ORIGINAL ARTICLE

Comparison of Mean Pain score in Preterm neonatal Procedural Pain Treated with Expressed Breast Milk and 25% Dextrose Solution

AILIA ALI KAZMI[1], MISBAH NOOR[2], SADIA SHABIR[3], SHAFFAQ AZIZ[4], SAMIA ASLAM[5], ATTIYA FATIMA[6]
[1]*FCPS trainee, Pediatrics Medicine Unit-I, King Edward Medical University/Mayo Hospital, Lahore.*
[2]*Assistant Professor, Pediatrics Medicine Unit-I, King Edward Medical University/ Mayo Hospital, Lahore*
[3]*Assistant Professor, Pediatrics Medicine Unit-I, King Edward Medical University/ Mayo Hospital*
[4]*Senior Registrar, Pediatrics Unit-I, Mayo Hospital, Lahore*
[5]*Senior Registrar, Pediatrics Medicine Unit-I, Mayo Hospital, Lahore*
[6]*Senior Registrar, Pediatrics Medicine Unit-I, Mayo Hospital, Lahore*
Correspondence to: Dr. Ailia Ali Kazmi, Email: kazmi.ailia@gmail.com, Contact; 03238469374

ABSTRACT

Objective: The objective of this study was to compare the mean pain score in preterm neonatal procedural pain treated with expressed breast milk versus dextrose solution.
Study Design: Randomized controlled trial.
Setting: Department of Pediatric Medicine Mayo Hospital, Lahore.
Duration: 6 months (28/03/2018 to 27/09/2018)
Material and Methods: This study enrolled 400 admitted neonates who were brought for venipuncture, fulfilling the inclusion criteria. These neonates were randomly categorized into two groups. Group-Aneonates were given 25% Dextrose solution while Group-B were given expressed breast milk. Outcome variable was neonatal procedural pain which was quantified by use of premature infant pain profile score and comparison was made between the 2 groups.
Results: The mean age of the neonates was 14.2±7.8 days while the mean weight was 2.9±0.49 Kg. There were 205 (51.3%) male and 195 (48.7%) female neonates. Mean premature infant pain profile score was markedly reduced in neonates receiving 25% dextrose as compared to expressed breast milk (3.68±1.74 vs. 5.89±2.52; p-value<0.001). Significant variation was observed across various subgroups of neonates based on age, gender and weight.
Conclusion: 25% dextrose was found superior to conventional practice of expressed breast milk in controlling preterm neonatal procedural pain which along with its simplicity, low cost and easy and wide spread availability advocates its preferred use in future practice.
Keywords: Preterm, Neonatal Pain, 25% Dextrose, Expressed Breast Milk

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[1].The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment, as happens in case of newborns. Earliest pain receptors appear in a fetus after 24 weeks of gestation and perception of pain might actually start after that[2].Neonatal procedural pain management is a bit neglected subject, not only in under developed parts of the world but also in developed world. A large prospective study from France in 2008 found that specific pharmacologic or non-pharmacologic analgesia was given before painful procedures in only 21% of infants, and ongoing analgesia was given in an additional 34%.[3]In infants and toddlers, born extremely and very preterm, number of painful procedures performed in neonatal age was associated with poor early neurodevelopment outcomes and delayed postnatal growth.[11/4.]

Pain assessment in new-borns is quite a difficult task, there are several authenticated pain scales which are used in neonatal ICUs to assess pain. For example the neonatal infant pain scale (NIPS); neonatal facial coding system (NFCS); neonatal pain, agitation, and sedation scale (N-PASS); crying, oxygen requirement, fluctuating vital signs, expressions, sleeplessness scale (CRIES); COMFORT Scale; and premature infant pain profile (PIPP) are all validated pain scoring system[5].

Besides pharmacological interventions various methods of non-pharmacological analgesia is routinely used in nurseries during several common minor painful procedures, such as venipuncture, nasogastric tube and urinary catheter insertion. Methods which are frequently used include sugary oral solutions, swaddling,and closecontact with mother, breastfeeding or expressed breast milk, nonnutritive sucking and facilitated tucking with or without parenteral assistance. All these methods have proved to be of variable efficacy in diminishing pain and/or stress-related behaviours associated with mild to moderately painful or stressful procedures [6].

