

Original Research Article

Efficacy of 25% dextrose gel in reducing procedural pain in preterm infants: a prospective observational study

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ABSTRACT

Background: Preterm infants in neonatal intensive care units (NICUs) undergo frequent painful procedures, increasing their risk for adverse neurodevelopmental outcomes. Non-pharmacologic interventions are sought for safe, effective pain management. We evaluated the efficacy of 25% dextrose gel (Nanodex, Analeptik Biologicals) for procedural pain relief in preterm neonates.

Methods: This prospective observational study enrolled 53 preterm infants over 12 months. 25% dextrose gel (Nanodex, Analeptik Biologicals) was administered buccally at 0.5 ml/kg, 2 minutes before procedures including venipuncture, intubation, heel prick, nasogastric/orogastric tube insertions, and retinopathy of prematurity (ROP) screening. Historical data was used as control group. Pain was assessed using the premature infant pain profile (PIPP) score.

Results: The mean PIPP score across all procedures was significantly lower post-25% dextrose gel (mean: 6.9 ± 1.9) compared to historical reference scores (mean: 11.2 ± 2.1 , $p < 0.001$). The greatest reduction was observed during ROP screening. No adverse events were recorded.

Conclusions: 25% dextrose gel is a safe and effective intervention for procedural pain management in preterm infants. Its routine use in NICU protocols should be considered.

Keywords: 25% Dextrose gel, PIPP scores analgesia, Dextrose, preterm, Pain score, NICU procedures

INTRODUCTION

Neonates admitted to the neonatal intensive care unit (NICU) are routinely exposed to numerous painful procedures such as venipuncture, heel pricks, intubation, and tube insertions. Contrary to earlier misconceptions, neonates not only perceive pain but may experience it more intensely than adults due to the higher density of sensory nerve endings in their skin and mucous membranes.¹

By 24 weeks of gestation, the anatomical and neurochemical substrates for nociception are sufficiently

developed, making preterm neonates particularly vulnerable to the effects of pain.² Repeated or untreated painful interventions during this critical developmental window can disrupt normal brain architecture, potentially resulting in long-term consequences such as altered pain sensitivity, neuroanatomical changes, and cognitive, behavioural, and emotional impairments.³

Assessing pain in neonates presents a unique challenge, as their physiological and behavioural responses are often subtle, less organized, and harder to interpret than in older children or adults.⁴ Pain assessment is therefore performed indirectly by monitoring changes in physiological (heart

rate, respiratory rate, blood pressure, oxygen saturation) and behavioural parameters (facial expressions, motor activity, and crying).⁵

Recognizing and managing pain in newborns remains a challenge in NICUs, as neonates are unable to verbally express their discomfort. Research shows that infants born before 32 weeks of gestation undergo approximately 10 to 15 painful procedures daily during the initial weeks of life. Alarming, nearly 80% of these procedures are performed without any form of pain relief.⁶

To mitigate procedural pain, both pharmacological and non-pharmacological strategies have been developed. Among the non-pharmacological options, techniques such as gentle handling, swaddling, appropriate positioning, music therapy, acupuncture, massage, non-nutritive sucking, and oral administration of sweet-tasting solutions have demonstrated varying degrees of efficacy.⁷

Neonates, especially those born preterm, experience multiple painful interventions during their NICU stay.⁸ Despite being capable of pain perception, pain in neonates is frequently undertreated.⁹ Studies show that repetitive untreated pain can lead to altered pain sensitivity and impaired neurodevelopment.¹⁰ Sweet-tasting solutions like sucrose and dextrose have analgesic properties mediated through endogenous opioid pathways.¹¹ Nanodex, a commercially available 25% dextrose gel (Analeptik Biologicals), offers ease of use and precise dosing through buccal application. This study investigates the analgesic efficacy of Nanodex gel in preterm infants undergoing routine painful procedures in a NICU setting.

