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Original Research Article

Comparison of efficacy of eutectic mixture of local anaesthetic with amethocaine on pain during venipuncture among term neonates in a tertiary care hospital, India

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ABSTRACT

Background: Neonates are frequently subjected to painful procedures which can adversely affect future pain perception. Pain control measures during invasive procedures include non-pharmacological and pharmacological methods. One pharmacological intervention that can be used prior to a needle insertion procedure is application of a topical local anaesthetic to numb the skin. Topical anaesthetics prevent nerve impulse transmission, promoting skin analgesia by acting on the free dermal terminations. This study compares the efficacy of eutectic mixture of local anaesthetic with amethocaine on pain during venipuncture among term neonates.
Methods: A randomized clinical trial was conducted with 70 term neonates who underwent venepuncture in neonatal intensive care unit of a tertiary care centre. A simple random sampling technique was used to enrol the neonates who met the inclusion criteria. Neonatal infant pain scale was used to collect the data. Descriptive and inferential statistics were used to analyse the data. frequency and percentage were used to describe the clinical and demographic variables of the study participants. The efficacy of topical local anaesthetics was analysed using independent student t test. Chi-square test was used to identify the association of level of pain with clinical and demographic characteristics of the neonate. The analysis was done with SPSS 21st version.
Results: Compared to amethocaine group, in eutectic mixture of local anaesthetic (EMLA) group only lesser number of neonates experienced severe level of pain and mild to moderate level of pain. Though mean pain score in EMLA group (3.457±1.633) was lesser than amethocaine group (4.000±1.514) it was not significant (p=0.347).
Conclusions: The study revealed the efficacy of topical anaesthetics in relieving pain in term neonates during venipuncture.

Keywords: Venipuncture, Term neonates, EMLA, Amethocaine, Pain

INTRODUCTION

Painful skin procedures are a major source of discomfort and distress to children, parents and health professionals. Neonates exhibit physiological, hormonal and behavioural response to pain similar to but more intense than adult. All these responses, results in adverse sequelae in the forms of poor neurologic outcomes and abnormal response to pain later in life including altered pain processing, impaired visual-perceptual ability and attention deficit disorder.[1]

Alleviation of pain is a basic right for every individual irrespective of age or size. The International Association for the study of pain (IASP) defined pain as 'An unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage.[2] Assessment of pain in a preverbal child is difficult, especially in the neonate. The most reliable way

of assessing pain is self-report by the individual. Even though infants are not able to verbalize, they do feel pain and express in various ways. From 24 weeks of Post-conceptional age, all the neurotransmitters and pain modulation receptors are present and responsive to painful stimuli. Thus, fetus and newborns feel pain. Pain in the newborns cause change in the behavior and physiological parameters. So, the evaluation of pain must be based on physiological changes and behavioural observations. Although behaviors such as vocalization, facial expression, and body movements are common to all infants, crying associated with pain is more intense and sustained. Most infants respond with increased body movement, alteration in physiological parameters.[3]

If the pain is not managed properly in the early neonatal period it may result in impairment in the neuro-developmental outcomes and also alter the pain threshold and stress related behavior when exposed to painful stimuli in the later life.[4-7]

Emerging studies provide clinical evidence for an adverse effect of neonatal pain or stress in newborns and they are recommending protocols for minimization of pain exposure and pain control measures to avoid adverse effects later in the neonate's life due to painful procedures during hospitalization.[8] Pain control measures during invasive procedures include non-pharmacological and pharmacological methods. One pharmacological intervention that can be used prior to a needle insertion procedure is application of a topical local anaesthetic to numb the skin[9]. Topical anaesthetics prevent nerve impulse transmission, promoting skin analgesia by acting on the free dermal terminations. Topical Anaesthetic may help to reduce discomfort associated with invasive procedures such as venipuncture, heel stick procedure and lumbar puncture in newborns.[10]

Eutectic mixture of local anaesthetic (EMLA) is currently a standard therapy to alleviate procedural pain in children in many hospitals. EMLA cream (lidocaine 2.5% and prilocaine 2.5%) is indicated for use on normal, intact skin before minor skin procedures including venipuncture.[11,12] Amethocaine is a new topical anaesthetic that requires a shorter application time for skin anaesthesia. Amethocaine is indicated for local topical anesthesia prior to venipuncture or venous cannulation. It is rapidly absorbed from mucous membranes.[13]

So far very few studies have been conducted to assess the effect of topical local anaesthetic on pain during venipuncture among term neonates. The studies that compared the effect of different topical local anaesthetic is still limited. It reflects the need for more research studies on topical local anaesthetics. The present research was carried out with an intention to compare the efficacy of eutectic mixture of local anaesthetic with amethocaine on pain during venipuncture among term neonates.

METHODS

The present study is a randomized clinical trial with registration code (CTRI/2018/09/021516). The study was carried out in the neonatal intensive care unit in Jawaharlal institute of post graduate medical education and research (JIPMER) hospital during October 2018 to January 2019 with seventy term neonates.

