary care hospital over a period of 2yr. Three hundred healthy infants of age group 6 weeks to 6 months reporting to Immunization clinic for immunization with DPT-HiB-Hepatitis B combination vaccine were taken for study. They were enrolled after obtaining informed written consent. The enrolled subjects were allocated into control group (75 infants who did not receive any local anesthesia) and intervention group. Intervention group further divided into Group A: 75 infants who applied with topical occlusive LA cream (Lidocaine and Prilocaine) 60 min before injection, kept covered in occlusive dressing. Group B: 75 Infants applied with topical LA spray without vapocoolant (10% Lidocaine spray), sprayed 10 sec before injection. Group C: 75 Infants applied with topical LA spray with vapocoolant (Benzocaine 0.36%, polyvinyl polymer 2.52% in propellant solvent), sprayed 10 sec before injection.

Inclusion criteria

All healthy infants from 6 weeks to 6 months age brought for immunization with DPT-HiB-Hepatitis B combination vaccine.

Exclusion criteria

- Any coexisting acute or chronic painful condition.
- CNS disorder.
- Infant on any medication.
- Any known sensitivity to the topical vapocoolant/anaesthetic or known history of G6PD deficiency.

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 G, 1 inch length needle inserted at 90° angle after standard skin preparation. Injection was given with infant lying on examination couch.

Primary data was recorded by the doctor posted in the clinic and blinded for study outcome. Distraction of the child by the parents during the vaccination was neither encouraged nor discouraged. Distraction of the child by the nurse delivering the vaccine during the vaccination was discouraged.

Outcome measures

Primary outcome

Pain scores by Modified Behavioral Pain Score as depicted in Table 1, the child is evaluated prior to the

procedure to give a baseline for comparison during and after the procedure, MBPS was recorded immediately before the injection, and at 15 seconds, 60 seconds and 5 minutes after injection.

Table 1: Modified behavior pain score.

Behaviour observed	Score
Facial expression	
Definite positive expression (i.e., smiling)	0
Neutral expression	1
Slightly negative expression (i.e., 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

Secondary outcomes

- Heart and respiratory rates at 5 minutes after vaccination.
- Frequency of adverse events.

Data was recorded in a preformatted form. The central tendencies and degree of dispersion were mentioned as mean and standard deviation. The statistical difference in the means of the groups was calculated using one way ANOVA test. The statistical difference in the means of Pain scores by Modified Behavioral Pain Score being the interval data was analyzed by Kruskal Wallis test. Statistical difference in the Frequency of adverse events was calculated chi square test. SPSS 17 software was used for statistical analysis.

RESULTS

Among the four groups of the patients studied we observed a statistical difference in the mean pain scores of the patients recorded at 15 second, 60 second and 5 min after vaccine injection (p value 0.0024 - 0.000) (Table 2). Group A (Infants with topical occlusive LA cream) showed minimum pain scores values recorded at 15 second, 60 second and 5 min after vaccine injection, followed by Group C (Infants with topical LA spray with vapocoolant) whereas Control group (Infants not received any local anaesthesia) and Group B (Infants with topical LA spray without vapocoolant) exhibited the maximum pain scores values.

Table 2: Comparison of pain score between groups.

	Control group	Group A	Group B	Group C
Pain score	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Before injection	0.8±0.8	0.7±0.8	0.7±0.8	0.7±0.8
At 15 sec	9.03±0.9	5.6±1.4	6.8±0.9	6.7±1.1
At 60 sec	6.6±0.9	4.1±1.1	5.2±1.2	5.0±0.9
At 5 min	2.9±0.8	0.8±0.7	2.8±0.8	1.8±0.8

Table 3: Pre-injection baseline parameters and HR and RR at 5 min of different groups.

	Control group	Group A	Group B	Group C	p value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Age	2.5±0.9	2.8±0.8	2.6±0.9	2.8±0.8	0.077
HR	102.8±9.4	102.3±9.0	101.5±8.2	101.3±7.7	0.679
HR at 5 min	120.6±10.4	108.5±7.9	113.9±9.1	111.8±8.3	
RR	43.3±10.4	43±9.4	43.3±10.4	43±9.4	0.994
RR at 5 min	54.2±10.5	47.1±9.5	51.3±9.2	50±10.1	
Mean Pain Score Before Inj	0.8±0.8	0.72±0.7	0.73±0.7	0.73±0.7	0.829

Table 4: Comparison of HR, RR and pain scores with history of previous injectable vaccine.

