CLINICAL INVESTIGATION

Oral dextrose v/s breast milk for the pain relief of newborn infants

Abstract

Aim: Pain management in newborn infants especially for mild to moderate pain is underused. The use of sucrose and glucose are found to be effective. This study is to find the effect of oral dextrose solution on pain relief in term neonates.

Methodology: In a randomized controlled clinical trial, 124 term neonates were enrolled in the study. They were randomized to receive oral dextrose (25%) or breast milk two minutes before venipunctures. Pain reactions were scored with the NIPS pain scoring system, heart rate, and oxygen saturation after venipunctures was recorded.

Results: There were significantly lower pain score in dextrose group after venipunctures (NIPS pain score: 4.67+1.04 and 6.62+0.82 at 1st minute, 2.04 ± 1.45 and 4.08 ± 1.05 at 2nd minutes and 1.63+0.76 and 3.02+1.08 at 3rd minute respectively) The mean heart rate of the group I (166.57 ± 12.25 /min) was high compared to the group II (144.8 ± 12.44 /min). There was desaturation noted in both the groups.

Conclusion: Using 2 ml of 25% oral dextrose solution is a useful, easy, non-expensive, and non-pharmacologic method for managing mild to moderate pain in neonates.

Keywords: pain • newborn • dextrose • breast milk • analgesia

Submitted: 29 June 2020; Accepted: 20 July 2020; Published online: 10 August 2020

Introduction

Newborn babies are undergoing a number of painful procedures before getting discharged. Even though surgical and major procedural pain management in newborn infants is effective, they are underused in minor procedures and nursing care. It has been found that the neuro-anatomical and chemical development for pain recognition starts at an early stage of life. These painful interventions can later affect the biopsycho-social development of the individual [1,2]. Physiological and behavioral parameters during the interventions can be used to evaluate the pain of newborn infants. These include heart rate, respiratory rate, blood pressure, saturation of oxygen, hormonal changes are the physiological parameters and facial mimicry, motor patterns, crying are the behavioral parameters [2]. A number of pharmacological and non-pharmacological techniques can be used for pain relief.

According to the International Association for the Study of Pain, mild to moderate pain is managed by a pacifier, sucrose, glucose, breast milk, kangaroo care, massage, sensorial saturation, and topical anesthetic cream or gel [3]. Sucrose and topical anesthetics are not readily available in all the health centers and are expensive while dextrose (25% solution) is available in all health centers and is cheap. Rest of the methods especially kangaroo care, massage, and sensorial stimulation are difficult in most of situations. Oral glucose solution has been used for the treatment of pain with good analgesic effect especially for mild to moderate pain or as adjuvant therapy for severe pain [4]. Most of the studies including a Cochrane review

Tharun C Varghese^{1*}, Anna Susan Paul², Santhosh Soans³

¹Department of Paediatrics, Amala Institute of Medical Sciences, Thrissur, Kerala, India

²Department of Community Medicine, Amala Institute of Medical Sciences, Thrissur, Kerala, India

³Department of Paediatrics, AJ Institute of Medical Sciences, Mangalore, Karnataka, India

*Author for correspondence: tharunvarg@gmail.com [5] observed minor side effects due to the use of oral glucose solution [5]. The main aim of this article is to find the effect of oral dextrose solution on pain relief in term neonates especially during venipunctures and to study the side effects if any.

Materials and Methods

A Randomized Controlled Clinical Trial (RCT) was conducted in the neonatal unit of a Level III hospital from August 2019 to Jan 2020 after getting consent from the institutional ethical committee.

The aim of the study is to assess the effect of 25% dextrose as an analgesic for mild to moderate pain in newborn infants.

Eligible infants which were included were 37 completed weeks of gestational age at birth; were between 1 and 7 days old; had 5 minute Apgar scores of 7 or more; were fed at least 1 hour before data collection; had no syndromes, congenital anomalies, or previous surgery; were not born to mothers with chronic infection; we're born to mothers not known to be a user of illicit drugs, and had a clinical indication for blood sampling. Infants were excluded if they were diagnosed with neurologic problems of any type, if they had received analgesic or sedative drugs within 24 hours of enrolment, or if their mother had any problem that hindered them from giving breast milk or those babies not satisfying the inclusion criteria.

