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Does Oral 25% Dextrose Effectively Reduce Procedural Pain in Neonates – A Randomized Controlled Trial

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Abstract
Background: *Neonates are subjected to frequent painful procedures. Neonates can perceive pain which can affect neurodevelopmental outcome. It is necessary to assess and manage pain during various procedures.*
Objective: *To compare the effect of oral 25% dextrose and placebo in reducing neonatal pain after venepuncture.*
Methods: *A randomised control study was done in a tertiary care hospital. Neonates were randomised into a placebo group using sterile water and intervention group using 25% dextrose. Two ml of test solution was administered to neonate two minutes before the procedure. Neonatal pain response was assessed at 0 – 30 sec, 1 -1½ min, 3 – 3½ min, 5 -5½ min after venepuncture using PIPP score. Cry time after venepuncture was recorded.*
Results: *Mean PIPP scores at 0 – 30 sec, 1 -1½ min, 3 – 3½ min, 5 -5½ min after venepuncture were 11.475, 10.125, 9.125, 7.575 in placebo group; 8.55, 7.225, 6.0, 4.5 in 25% dextrose group respectively. Mean cry time was 105.65 sec in placebo group and 60.85 sec in 25% dextrose group.*
Conclusion: *Oral 25% dextrose significantly reduced neonatal pain compared to placebo after venepuncture.*
Keywords: *25% dextrose, PIPP, Venepuncture.*
Abbreviations: *25% D - 25% dextrose, PIPP – Premature Infant Pain Profile, sec – seconds, min – minutes.*

Introduction

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential damage to tissue.[(1)] Neonates undergo large number of painful procedures as a part of their routine care . Nearly 10% of neonates are subjected to more than 300 painful procedures within the first week of life. [(2)]

Earlier it was thought that neonates were not able to perceive pain. Now it is known that neonates have the necessary neuronal connections to perceive the affective components of pain.[(3)] Neonatal response to pain includes physiological, behavioural, metabolic and hormonal changes.[(4)] In addition to short term effects, evidence have demonstrated that neonatal pain influences

neurodevelopment and affects future perception of painful stimuli.[5] Neonates lack the ability to verbalise pain and hence caregivers must be able to recognise, assess and manage pain.[6]

Various types of pharmacologic and non pharmacologic methods have been described for neonatal pain management.[7] Recent Cochrane reviews have discussed non pharmacologic interventions to reduce pain in neonates during routine procedures.[8,9] Oral sweet solutions like sucrose and dextrose have been found to have pain relieving effects.[9,10] Trials using 25% dextrose[6,10,11,12] to reduce procedural pain in neonates have been done. Thus the following trial was done with the objective of determining the efficacy of oral 25% dextrose in comparison with placebo in reducing neonatal pain response after venepuncture with the help of PIPP pain scale.

Methodology

Study centre

This randomized controlled trial was done in Rajah Muthiah Medical College and Hospital, Chidambaram. 40 term neonates admitted in the hospital were enrolled in each group after informed parental consent.

Inclusion and Exclusion Criteria

Eligible term neonates 37 weeks or more of gestational age who were started on breastfeeding and were fed 1 hour before the procedure and required venepuncture for blood sampling were included. Neonates who were sick, had birth asphyxia or congenital malformations or feeding intolerance, those who were on sedatives, phenobarbitone were excluded from the trial. Neonates who had more than one prick were excluded from the trial. The trial was cleared by the institutional ethical committee.

Method of study

The eligible neonates were randomised into two groups – placebo group and oral 25% dextrose group using random closed envelope method where envelopes with codes for the groups were used. Neonates included in the trial were allocated to the group encoded in the envelope chosen by the parents.

The neonates were taken to a quiet room and placed under a radiant warmer. A pulse oximeter probe was firmly attached to the foot of the neonate. The behavioural state of the neonate was scored by observing the baby for 15 seconds. . Baseline heart rate and oxygen saturation of the neonates were recorded.

