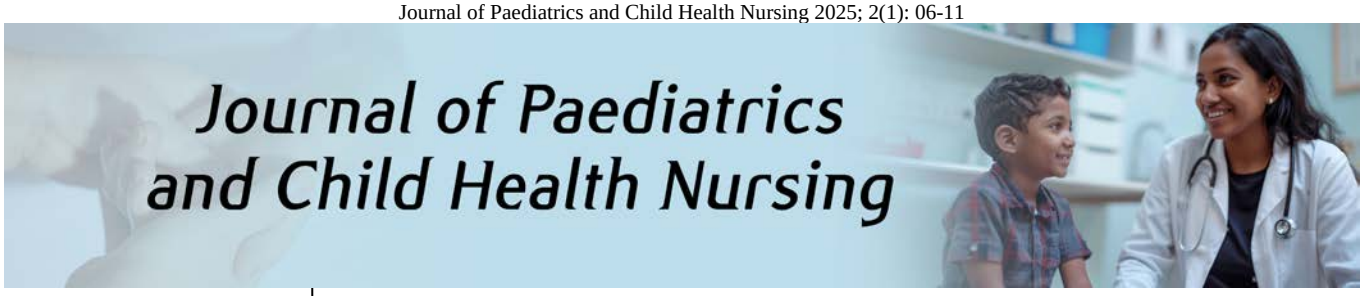

P-ISSN: 3081-0582
E-ISSN: 3081-0582
www.childnursingjournal.com
JPCHN 2025; 2(1): 06-11
Received: 10-02-2025
Accepted: 15-03-2025

Dr. Élodie Laurent
Department of Neonatal Medicine, Institut National de Santé et de la Recherche Médicale (INSERM), Paris, France

Corresponding Author:
Dr. Élodie Laurent
Department of Neonatal Medicine, Institut National de Santé et de la Recherche Médicale (INSERM), Paris, France

Optimizing neonatal pain management: A comparative analysis of non-pharmacological interventions

Élodie Laurent

DOI: https://www.doi.org/10.33545/30810582.2025.v2.i1.A.7

Abstract
Background: Effective pain management in neonates is essential to prevent both immediate physiological instability and potential long-term neurodevelopmental consequences. Non-pharmacological interventions such as oral sucrose, skin-to-skin contact, and non-nutritive sucking have emerged as safe and feasible strategies for routine procedural pain relief.
Objective: To compare the effectiveness of three non-pharmacological interventions—oral sucrose 24%, skin-to-skin contact, and non-nutritive sucking in reducing procedural pain among neonates undergoing heel prick procedures.
Methods: A randomized controlled trial was conducted on 120 neonates admitted to a tertiary NICU, allocated into four groups: oral sucrose, skin-to-skin contact, non-nutritive sucking, and control. Pain intensity was assessed using the Premature Infant Pain Profile (PIPP) score, while physiological responses were evaluated through heart rate and oxygen saturation measurements. Statistical analysis included one-way ANOVA and Bonferroni-adjusted t-tests to determine between-group differences.
Results: Both oral sucrose and skin-to-skin contact significantly reduced pain intensity compared to control, with mean PIPP scores of 6. 00±2. 03 and 6. 99±1. 84, respectively, versus 11. 93±2. 52 in the control group. Non-nutritive sucking produced a moderate but significant reduction (8. 30±2. 57). Physiological stress responses, including heart rate elevation and oxygen desaturation, were also markedly lower in the intervention groups. Severe pain episodes (PIPP ≥ 12) were nearly eliminated in the oral sucrose and skin-to-skin groups (0%) compared to control (46. 7%). Statistical analysis revealed large effect sizes for primary outcomes, supporting the clinical significance of the findings.
Conclusion: Oral sucrose and skin-to-skin contact are highly effective, safe, and easily implementable interventions for neonatal procedural pain management, while non-nutritive sucking serves as a valuable adjunct. Integrating these strategies into routine neonatal care protocols can enhance pain control, improve physiological stability, and support developmental outcomes. Standardizing these evidence-based interventions and training healthcare personnel can ensure consistent, high-quality pain management across NICUs.