All the newborn infants were randomized into two groups; group I (having 25% dextrose as an analgesic) and group II (having breast milk as control). The allocation was achieved by using concealed envelopes containing intervention codes (I or II). Envelopes were exclusively accessed by research assistants. Interventions investigated were 2 ml of expressed breast milk (Control group-II) and 2 ml of 25% dextrose (Study group-I), given by a needleless syringe to the anterior portion of the tongue 2 minutes before the peripheral venipuncture. Research assistants prepared syringes containing both solutions for all infants. Syringes were covered and labeled according to the groups. Neonates were kept under the warmer in servo mode during data collection. An oxygen saturation monitor was applied to the infant's hand or foot to monitor heart rate and oxygen saturation.

The research person offered the assigned solution to the infant after two minutes without any further handling.Neonates were kept in a semi-seated position and the duration of administration varied between 10 and 30 seconds according to the ability to swallow. By the end of solution administration, research assistants confirmed whether neonates had swallowed the entire volume offered and removed any solution residue from the infants' faces. All the infants who failed to swallow the entire volume offered were excluded to minimize the bias. After an additional 2 minutes, all the infants undergo peripheral venipunctures. Infants with repeated pricks were excluded from the study. If the time taken for venipunctures was more than one minute, the infant was excluded from the study. All the venipunctures is done by a single research person to minimize the bias.

The primary outcome was measured in terms of pain intensity as assessed with the NIPS (neonatal infant pain scale), heart rate, and oxygen saturation. The NIPS is a composite pain measure that includes physiologic indicators respiratory patterns and behavioral indicators like facial expression, cry, movements of arms, legs, and state arousal. Total pain scores of NIPS range from 0-7 (0-2=mild to no pain, 3-4=mild to moderate pain and >4=severe pain). Behavioral and physiologic indicators were assessed and documented at the bedside during and after the procedure by a single research assistant for all infants.

Heart rate baseline will be calculated for all infants 5 minutes prior to the procedure and an increase of heart rate of more than 10% of the baseline is considered significant. Baseline oxygen saturation is also checked 5 minutes prior to the procedure and the need for oxygen supplementation for maintaining saturation is considered significant.

All the infants are assessed at 1, 2, and 3 minutes after the procedure for pain. The heart rate and oxygen saturation were checked after 3 minutes of the procedure.

Statistical analysis was performed with SPSS 14.0 software by using a t-test and chi-square test. Values of P<0.05 were considered statistically significant (Table 1).

Results

A total of 485 infants were there in the study period, out of which 297 were excluded from the study as they didn't satisfy the inclusion criteria. The rest of the 188 term neonates were included in the study. Two groups of 94 each were randomized as Group I and II; but 18 of them were excluded as they didn't take the whole solution given to them, 22 were not

Table 1. Neonatal/Infant Pain Scale (NIPS)-Recommended for children less than 1 year old. (A score greater than 3 indicates pain).

indicates pain).		1
	Pain assessment	Score
	Facial expression	
0-relaxed muscles	Restful face, neutral expression	
1-grimace	Tight facial muscles; furrowed brow, chin, jaw (negative facial expression-nose, mouth brow)	
	Cry	
0-no cry	Quiet, not crying	
1-whimper	Mild moaning, intermittent	
2-vigorous cry	Loud scream; rising, shrill, continuous	
	Breathing pattern	
0-relaxed	Usual pattern for this infant	
1-change in breathing	Indrawing, irregular, faster than usual; gagging, breath holding	
	Arms	
0-relaxed/restrained	No muscular rigidity, occasional random movements of arms	
1-flexed/extended	Tense, straight arms, rigid and/or rapid extension, flexion	
	Legs	
0-relaxed/restrained	No muscular rigidity, occasional random movement of legs	
1-flexed/extended	Tense, straight legs, rigid and/or rapid extension, flexion	
	State of arousal	
0-sleeping/awake	Quiet, peaceful, sleeping or alert, random leg movements	
1-fussy	Alert, restless and thrashing	