Two ml of the test solution according to the group allocated was administered on the anterior aspect of the tongue of the neonate through a dropper by the principle investigator. Two minutes later, venepuncture was done with 23 gauge needle by a trained neonatal nurse. Another trained neonatal nurse blinded to the group allocation recorded the heart rate, oxygen saturation and cry time. Cry time was defined as the total duration of audible cry after removal of needle and was measured in seconds. An independent observer blinded to the group allocation noted down the duration of facial response to pain (brow bulge, eye squeeze, nasolabial furrow). Thus the maximum heart rate, minimum oxygen saturation and duration of facial response to pain were recorded between 0-30 sec, 1-1½ minute, 3-3 ½ minute, 5-5½ minute after venepuncture and recorded in the proforma. PIPP score was calculated from these parameters.

The PIPP score is a composite pain measure that includes contextual, behavioural and physiological indicators of pain. Each indicator is scored in a 4 point scale. A Score <6 represents absence of pain, score between 6-10 represents mild to moderate pain while score >10 represents severe pain.[13]

PIPP score and cry time were recorded for neonates of both the groups.

Data Analysis

The data collected was entered into Microsoft Excel spreadsheet and analysed using SPSS version 21.0. Statistical analysis was done using T test to compare the efficacy between the groups in reducing Mean PIPP score and cry time. A p value<0.05 was accepted to be statistically significant difference.

Results

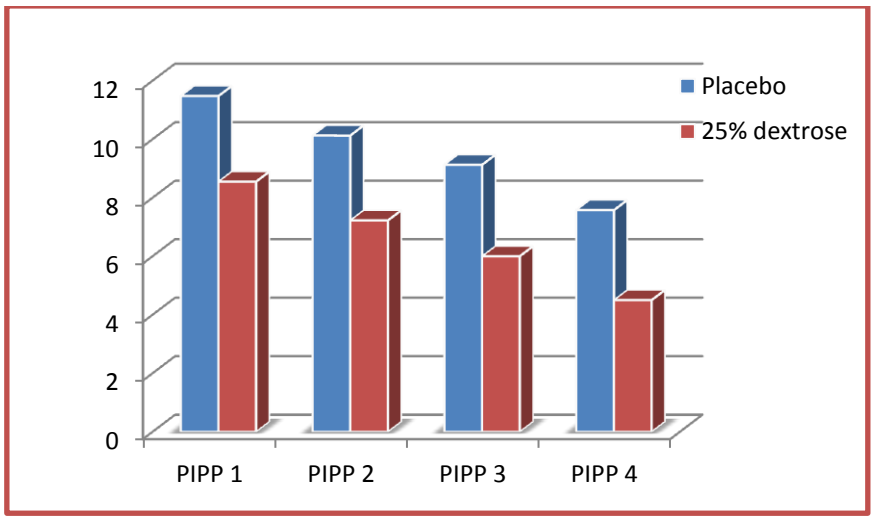
There was no statistically significant difference with regard to sex, mode of delivery, gestational and postnatal age, birth weight among the neonates of the two groups.

The mean PIPP score of neonates at 0 – 30 sec was 11.475 in placebo group vs 8.55 in 25% D group. At 1 – 1 ½ min, mean PIPP score was 10.125 in placebo group and 7.225 in 25% D group. A mean PIPP score of 9.125 and 6.0 were recorded in placebo group and 25% D group at 3 – 3 ½ min. At 5 – 5 ½ min, score was 7.575 in placebo group vs 4.5 in 25% dextrose group (Table 1, Figure 1).