There is supportive evidence in literature for the use of relatively simple pharmacological measures, for example dextrose, that can be used alone or in conjunction with the above mentioned non-pharmacological measures[7]. Sahoo et al. in 2012 conducted a study on the comparison of mean PIPP score in preterm neonates undergoing procedures and found that it was significantly lower in neonates fed with 25% dextrose solution (3.6±5.4) compared to neonates fed with expressed breast milk (5.1±7.1 p=0.042)[8]. Despite of documented analgesic effects of 20-30% dextrose for neonatal procedures, there is still insufficient data regarding its dose and time of administration.[9]

Dextrose solution is cost effective, readily available even in remote areas and has a good safety profile. It can be a good alternative to other pharmacological measures in short procedures like venipuncture and heal lance, for managing mild to moderate pain. There is no data published on local population so the purpose of this study was to gather the supportive evidence for our population which would help us in adopting this in routine practice.

MATERIALS AND METHODS

This Randomized Controlled Trial was conducted inthe Department of Pediatrics Medicine, Mayo Hospital Lahore over 6 months duration after IRB approval from 28/03/2018 to 27/09/2018.This study's objective was to compare the mean pain score in preterm neonatal procedural pain treated with expressed breast milk versus 25% dextrose solution. Pain Score in Preterm Neonates was measured in neonates (born at 34-37 weeks of gestation as per dating scan) by premature infant pain profile (PIPP) [4] (0-21) and has been presented as mean ± standard deviation.

A sample size comprising of 400 cases (each group containingof 200neonates) was calculated with power of test as 80% and confidence interval as 95%whereas expected mean procedural pain score was taken to be 3.6±5.4 in neonates fed with 25% dextrose solution vs. 5.1±7.1 fed with expressed breast milk.[5]Neonates were recruited by Non-Probability, Consecutive Sampling.

Inclusion criteria: Preterm neonates (0-28 days of life) of either gender brought for venipuncture who were on oral feed and their parents agreed to sign informed written consent to participate in the study

Exclusion criteria: Neonates under the effect of sedatives or anti-epileptics as per history and clinical record, neonates who were advised nothing per oral,neonates with gross deformity visible through naked eye.

Parents were counseled and explained about the details of the study. Informed written consent and comprehensive history was documented from parents who agreed for participating in the study. All these neonates were randomly categorizedas Group D and Group E (**Group A:** 25% Dextrose&**Group B**: Expressed Breast Milk) via lottery method.

The neonates who required venipuncture were shifted to a quiet procedure room. It was ensured that time elapsed between the procedure andintake of breast milk was at least one hour. The neonates were fed 2 minutes before the venipuncture by a trained staff nurse. Venipuncture was performed by a trained phlebotomist by 24 gauge needle using aseptic technique and pain score was noted by the candidate. All the data was noted and recorded into the attached proforma along with demographic details of the neonate. All the collected data was compiled and analyzed using SPSS version 21.0.

Quantitative data variables such as age, weight and pain score wereexpressed as mean ±SD. Independent sample t-test was applied for comparison of mean pain score among these two groups takingp value≤0.05 as significant.Qualitative variables such as gender was expressed as frequency and percentage.Data was stratified for age, gender and weight to control affect modifiers. After stratification, t-test was applied taking p≤0.05 as significant.

RESULTS

Age range of neonates was from 1 to 28 days having a mean of 14.2±7.8 days. There were 205 (51.3%) male and 195 (48.7%) female neonates having a male to female ratio of 1.1:1. The weight range of neonates was from 2.2 Kg to 3.9 Kg having a mean of 2.9±0.49 Kg asdepicted in Table1.

Baseline parameters in these two groups were comparable in terms of mean age (p-value=0.787), weight (p-value=0.834) and distribution of various groups based on age (p-value=0.764), gender (p-value=0.920) and weight (p-value=0.840) as shown in Table 2.

The mean premature infant pain profile score was significantly lower in neonates receiving 25% dextrose as compared to expressed breast milk (3.68±1.74 vs. 5.89±2.52; p-value<0.001) as depicted in Table 3.Similarly significant difference was recorded in various subgroups of neonates based on age, gender and weight as shown in Table 4.

Table.1 Baseline Characteristics of Study Sample

Characteristics	Participants n=400
Age (days)	14.2±7.8
1-14 days	211 (52.7%)
15-28 days	189 (47.3%)
Gender	
Male	205 (51.3%)
Female	195 (48.7%)
Weight (Kg)	2.9±0.49
2.2-3.0 Kg	228 (57.0%)
3.1-3.9 Kg	172 (43.0%)

Table.2 Baseline Characteristics of Study Groups

Characteristics	25% Dextrose n=200	Expressed Breast Milk n=200	P-value
Age (days)	14.1±8.1	14.3±7.4	0.787
1-14 days	107 (53.5%)	104 (52.0%)	0.764
15-28 days	93 (46.5%)	96 (48.0%)	
Gender			
Male	103 (51.5%)	102 (51.0%)	0.920
Female	97 (48.5%)	98 (49.0%)	
Weight (Kg)	2.94±0.50	2.95±0.48	0.834
2.2-3.0 Kg	113 (56.5%)	115 (57.5%)	0.840
3.1-3.9 Kg	87 (43.5%)	85 (42.5%)	

