International Journal of Contemporary Pediatrics
Sharma A et al. Int J Contemp Pediatr. 2021 Nov;8(11):1815-1818
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20214151

Original Research Article

Efficacy of eutectic mixture of local anesthetics in alleviating pain associated with lumbar puncture in newborns: a placebo compared randomized controlled trial

Akshi Sharma, Rakesh Sharma, Mangla Sood*, Pancham Kumar

Department of Pediatrics, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India

Received: 01 October 2021
Accepted: 14 October 2021

***Correspondence:**
Dr. Mangla Sood,
E-mail: drmanglasood@gmail.com

ABSTRACT

Background: Lumbar puncture (LP) is one of the most commonly encountered painful procedure in paediatric medicine. Research has shown that neonates too experience pain from noxious stimuli that can be more intense than what is experienced by an adult, and so have the right to receive safe, efficient and effective pain management. Objective was to determine efficacy of topical eutectic mixture of local anesthetics (EMLA) in alleviating pain associated with lumbar puncture among newborns admitted to sick newborn care unit (SNCU).
Methods: The study was a one-year tertiary care teaching hospital-based randomised comparative double blinded trial among 42 neonates aged 32 weeks or more admitted to SNCU and required a diagnostic lumbar puncture, randomly assigned to one of two groups. Half hour before the procedure, 1 g of topical EMLA cream was applied to LP site in intervention group versus placebo in other group. At different stages, the heart rate, transcutaneous oxygen saturation level, and total behaviour score were captured on a video camera and rated using the neonatal facial coding system.
Results: EMLA dramatically lowers pain sensitivity when compared to placebo. Total behavioural score means±standard deviation (SD) at the moment of needle insertion (EMLA: 1.05±1.24; placebo: 2.71±1.76, p≤0.001) and post procedural 5 minute later was (EMLA: 0.05±0.22; placebo: 0.81±0.92, p≤0.01). Similarly, oxygen saturation level when needle was in spinal place (EMLA: 96.76±2.45; placebo: 94.29±3.62, p=0.01) and post procedural 1 hour later was (EMLA: 98.81±1.94; placebo: 97.48±2.18, p=0.04). The heart rate of all newborns in both groups was greater than it was at baseline, although the difference was not significant.
Conclusions: EMLA is an effective agent in reducing pain associated with LP among newborns.

Keywords: Infant, Newborn, Lumbar puncture, Lidocaine, Prilocaine drug combination, Pain management

INTRODUCTION

In hospital settings, lumbar puncture (LP) is one of the most common unpleasant procedures in paediatric medicine. Due to concerns about the harmful effects of various local anaesthetic drugs, LP in newborns has traditionally been conducted without the use of a local anaesthetic agent. Long-held medical beliefs that neonates are incapable of feeling pain have been disproved by research, which has shown them capable of both perceiving and responding to unpleasant stimuli in a consistent manner.[1] Since then, several studies have been undertaken all around the world to document the physiological, behavioural, and biochemical responses of newborns to painful operations.[2,3] Because repeated painful stimuli can lead to behavioural and mental issues, psychosis, intractable pain states, and changed pain responses later in life, babies have the right to safe, efficient, and effective pain management.[4]

Eutectic mixture of local anesthetics (EMLA) is a 1: 1 oil in water emulsion of 2.5 percent lidocaine and prilocaine,

used to treat pain in newborns and toddlers since 1980. It has been proven to reduce pain during circumcision, venepuncture, and percutaneous venous catheter placement.[2,4,5] Because there is inadequate data to advocate its use for LP procedure, the current study was designed to investigate the efficacy of topical EMLA in alleviating pain associated with lumbar puncture in newborns.

METHODS

Study design, settings, and participants

This was a hospital based randomised comparative double blinded study conducted over a period of one year from December 2018 to November 2019 in sick newborn care unit (SNCU) of tertiary care teaching hospital in Shimla, Himachal Pradesh, India. Inclusion criteria for the study was sick newborns admitted with gestational age of 32 weeks or older, born through uncomplicated vaginal or caesarean delivery, with 5-minute Apgar score of 7 or higher, and required diagnostic LP procedure to rule out meningitis for seizures or as a part of a septic work- up as per intensive care treatment protocols. Newborns with lumbosacral structural, major congenital or neurodevelopment anomalies, or received any sedatives or analgesics (phenobarbitone, phenytoin), hemodynamically unstable, had coagulopathy, methemoglobinemia in blood gas, glucose-6-phosphate dehydrogenase (G6PD) deficiency, severe hepatic or renal disease, requiring any kind of supportive treatment (ventilatory support, ionotropic support) after birth or when mothers had received any drug which causes central nervous system (CNS) depression in the baby (anti–depressants, benzodiazepines) were excluded from the study. Study was approved by the institute ethic board.