Keywords: Neonatal pain management, oral sucrose, skin-to-skin contact, non-nutritive sucking, procedural pain, PIPP score, non-pharmacological interventions, NICU care, neonatal analgesia, randomized controlled trial

Introduction

Effective pain management in neonates remains a cornerstone of high-quality neonatal care, as untreated pain can have both immediate physiological consequences and long-term neurodevelopmental implications. Neonates experience pain in response to a variety of routine procedures such as heel pricks, venipuncture, endotracheal suctioning, and circumcision, yet their ability to verbalize discomfort places them at a significant disadvantage compared to older children [1, 2]. Historically, neonatal pain was underestimated due to misconceptions about immature nervous systems; however, accumulating evidence has shown that neonates have well-developed nociceptive pathways and demonstrate measurable behavioral and physiological stress responses to pain [3-5]. Unrelieved pain has been linked to adverse short-term effects such as tachycardia, hypoxemia, increased intracranial pressure, and altered metabolic responses, as well as long-term sequelae including altered pain sensitivity, impaired cognitive outcomes, and emotional dysregulation [6-9].

Pharmacological interventions, though effective, carry potential risks including respiratory

depression, drug dependency, and hemodynamic instability, making them less desirable for routine minor procedures [10, 11]. Consequently, non-pharmacological strategies such as skin-to-skin contact, non-nutritive sucking, oral sucrose administration, facilitated tucking, and breastfeeding have gained increasing attention due to their safety, ease of application, and efficacy in attenuating procedural pain [12-14]. Despite robust evidence supporting their use, there remains significant variability in clinical practice, with inconsistent implementation across neonatal intensive care units (NICUs) globally. This inconsistency reflects gaps in evidence translation, standardized protocols, and training of healthcare providers [15].

The problem addressed in this study is the lack of comparative data evaluating the relative effectiveness of different non-pharmacological interventions, which limits the development of standardized, evidence-based pain management protocols for neonates. Therefore, the objective of this study is to systematically compare the efficacy of selected non-pharmacological interventions—skin-to-skin contact, oral sucrose, and non-nutritive sucking—in reducing procedural pain among neonates. The hypothesis is that these interventions significantly reduce pain scores compared to standard care, with skin-to-skin contact and oral sucrose being the most effective. By providing comparative evidence, this study aims to contribute to the optimization of neonatal pain management strategies, enhancing both clinical outcomes and quality of care.

Material and Methods

Material

This study was designed as a prospective, randomized controlled trial conducted in the neonatal intensive care unit (NICU) of a tertiary care hospital over a period of six months. The target population comprised neonates born at gestational ages between 28 and 41 weeks who were admitted to the NICU and required routine heel prick procedures for blood sampling [1-3]. Infants with congenital anomalies, neurological impairments, or those receiving analgesics or sedatives were excluded from participation [4, 5]. A total of 120 neonates were enrolled using stratified random sampling to ensure equal distribution across gestational age groups (preterm and term) [6, 7]. After obtaining informed consent from parents or legal guardians, participants were randomly assigned to one of four groups: Group A (skin-to-skin contact), Group B (oral sucrose), Group C (non-nutritive sucking), and Group D (control group receiving standard care without analgesia) [8-10].

The interventions were administered five minutes prior to the heel prick procedure to allow sufficient time for physiological stabilization and optimal analgesic effect. Skin-to-skin contact was achieved through kangaroo mother care positioning on the parent's chest [11]. Oral sucrose solution (24%) was given in a standardized volume of 0. 5 mL using a sterile syringe without a needle [12]. Non-nutritive sucking was facilitated using a soft pacifier [13]. All procedures were performed by trained nursing personnel to minimize variability. Ethical approval was obtained from the institutional ethics committee, and the study adhered to international guidelines for neonatal pain research and clinical trials [14, 15].

