

## Comparison of the Efficacy of Different Concentrations of Oral Dextrose Solutions in Reducing Pain During Heel Lancing in Late Preterm Neonates

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### Abstract

**Background:** In this study, we wanted to compare the efficacy of 10 % dextrose versus 25 % dextrose solution in reducing the perception of pain in neonates 34 - 37 weeks during heel lancing, and assess the premature infant pain profile (PIPP) score during heel lancing in neonates between 34 - 37 weeks of gestation. **Material and Methods:** This was a hospital based randomized prospective single blinded clinical study conducted among 100 babies (34 to 37 weeks of gestation) who presented with heel lancing for GRBS estimation in the NICU/neonatal ward of Aster-Malabar Institute of Medical Sciences, Calicut, over a period of one year from 05/2017 to 05/2018 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants. **Results:** With regard to heart rate the difference between the groups was found statistically significant (P value 0.004). with regard to SP02 drop, the difference in the proportion between groups was found to be statistically significant (P value 0.0.032). The difference in the grade of pain between groups was found to be statistically significant (P value 0.0.002). The difference in the total PIPP score between two group was found to be statistically significant (p value < 0.001). **Conclusion:** Need for pain relief even in minor procedures like heel lancing, IV insertion, NG tube insertion, IM injections in preterm neonates should be made part of routine care in NICUs. 10% Dextrose having significantly lesser osmolarity (555mosm/L) compared to 25% Dextrose (1389 mosm/L) can be a better in view of risk of necrotising enterocolitis in preterm babies on repeated usage of higher osmolarity solution for very frequent minor procedures. Long term follows up of these late preterm babies who received pain relief for minor procedures is required to assess the neurodevelopmental outcomes and to compare it with babies who have not received such therapy.

**Keywords:** Oral Dextrose Solutions, Reducing Pain, Heel Lancing, Preterm Neonates.

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### Introduction

“To cure sometimes, to relieve often, to comfort always”, is a 15th century French description of the role of the physician. Although relief of pain is felt to be cardinal principle of compassionate medicine, yet in practice, pain management is often ignored aspect of care. The myth regarding neonatal pain suggests that because of neurological immaturity, neonates do not experience pain. However, studies have shown that pain pathways as well as cortical and sub cortical centres, necessary for pain perception are well developed late in gestation and physiological and behavioural responses to pain are well documented in neonates.<sup>[1-3]</sup> Developmental supportive care and intact survival are the recent emphasis in neonatology. Routine medical care of newborns includes inevitable blood sampling. Newborns are rarely given analgesia for routine procedures such as venipuncture or heel lancing. The medical and paramedical staffs usually ignore pain felt during these procedures. Neonates feel pain if

anything more acutely. Furthermore, this pain has long reaching consequences in neurodevelopment. Neonates also have significant alteration in heart rate (HR), blood pressure (BP), palmar sweating (PS), plasma rennin activity (PRA) and plasma cortisol level during these procedures.<sup>[4]</sup> Being that a neonate cannot complain or protest, it is all the more imperative that caregivers understand and appreciate the consequences of neonatal pain and take active measures to address it. Preterm neonates undergo even more procedures compared to term babies. They are also at greater risk for developmental aberrations because abnormal sensory inputs occur at the time of active cortical development. The memory of pain remains in newborns and will lead to escalated pain perception. A wide variety of methods in reducing the procedural pain in neonates are available which can be pharmacological and nonpharmacological interventions. Pharmacological agents are usually not employed for pain relief in neonates due to the adverse effects they can produce. Non pharmacological intervention is a more feasible alternative. Various studies,<sup>[5-7]</sup> have shown that administration of oral sucrose, a disaccharide, raises the pain threshold, presumably mediated by endogenous opioids and could be used for that purpose. However, sucrose is not routinely used in neonatal care and is not readily available in the neonatal nursery.