Table 1. Comparison of Mean PIPP Score [Mean (SD)] in the study population after venepuncture

PIPP at various time intervals after venepuncture		**Mean PIPP score (Standard Deviation)**	
		Placebo group	**25% D group**
PIPP at 0 – 30 sec	**PIPP 1**	11.475 (1.04)	8.55 (1.78)
PIPP at 1– 1 ½ min	**PIPP 2**	10.125 (0.99)	7.225 (1.51)
PIPP at 3– 3 ½ min	**PIPP 3**	9.125 (1.32)	6.0 (1.32)
PIPP at 5– 5 ½ min	**PIPP 4**	7.575(1.38)	4.5 (1.52)

Figure 1. Comparison of mean PIPP score of study population after venepuncture



Difference between the mean PIPP score of neonates at various time intervals after venepuncture between the two groups was studied. Statistically significant difference in the mean PIPP score between neonates of placebo group and 25% D group was observed at all time intervals after venepuncture. (Table 2)

Table 2: Comparison of differences in mean PIPP score between the groups

PIPP at various time intervals after venepuncture		**Groups**	**Difference in mean PIPP score**	**t value**	**p value**
PIPP at 0 – 30 sec	**PIPP 1**	placebo vs 25% dextrose	2.9250	8.970	<0.05*
PIPP at 1– 1 ½ min	**PIPP 2**	placebo vs 25% dextrose	2.9000	10.150	<0.05*
PIPP at 3– 3 ½ min	**PIPP 3**	placebo vs 25% dextrose	3.1250	10.569	<0.05*
PIPP at 5– 5 ½ min	**PIPP 4**	placebo vs 25% dextrose	3.0750	9.49	<0.05*

Mean cry time after venepuncture was 105.65 sec and 60.85 sec in the placebo group and 25% dextrose group respectively**.** (Table 3)

Table 3 : Mean cry time after venepuncture in study population

Cry time	Groups	Mean Cry time	Standard Deviation
Cry time	placebo	105.650	7.7775
	25% dextrose	60.850	8.8130

There was a significant difference in mean cry time between the neonates of placebo group and the 25% dextrose group with p value <0.05. (Table 4)

Table 4: Comparison of difference in mean cry time between the groups

Cry time	Groups	Difference in mean cry time	t value	p value
Cry time	Placebo vs 25% dextrose	44.8000	24.106	<0.05*

Discussion

This study assessed the efficacy of oral 25% dextrose in reducing pain during venepuncture in neonates with the help of PIPP score.

Oral sweet solutions stimulate sensory afferents in the oral cavity producing pleasurable sensation. This positive hedonic effect induced analgesia suggests that the taste of sweetness is involved.[14]

Pain reducing effect of sweet solutions is thought to be mediated by two mechanisms – orotactile stimulation producing an initial effect and oro gustatory stimulation prolonging the effect by releasing endogenous opioids. [15]

The neonates in placebo group had significantly higher PIPP score at all time intervals after venepuncture. Analysis revealed significant difference in mean cry time between the neonates of placebo group and 25% dextrose group. Neonates in 25% dextrose group had statistically significant lower PIPP score and reduced cry time after venepuncture.

Similarly, studies conducted by Sahoo et al [6] and Mariano et al [11] also showed that 25% dextrose decreased mean PIPP score and cry time after procedure compared to placebo . Costa et al aimed to evaluate the effect of 25% glucose during ophthalmic examination for retinopathy of prematurity in preterm infants using Neonate infant pain scale. The score was 2.6±1.1 in glucose group and 4.5±1.3 in control group indicating that 25% glucose was effective for pain relief.[12]In a study by Fusun Okan et al, pain relieving effect of glucose was compared to placebo after heel lancing. Pain response was assessed with Neonatal Facial Coding System (NFCS). After the heel prick, neonates in glucose group had significantly reduced duration of first cry and total crying time ($P = 0.005$ and $P = 0.007$). Neonates receiving placebo had a significantly higher NFCS score at 4 and 5 min after the heel prick ($P = 0.009$ and 0.046 respectively).[16]

One of the strength of the study was the use of a validated pain scale – PIPP pain scale.[17] The fact that observers were masked to group allocation was yet another strength. Limitation of our study was that the long term effect of painful stimuli could not be studied. Our study included only term neonates and hence further studies for pain management in preterm neonates are needed.

Conclusion

Neonatal pain should be appropriately assessed and managed. In this study,it was found that 25% dextrose significantly reduced mean PIPP score and cry time compared to placebo after venepuncture. Thus 25% dextrose was found to effectively reduce procedural pain in neonates.

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