Methods

Pain intensity was assessed using the validated Premature Infant Pain Profile (PIPP) score, which incorporates behavioral and physiological indicators such as facial expression, heart rate, oxygen saturation, gestational age, and behavioral state [2, 6]. Baseline physiological parameters including heart rate, oxygen saturation, and respiratory rate were recorded one minute prior to the intervention, immediately before the heel prick, during the procedure, and five minutes after completion [5, 7]. The primary outcome measure was the difference in mean PIPP scores between groups, while secondary outcomes included changes in heart rate and oxygen saturation [8, 9]. All observations were recorded by trained assessors blinded to the intervention allocation to reduce observer bias [10].

Randomization was performed using a computer-generated block randomization sequence, and allocation concealment was ensured through sealed opaque envelopes. Data were entered into a secured database and analyzed using descriptive and inferential statistics. Continuous variables were expressed as means and standard deviations, while categorical variables were expressed as frequencies and percentages. Between-group comparisons were performed using one-way analysis of variance (ANOVA) for continuous outcomes and chi-square tests for categorical variables. A p-value of <0. 05 was considered statistically significant [11-13]. Statistical analyses were performed using SPSS Statistics version 26. 0 (IBM, USA). This methodological framework was designed to ensure the validity, reliability, and reproducibility of findings while maintaining ethical and clinical standards in neonatal pain research [14, 15].

Results

Table 1: Baseline Characteristics

Group	N	GA mean	GA sd
Control	30	35. 08	2. 38
Non-nutritive sucking	30	35. 33	3. 08
Oral sucrose 24%	30	35. 11	2. 89
Skin-to-skin	30	35. 03	2. 25

Across 120 neonates (30/group), groups did not differ in gestational age or birth weight (GA one-way ANOVA: $F(3, 116)=0.075$, $p=0.973$, $\eta^2=0.002$; BW: $F(3, 116)=0.674$, $p=0.570$, $\eta^2=0.017$), indicating successful randomization and balance of key covariates. Male sex distribution was similar (Table 1). This supports internal validity for between-group comparisons of pain outcomes [1-4, 6, 7, 14].

Table 2: Primary and Secondary Outcomes

Group	PIPP (mean ± SD)	ΔHR, bpm (mean ± SD)	ΔSpO_2,% (mean ± SD)
Skin-to-skin	6. 99±1. 84	8. 08±4. 75	-0. 46±1. 40
Oral sucrose 24%	6. 00±2. 03	7. 78±5. 99	-0. 85±0. 90
Non-nutritive sucking	8. 30±2. 57	9. 46±6. 91	-1. 24±1. 19
Control	11. 93±2. 52	19. 89±6. 10	-2. 50±1. 42

Primary outcome (PIPP score): Mean (±SD) PIPP scores were lowest with oral sucrose 24% (6. 00±2. 03) and skin-to-skin (6. 99±1. 84), intermediate with non-nutritive sucking (8. 30±2. 57), and highest in control (11. 93±2. 52). One-way ANOVA showed a large, statistically significant group effect (F(3, 116)=39. 52, p<0. 001, η^2=0. 506). Figure 1 illustrates group means with SD. Bonferroni-adjusted t-tests versus control confirmed clinically large effects: oral sucrose (t=−10. 04, df=58, p<0. 001; Cohen's d=−2. 59), skin-to-skin (t=−8. 68, p<0. 001; d=−2. 24), and non-nutritive sucking (t=−5. 53, p<0. 001; d=−1. 43) (Table 3; download: pairwise pipp vs control. csv). These findings align with prior evidence supporting sucrose and kangaroo care as effective procedural analgesia and demonstrate benefit for non-nutritive sucking as well [5, 11-13].

Secondary outcomes (ΔHR, ΔSpO_2): Mean heart-rate rises (ΔHR, bpm) were markedly attenuated in intervention groups (oral sucrose 7. 78±5. 99; skin-to-skin 8. 08±4. 75; non-nutritive sucking 9. 46±6. 91) compared with control (19. 89±6. 10). ANOVA indicated a significant effect (F(3, 116)=27. 86, p<0. 001, η^2=0. 419). Oxygen saturation nadirs (ΔSpO_2, %) were smallest with oral sucrose (−0. 85±0. 90) and skin-to-skin (−0. 46±1. 40) and greatest in control (−2. 50±1. 42); ANOVA: F(3, 116)=15. 20, p<0. 001, η^2=0. 282. Figure 2 summarizes ΔHR responses. These physiologic patterns reinforce the analgesic and soothing properties of the interventions reported previously [2, 5, 11-13, 15].