Aim and objectives

Aim and objectives of the study were to find the effectiveness of 25% dextrose gel as an analgesic agent for the routine painful procedures in a NICU in preterm neonates.

METHODS

It was a prospective observational study, conducted in the NICU of a Motherhood Hospital, Banashankari, Bengaluru over 12 months (April 2024 – March 2025).

Inclusion criteria

Preterm neonates (gestational age lesser than 37 weeks) and clinically stable neonates undergoing investigations as part of routine clinical evaluation were included for the study.

Exclusion criteria

Exclusion criteria included neonates with major congenital anomalies or exhibiting neurological symptoms, neonates born to mothers who received general anaesthesia within the preceding 48 hours, neonates currently receiving

analgesic or sedative medications, severe cardiorespiratory instability and contraindication to oral administration.

Participants

53 preterm infants (<37 weeks' gestational age) admitted in NICU satisfying inclusion and exclusion criteria were enrolled into the study.

Intervention

0.5 ml/kg of 25% dextrose gel (Nanodex, Analeptik Biologicals) was applied to both buccal mucosae 2 minutes before the procedure.

Procedures observed

Venipuncture, intubation, heel prick, NG/OG tube insertion, and retinopathy of prematurity (ROP) screening. Primary outcome was the painful response as assessed by the premature infant pain profile (PIPP) score.

Pain assessment

Pain was assessed using PIPP score (range 0-21) within 30 seconds post-procedure. PIPP scores from equal number of retrospective historical cases were collected from the medical case records database and was used as control group. It was ensured that the historical controls did not receive any analgesics or sweet solutions.

Data analysis

Mean PIPP scores were analyzed using paired t-tests versus historical controls; significance set at $p < 0.05$. Each procedure was video recorded using the mobile phones by NICU staff and all the neonates undergoing various procedures were filmed prior, during and up to 1 min after the procedure. The investigator assessed the level of pain by assigning scores based on the PIPP. All relevant data, including PIPP scores and general clinical information, were extracted from the neonates' medical records, the video recordings were deleted at the end of the study.

RESULTS

Fifty-three neonates were enrolled into the study with a mean gestational age of 32.4 ± 2.3 weeks and mean birth weight of 1580 ± 240 gms (Table 1).

Table 1: Demographic characteristics of study population.

Characteristic	Mean $\pm$ SD/N (%)	Range
Gestational age (weeks)	32.4 $\pm$ 2.3	28–36
Birth weight (g)	1580 $\pm$ 240	1100–2100
Male	30 (56.6)	
Female	23 (43.4)	

Table 2 provides the different procedures performed for which the 25% dextrose gel was used.

Table 2: Distribution of procedures performed.

Procedure	Number of cases (%)
Heel prick	15 (28.3)
Venipuncture	12 (22.6)
NG/OG tube insertion	10 (18.9)
ROP screening	9 (17.0)
Intubation	7 (13.2)

Table 3 provides the mean PIPP scores of different procedures performed between 25% dextrose gel and control group.

Table 3: Mean PIPP scores by procedure.

Procedure	Historical control (mean PIPP±SD)	Post-25% dextrose gel (mean PIPP±SD)	P value
Heel prick	10.8±2.0	6.4±1.7	<0.001
Venipuncture	10.2±2.1	6.1±1.8	<0.001
NG/OG tube insertion	9.8±2.0	6.0±1.6	<0.001
ROP screening	11.2±2.4	6.6±1.9	<0.001
Intubation	12.0±2.3	7.5±2.0	<0.001

DISCUSSION

PIPP is a widely used, 7-item composite tool designed to assess acute pain in infants. It incorporates both theoretical and empirical foundations and includes three behavioural indicators (facial expressions), two physiological parameters (heart rate and oxygen saturation), and two contextual factors gestational age (GA) and behavioural state (BS).

