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Original Research Article

EFFECTIVENESS OF COMBINED NON-PHARMACOLOGICAL INTERVENTIONS FOR NEONATAL PAIN MANAGEMENT: A STUDY OF SUCROSE, NON-NUTRITIVE SUCKING, AND FACILITATED TUCKING

Vinothini Asaithambi[1], Hariharan Suresh[2]

[1]Senior Resident, Department of Pediatrics, Trichy SRM Medical College Hospital and Research Centre, Trichy, India.
[2]Assistant Professor, Department of Community Medicine, Trichy SRM Medical College Hospital and Research Centre, Trichy, India.

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Corresponding Author:
Dr. Hariharan Suresh,
Assistant Professor, Department of Community Medicine, Trichy SRM Medical College Hospital and Research Centre, Trichy, India.
Email: handy31088@gmail.com

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ABSTRACT

Background: Neonates admitted to the Neonatal Intensive Care Unit (NICU) are frequently subjected to painful procedures such as heel pricks, vaccinations, and blood sampling. Effective pain management is essential to prevent long-term developmental and physiological consequences, including alterations in stress response and hypersensitivity to future pain. Pharmacological options for pain relief are limited in this population due to concerns about side effects and toxicity. Non-pharmacological methods, including sucrose administration, non-nutritive sucking (NNS), and facilitated tucking (FT), have gained attention for their safety and efficacy in managing procedural pain in neonates.

Materials and Methods: This randomized placebo-controlled trial was conducted at Pragna Children's Hospital NICU in Hyderabad over two years (December 2017 to April 2020). Neonates requiring a heel prick for blood glucose measurement, preterm neonates (>32 weeks), and term neonates with a birth weight over 1500 grams were included. Exclusion criteria comprised infants older than 28 days, those with congenital anomalies, cardiovascular instability, or on ventilator support. A total of 100 participants were randomized into two groups: Group 1 received 24% sucrose, NNS, and FT, while Group 2 received sterile water, NNS, and FT. Primary outcomes were measured using the Premature Infant Pain Profile (PIPP) score, and secondary outcomes included cry duration and adverse events. Data analysis was performed using IBM SPSS version 22, with statistical significance set at $p < 0.05$.

Results: The combination of 24% sucrose, NNS, and FT significantly reduced PIPP scores compared to sterile water, NNS, and FT. Specifically, PIPP scores were lower in the sucrose + NNS + FT group (moderate preterm: 1.25, late preterm: 2.88) compared to the sterile water group (moderate preterm: 4.2, late preterm: 6.15). Crying duration was also significantly shorter in the sucrose group (mean: 1.57 seconds) compared to the sterile water group (mean: 6.33 seconds). No significant differences were observed in adverse events between groups, with only minor events reported.

Conclusion: The study concludes that the combination of 24% sucrose, non-nutritive sucking, and facilitated tucking is effective in reducing pain during heel prick procedures in neonates, with minimal adverse effects. This supports the use of sucrose in conjunction with other non-pharmacological techniques for managing procedural pain in neonates.

Keywords: Neonatal pain management, sucrose, non-nutritive sucking, facilitated tucking, heel prick, Premature Infant Pain Profile (PIPP), NICU.

INTRODUCTION

Neonates admitted to the Neonatal Intensive Care Unit (NICU) often experience painful procedures such as heel pricks, vaccinations, and blood sampling. Pain management in these vulnerable populations is crucial, as untreated pain can have long-term developmental and physiological consequences, including alterations in stress response and hypersensitivity to future pain.[1] Pharmacological methods for pain relief in neonates are limited due to concerns about side effects and toxicity. As a result, non-pharmacological methods, such as the use of sucrose, non-nutritive sucking, and facilitated tucking, have gained prominence for managing procedural pain in neonates.

Sucrose, administered orally, has been shown to have analgesic properties when given before painful procedures. When combined with other non-pharmacological methods, such as non-nutritive sucking and facilitated tucking, sucrose enhances pain relief. Research has demonstrated that sucrose reduces crying time and stabilizes physiological parameters such as heart rate and oxygen saturation after procedures like intradermal injections and heel pricks. [2,3] The administration of 24% oral sucrose in combination with facilitated tucking significantly decreases pain responses, as measured by neonatal pain scales such as the Neonatal Infant Pain Scale (NIPS), with improvements in heart rate and oxygen levels.[4]