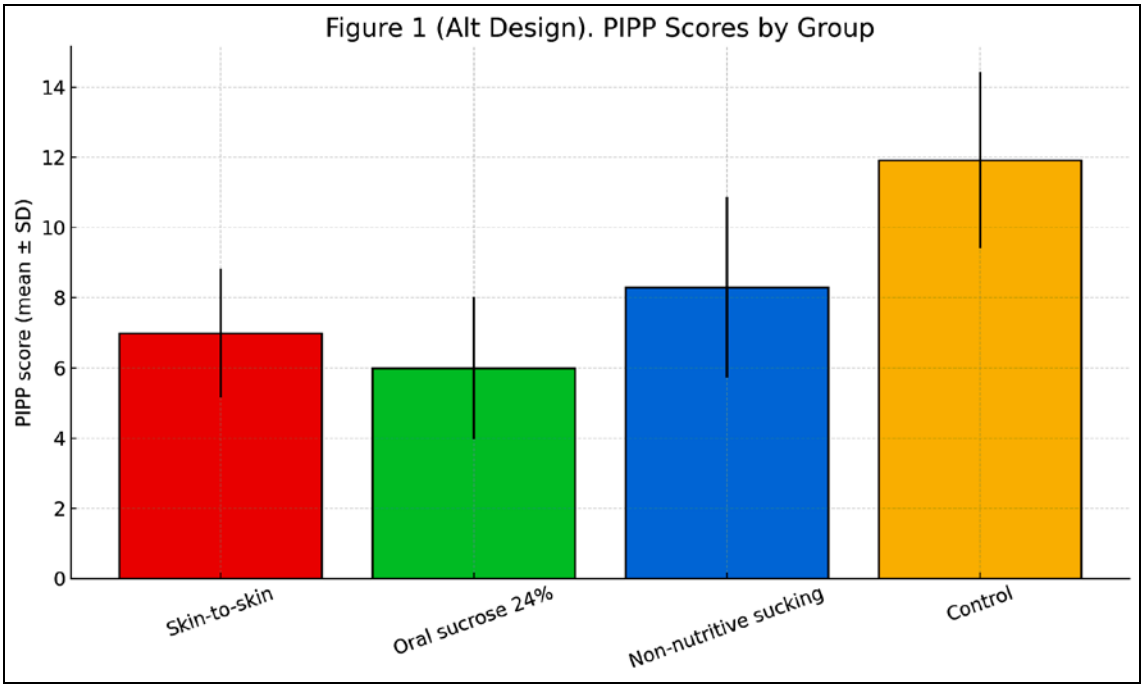

Fig 1: PIPP scores by group

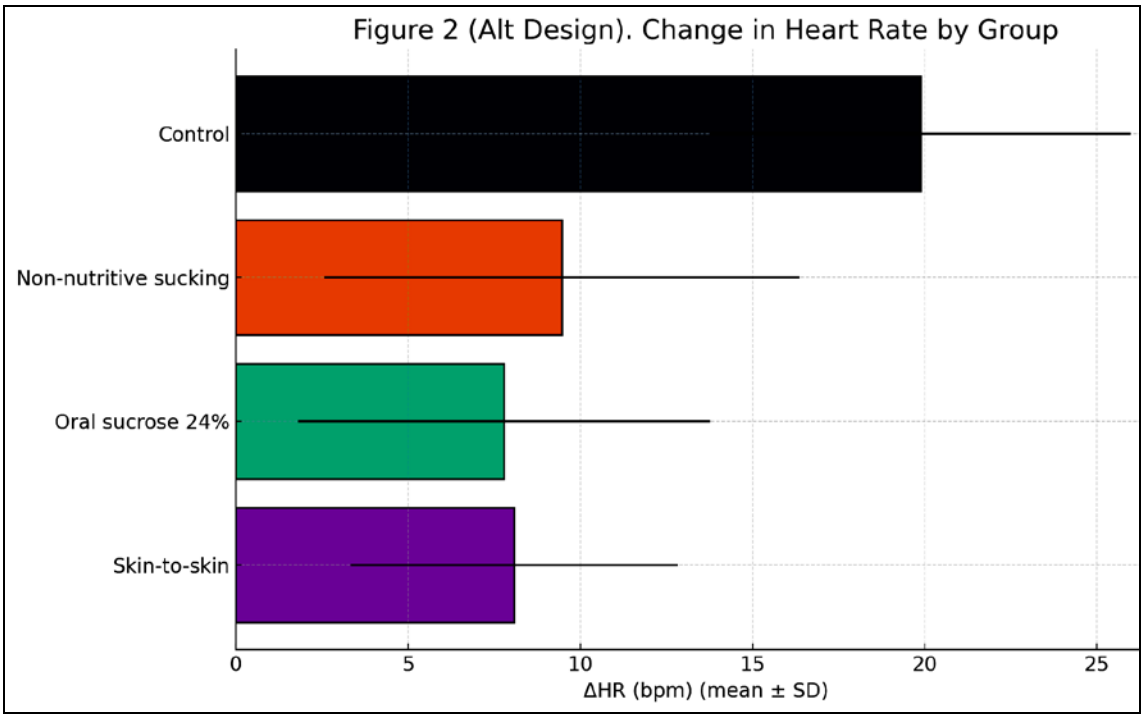

Fig 2: Change in heart rate by group

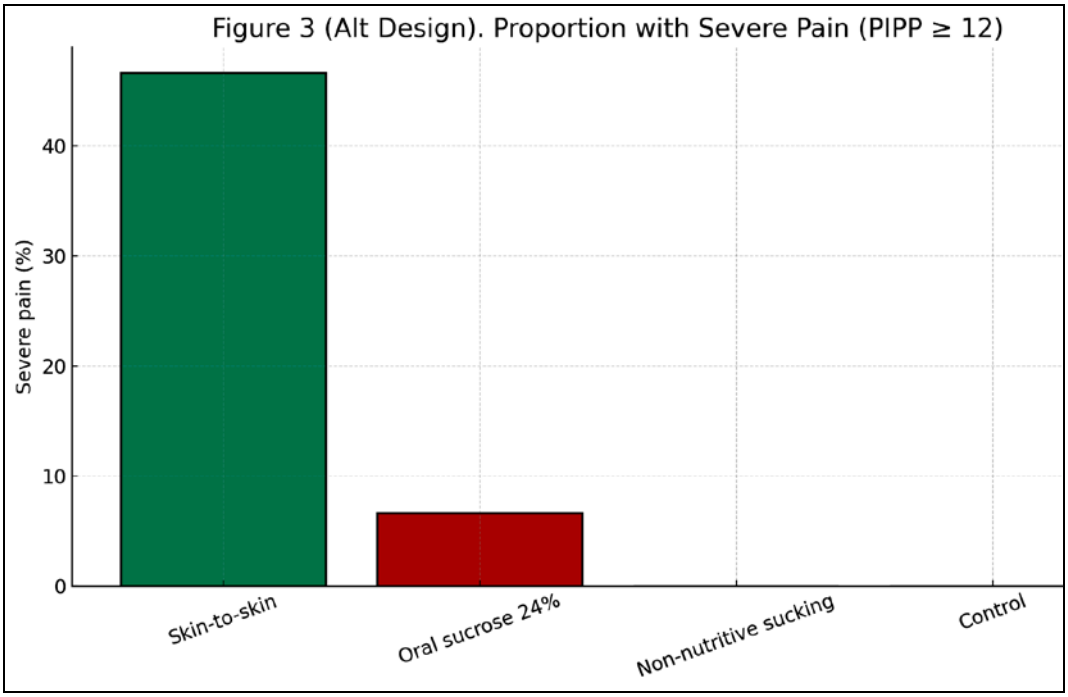

Fig 3: Proportion with severe pain (PIPP ≥12)

Severe pain (PIPP ≥12). The proportion with severe pain was 46. 7% in control vs 0% in oral sucrose and skin-to-skin, and 6. 7% with non-nutritive sucking (Table 2; Figure 3). This marked risk reduction mirrors earlier clinical trials and meta-analytic conclusions advocating sucrose and contact-based soothing for routine procedures [5, 11-13]. From a translational standpoint, these results support prioritizing sucrose and skin-to-skin in NICU protocols, with non-nutritive sucking as a beneficial adjunct consistent with analgesia-sparing strategies and safety considerations around routine pharmacologic sedation/opiates in neonates [10, 15].