A computer-generated sequence was used to divide 42 babies into two groups. Half an hour before lumbar puncture, the intervention group received 1 g of EMLA cream. At the same time, controls got placebo (an inert oil that could not be distinguished from EMLA in terms of appearance and odour). The hospital pharmacy packaged 1 g of both the intervention and placebo into opaque similar sterile ampules and serially labelled them. For allocation concealment, serially labelled opaque envelops were under charge of the unit in charge, who was not a member of the research team. Envelopes were opened and intervention was used only when parents consented to participate.

Study procedure

After parents/ caregivers informed consent and after breast feeding, newborns were shifted to pre-warm procedure room and placed under radiant warmer. Medicine was uniformly applied to an area of 9 cm^2 at the site of the procedure and covered with tegaderm for 30 minutes before the scheduled time by the staff nurse. The dressing was removed immediately prior to the procedure. LP was done at the same state of arousal in all the neonates (at stage iii or iv),[6] in the same room and surrounding under the same radiant warmer. Same doctor carried out all LP to remove bias. After removal of dressing, the skin was wiped dry, disinfected with povidone – iodine solution, followed by alcohol and draped with sterile drapes following all standard aseptic instructions. LP was performed with a 24-gauge needle.

The procedure comprised of 7 events: baseline (pre-procedural 30 minutes before medicine application); preparation; needle insertion; needle in place; needle withdrawal; 5-minute after needle withdrawal; and 1-hour after needle withdrawal.

Physiological responses (heart rate, transcutaneous oxygen saturation level) were monitored using a compact vital sign monitor (PHILIPS-IntelliVue MP 50). Facial expressions were recorded during events on mobile phone camera mounted on a tripod at the bedside, which captured close-up view of the neonate's face continuously. These videotapes were decoded by different researcher was never present during the procedure, trained for using neonatal facial coding system (NFCS) developed by Grunau and Craig and simplified by Rushforth and Levene.[7,8]

Eight items of facial action (brow bulge, eye squeeze, nasolabial furrow, and open mouth, mouth stretch, tongue tautening, tongue protrusion and chin quiver) and the presence of crying were used as measures of behavioural response to pain. Each response was given a score of 1 if present and 0 if absent, for a possible total ranging from 0 to 8. After the procedure, all newborns were closely monitored for a period of 24 hours for the presence of any local or systemic adverse effects linked EMLA application.

Statistical analysis

Data was analysed and statistically evaluated using Epi Info software of CDC.[9] After checking for normality using Kolmogorov-Smirnov test, quantitative data was expressed in mean, standard deviation while qualitative data was expressed in percentage. The difference between means of two groups was compared by Student t test or Mann Whitney U test. P value less than 0.05 was considered statistically significant.

RESULTS

Demographic data of both the groups was comparable. The mean birth weight of intervention and placebo group was 2423±723.81 g and 2385±743.16 g respectively, mean gestational age was 36.91±2.53 weeks for the intervention and 37.52±2.67 weeks for the placebo group. The LP was performed at a mean postconceptional age of 9.57±7.66 days in intervention and 9.95±8.11 days in placebo group. The male to female ratio was 13:8 in the intervention and 14:7 in the placebo group.

Mean±SD total behaviour score, heart rate, and oxygen saturation levels for the intervention and placebo group at different events are presented in Table 1 and Figure 1 and 2. Total behavioural score was significantly lesser in intervention group at all steps except at the time of needle withdrawal and one-hour post LP. Behavioural score for both groups was significantly higher compared to baseline for all events except half hour before procedure and one-hour post procedure. Heart rate for both groups was higher from baseline at all events except 5-minute post procedure and 1-hour post procedure, without any significant difference between both the groups (Figure 1).

Oxygen saturation level was found significantly different between both the groups when needle was in spinal space. The mean difference between events ranged between 1% and 4%. The percentage change from the baseline value was found to be very small in the intervention group compared with the placebo group during other times (Figure 2).

Table 1: Behavioural score comparison between both groups at different interval.