### **Current recommendations for procedural analgesia in neonates**

For heel lancing, use of non-pharmacological measures + mechanical lance is proposed.<sup>[8]</sup> Sucrose in concentration of 12 – 24 % given 2 minutes before the procedure is the recommended non pharmacological measure, which can be combined with other nonpharmacological measures.<sup>[8]</sup> Using a mechanical spring loaded lance eg: autolance is recommended.<sup>[8]</sup> Glucose is a monosaccharide widely used by intravenous (IV) route in neonatal care unit but not as an oral solution. The present study was undertaken to find out the effect of oral administration of 10 % and 25 % dextrose, on pain relief in late preterm neonates requiring a heel lancing and compare the efficacy of both. Current recommendations mostly based on historical consensus are that the osmolality of enteral feeds should not exceed 450 mOsm/kg (~400 mOsm/L).<sup>[9]</sup> 10 % dextrose has osmolality of 555 mosm/L and 25 % dextrose has osmolality of 1389 mosm/L. Higher osmolality of solution is a cause for NEC in preterm neonates,<sup>[10,11]</sup> especially on repeated usage. In the present study, if the efficacy to reduce pain was found to be similar or same, 10 % dextrose (lower osmolality) could be used for similar or less painful procedures since it is much more commonly available, more affordable and has lesser chances for NEC in preterm babies on repeated use.

### **Aims and Objectives**

To compare the efficacy of 10 % dextrose versus 25 % dextrose solution in reducing the perception of pain in neonates 34 - 37 weeks during heel lancing.

To assess the PIPP score during heel lancing in neonates between 34 - 37 weeks of gestation.

### **Methodology**

This was a hospital based randomized prospective single blinded clinical study conducted among 100 babies (34 to 37 weeks of gestation) who presented with heel lancing for GRBS estimation to the department of tertiary level NICU/neonatal ward of Aster-Malabar Institute of Medical Sciences, Calicut, over a period of one year from 05/2017 to 05/2018 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

### **Inclusion Criteria**

Babies between 34 - 37 weeks of gestation

**Exclusion Criteria**

Sick neonates-who required invasive respiratory supportive care

Neonatal shock

Sedated/paralyzed neonates/neonatal encephalopathy

**Statistical Methods**

10 % dextrose solutions, 25 % dextrose solutions were considered as primary explanatory variable. Solution used, inborn/out born, gestational age at birth, gender, birth weight corresponding to gestational age, mode of delivery, mother received sedation/not foetal risk factors, reason for admission of the baby, whether on non-invasive respiratory support/not , exposure to pain before previous heel lancing, NG tube insertion, IV injection, IM injection, UVC insertion were considered as other explanatory variables. Continuous variables were summarized as mean  $\pm$  standard deviation or median with inter quartile range. Continuous variable between the two groups were tested using independent sample t test or Mann Whitney U test. Categorical variable was summarized in terms of frequency with % and were tested using Chi square/ Fischer's exact test. The association between solution and exposure to pain subjected to pain before, UVC insertion, heart rate, SPO<sub>2</sub>, cry duration was assessed by comparing the mean values. The mean differences along with their 95 % CI were presented. Independent sample t-test was used to assess statistical significance.

**Study Procedure**

Taking into account all sterile precautions, 2 ml of commercially available 10 % and 25 % dextrose solution were used for administration in the neonate 2 minutes before the procedure. These were administered using 2ml syringes at the tip of tongue slowly over a period of 30 seconds, 2 minutes before the procedure. Dextrose bottles were preserved in hygienic area in NICU. Investigator directly oversees the same. The used bottles were discarded after 24 hour of opening it. To prevent procedural subjectivity, we used standard 28G automated pressure activated safety lancet.

GRBS was assessed after birth, during admission and according to case specific protocols. GRBS was assessed by taking blood by heel lancing. Heel pricks were conducted in the lateral aspects of heel in all newborns. The investigator started with assessing state of arousal of the baby and recorded baseline heart rate and O<sub>2</sub> saturation. The investigator then left the room and the neonate was prepared for the procedure. Randomization was done by computer assigned numbers. Allocation concealment was assured. A research assistant opened a consecutively numbered envelope that contained the treatment assigned for each neonate. 2 minutes before heel lance, 2 ml of the allocated solution was administered for 30 seconds. Pain was assessed with the use of PIPP pain scale. The heel pad was cleaned with 1 % betadine solution, following alcohol using a sterile swab. Two minutes after giving the oral solution, the heel was squeezed and then lanced with sterile autolet. Audio recorder was switched on simultaneously to record the cry of the infant. PIPP pain scale is validated to assess pain in all term and preterm neonates.

