



Effectiveness of white noise for reducing invasive procedural pain in neonates: A co-designed randomized controlled trial protocol

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ABSTRACT

Objective: To develop a white-noise intervention protocol through a co-design approach and evaluate the effectiveness of white noise in reducing pain associated with invasive procedures in term neonates. **Methods:** This study comprises two phases. Phase 1 will use a co-design approach involving researchers, physicians, nurses, and parents/legal guardians to refine the intervention protocol. Phase 2 will be a two-arm, parallel-group randomized controlled trial conducted in the Neonatal Unit of Phenikaa University Hospital. A total of 70 term neonates scheduled to undergo invasive procedures will be recruited. Participants will be randomly allocated in a 1:1 ratio to either the white-noise group or the usual-care group. **Conclusion:** This standardized protocol may provide a basis for evaluating and integrating white noise into non-pharmacological pain management for neonates.

Keywords: White noise; pain; neonates; intervention study; co-design.

INTRODUCTION

Hospitalized neonates may undergo multiple painful procedures, including heel lancing, venipuncture, injections, and intravenous catheter insertion. Preventing and managing procedural pain is an essential component of neonatal care because repeated pain exposure may trigger acute stress responses and be associated with adverse longer-term outcomes ¹.

Non-pharmacological pain-relief strategies may be used alone or in combination with routine care, depending on the procedure and the infant's clinical condition. White noise is a continuous sound with a broad frequency spectrum that is thought to mask inconsistent environmental

noise and support infants' behavioral regulation ². Several trials have reported that white noise may reduce pain scores or crying duration; however, findings across studies remain inconsistent ³⁻⁵. Systematic reviews have also identified substantial variations in sound type, intensity, timing of initiation, and duration of the intervention ⁶.

The Neonatal Infant Pain Scale (NIPS) is a behavioral pain-assessment tool developed for neonates. It includes six components and yields a total score ranging from 0 to 7 ⁷. To comprehensively assess pain responses, NIPS scores should be supplemented by physiological indicators such as peripheral oxygen saturation (SpO₂), heart rate, and crying duration. In addition to clinical

effectiveness, developing an intervention with the involvement of healthcare professionals and parents/legal guardians may improve its contextual appropriateness and feasibility in real-world practice ⁸.

The preparatory co-design phase aims to develop and refine a contextually appropriate white-noise intervention protocol. The primary objective of the randomized trial is to evaluate the effect of white noise, added to standardized usual care, on NIPS scores during the invasive procedure (T1), and at 5 minutes after the procedure (T2). Secondary objectives are to evaluate heart rate, peripheral oxygen saturation, crying duration, and intervention feasibility at baseline (T0), during the invasive procedure (T1), and at 5 minutes after the procedure (T2).

METHODS

Study design and setting: This study protocol consists of a co-design phase followed by a two-arm, parallel-group randomized controlled trial with a 1:1 allocation ratio.

Co-design phase: The co-design group will include researchers, two to three neonatologists, five to eight neonatal nurses, and five to eight parents or legal guardians of infants previously treated in the unit. Participants will be purposively recruited to ensure diversity of experience. At least two facilitated discussion sessions, each lasting approximately 15 minutes, will be conducted using a semi-structured discussion guide. With participants' consent, sessions will be audio-recorded and transcribed verbatim; field notes will also be collected. Two researchers will independently code the transcripts and develop a shared coding framework through discussion. Coding disagreements will be resolved by consensus

or, when necessary, consultation with a third researcher. Findings will be returned to participants during the subsequent session to refine the protocol and document the rationale for final decisions.

The discussions will address the following topics: selection of the audio track; equipment and equipment-cleaning procedures; sound-volume level; speaker placement distance; intervention initiation and discontinuation times; approaches to minimizing interference with professional communication; safety criteria; and an adherence-monitoring checklist.

Participants' views will be documented, synthesized thematically, and fed back to the group during the subsequent session. The final protocol will be approved after consensus is reached among the expert group and will undergo feasibility testing using a simulated procedure before participant recruitment. The outputs of this phase will include an intervention manual, an adherence checklist, and guidance on video-data confidentiality.

Participants: Neonates admitted to the Neonatal Unit who meet all the following eligibility criteria: (1) gestational age of 37–42 weeks; (2) an indication for an invasive procedure, including heel prick blood sampling, blood sampling for testing, intravenous injection/infusion; and written informed consent from a parent or legal guardian.

Exclusion criteria: (1) they have severe congenital anomalies; (2) postoperative; (3) received sedatives, muscle relaxants, or anticonvulsants; (4) hearing impairment; (5) received oxygen therapy or respiratory support; (6) have a temperature above 37.5°C; (7) or have clinically unstable conditions as determined by the treating physician.

Sample size: The sample size will be calculated for a two-sided comparison of two independent means, assuming a standardized effect size of Cohen's $d = 0.80$ ⁹, a significance level of 0.05, 80% statistical power, and a 1:1 allocation ratio. The calculation indicated that 26 neonates per group were required. Allowing 30% missing primary outcome data, the planned recruitment target was 70 neonates, with 35 allocated to each group.

Randomization, allocation concealment, and blinding:

The randomization sequence will be generated by an independent statistician using random-number-generation software, with permuted blocks of four. An independent statistician, who is not involved in recruitment, intervention delivery, or outcome assessment, will generate the allocation sequence. An independent staff member will prepare the sequentially numbered, opaque, sealed envelopes.