Behavioural score	Group 1 intervention (n=21)	Group 2 control (n=21)	Mean difference (95% CI)	P value
Prior to 1 hour before procedure	0.0±0.0	0.0±0.0	-	-
At the time of preparation	1.52±1.36	2.43±1.32	-0.90 (-1.74 to -0.06)	0.03
At the time of needle insertion	1.05±1.24	2.71±1.76	-1.66 (-2.61 to -0.71)	<0.01
Needle in place	0.38±0.74	1.48±1.63	-1.09 (-1.88 to -0.30)	0.02
At the time of needle withdrawal	0.48±0.87	1.30±1.59	-0.82 (-1.63 to 0.01)	0.08
Post-procedure (5 minute after)	0.05±0.22	0.81±0.92	-0.76 (-1.18 to -0.34)	<0.01
Post-procedural (1 hour after)	0.0±0.0	0.0±0.0	-	-

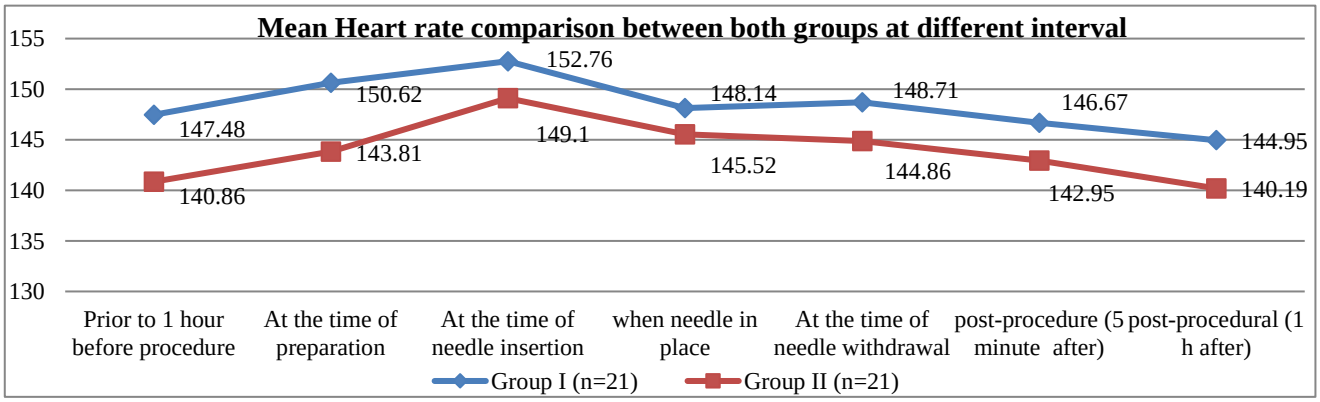

Figure 1: Mean heart rate comparison between both groups at different interval.

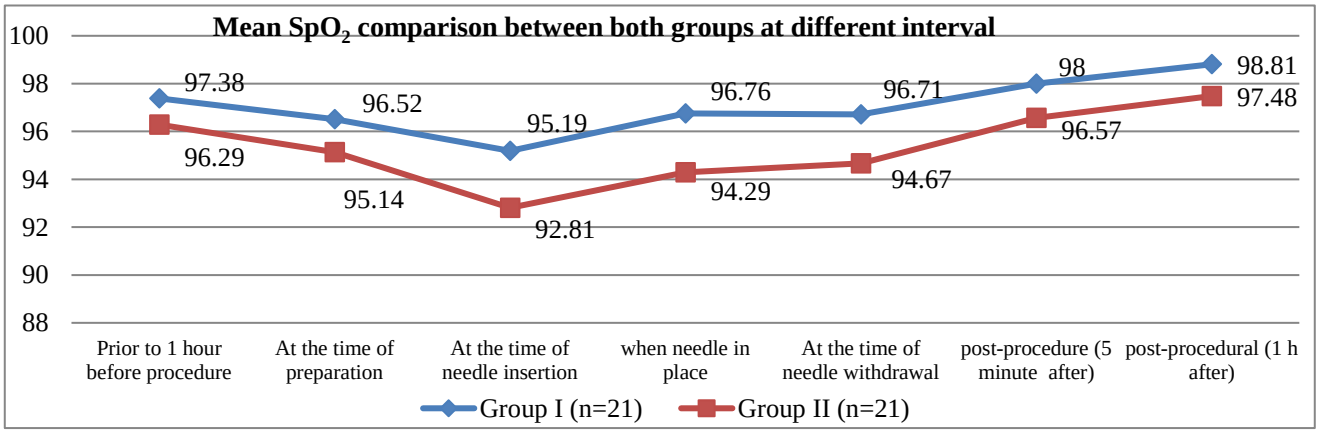

Figure 2: Mean SpO_2 comparison between both groups at different interval.