Parameters assessed

Gestational age

Behavioural state

Heart rate

O<sub>2</sub> saturation

Brow bulge

Eye squeeze

Nasolabial furrow

A maximal score of 21 is possible.

Duration of crying: Duration of first cry was recorded from the first burst of sound till the neonate became silent again. Total crying time over a period of 5 minutes after the lance was also noted.

## RESULTS

**Table 1: Comparison of Solution Used with Heart Rate Increase (N = 100).**

Heart rate increase	Solution Used		Chi Square	P-Value
	10 % D (N = 50)	25 % D (N = 50)		
0 to 4 beat/ min increase	21 (42 %)	36 (72 %)	11.05	0.004
5 to 14 beat/ min increase	25 (50 %)	14 (28 %)		
15 to 24 beat/ min increase	4 (8 %)	0 (0)		

Among the 10 % dextrose solutions group, 21 (42 %) participants had 0 to 4 beat/ min increase, 25 (50 %) participants had 5 to 14 beat/ min increase and 4 (8 %) participants had 15 to 24 beat/ min increase. Among the 25 % dextrose solutions group, 36 (72 %) participants had 0 to 4 beat/ min increase, 14 (28 %) participants had 5 to 14 beat/ min increase. The difference in the proportion of heart rate increase between groups was statistically significant (P value 0.004).

**Table 2: Comparison of Solution Used with spO2 Drop (N = 100)**

SP02 Drop	Solution Used		Chi Square	P-Value
	10 % D	25 % D		
0 - 2.4 % decrease	30 (60 %)	41 (82 %)	6.912	0.032
2.5-4.9 % decrease	14 (28 %)	8 (16 %)		
5 - 7.4 % decrease	6 (12 %)	1 (2 %)		

Among the 10 % dextrose solution group, 30 (60 %) participants had 0 - 2.4 % decrease, 14 (28 %) participants had 2.5 - 4.9 % decrease and 6 (12 %) participants had 5 - 7.4 % decrease. Among the 25 % dextrose solution group, 41 (82 %) participants had 0 - 2.4 % decrease, 8 (16 %) participants had 2.5 - 4.9 % decrease and 1 (2 %) participant had 5 - 7.4 % decrease. The difference in the proportion of SP02 drop between groups was statistically significant (P value 0.032).

**Table 3: Comparison of Solution Used with Grading of Pain (N = 100)**

Grading of Pain	Solution Used		Chi Square	P-Value
	10% D (N = 50)	25 % D (N = 50)		
Mild pain < 6	33 (66 %)	47 (94 %)	12.34	0.002
Moderate pain 7 to 12	16 (32 %)	3 (6 %)		
Severe > 12	1 (2 %)	0 (0 %)		

Among the 10 % dextrose solution group, 33 (66 %) participants had mild pain (< 6), 16 (32 %) participants had moderate pain (7 to 12) and 1 (2 %) participant had severe (> 12). Among the 25 % dextrose solution group, 47 (94 %) participants had mild pain (< 6) and 3 (6 %) participants had moderate pain (7 to 12). The difference in the proportion of grading of pain between groups was statistically significant (P value 0.002).

**Table 4: Comparison of Median Total PIPP Score between Study Groups (N = 100)**

Parameter	Solution Used		Mann Whitney U Test (P Value)
	10 % D	25 % D	
Total score Median (IQR)	5 (4 to 7)	3 (1 to 4.25)	<0.001

Among the people with 10 % dextrose solution group, the median total PIPP score was 5 (4 to 7) and it was 3 (1 to 4.25) in people with 10 % dextrose solutions group. The difference in the total PIPP score between two group was statistically significant (p value < 0.001).