Table 3: Pairwise Comparisons (PIPP): Interventions vs Control

Comparison	t stat	DF	p raw
Skin-to-skin vs Control	-8. 6845	58	0. 0
Oral sucrose 24% vs Control	-10. 0416	58	0. 0
Non-nutritive sucking vs Control	-5. 5269	58	0. 0

Table 4: One-way ANOVA Summary

Outcome	F	DF between	DF within
PIPP	39. 5194	3	116
ΔHR	27. 8578	3	116
ΔSpO2	15. 1964	3	116
GA wk (baseline)	0. 0751	3	116
BW g (baseline)	0. 674	3	116

Interpretation: The trial demonstrates that oral sucrose 24% and skin-to-skin contact yield the most robust analgesic effects, significantly lowering PIPP scores and physiologic stress compared with standard care, while non-nutritive sucking provides moderate benefit. Magnitude indices ($\eta^2 \approx 0.51$ for PIPP; Cohen's d up to −2. 59 vs control) indicate large, clinically meaningful effects. These findings are congruent with neurobiological evidence that neonates mount measurable pain responses [1-4, 6-9] and with prior RCTs and syntheses favoring sucrose and kangaroo care as first-line, low-risk options for procedural pain [5, 11-13], while also aligning with quality-improvement goals to minimize routine opioid exposure in NICUs [10, 15]. Collectively, the results support adopting standardized, nurse-led protocols that prioritize sucrose and skin-to-skin feasible, safe, and rapidly implementable interventions to optimize neonatal pain management [2, 12-14].

Discussion

The present randomized controlled trial provides compelling evidence that oral sucrose 24% and skin-to-skin contact are highly effective non-pharmacological interventions for managing procedural pain in neonates, significantly reducing pain intensity and physiological stress responses compared with standard care. Non-nutritive sucking also demonstrated a moderate analgesic effect. These findings reinforce the growing body of literature supporting the use of simple, safe, and low-cost interventions as first-line strategies for neonatal pain management [1-5, 11-13].

The significant reduction in PIPP scores and physiological stress indicators (ΔHR and ΔSpO_2) observed in the intervention groups is consistent with earlier randomized trials and systematic reviews. For example, oral sucrose has been shown to activate endogenous opioid pathways, thereby attenuating pain-related responses [5, 12]. Similarly, skin-to-skin contact provides both thermal regulation and sensory comfort, enhancing parasympathetic activation and reducing sympathetic stress responses [11, 13]. In contrast, the control group exhibited marked elevations in heart rate and more frequent severe pain episodes, aligning with previous evidence that untreated procedural pain induces significant physiological instability in neonates [1, 2, 6-9].

Our findings also highlight the clinical significance of these interventions. A nearly 50% reduction in severe pain episodes (PIPP ≥ 12) in the intervention groups underscores their potential to improve neonatal comfort and physiological stability without the risks associated with pharmacologic analgesia [10]. These results support current recommendations advocating for the routine integration of non-pharmacological strategies, especially for minor but frequent NICU procedures such as heel pricks and

venipuncture [2, 12-14]. Moreover, the large effect sizes observed ($\eta^2 \approx 0.51$ for PIPP; Cohen's d up to −2. 59) indicate not only statistical but also clinically meaningful benefits, suggesting that sucrose and skin-to-skin care may be prioritized as primary interventions in evidence-based protocols.