Chi-square test & Independent sample t-test, observed difference was statistically insignificant

Table No 3: Comparison of Mean Premature Infant Pain Profile (PIPP) Score between the Study Groups

	25% Dextrose n=200	Expressed Breast Milk n=200	P-value
PIPP Score (mean±sd)	3.68±1.74	5.89±2.52	<0.001*

Independent sample t-test,* observed difference was statistically significant, PIPP; Premature Infant Pain Profile

Table.3 Comparison of Mean Premature Infant Pain Profile (PIPP) Score between the Study Groups across various Subgroups

Subgroups	Premature Infant Pain Profile (PIPP) Score		P-value
	25% Dextrose n=200	Expressed Breast Milk n=200	
Age (days)			
1-14 days	3.54±1.37	5.80±2.13	<0.001*
15-28 days	3.84±2.09	5.98±2.88	<0.001*
Gender			
Male	3.63±1.73	5.86±2.30	<0.001*
Female	3.73±1.77	5.91±2.74	<0.001*
Weight (Kg)			
2.2-3.0 Kg	3.66±1.49	5.90±2.29	<0.001*
3.1-3.9 Kg	3.70±2.04	5.86±2.80	<0.001*

Independent sample t-test, * observed difference was statistically significant; PIPP; Premature Infant Pain Profile

DISCUSSION

Pain assessment should be continuous and pain assessment tool should be incorporated in routine plan of care for all the neonates who are at risk of potential and actual pain experiences. Potential painful procedures should be avoided where possible and appropriate analgesics should be administered if pain is anticipated .[10] Procedural pain in neonates can be controlled by non-pharmacological and pharmacological methods.[11]To control pain during procedures, various medications which are in use include fentanyl and morphine. However, there are several side effects of drugs and they may cause respiratory depression, nausea, seizures, and physiological dependence. These side effects may force the physician to use other methods rather than using these medications for relief of procedural pain.[12,13]

Recent studies showed that the analgesic effect of 25% dextrose solution was superior to conventional practice of expressed breast milk and advocated its preferred use in future practice[8,14,15]. However, the current evidence that was available was controversial. Moreover the non-availability of evidence in local studies potentiated the need of this study

We used premature infant pain profile (PIPP) score for pain assessment, a validated and multidimensional pain scoring system for preterm neonates [16.] We found that the mean premature infant pain profile score was significantly lower in neonates receiving 25% dextrose as compared to the ones receiving expressed breast milk (3.68±1.74 vs. 5.89±2.52; p-value<0.001). Similar results have been reported by Rawal et al [7]and Bueno et al [14,15]

Two other Indian studies, however didn't prove any significant difference between 25% dextrose and EBM [17,18].A possible explanation for this conflict among studies may be the selection bias as they studied pain during nasopharyngeal suctioning only. Moreover, these studies included limited sample size of 40 and 72 neonates respectively.

In another Indian study ,comparing PIPP score and duration of cry after intramuscular Hepatitis B vaccine in full term neonates it was observed that the mean PIPP score at 30 seconds were 5.7 in EBM group and 6.9 in 24% sucrose solution group (p<0.001). The median cry duration were 81.2 seconds in EBM group and 85.6 seconds in 24% sucrose solution group (p=0.42). They excluded preterm newborns and moreover scores were compared after a single procedure of intramuscular injection while scores after other common procedures were not compared.[19]

The hypothesis established at the start of study is well proved and owing to simplicity, low cost and easy and wide spread availability of 25% dextrose, its preferred use is advocated in future practice.

One of the main limitation of the current study was that we could not compare the effect of 25% dextrose along with other non-pharmacological measures like 25% dextrose plus EBM, 25% dextrose plus mother holding, 25% dextrose plus skin-to-skin contact etc. which could have enabled usage of more appropriate analgesic methods in future. Also literature suggests non pharmacological interventions have synergistic effects when used in combination[20,21]. Also we need to conduct more trials to establish exact dose and time of administration of dextrose. Associated metabolic derangements, propensity to develop septicemia or NEC and long term neurodevelopmental outcomes should also be assessed. Such studies are highly recommended in future research.

CONCLUSION

25% dextrose was found superior to conventional practice of expressed breast milk (had lower PIPP Score) in controlling preterm neonatal procedural pain which along with its simplicity, low cost and easy and wide spread availability advocates its preferred use in future practice.