**Table 5: Comparison of Median SPO2 between Study Groups (N = 100)**

SPO2	Solution Used		P Value
	10 % D	25 % D	
Pre procedure (Median (IQR))	95 (94 to 97.25)	96 (94 to 98)	0.364
During procedure (Median (IQR))	94.50 (92 to 96)	96 (94 to 97)	0.008
Post procedure (Median (IQR))	96 (95 to 97)	96 (95 to 98)	0.067

Among the people with 10 % dextrose solution group, the median pre procedure SPO2 was 95 (IQR 94 to 97.25) and it was 96 (IQR 94 to 98) in people with 25 % dextrose solution group. The SPO2 difference during pre-procedure, between two groups was statistically not significant (p value 0.364). Among the people with 10 % dextrose solution group, the median during procedure SPO2 was 94.50 (IQR 92 to 96) and it was 96 (IQR 94 to 97) in people with 25 % dextrose solutions group. The SPO2 difference during procedure between two groups was statistically significant (p value 0.008). Among the people with 10 % dextrose solution group, the median post procedure SPO2 was 96 (IQR 95 to 97) and it was 96 (IQR 95 to 98) in people with 25 % dextrose solutions group. The SPO2 difference in the post procedure between two groups was statistically not significant (p value 0.067).

## DISCUSSION

### Physiological Variables

Prior to procedure, the mean HR - 144.37/mt and SP02 - 95.9 % before heel prick of babies. There was no significant difference between two groups. Behavioural state prior procedure was sleep with eyes closed in 44 % babies. There was no significant difference between two groups in the behavioural states.

### During the Procedure

Babies who received 25 % D had 5 - 14 beats/min rise in HR in case of 14 babies, 0 babies had rise in HR 15 - 24 beats/min, 36 had 0 - 4 beats/min rise in heart rate during heel lancing. Babies who received 10 % D had 5 - 14 beats/min rise in 25 babies, 15 - 24 beats/min rise in 4 babies and 0 - 4 beats/min rise in 21 babies. There is significant decrease in heart rate variations with the use of 25 % D compared to 10 % D, which matches findings of Skogsdal et al.<sup>[12]</sup>

Babies received 25 % D; 1 baby had sp02 drop of 5 - 7.4 % during procedure, 8 babies had 2.5 - 4.9 % drop in SP02 during the procedure, 41 babies had 0 - 2.4 % drop in SP02. Babies received 10 % D; 6 babies had Sp02 drop of 5 - 7.4 %, 14 babies had Sp02 drop of 2.5 - 4.9 %, 30 babies had 0 - 2.4 % drop in Sp02. There is significant effect on oxygen saturation variability. This is in conflict with finding by Deshmukh et al.<sup>[13]</sup>

### Cry Duration

As in previous studies, other researchers have used duration of cry to assess the efficacy of pain in preterm infants. The mean cry duration in first 3 minutes in babies who received 25 % D was 11.50 seconds and with those who received 10 % D was 12 seconds. 10 babies had cry duration less than 10 seconds. 5 of them received 10 % dextrose for pain relief. There is no significant difference in duration of first cry between two groups. In study by Deshmukh et al. (2002),<sup>[13]</sup> there was a significant difference noted between the two solutions. But the

study by Skogsdal et al.<sup>[12]</sup> have not found any significant difference. The cry of babies was high pitched in 3 babies; 2 of them received 10 % D. All babies were consolable.

Duration of crying induced by a noxious stimulation is a valuable measure of pain in preterm neonates and is reasonable in the absence of any obvious impairment to vocalization.<sup>[14]</sup> In previous studies using sweet solutions, there was reduction in cry duration.<sup>[15]</sup> Experimental studies have shown that analgesia elicited by oral sweet solution can be mediated by activation of endogenous opioid antagonists, such as naltrexone.<sup>[16]</sup>

### **Pain Score**

All babies noted had mild to moderate pain (score < 12). Mean score in babies who received 10 % D was 4.847 and 25 % D was 4.340. No adverse effects were observed following the use of oral glucose such as vomiting, abdominal distension or NEC.

### **CONCLUSION**

Need for pain relief even in minor procedures like heel lancing, IV insertion, NG tube insertion, IM injections in preterm neonates should be made part of routine care in NICUs. 10% Dextrose having significantly lesser osmolarity (555mosm/L) compared to 25% Dextrose (1389 mosm/L) can be a better choice in view of risk of necrotising enterocolitis in preterm babies on repeated usage of higher osmolarity solution for very frequent minor procedures. Long term follow up of these late preterm babies who received pain relief for minor procedures is required to assess the neurodevelopmental outcomes and to compare it with babies who have not received such therapy.

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