		History of previous injectable vaccine		p value
		Yes (60)	No (240)	
		Mean±SD	Mean±SD	
Pain score	Before vaccination	0.75±0.769	0.73±0.787	0.471
	At 15 sec	7.82±1.712	7.03±1.651	0.085
	At 60 sec	5.32±1.535	5.21±1.332	0.214
	At 5 min	2.72±0.804	2.28±0.771	0.068
Heart rate	Before vaccination	102.68±9.593	102.82±8.324	0.543
	At 5 min	117.27±10.489	113.55±9.845	0.021
Respiratory rate	Before Vaccination	45.62±9.494	44.29±9.985	0.26
	At 5 min	57.62±10.213	50.28±10.094	0.083

Table 5: Incidence of adverse effects in different groups.

Adverse effect	Control group	Group A	Group B	Group C	p value
Local skin reaction	-	-	-	-	-
Erythema	2	1	-	-	0.879
Induration	2	-	3	1	0.485
Abscess	1	0	1	1	0.870
Systemic effect	-	-	-	-	-
Fever	44	34	26	30	0.064
Seizure	-	-	-	-	-
Persistent crying	5	-	-	3	0.657
Rash	-	-	-	-	-
Feed intolerance	-	-	-	-	-
Restriction of movement	6	-	2	-	0.343
Red coloured urine	-	-	-	-	-

Among the four groups of the patients studied we observed a statistical difference in the mean heart rate of the patients recorded at 5 min after vaccine injection (p value 0.0012-0.000). We used one sided ANOVA test to estimate the statistical difference among the groups.

Group A (Infants with topical occlusive LA cream) showed minimum increase in the heart rate recorded at 5 min after vaccine injection, followed by Group C (Infants with topical LA spray with vapocoolant) whereas Control group (Infants not received any local anaesthesia) and

Group B (Infants with topical LA spray without vapocoolant) exhibited the maximum increase (Table 3).

Among the four groups of the patients studied we observed a statistical difference in the mean respiratory rate of the patients recorded at 5 min after vaccine injection (p value 0.0017-0.000). Group A (Infants with topical occlusive LA cream) showed minimum increase in the respiratory rate recorded at 5 min after vaccine injection, followed by Group C (Infants with topical LA spray with vapocoolant) whereas Control group (Infants not received any local anaesthesia) and Group B (Infants with topical LA spray without vapocoolant) exhibited the maximum increase (Table 3).

When the patients were grouped in two groups based on history of injectable vaccination, we observed that the group of patients with positive previous history of injectable vaccination had no statistically significant with negative history of injectable vaccination, in heart rate, pain score and respiratory rate (Table 4).

It was also observed that there was no statistical difference in the adverse effects among the groups of patient studied (Table 5).

DISCUSSION

Immunization has a key role in maintaining global public health; numerous individuals either refuse or delay immunization.^{3,4} One of the well-documented barriers to immunization is pain from the requisite needle puncture. Several methods have been employed to reduce injection pain during immunization in children.

In our study we used topical occlusive local anesthetic (LA) cream, topical LA spray with vapocoolant, topical LA spray without vapocoolant and compared their effect by using MBPS.⁵ Among the four groups of the patients studied we observed that the mean pain scores after vaccine injection were minimum in Group A (Infants with topical occlusive LA cream) this was followed by Group C (infants with topical LA spray with vapocoolant), whereas Control group of infants who did not receive any local anesthesia and Group B (Infants with topical LA spray without vapocoolant) exhibited the higher pain scores values.

Our findings of topical occlusive cream being the most effective in preventing injection pain are similar to various other studies. Taddio et al studied Eutectic Mixture of local anesthetics (EMLA) to prevent injection pain in 49 infants.¹ O'Brein L et al in their double blind randomized placebo controlled trial using 4% amethocaine gel found MBPS pain score to be significantly lower in the amethocaine group.⁶ Similarly, Halperin SA et al studied the role of lidocaine-prilocaine patch (EMLA) in decreasing the pain associated with MMR vaccine, and found that MBPS score was significantly lower in those who received the patch.^{7,8}

EMLA patch was also shown to be beneficial in children of age group 4-6 years who were studied for intramuscular injection pain using Faces pain scale and Visual Analogue scale.⁹