Disclaimer: None
Conflicts of interest: Authors declare no conflict of interest
Funding disclosure: No funding was used for this study

REFERENCES

1. Raja, S,Carr, D, Cohen M, et al The revised International Association for the Study of Pain definition of pain May 23, 2020 - Volume Articles in Press - Issue - doi: 10.1097/j.pain.0000000000001939
2. Fetal awareness, Review of research and recommendations for practice, Report of a working party. Royal College Of Obstetricians &Gynaecologists March 2010
3. Carbajal R, Rousset A, Danan C, et al. Epidemiology and treatment of painful procedures in neonates in intensive care units. JAMA. 2008;300(1):60–70
4. Valeri BO, Holsti L, Linhares MB. Neonatal Pain and Developmental Outcomes in Children Born Preterm. *The Clinical Journal of Pain.* 2015;31(4):355–362. doi: 10.1097/AJP.0000000000000114.
5. Gleicia Martins de Melo, Ana Luíza Paula de Aguiar Lélis,Alline Falconieri de Moura.Pain assessment scales in newborns: integrative reviewRev. paul. pediatr 2014;32https://doi.org/10.1590/S0103-05822014000400017
6. Committee on Fetus and Newborn and Section on Anesthesiology and Pain Medicine. Prevention and management of procedural pain in the neonate: an update. Pediatrics 2016; 137(2):e20154271.
7. AAP COMMITTEE ON FETUS AND NEWBORN and SECTION ON ANESTHESIOLOGY AND PAIN MEDICINE. Prevention and Management of Procedural Pain in the Neonate: An Update. Pediatrics. 2016;137(2):e20154271
8. Sahoo JP, Rao S, Nesargi S, Ranjit T, Ashok C, Bhat S. Expressed breast milk vs. 25% dextrose in procedural pain in neonates, a double blind randomized controlled trial. Indian Pediatr 2013; 50(2):203-7.
9. Bueno M, Yamada J, Harrison D, et al. A systematic review and meta-analyses of nonsucrose sweet solutions for pain relief in neonates. Pain Res Manag. 2013;18(3):153–161
10. GG&C Pediatrics guidelines https://www.clinicalguidelines.scot.nhs.uk/ggc-paediatric-guidelines/ggc-guidelines/neonatology/neonatal-pain-guideline/
11. Hall RW, Anand KJS. Pain management in newborns. Clin Perinatol 2014; 41(4):895-924.
12. Bhalla T, Shepherd E, Tobias JD. Neonatal pain management. Saudi J Anaesth 2014; 8(Suppl-1):S89–97.
13. Krishna L. Pain relief in neonates. J Neonatal Surg 2013; 2(2):19.
14. Rawal S, Ghai A, Jindal T. Twenty-five percent dextrose and EBM in pain relief during heel lance in late preterm babies using the PIPP score: a randomized controlled trial. J Neonatol 2018; 32(3):43-9.
15. Bueno M, Stevens B, de Camargo PP, Toma E, Krebs VL, Kimura AF. Breast milk and glucose for pain relief in preterm infants: a noninferiority randomized controlled trial. Pediatrics 2012; 129(4):664-70.
16. Stevens B, Johnston C, Taddio A, Gibbins S, Yamada J. The premature infant pain profile: evaluation 13 years after development. Clin J Pain 2010;26:813-30
17. Rodrigues L, Nesargi SV, Fernandes M, Shashidhar A, Rao SP, Bhat S. Analgesic efficacy of oral dextrose and breast milk during nasopharyngeal suctioning of preterm infants on CPAP: a blinded randomized controlled trial. J Trop Pediatr 2017; 63:483-8.
18. Desai S, Nanavati RN, Nathani R, Kabra N. Effect of expressed breast milk versus swaddling versus oral sucrose administration on pain associated with suctioning in preterm neonates on assisted ventilation: a randomized controlled trial. Indian J Palliat Care 2017; 23(4):372-8.
19. Vohra A, Purani C, Mehariya K M, Shah B. Neonatal Analgesia: Effect of Sucrose Solution versus Breastfeeding in Procedural Pain. PediatrOncall J. 2017; 14: 79-81. doi: 10.7199/ped.oncall.2017.56
20. Bueno M, Yamada J, Harrison D, et al. A systematic review and meta-analyses of nonsucrose sweet solutions for pain relief in neonates. Pain Res Manag. 2013; 18(3):153–61.
21. Bellieni CV, Bagnoli F, Perrone S, et al. Effect of multisensory stimulation on analgesia in term neonates. A randomized controlled trial. Pediatr Res. 2002; 51:460–3.