An inclusion criterion was the term neonates admitted in neonatal intensive care unit and underwent venipuncture procedure. Term neonates who were sick and who were on opioid analgesic or on sedatives were excluded from the study. Block randomization with varying block size generated through the computer was used to randomize the participants into study groups. Allocation concealment was done by using sealed opaque and serially numbered envelopes. Enrolment, intervention allocation, follow-up and analysis details of the participants were shown in Figure 1.

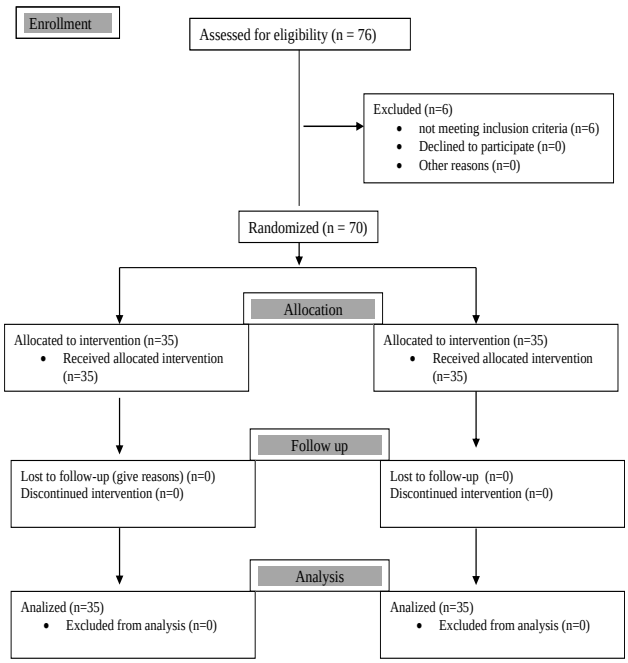

Figure 1: Consent flow diagram.

Demographic and clinical variables proforma was used to collect the basic data of the neonate like gender, age, gestational week and birth weight. Neonatal infant pain scale [NIPS] was used to assess the pain level of the neonate. The NIPS was developed by Lawrence et al in 1993 to evaluate the behavioural and physiological pain responses of preterm and term infants.

NIPS has six indicators. It includes facial expression, cry, breathing pattern, state of arousal, position of legs and position of arms. Each indicator has a score of 0 and 1 except cry, which has 0,1 and 2. Total, score is 7. Interpretation of scores includes 0-2 as no pain to mild

pain, 3-4 as mild to moderate pain and more than 4 as severe pain.

In group one, for the neonate's eutectic mixture of local anaesthetic (EMLA) was applied on the venipuncture area 45 minutes before the procedure and at the time of venipuncture the pain experienced by the neonates were assessed using NIPS. In group two, 20 minutes before the venipuncture Amethocaine, the local anaesthetic was applied on the venipuncture area and during the procedure the pain was assessed.

Both descriptive and inferential statistics were used to analyse the data. Descriptive statistics [frequency, percentage] was used to describe the clinical and demographic variables. Unpaired t test was used to compare the efficacy of EMLA and Amethocaine. Chi-square test was used to identify the association between the level of pain with demographic and clinical variables of the neonates. Data analysis was done with SPSS 21st version.

RESULTS

In both EMLA and Amethocaine group more than 50% were males. In EMLA group 54.3% were in the gestational age of 39-40 weeks and in amethocaine group 62.9% were in 37-39 weeks. Pertaining to birth weight in both the groups majority of the neonates had 2.5-3.5 kg. Regarding age in both the groups majority were below 5 days of age (Table 1).

In EMLA group only 28.6% had severe pain compared to 37.1% in Amethocaine group. Mild to moderate pain also less in EMLA group (EMLA-40%, amethocaine-42.9%). Only 20% had no pain to mild pain in the amethocaine group whereas in the EMLA group it was 31.4% (Table 2).

Comparison of level of pain between the two groups revealed that though the mean pain score was less in EMLA group, it was not statistically significant (p=0.347) (Table 3).

There was no association between the level of pain and demographic and clinical variables in EMLA group (Table 4). Whereas in amethocaine group gestational age had association (Table 5).

Table 1: Clinical characteristics of term neonates in both groups (n=70).

Clinical variables	EMLA group		Amethocaine group		Statistical significance
	N	%	N	%	
Gender					x^2=.058 P=(500) df=1
Male	20	57.1	19	54.3	
Female	15	42.9	16	45.7	
Gestational age (weeks)					x^2= 2.072 P=(0.115) df=1
37-39	16	45.7	22	62.9	
39-40	19	54.3	13	37.1	
Birth weight (kg)					x^2 = 1.609 P=(0.171) df=1
1.5-2.5	4	11.4	8	22.9	
2.5-3.5	31	88.6	27	77.1	
Age (days)					x^2= 1.296 P=(0.197) df=1
Less than 5	29	82.9	25	71.4	
More than 5	6	17.1	10	28.6	

Table 2: Level of pain in EMLA and amethocaine group (n=70).