Topical occlusive cream has thus been found effective in decreasing injection pain. The eutectic mixture of local anesthetics in topical occlusive cream penetrates intact skin, causes dermal anesthesia, and significantly reduces puncture pain.¹⁰

In our study, we found that Group C (topical LA spray with vapocoolant group) had lower pain scores after injection, as compared to the topical LA spray without vapocoolant (Group B) or control group. This indicates that use of vapocoolant along with local anesthetic provides additional benefit in decreasing injection pain. Evelyn Cohen Reis et al in their study using vapocoolant spray (ethyl chloride vapocoolant) reported that it was equally effective as EMLA cream in reducing immunization pain in school aged children.⁴ They also observed that vapocoolant spray is less expensive and faster acting than EMLA cream and thus may help overcome the resistance of physicians and parents to multiple injections that lead to missed opportunities to immunization. Maikler VE also studied the effect of cooling using skin refrigerant/anesthetic during routine DPT vaccine administration, and found fewer distress behaviors in this group as compared to compressed air.¹¹

In case of vapocoolant immediate topical analgesia is provided based on the chilling effect of evaporation, which is attained by spraying the determined surface with volatile liquid sprays (e.g. ethyl chloride, fluorohydrocarbon).^{12,13} Rapid evaporation of the volatile liquid spray from the skin surface causes a decrease in temperature and results in temporary interruption of pain sensation, possibly through desensitization of pain receptors or activation of ion channels involved in pain transmission.

Among the four groups of the patients studied we observed a statistical difference in the heart rate, respiratory rates and the mean pain score of the patients. Group A (Infants with topical occlusive LA cream) showed minimum increase in the heart rate and respiratory rates recorded at 5 min after vaccine injection and it was followed by Group C (Infants with topical LA spray with vapocoolant). Control group (Infants not received any local anesthesia) and Group B (Infants with topical LA spray without vapocoolant) exhibited the maximum increase in the heart rate and respiratory rates recorded at 5 min after vaccine injection. This different response of heart rate and respiratory rate following injection in the four groups was commensurate with the observed post-injection pain scores in these groups. The group (Group A) with minimal pain scores showed minimal rise in heart rate and respiratory rate following injection. There are few studies which have measured the heart rate and respiratory rate changes following

intramuscular vaccine injection. However it is well known in neonates that the physiological stress response to pain due to release of catecholamines causes rise in heart rate and blood pressure. A similar catecholamine response following intramuscular vaccine injection may be responsible for the findings of our study.

In our study, we observed that there was no statistically significant difference in the post injection pain scores at 15 sec, 60 sec and 5 min between the group of patients with history of previous injectable vaccination, and the group with negative history of previous injectable vaccination. However some authors have reported that previous experience of pain affects the subsequent response to the next painful experience. Geyer J et al demonstrated difference in response to vaccination among infants who had undergone circumcision with anesthesia as compared to those who had not received anesthesia.¹⁴ More studies are needed to prove or refute the role of previous vaccination experience on pain perception in infants. We observed no significant difference in the incidence of adverse effects in the four groups. Other studies have not shown any specific adverse effects following the use of topical occlusive LA cream or vapocoolant.

The finding of our study showing that topical occlusive LA cream significantly decreases injection pain in infants has applicability in clinical practice. If this finding is supported by large randomized controlled trials, topical occlusive LA cream can be routinely used in infants before administering intramuscular vaccine injections. LA spray with vapocoolant which also showed lower pain scores in our study needs to be evaluated in larger studies, as it has inherent advantages of faster onset of action. The limitations of our study were that it was confined to studying only effect of local anesthetics in reducing injection pain during immunization in infants. Other potentially confounding factors like injection site selection, needle length, vaccine temperature, injection formulation, distraction techniques, site pressure, injection technique and parental behavior were not included in this study. A large randomized controlled trial in Indian conditions which includes all these factors would be revelatory.

CONCLUSION

Topical occlusive local anesthetic cream and topical LA spray with vapocoolant were effective in alleviating injection pain perceived by infants during vaccination, and were found to be better than topical LA spray without vapocoolant or no topical anesthetic. Use of topical occlusive LA cream led to lower pain scores than use of LA spray with vapocoolant. Infants with previous history of receiving injectable vaccine had no significant difference in pain score when compared to infants without previous history of receiving injectable vaccine. There was no significant difference in the profile of side

effects following vaccine injection in the four studied groups of the patients.

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