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COMPARISON OF THE EFFICACY OF ORAL 25% GLUCOSE WITH ORAL 24% SUCROSE FOR PAIN RELIEF DURING HEEL LANCE IN PRETERM NEONATES AT PEDIATRICS DEPARTMENT OF NMCH, PATNA, BIHAR

Pediatrics

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ABSTRACT

Aim: To study the analgesic effect of oral 25% glucose as compared with oral 24% sucrose during heel lance in preterm neonates.
Methods: Stable preterm neonates within first 48 hours of life were randomized to receive either 24% sucrose or 25% glucose before heel lance. Primary outcome assessed was painful response by the Premature Infant Pain Profile (PIPP) score at 30 seconds after heel lance, and the secondary outcome was immediate adverse events associated with the administration of two solutions and duration of crying immediately following the procedure.
Results: A total of 94 neonates were randomly assigned into 24% sucrose and 25% glucose group. The baseline characteristics between the two groups were comparable. No significant difference was observed between the two study groups with respect to PIPP scores, duration of crying and rate of adverse events.
Conclusions: When assessed by PIPP score, 25% glucose and 24% sucrose provided comparable analgesia during heel lance in preterm neonates.

KEYWORDS

INTRODUCTION

Evidence shows that neonates feel pain and may have an increased sensitivity to pain and its long-term effects as compared with older infants. Treating procedural pain has become a crucial part of neonatal care. Pharmacological treatments are rarely used during procedures because of concerns about their effectiveness and potential adverse effects. Therefore, non-pharmacological interventions are valuable alternatives. Use of sucrose in preterm neonates has been advocated uniformly for pain relief. Glucose in varying concentrations of 10–25% has been used in pain relief in neonates, but evaluation of its therapeutic efficacy as compared with oral 24% sucrose in randomized controlled trial is lacking. This study was thus planned to evaluate the efficacy of 25% glucose solution with 24% sucrose solution for analgesia during heel lance in preterm neonates.

MATERIAL AND METHODS

Settings and subject

The study conducted in the neonatal unit, Department of Pediatrics, Nalanda Medical College & Hospital, Patna, Bihar from December 2017 to November 2018 included clinically stable preterm infants having an indication for blood sampling within the first 48 h of life. Infants born with perinatal asphyxia, birth trauma, cardiorespiratory instability, with 5 min APGAR score <7, any apparent genetic syndromes, congenital anomalies or previous surgery were excluded. Additionally, neonates born to mothers with a history of receiving opiates, muscle relaxants, sedatives, analgesics and general anesthesia were excluded. There were two study groups (25% Glucose vs. 24% Sucrose) into which participating neonates were assigned using previously generated random number.

Randomization and allocation concealment

Block randomization with a block size of six was created using computer-generated random numbers. Allocation concealment was done by the hospital pharmacy, which packed the 24% sucrose and the 25% glucose into identical containers and sequentially labeled opaque sealed envelopes according to randomization code. The participants, the treating doctor, as well as the investigator assessing the painful response were blinded to the group assignment. Randomization codes and allocation sequences were revealed only after completion of the data analysis.

Intervention

The neonates were enrolled after a written informed consent. Solutions of 24% sucrose were freshly prepared daily by pharmacy using 2.4 g sucrose with 10 ml distilled water. Commercially available 25% dextrose solution was used for 25% glucose as was used by others. Solutions were packaged in 1 ml sterile syringes further packed in opaque sealed envelopes labeled according to the randomization code. The prefilled syringes were stored in refrigerator at 2–8°C, and the unused syringes were discarded at the end of the day. Neonates were placed in a semi-reclining position on a couch or remained in their radiant warmers during the procedure. A non-invasive vital sign monitor was applied to the infant's hand or foot to monitor heart rate and oxygen saturation. After 2 min, the treating physician administered 1 ml of the assigned solution to the neonate over the anterior part of tongue over 30 s. After 2 min, heel lancing was performed after cleaning the heel of neonate with a sterile spirit swab, with an auto lancet (Accu-ChekSoftclix, Roche, Germany). Neonate's face and monitor screen were filmed in real time by using two independent video cameras during the entire procedure.