DISCUSSION

LP being a painful procedure, newborns experiences pain in the form of increased heart rate, decreased oxygen saturation level, facial responses and crying during the procedure. Maximum pain response was noted while positioning the neonate and insertion of needle in spinal space. EMLA cream effectively attenuated the pain

response during the time of needle insertion and needle in space. Maximum pain responses and crying occurred during needle insertion in the placebo group. Though the pain of LP could not be eliminated completely by EMLA application, significant changes from baseline during most events occurred. Positioning of newborn for LP resulted in crying, facial expression and heart rate changes with decreased oxygen saturation, without any difference in EMLA vs placebo group.

Our study has similarities with Kaur et al where EMLA was found effective for reducing the pain associated during LP needle insertion and withdrawal.[10] Total behaviour score was also lower in EMLA group compared to placebo.

Orthotoludin a metabolite of prilocaine, can lead to methemoglobinemia.[11] Excessive amounts of EMLA, a large application area, prolonged application time, diseased and/or inflamed skin (e.g. vascular malformations, molluscum contagiosum, eczema, previously abraded skin), age less than 3 months, and concurrent use of a methaemoglobin-inducing agent are all possible factors that contributed to the development of systemic toxicity.[11] But a single application of 1 g EMLA for LP was found safe without clinical side effect among any newborn even after 24 hours observation in our study. We did not measure the serum levels of lidocaine, prilocaine or performed blood gas for methemoglobinemia post application.

Limitations

Our study is limited with small sample size, we used only NFCS, a comparatively easier one. In newborns and infants, pain tends to manifest as crying, facial expressions and body movements. The NFCS tests only facial expression, other scales like face, legs, activity, cry and cognoscibility pain scale (FLACC) measures pain using different behavioural indicators. We also did not be compare other methods of neonatal pain control like oral sucrose, skin-skin contact, breast feeding with EMLA.

CONCLUSION

This study concluded that EMLA is effective in reducing acute pain in newborns in LP procedure. The effect of EMLA may differ with weight, gestational age and amount of subcutaneous fat. Hence further studies with larger sample size and different methods of pain assessment may be conducted in future.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Anand KJS, Hickey PR. Pain and Its Effects in the Human Neonate and Fetus. N Engl J Med. 1987;317(21):1321-9.
2. M Holsti L, Grunau RE, Shany E. Assessing pain in preterm infants in the neonatal intensive care unit: moving to a 'brain-oriented' approach. Pain Manag. 2011;1(2):171-9.
3. Hui-Chen F, Hsiu-Lin C, Shun-Line C. The Effect of EMLA Cream on Minimizing Pain during Venipuncture in Premature Infants. J Trop Pediatr. 2013;59(1):72-3.
4. Sharara-Chami R, Lakissian Z, Charafeddine L, Milad N, El-Hout Y. Combination Analgesia for Neonatal Circumcision: A Randomized Controlled Trial. Pediatrics. 2017;140(6):e20171935.
5. Spence K, Henderson-Smart D, New K, Evans C, Whitelaw J, Woolnough R. Evidenced-based clinical practice guideline for management of newborn pain. J Paediatr Child Health. 2010;46(4):184-92.
6. Prechtl HFR. The behavioural states of the newborn infant (a review). Brain Res. 1974;76(2):185-212.
7. Garcia OC, Reichberg S, Brion LP, Schulman M. Topical anesthesia for line insertion in very low birth weight infants. J Perinatol. 1997;17(6):477-80.
8. Grunau RVE, Craig KD. Pain expression in neonates: facial action and cry. Pain. 1987;28(3):395-410.
9. Centers for Disease Control and Prevention. Epi InfoTM. Available at: https://www.cdc.gov/epiinfo/index.html. Accessed on 08 October 2021.
10. Kaur G, Gupta P, Kumar A. A Randomized Trial of Eutectic Mixture of Local Anesthetics During Lumbar Puncture in Newborns. Arch Pediatr Adolesc Med. 2003;157(11):1065.
11. Tran AN, Koo JY. Risk of systemic toxicity with topical lidocaine/prilocaine: a review. J Drugs Dermatol. 2014;13(9):1118-22.

Cite this article as: Sharma A, Sharma R, Sood M, Kumar P. Efficacy of eutectic mixture of local anesthetics in alleviating pain associated with lumbar puncture in newborns: a placebo compared randomized controlled trial. Int J Contemp Pediatr 2021;8:1815-8.