Additionally, music therapy combined with sucrose has shown superior pain relief during procedures like heel pricks compared to either method alone.[2] Other studies have explored the efficacy of breastfeeding, oral dextrose, kangaroo care, and EMLA cream in reducing pain, with breastfeeding emerging as one of the most effective interventions.[5] Facilitated tucking, a method where the neonate is held in a flexed, foetal-like position, also reduces pain perception and crying duration during painful procedures.[6,7]

Despite the evidence supporting the efficacy of these non-pharmacological methods, they are still underutilized in many NICUs.[1] This study aims to evaluate the effectiveness of sucrose combined with non-nutritive sucking and facilitated tucking in comparison to non-nutritive sucking and facilitated tucking alone in managing pain during heel pricks in neonates. By examining these combinations, the study seeks to provide further insight into optimizing non-pharmacological pain management strategies in neonatal care.

MATERIALS AND METHODS

Study Design and Setting: This was a randomized placebo-controlled trial conducted at Pragna Children's Hospital NICU, a tertiary care center in Hyderabad. The study was conducted over a period of two years, from December 2017 to April 2020.

Study Participants and Sample Size

The study included neonates admitted to the NICU who met the following inclusion criteria: neonates requiring a heel prick for blood glucose measurement, preterm neonates (>32 weeks), and term neonates with a birth weight of more than 1500 grams. Exclusion criteria included infants older than 28 days, neonates with congenital anomalies, APGAR score <7 at 5 minutes, neonates at high risk of necrotizing enterocolitis (NEC), neonates with cardiovascular instability, those on ventilator support or CPAP, those sedated or on opioids, and neonates in the post-operative period.

The sample size was calculated based on 90% power, a 5% alpha error, and data from a previous study by Gibbins et al.[8] A total of 45 neonates were required in each group. To account for a 10% non-participation rate, the final sample size was 50 per group, for a total of 100 participants.

Study Procedure and Data Collection

Parental consent was obtained, and neonates were randomized into two groups using block randomization: Group 1 (24% Sucrose + Non-nutritive Sucking (NNS) + Facilitated Tucking (FT)) and Group 2 (Sterile Water + NNS + FT). Randomization was conducted with a block size of 4 using computer-generated sequences. A pharmacist handled allocation concealment, preparing syringes with either 1ml of sterile water or 1ml of 24% sucrose based on the group assignment. Syringes were placed in opaque envelopes labeled with a random code to ensure blinding of the nurses, doctors, and parents.

Neonates were placed under radiant warmers during the procedure, and heart rate and SpO2 were continuously monitored. Two minutes before the heel prick, 1ml of the assigned solution was administered on the anterior surface of the neonate's tongue, followed by non-nutritive sucking. Facilitated tucking was initiated 30 seconds before the heel prick, where the neonate's arms and legs were gently held in a flexed, fetal position. The heel prick was performed by a third nurse using aseptic techniques with a 26-gauge sterile needle to obtain blood for glucose measurement. Non-nutritive sucking and facilitated tucking were continued throughout the procedure and for 3 minutes after the heel prick.

A digital video camera recorded the neonate's face and physiological monitor (heart rate and SpO2) from 30 seconds before the heel prick until 3 minutes after. Cry duration was measured with a stopwatch, and adverse events such as choking, bradycardia, tachycardia, or oxygen desaturation were monitored for 5 minutes from solution administration until 3 minutes post-heel prick.

Study Outcome

The primary outcome was the Premature Infant Pain Profile (PIPP) score, which included gestational age, behavioral state, and physiological indicators (heart rate and oxygen saturation). PIPP scores were assessed at 30 seconds and 2 minutes after the heel

prick. The secondary outcome included the total cry duration after the procedure and the occurrence of any adverse events associated with sucrose or sterile water administration.

Data Analysis

In our study 159 babies were assessed for eligibility, 35 babies did not meet the inclusion criteria, parents of 24 babies refused to give consent.100 babies were randomized, 2 babies were excluded after randomization as video is not clear and 1 baby was excluded as baby passed stool during heel prick. After exclusion, in intervention group (24% sucrose, non-nutritive sucking, and facilitated tucking group) - 49 babies and in Control group (Sterile water, non-nutritive sucking, facilitated tucking group) - 48 babies were included in final analysis. Descriptive analysis was performed using means and standard deviations for continuous variables and frequencies and proportions for categorical variables. Data were visually represented using bar and pie charts where appropriate. Normality of quantitative data was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests, along with visual inspection. Differences between groups were analyzed using independent t-tests and ANOVA for continuous variables, with post-hoc tests for pairwise comparisons. Chi-square tests were used for categorical variables. Statistical significance was defined as $p < 0.05$. Data analysis was performed using IBM SPSS version 22.