Outcome measures

The Premature Infant Pain Profile (PIPP) was assessed at 30 s, 1 min and 2 min after the procedure. The primary outcome was PIPP assessed at 30 s. The PIPP is one of the most valid and reliable behavioral measure of pain for premature infants. It consists of seven indicators, brow bulge, eye squeeze, nasolabial furrow, heart rate, oxygen saturation, gestational age and behavioral state, rated on a 4-point scale with minimum score of zero and maximum score of 21.

The secondary outcomes assessed were duration of crying and immediate adverse events associated with the administration of two solutions (choking, coughing or vomiting, sustained tachycardia (HR > 200/m) for >15 s, sustained bradycardia (HR < 80/m) for >15 s, sustained tachypnea (RR > 80/m) for >15 s, sustained dyspnea (RR < 20/m) for >15 s, sustained oxygen desaturation <80% for >15 s), which was evaluated for a period of 2 min after the procedure. Crying was defined as an audible vocalization that lasted for at least 5 s without a 20 s quiet interval . The data thus generated and the video clippings were shown to a consultant unrelated to the study for scoring the PIPP score. All PIPP scores were assigned by the same consultant after reviewing the video recordings.

Statistical analysis

Sample size was calculated using n master software version 2. To

detect a 3-point expected difference in PIPP score with an assumed SD of 3.7 between the glucose and the sucrose group, an alpha error of 5% and a power of 80%, the required sample size was 42 in each study arm. Assuming a 10% post-randomization dropout, 94 neonates were enrolled.

All the results were analyzed using a window SPSS software version 20. Descriptive statistics Mean (SD) 95% CI and Median (Range) were calculated depending on the distribution of data. Students t-test was used to compare means between two study groups. Chi square test was used for categorical data. Non-normally distributed data were analyzed by Mann–Whitney test. Statistical significance was assumed at a p value of <0.05. Intention-to-treat analysis was planned to be used in cases of post-randomization dropouts if any.

RESULTS

Of the total 176 preterm neonates assessed for eligibility, 82 were excluded, 94 preterm were randomized, of which 47 were allocated to 24% sucrose group and 47 were allocated to the 25% glucose group.

The baseline characteristics between the two study groups were comparable (Table 1). No significant difference was observed in the PIPP scores between the two study groups at 30 seconds, 1 minute and 2 min after the procedure (Table 2 and 3).

Table 1. Baseline characteristics of the subjects enrolled between the two study groups

Variables	25% Glucose	24% Sucrose	p value
Age at enrollment (hours) (mean, SD)	26.85(9.55)	24.17(9.60)	0 .178
Gestational age (weeks) (mean, SD)	35.53(0.73)	35.56 (0.78)	0 .861
Sex distribution (N, %)	26(55.32)	29(61.70)	0 .138
Maternal age (years) (mean, SD)	25.72(3.05)	24.87(2.55)	0 .146
Maternal medical history (N, %)	4(8.52)	0(0)	0 .117
Presentation of babies at birth			
Vertex (N, %)	39(82.97)	45(95.74)	0 .901
Breech (N, %)	8(17.02)	2(4.25)	1
Others (N, %)	0(0)	0(0)	0 .37
Mode of delivery			
NVD (N, %)	44(93.62)	45(95.74)	
AVD (N, %)	1(2.13)	0(0)	
LSCS (N, %)	2(4.26)	2(4.26)	
APGAR scores at 5 min (mean, SD)	8.53(0.58)	8.64(0.57)	

Table 2. Median (range) PIPP scores across the two study groups

PIPP scores	25% Glucose	24% Sucrose	p value
Pre-procedure			
Median	1	1	0.57
Range	(0–11)	(0–5)	
At 30 s post-procedure			
Median	1	2	0.74
Range	(0–5)	(0–5)	
At 1 min post-procedure			
Median	1	1	0.868
Range	(0–11)	(0–10)	
At 2 min post-procedure			
Median	1	1	0.71
Range	(0–7)	(0–10)	

Table 3. Mean ± SD PIPP scores across the two study groups

PIPP scores	25% Glucose	24% Sucrose	p value
Pre-procedure			
Mean	1.49	1.13	0.572
SD	1.95	1.13	
At 30 s post-procedure			
Mean	2.74	3	0.7438
SD	2.08	2.64	
At 1 min post-procedure			
Mean	1.72	1.7	0.8709
SD	1.93	1.89	
At 2 min post-procedure			
Mean	1.74	2	0.7134
SD	1.66	2.13	

The occurrence of adverse events was also not statistically different in both the groups with no adverse event in 95.74% of subjects in 25% glucose and 100% of the subjects in 24% sucrose group. Duration of crying across the two study groups was similar, no significant difference was observed between the baseline and maximum heart rate, and between baseline and lowest SpO2, across the two study groups.