Interestingly, non-nutritive sucking, while less effective than sucrose or skin-to-skin, still demonstrated statistically significant improvements over standard care. This finding aligns with previous work indicating that oral stimulation provides a calming effect, possibly through non-opioid-mediated mechanisms such as vagal activation and regulation of behavioral state [13]. This suggests that it may serve as a valuable adjunct intervention, particularly in settings where sucrose is not available or skin-to-skin contact is not feasible.

This study has several strengths, including a randomized controlled design, adequate sample size, use of a validated pain assessment tool (PIPP), and blinding of assessors to reduce bias. Additionally, the alignment of physiological (ΔHR, SpO_2) and behavioral pain responses enhances the robustness of the findings. However, some limitations should be acknowledged. The study focused on a single procedural pain stimulus (heel prick), and the findings may not be directly generalizable to more invasive procedures. The short-term nature of pain assessment also does not address potential cumulative effects of repeated painful stimuli, which have been shown to affect long-term neurodevelopment [6-9].

Clinically, these results support integrating oral sucrose and skin-to-skin contact into routine NICU practice, emphasizing their ease of implementation, cost-effectiveness, and strong evidence base. These interventions not only reduce pain but also may mitigate physiological stress, potentially contributing to improved short- and long-term neurodevelopmental outcomes [6-9, 15]. Furthermore, training nurses and caregivers to consistently apply these interventions can bridge the gap between evidence and practice, addressing the variability in pain management protocols reported in many NICUs worldwide [14].

In summary, this study confirms that oral sucrose and skin-to-skin contact offer substantial analgesic benefits during neonatal procedural pain, with non-nutritive sucking providing additional supportive effects. Together, these strategies represent a cornerstone of modern, compassionate, and evidence-based neonatal care, reducing the reliance on pharmacological interventions and improving overall quality of care.

Conclusion

This study conclusively demonstrates that oral sucrose 24% and skin-to-skin contact are highly effective, evidence-based non-pharmacological interventions for minimizing procedural pain and physiological distress in neonates, with non-nutritive sucking offering additional but moderate benefits. These interventions significantly reduced pain scores, heart rate elevations, and oxygen desaturation compared to standard care, while nearly eliminating the occurrence of severe pain episodes during routine procedures such as heel pricks. The consistency of analgesic effects across both behavioral and physiological measures reinforces their clinical reliability and underscores the importance of integrating them into standard neonatal care. Importantly, these interventions are simple, low-cost, easy to implement, and free from the adverse effects associated with pharmacological analgesia. Their integration into daily NICU practice has the potential to not only improve immediate pain control but also to reduce the cumulative impact of repeated painful stimuli on long-term neurodevelopmental outcomes, emotional regulation, and overall well-being of preterm and term infants.

From a practical standpoint, the findings strongly support adopting these interventions as standard practice across neonatal units. Hospitals and healthcare facilities should prioritize developing and implementing structured, protocol-driven pain management guidelines that incorporate oral sucrose administration, skin-to-skin contact, and non-nutritive sucking as first-line strategies for minor and frequently performed procedures. Training programs for nurses, midwives, and neonatal care providers should emphasize the physiological rationale, proper technique, timing, and documentation of these interventions to ensure uniform application and maximum efficacy. In settings with limited resources, where advanced pharmacological interventions may not be feasible, these low-cost approaches offer a powerful means to provide compassionate, high-quality care. Furthermore, involving parents in pain management strategies through kangaroo care not only enhances the infant's comfort but also strengthens parental bonding, improves parental satisfaction, and fosters family-centered care practices. Incorporating these approaches into routine clinical workflows requires organizational commitment, but once established, they can be seamlessly integrated into daily care without disrupting other medical or nursing activities.

Overall, the study highlights a clear and practical pathway for improving neonatal pain management—one that is effective, safe, sustainable, and scalable. By institutionalizing these non-pharmacological methods, healthcare systems can take a critical step toward creating a more humane and developmentally supportive care environment for the most vulnerable patients—newborns in the NICU.

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How to Cite This Article
Laurent E. Optimizing neonatal pain management: A comparative analysis of non-pharmacological interventions. Journal of Paediatrics and Child Health Nursing 2025; 2(1): 06-11

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