Table 2. Showing no statistical differences between the 2 groups.						
Characteristics	Dextrose (62) Group I	Breast milk (62) Group II	p-value			
Gestational age (wks)	39.4 ± 1.14	38.6 ± 1.24	0.42			
Birth weight (gram)	2978.54 ± 250.16	2876 ± 287.8	0.48			
Postnatal age (day)	4.73 ± 1.25	4.53 ± 1.43	0.52			
Gender (Male/Female)	32/30	28/34	0.29			

 Table 3. There was no side effects noted in any of the neonates in the study group and all children were observed for the next 30 days for it.

 (Dextrose) Group I
 (Breast milk) Group II

		(Dextrose) Group I	(Breast milk) Group II	p-value
	Pain Score (at 1 min)	4.67 ± 1.04	6.62 ± 0.82	0.04
	Pain Score (at 2 min)	2.04 ± 1.45	4.08 ± 1.05	0.02
	Pain score (at 3 min)	1.63 ± 0.76	3.02 ± 1.08	0.01
	Heart rate/min (at 3 min)	166.57 ± 12.25	144.8 ± 12.44	0.13

willing to undergo the study, 24 had to be pricked again or the duration taken was more than 1 minute. Hence the remaining 124 babies; 62 of each group (I and II) have been studied and evaluated. The mean gestational age of group I was 39.4+1.14 weeks and that of group II was 38.6+1.24 weeks. The mean birth weight of the two groups was 2978.54 ± 250.16 grams and 2876 ± 287.8 grams respectively. The postnatal age of the two groups was 4.73 ± 1.25 days and $4.53 \pm$ ± 1.43 days respectively. The total number of male neonates in these groups were 32 and 28 respectively. On statistical analysis, it had been found that there are no significant differences between the two groups (Table 2).

Neonatal/Infant Pain Scale (NIPS) had been used in

both groups at 1, 2 and 3 minutes after the procedure with heart rate and saturation at 3^{rd} minute after the procedure. The mean values were 4.67+1.04 and 6.62+0.82 at 1^{st} minute, 2.04 ± 1.45 and 4.08 ± 1.05 at 2^{nd} minutes and 1.63+0.76 and 3.02+1.08 at 3^{rd} minute respectively. The mean heart rate of the group I (166.57 ± 12.25/min) was high compared to group II (144.8 ± 12.44/min). There was desaturation noted in both the groups. On statistical analysis, it had been found that there was a significant decrease in the pain score in the study group than in the control group in all three times. This shows that 25% dextrose is an effective analgesic for mild to moderate pain, especially in venipunctures as compared to breast milk with a considerable reduction in pain during and after the procedure. Even though there was an increase in heart rate in the study group than in the control group the difference was not statistically significant (Table 3).

Discussion

In this study, we assessed the efficacy of 25% dextrose for managing of infants pain in neonatal peripheral venipunctures and was found to be a statically significant reduction in pain during and after the procedure like Chermount et al. [6] when compared to control group.

This study also showed heart rate was increased in the group receiving dextrose when compared to the control group though like Gradin et al. [7] but it was not statistically significant. Various other studies also showed a similar increase in the heart rate during painful procedures [8-10].

There is no desaturation noted in any of the infants in both groups which is against the findings of Singh et al. [10] and Williamson et al. [11] in these studies they noted desaturation after the painful procedures.

All the infants were closely monitored for side effects of dextrose for 3 days and didn't find any. There was no nausea, vomiting, feeding intolerance, or NEC in any of the infants.

The use of 2 ml of 25% dextrose in term neonates during mild to the moderate painful procedure is effective.

The mechanism of action of glucose in pain relief could not be studied but various studies have shown a role of endogenous opioids [12-14] or a pre-absorptive mechanism [15] in pain relief. This study suggests great promise for future research and policy formation regarding the pain management of newborn infants.