Level of pain among term neonates	EMLA group		Amethocaine group	
	N	%	N	%
No pain to mild pain	11	31.4	7	20
Mild to moderate pain	14	40	15	42.9
Severe pain	10	28.6	13	37.1

Table 3: Comparison of mean pain scores in EMLA and amethocaine group (n=70).

Level of pain among term neonates	EMLA group		Amethocaine group		T	P
	Mean	S. D.	Mean	S. D.		
	3.457	1.633	4.000	1.514	-1.445	0.3457

Table 4: Association between the level of pain and clinical variables in EMLA group.

Clinical variables	EMLA group						X^4	Df	P value
	Level of pain								
	No pain to mild		Mild to moderate		Severe				
	N	%	N	%	N	%			
Gender									
Male	6	30	11	55	3	15	5.664	2	0.059
Female	5	33.3	3	20	7	46.7			
Gestational age (weeks)									
37-39	8	50	5	31.2	3	18.8	4.794	2	0.091
39-40	3	15.8	9	47.4	7	36.8			

Continued.

Clinical variables	EMLA group						X^4	Df	P value
	Level of pain								
	No pain to mild		Mild to moderate		Severe				
	N	%	N	%	N	%			
Birth weight (kg)									
1.5-2.5	2	50	1	25	1	25	0.770	2	0.681
2.5-3.5	9	29	13	41.9	9	29.1			
Age (days)									
Less than 5	8	27.6	11	37.9	10	34.5	3.045	2	0.218
More than 5	3	50	3	50	0	0			

Table 5: Association between the level of pain and clinical variables in amethocaine group.

Clinical variables	Amethocaine group						X^4	Df	P value
	Level of pain								
	No pain to mild		Mild to moderate		Severe				
	N	%	N	%	N	%			
Gender									
Male	3	15.8	9	47.4	7	36.8	0.567	2	0.753
Female	4	25	6	37.5	6	37.5			
Gestational age (weeks)									
37-39	5	22.7	14	63.6	3	13.6	14.99	2	0.001**
39-40	2	15.4	1	7.7	10	76.9			
Birth weight (kg)									
1.5-2.5	3	37.5	4	50	1	12.5	3.407	2	0.182
2.5-3.5	4	14.8	11	40.7	12	44.5			
Age (days)									
Less than 5	4	16	12	48	9	36	1.217	2	0.533
More than 5	3	30	3	30	4	40			

**P<0.01

DISCUSSION

The quantification of pain in newborn still remains a challenge among the health care personnel. There is raise in need on concentration about neonatal pain, its assessment and management of acute pain produced due to painful procedures in clinical settings. A variety of pain assessment approaches namely behaviour observation, physiological parameters assessment has been used to accurately quantify neonates pain perception.[15]

Acute episodic pain may lead to early neurologic injury while repeated and prolonged exposure to pain may alter subsequent psychokinetic development and long-term neuro developmental, behavioural and socio-emotional outcome.[16,17]

Mean pain score in EMLA group was lesser than amethocaine group but it was not statistically significant. The study results were in accordance with those of Lawerance et al study where 30 children were recruited in the study and compared the efficacy of two local anaesthetics EMLA and ELA-Max. In group one EMLA was applied to dorsal aspect of hand 45 minutes before venipuncture and in group two ELA-Max was applied 30 minutes before venipuncture. children pain score was rated using Oucher pain scale and the results revealed that there was no statistical difference in pain scores[1,8] Bishai et al conducted a randomized cross over study to compare the relative efficacy of amethocaine gel and lidocaine-prilocaine cream. In group one, one gram of amethocaine was applied 30 minutes before port-a-cath puncture and in group two, one gram of lidocaine-prilocaine was applied 60 minutes before the procedure. Visual analogue scale was used to assess the pain score. The study results showed that the mean pain score in amethocaine group was 2.0 and in EMLA group it was 1.5 and there was no statistically significant difference and p=0.09.[19] Similar findings were noted in a randomized double blind controlled study conducted by Newbury et al to compare the efficacy of EMLA and Amethocaine. Sixty-five participants who underwent intravenous cannulations were enrolled. The results revealed that there was no statistically difference between the two groups and p=0.53.[13] Janet et al conducted a randomised trial among 69 participants to compare the efficacy of ELA-Max and 1% lidocaine on pain among children who underwent peripheral intravenous insertion. Visual analogue scale was used to assess the pain score. Data were analysed with chi square and t test. The results

revealed that there were no significant differences between the groups.[20]

The findings of the study are not generalizable due to small sample size and also only term neonates were enrolled in the study.

CONCLUSION

Though many non-pharmacological methods were practiced in neonatal intensive care units in pain management during invasive procedures use of topical anaesthetic to be included in the pain management protocol.

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Ethical approval: The study was approved by the Institutional Ethics Committee-JIP/IEC/2018/028.

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