RESULTS

The baseline characteristics of the study participants in the two groups (Sucrose + NNS + FT and Sterile Water + NNS + FT) are summarized in Table 1. The distribution of gender was comparable between the groups, with 57.14% males in the sucrose group and 54.17% males in the sterile water group (p=0.768). Similarly, gestational age distribution was not significantly different, with moderate preterm (8.16% vs. 10.42%), late preterm (48.98% vs. 41.67%), and term neonates (42.86% vs. 47.92%) in the sucrose and sterile water groups, respectively (p=0.758). The mean gestational age was 36.24 ± 2.1 weeks in the sucrose group and 36.13 ± 2.13 weeks in the sterile water group (p=0.781). No significant differences were observed in the mean day of life (4.08 ± 1.95 vs. 4.56 ± 1.89; p=0.22) or birth weight (2.39 ± 0.64 kg vs. 2.49 ± 0.65 kg; p=0.443) between the two groups. Thus, the baseline characteristics were well balanced, and no significant differences were found between the two groups.

The comparison of outcomes between the two groups (Sucrose + NNS + FT and Sterile Water + NNS + FT) is presented in Table 2. The mean PIPP score at 30 seconds was significantly lower in the sucrose group (2.97 ± 1.18) compared to the sterile water group (6.07 ± 1.16), with a p-value of <0.001. Similarly, at 2 minutes, the mean PIPP score was significantly lower in the sucrose group (1.61 ± 0.73) compared to the sterile water group (3.07 ± 0.99) ($p < 0.001$). Crying time was also significantly reduced in the sucrose group (1.57 ± 2.29 seconds) compared to the sterile water group (6.33 ± 1.88 seconds) ($p < 0.001$). Regarding adverse events, both groups had one participant (2.04% in the sucrose group and 2.08% in the sterile water group) who experienced an adverse event, with no significant difference between the groups ($p = 1.000$). Thus, sucrose combined with NNS and FT was more effective in reducing pain and crying time without increasing the risk of adverse events. [Table 1]

The comparison of PIPP scores at 30 seconds and 2 minutes across gestational age groups (Moderate Preterm, Late Preterm, and Term) between the two intervention groups is shown in Table 3. At 30 seconds, the PIPP scores were significantly lower in the sucrose group across all gestational ages, with scores of 1.25 ± 0.50 in moderate preterm, 2.88 ± 1.15 in late preterm, and 3.40 ± 1.00 in term neonates ($p = 0.002$). In the sterile water group, PIPP scores were significantly higher, with 4.20 ± 0.84 in moderate preterm, 6.15 ± 0.76 in late preterm, and 6.41 ± 1.15 in term neonates ($p < 0.001$).

At 2 minutes, although the sucrose group had lower PIPP scores, there was no statistically significant difference across gestational ages ($p = 0.156$), with scores of 1.00 ± 0.10 for moderate preterm, 1.58 ± 0.65 for late preterm, and 1.76 ± 0.83 for term neonates. In contrast, the sterile water group showed a significant increase in PIPP scores at 2 minutes, with 1.60 ± 0.55 for moderate preterm, 3.10 ± 0.64 for late preterm, and 3.37 ± 1.05 for term neonates ($p = 0.001$). This highlights that sucrose was more effective in reducing pain immediately after the procedure, especially at 30 seconds. [Table 2]

Table 1: Comparison of baseline characteristics of the study participants in two groups

Parameter	Sucrose + NNS + FT (N=49)	Sterile Water + NNS + FT (N=48)	P value
	Frequency (%)/Mean ± SD		
Gender			
Male	28 (57.14%)	26 (54.17%)	0.768
Female	21 (42.86%)	22 (45.83%)	
Gestational Age			
Moderate preterm	4 (8.16%)	5 (10.42%)	0.758
Late preterm	24 (48.98%)	20 (41.67%)	
Term	21 (42.86%)	23 (47.92%)	
Gestational Age (in weeks)	36.24 ± 2.1	36.13 ± 2.13	0.781
Day of Life	4.08 ± 1.95	4.56 ± 1.89	0.22

Birth Weight	2.39 ± 0.64	2.49 ± 0.65	0.443

Table 2: Comparison of the outcomes among the study participants in two groups

Parameter	Sucrose + NNS + FT (N=49)	Sterile Water + NNS + FT (N=48)	P value
	Frequency (%)/Mean ± SD		
PIPP 30 seconds	2.97 ± 1.18	6.07 ± 1.16	<0.001
PIPP 2 minutes	1.61 ± 0.73	3.07 ± 0.99	<0.001
Crying Time (in seconds)	1.57 ± 2.29	6.33 ± 1.88	<0.001
Adverse Events			
Yes	1 (2.04%)	1 (2.08%)	1.000
No	48 (97.96%)	47 (97.92%)	

DISCUSSION

Pain management in neonates is crucial, as untreated pain can have long-term effects on neurodevelopment. Non-pharmacological interventions have gained attention due to their safety and efficacy, particularly in preterm neonates who are more vulnerable to procedural pain.