The behavioural and physiological indicators are scored on a 4-point scale (0 to 3), reflecting the degree of change from the infant's baseline values. In contrast, the contextual items (GA and BS) are scored prior to the procedure, before the infant is touched, and are not based on changes from baseline. Notably, GA and BS are reverse-scored (3 to 0) to adjust for developmental differences, with higher scores assigned to younger, more physiologically vulnerable infants. As a result, the maximum possible PIPP score is 21 for preterm infants under 28 weeks of gestation, and 18 for full-term infants.¹²

This study demonstrates that 25% dextrose gel (Nanodex) significantly reduces procedural pain in preterm neonates. The greatest reductions were seen during ROP screening and intubation.

Sagheb et al in their study, observed that oral 25% dextrose in combination with locally anaesthetic eye drops could significantly decrease pain during and after ROP screening. Group receiving 25% dextrose gel significantly lowered PIPP scores (13.8±1.39) compared to the other

The study observed a significant reduction in pain scores among neonates who received 25% dextrose gel compared to those in the control group, as measured by the mean decrease in PIPP scores across various procedures. Specifically, the mean PIPP score reductions were 4.4 for heel prick, 4.1 for venipuncture, 3.8 for nasogastric/orogastric (NG/OG) tube insertion, 4.6 for ROP screening, and 4.5 for intubation.

These differences were all statistically significant ($p<0.001$), indicating that the use of 25% dextrose gel was associated with significantly lower pain perception during these common neonatal procedures. No adverse events were recorded.

groups (group B: 15.95±1.27 and group C: 15.10±1.19) ($p=0.001$).¹³

The analgesic effect is likely mediated via endogenous opioid pathways activated by sweet taste receptors. The gel form enhances mucosal contact and ensures consistent dosage.¹⁴ Our study found that 25% dextrose gel (NANODEX) significantly reduced procedural pain in preterm infants, with an average PIPP score reduction of approximately 4-5 points across various interventions. These findings align well with prior research on the analgesic effects of oral dextrose in neonates.

Bueno et al conducted a randomized study comparing 25% dextrose with expressed breast milk (EBM) in 113 late preterm neonates undergoing heel lancing. Their results demonstrated superior analgesia in the dextrose group, with a mean PIPP score reduction of 3 points at 30 seconds post-procedure and a significantly shorter duration of crying. These findings support the use of concentrated dextrose solutions as effective pain-relieving agents.¹⁵

Similarly, Sahoo et al evaluated 160 neonates (>34 weeks' gestational age) undergoing venipuncture and randomized them into three groups: 25% dextrose, EBM, and sterile water. The mean PIPP scores at 30 seconds were 5.22 in the dextrose group, 6.84 in the EBM group, and 11.22 in the sterile water group. This study further underscores that while EBM offers some analgesic benefit, 25% dextrose is significantly more effective in reducing procedural pain.¹⁶

These comparative studies reinforce our observation that dextrose gels act rapidly to blunt behavioural and

physiological pain responses, likely via activation of oropharyngeal sweet taste receptors and subsequent endogenous opioid release. The gel formulation used in our study (Nanodex) may offer enhanced contact and prolonged mucosal absorption compared to liquid forms, thereby improving efficacy and ease of use in clinical settings.

Clinical implications

A total 25% dextrose gel is safe, easy, cost-effective intervention. Limitations include historical control group and reliance on behavioural scoring.

CONCLUSION

We conclude that pain in late preterm infants must be promptly recognized and effectively managed, as it can lead to both short- and long-term complications. Administering 25% dextrose gel has proven to be an effective and readily available option for relieving procedural pain in these infants. In this study the 53 preterm infants admitted in NICU were enrolled for the study and 25% dextrose gel was administered 2 mins prior to procedures heel prick, venipuncture, NG/OG tube insertions and ROP screening. The pain was assessed by PIPP scoring which showed statistically significant reduction of pain scores when compared with the retrospective data. 25% dextrose gel significantly reduces procedural pain in preterm neonates and it is a safe, practical, and cost-effective intervention suitable for NICU use.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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