The limitation of this study was that preterm infants were not included as they undergo more painful procedures than the term infants. The small sample size was also a limitation. In this study, we were unable to explain the cause of tachycardia in the study group as compared to the control group.

Conclusion

Using 2 ml of 25% oral dextrose solution is a useful, easy, non-expensive, and non-pharmacologic method for managing mild to moderate pain or as an adjuvant for severe pain in newborn infants. Compared to other methods oral dextrose is a more practical, safe, and effective method in Indian settings.

Executive summary

Aim: Pain management in newborn infants especially for mild to moderate pain is underused. The use of sucrose and glucose are found to be effective. This study is to find the effect of oral dextrose solution on pain relief in term neonates.

Methodology: In a randomized controlled clinical trial, 124 term neonates were enrolled in the study. They were randomized to receive oral dextrose (25%) or breast milk two minutes before venepuncture. Pain reactions were scored with the NIPS pain scoring system, heart rate, and oxygen saturation after venepuncture was recorded.

Results: There were significantly lower pain score in dextrose group after venepuncture (NIPS pain score: 4.67 + 1.04 and 6.62 + 0.82 at 1st minute, 2.04 ± 1.45 and 4.08 ± 1.05 at 2nd minutes and 1.63 + 0.76 and 3.02 + 1.08 at 3rd minute respectively) The mean heart rate of the group I (166.57 \pm 12.25/min) was high compared to the group II (144.8 \pm 12.44 /min). There was desaturation noted in both the groups.

Conclusion: Using 2 ml of 25% oral dextrose solution is a useful, easy, non-expensive, and non-pharmacologic method for managing mild to moderate pain in neonates.

References

- 1. Grunau R. Early pain in preterm infants. A model of long term effects. *Clin Perinatol* 29: 373-394 (2002).
- Batton DG, Barrington KJ, Wallman C, et al. Prevention and management of pain in the neonate: An update. *Pediatrics* 118: 2231-2241 (2006).
- Anand KJS, Bergqvist L, Whit Hall R, et al. Acute pain management in newborn infants. *Pain: Clin Updates* 19: 1-6 (2011).
- 4. Dilen B, Elseviers M. Oral glucose as pain relief in newborns: Results of a clinical trial. *Birth* 37: 98-105 (2010).
- Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. *Cochrane Database Syst Rev* 1: CD001069 (2010).
- Chermont AG, Falcão LF, de Souza Silva EH, et al. Skin-toskin contact and/ or oral 25% dextrose for procedural pain relief for term newborn infants. *Pediatrics* 124: e1101-1107 (2009).
- 7. Gradin M. Effect of oral glucose on the heart rate of healthy newborns. *Acta Paediatr* 94: 324-328 (2005).

- Skogsdal Y, Eriksson M, Schoclin J. Analgesia in newborns given oral glucose. *Acta Pediatr* 86: 217-220 (1997).
- 9. Owen ME. Pain in infancy-conceptual and methodological issues. *Pain* 20: 213-230 (1984).
- Singh H, Singh D, Soni RK. Comparison of pain response to venepuncture between term and preterm neonates. *Indian Pediatr* 37: 179-181 (2000).
- Williamson PS, Williamson RM. Physiologic stress reduction by a local anesthetic during newborn circumcision. *Pediatrics* 71: 36-40 (1983).
- 12. Anand KJS, Hickey PR. Pain and its effect in human neonate and fetus. *N Engl J Med* 317: 1321-1329 (1987).
- 13. Blass EM, Hoffmeyer LB. Sucrose as an analgesic for newborn infants. *Pediatrics* 87: 215-218 (1991).
- Barr RG, Quek VS, Caussineau D, et al. Effect of intra-oral sucrose on crying, mouthing and hand mouth contact in newborn and one week old infants. *Dev Med Child Neurol* 36: 606-609 (1994).
- Blass EM, Fitzgerald E, Kehoel P. Interaction between sucrose, pain and isolation distress. *Pharmacol Biochem Behav* 26: 483-489 (1987).