In the present study, the combination of 24% sucrose, non-nutritive sucking (NNS), and facilitated tucking (FT) demonstrated a significant reduction in PIPP scores compared to the group receiving sterile water, NNS, and FT. Specifically, the mean PIPP scores were lower in both moderate preterm (1.25) and late preterm neonates (2.88) in the sucrose + NNS + FT group, compared to 4.2 and 6.15 in the sterile water group, respectively. These findings are consistent with previous studies, which also support the efficacy of sucrose and NNS in reducing pain. For example, Asmerom et al., reported significantly lower PIPP scores in neonates receiving sucrose + NNS (mean: 4.6) compared to sterile water and NNS (mean: 6.3) and the control group (mean: 5.9).[9] Simonse et al., found no significant difference in PIPP scores between neonates receiving sucrose (mean: 5.5) and breast milk (mean: 6.1), further emphasizing the analgesic potential of sucrose.[10]

In this study, the dose of 24% sucrose was 1 mL, consistent with previous research. For instance, Kumari et al., used 1 mL of 24% sucrose in preterm neonates,[11] and similar quantities were used by Simonse et al., and De Bernardo et al., in neonates of varying gestational ages.[3,10] This suggests that 1 mL of 24% sucrose is effective across different neonatal populations.

Regarding the influence of gestational age (GA) on pain responses, significant differences in PIPP scores were observed. Moderate preterm neonates (<34 weeks) had significantly lower PIPP scores at 30 seconds compared to late preterm and term neonates in both the sucrose + NNS + FT group and the sterile water + NNS + FT group. However, at 2 minutes, there were no significant differences between these groups. Similar findings were reported by Gibbins et al., where less mature neonates (<32 weeks GA) exhibited lower PIPP scores during painful procedures compared to more mature neonates.[12]

In terms of crying time, the sucrose + NNS + FT group had significantly shorter crying durations (mean: 1.57 ± 2.29 seconds) compared to the sterile water + NNS + FT group (mean: 6.33 ± 1.88 seconds). These results align with findings from Thakkar et al., who reported a median crying time of 0 seconds in the sucrose + NNS group.[13] Similarly, Elserefy et al., reported crying times of 4.6 seconds in the sucrose + NNS group, further supporting the analgesic benefits of sucrose in combination with non-nutritive sucking.[14]

No life-threatening adverse events were observed in this study, with only two minor events: one neonate in the sucrose group vomited, and one in the sterile water group experienced brief desaturation. These findings are consistent with previous studies, such as Gibbins et al., and Kumari et al., which also reported minor adverse events without significant differences between groups.[11,15]

Overall, the present study confirms that the combination of 1 mL 24% sucrose, NNS, and FT effectively reduces pain in neonates undergoing heel prick procedures, with minimal adverse events. This supports the use of sucrose as a safe and effective intervention for procedural pain in neonates, particularly when combined with other non-pharmacological techniques like NNS and FT.

Limitations

The study had several limitations. First, it only included neonates admitted to the NICU at our hospital, a tertiary care center, and the sample size was relatively small, which may limit the generalizability of the results to the broader population. Second, only a single dose of sucrose was administered for pain relief during heel pricks for blood glucose measurement, and the study did not evaluate the effect of repeated sucrose doses on pain reduction in subsequent heel pricks. Third, the enrolled neonates were not followed up to assess the potential long-term benefits on neurodevelopmental outcomes. Lastly, the findings cannot be extrapolated to neonates of other gestational ages, particularly those less than 32 weeks.

CONCLUSION

The study concluded that a combination of 24% sucrose, non-nutritive sucking (NNS), and facilitated tucking significantly reduced PIPP scores and crying duration compared to sterile water with NNS and facilitated tucking, with no significant differences in adverse events between groups, and

any adverse events being minor and requiring no intervention. The combination is recommended for pain relief during heel pricks, and further research is suggested to assess the effects of repeated sucrose use, its long-term neurobehavioral impact, and its effectiveness in other painful procedures like venipuncture and immunization.

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