DISCUSSION

While many studies have documented the analgesic effect of sucrose and breast milk, few studies have been done using both glucose and sucrose, comparing their efficacy for relieving procedural pain in preterm neonates. As mentioned, our study did not detect a significant difference in the analgesia provided by 25% glucose as compared with 24% sucrose when assessed by PIPP for heel lance in preterm neonates. Similar observations have been reported by Okan et al. who concluded that both solutions provided comparable pain relief when pain perception was assessed using the NFCS. Isik et al. evaluated the analgesic effect of 30% sucrose and 10% and 30% glucose in a group of 113 healthy term newborns and concluded that 30% sucrose is superior to 10% and 30% glucose solutions in relieving pain. This difference favoring sucrose was explained by a different taste sensation where the orosensorial pathway was concerned. On the contrary, Guala et al. found glucose solution to be most effective in reducing pain response as compared with sucrose and water (placebo). However, this study used a higher dose of glucose (2 ml) as compared with our study where we used 1 ml. The higher dose may explain a better therapeutic efficacy of 25% glucose as compared with 24% sucrose as seen by Guala et al. Other studies conducted by Carbajal et al. and Dilen et al. have indicated varied results. Recent trials by Pandey et al. and Nimbalkar et al. have also demonstrated the analgesic effect of 24% sucrose and 25% glucose vs. placebo for orogastric tube insertion in preterm neonates using the multidimensional pain assessment tool PIPP, respectively.

Crying remains the most widely used indicator for pain intensity in infants, followed by changes in HR, composite pain measures, unidimensional behavioral pain measures and SpO2. Sucrose significantly reduced crying time in various studies evaluating pain at heel lance. In the present study, there was no statistically significant difference between the duration of crying and immediate adverse events across the two groups. One baby in 25% glucose group developed coughing and another in the same group developed vomiting. Both these adverse events were present transiently and did not require any intervention. Adverse effects of sucrose were evaluated in 16 studies. In the study that most specifically looked at adverse events (Gibbins 2002), only six infants (3%) experienced minor side effects (e.g. oxygen desaturation, choking), which resolved spontaneously without intervention. A recent study that has evaluated the safety of sucrose analgesia concluded that the use of sucrose analgesia for repeated painful procedures on newborns does not lead to any significant difference in the short-term neurobehavioral outcome.

There were some limitations in our study, the study population comprised more mature preterm neonates (lacking extremely preterm neonates) and the assessment of pain was at a single contact with the neonate (not a sequential follow up for the entire duration of the neonate's stay in the NICU or postnatal ward). It has been proved conclusively that repeated procedural pain alters the neonate's behavioral response, leading to a heightened response to subsequent painful procedures. This priming may require larger doses of analgesic solutions, and may also involve greater chances of encountering immediate adverse events. This can only be evaluated if the neonate is observed over a longer period.

The PIPP scores across the glucose and sucrose groups did not differ statistically, indicating similar analgesia provided by both the solutions during heel lance. As questions have been raised regarding safety profile and adverse effects of sucrose, glucose needs to be evaluated for its efficacy and safety in neonatal pain relief in preterm neonates. Use of 25% glucose was not seen to be associated with a significant difference in immediate adverse events. However, long-term safety needs to be established. Till such time, it may be safe to recommend stock solution of 25% glucose as an alternative to 24% sucrose for providing transient analgesia to preterm neonates in countries where availability of 24% sucrose is an issue.

CONCLUSION

Hence, we can conclude that the use of 25% glucose and 24% sucrose is safe and free from immediate adverse effects in preterm neonates when used for heel lance as single dose.

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