Recruitment staff will assess eligibility and obtain written informed consent without access to the allocation sequence. After enrollment is completed, a designated staff member who is not involved in outcome assessment will open the next envelope in sequence. The participant's study identification number and the date and time of envelope opening will be recorded.

Because of the nature of the intervention, intervention providers and caregivers cannot be blinded. However, NIPS scores and crying duration will be assessed from coded video recordings without information identifying group allocation or assessment time point. Two trained assessors will independently rate the recordings, and inter-rater agreement will be reported. If

agreement cannot be reached, principal investigator will adjudicate the discrepancy. The final agreed or adjudicated score will be used in the outcome analysis.

Intervention and usual care:

Participants in the intervention group will listen to the white-noise audio track approved by the co-design group, "Calm Rain for Colic Baby Sleep". The sound will be played using an iPhone 13 set to airplane mode and positioned 30 cm from the infant's ear. The sound intensity will be checked before each session using a calibrated sound-level meter and maintained below 50 dB at the infant's ear^{9, 10}. The intervention will begin 2 minutes before the procedure, continue throughout the procedure, and be maintained for at least 5 minutes after completion. The intervention will be discontinued if clinically indicated by a physician, requested by a parent, if equipment malfunctions, or if the infant shows signs of intolerance.

The control group will receive routine care according to the hospital's standard clinical practice. Invasive procedures were performed by the same nurses who provided care to participants in the intervention group to minimize potential operator-related variability.

Outcome measures: The primary outcome will be the NIPS score during the invasive procedure (T1). Secondary outcomes will include the NIPS score five minutes after the procedure, heart rate, peripheral oxygen saturation (SpO_2), and crying duration. Baseline NIPS, heart rate, and SpO_2 will be assessed before intervention initiation. Feasibility, safety, and acceptability outcomes will also be documented.

Outcome category	Outcome	Definition and measurement	Assessment time point
Primary	NIPS score during the procedure	Total NIPS score, ranging from 0 to 7, assessed from video recordings within a prespecified observation window following the first needle insertion. The duration of the observation window and scoring rule will be finalized before recruitment and applied consistently to both groups.	T1: during the procedure
Secondary	NIPS score after the procedure	Total NIPS score assessed from video recordings using a standardized observation window.	T2: 5 minutes after procedure completion
Secondary	Heart rate	Heart rate in beats per minute, obtained from the bedside monitor and calculated as the mean of valid readings within a predefined 30-second assessment window. Readings affected by movement artifacts or poor signal quality will be excluded according to prespecified criteria.	T0, T1, and T2
Secondary	SpO ₂	Peripheral oxygen saturation (%), obtained from the bedside monitor and calculated as the mean of valid readings within the same predefined 30-second assessment window used for heart rate. Readings affected by artifacts or poor signal quality will be excluded according to prespecified criteria.	T0, T1, and T2

Outcome category	Outcome	Definition and measurement	Assessment time point
Secondary	Crying duration	Elapsed time, in seconds, from the onset of crying at or after the first needle insertion until crying has ceased continuously for ≥ 30 seconds. A value of 0 will be recorded if the infant does not cry during the observation period.	From the first needle insertion until the crying-cessation criterion is met
Baseline measure	NIPS score before intervention	Total NIPS score assessed before white-noise initiation in the intervention group and before the corresponding observation period in the control group.	T0: before intervention initiation and procedural handling
Feasibility	Protocol adherence and intervention interruptions	Proportion of intervention sessions completed according to all required checklist items; number, timing, duration, and reasons for interruptions or protocol deviations.	Throughout each study session
Safety	Adverse events and intervention discontinuation	Number, type, timing, severity, and clinical management of adverse events; reasons for intervention discontinuation.	Throughout each study session
Acceptability	Staff and parent/legal guardian feedback	Feedback collected using a prespecified brief questionnaire or interview guide addressing perceived acceptability and practical concerns.	After the study session

Video recording will begin 2 minutes before the procedure and continue until 5 minutes after the procedure or until the infant has stopped crying, whichever occurs later. The camera will be positioned using a standardized angle to allow clear observation of the infant's face and limbs. Video recordings and monitor data will be assigned study codes and stored in password-protected devices or folders. Access will be restricted to authorized research team members.

Data analysis:

Data will be analyzed using SPSS version 23.0. Maternal and neonatal characteristics will be described using means $\pm$ standard deviations or medians (interquartile ranges) for continuous variables, and frequencies and percentages for categorical variables. Participants will be analyzed according to their original randomized assignment, regardless of adherence, intervention interruption, or receipt of additional pain-relief measures.

The amount and reasons for missing data will be reported by group, and the prespecified missing-data method and sensitivity analyses will be described. Any per-protocol analysis will be presented as supplementary rather than replacing the primary intention-to-treat analysis.

Baseline comparisons between groups will use independent-samples *t* tests or Mann–Whitney *U* tests for continuous variables, and chi-square tests or Fisher's exact tests for categorical variables, as appropriate for variable distributions and expected cell frequencies. Intervention effects over time will be estimated using mixed-effects models for repeated measures, including fixed effects for group, time, and the group $\times$ time interaction, with participant included as a random effect.

Ethical considerations:

The study was approved by the Biomedical Research Ethics Committee of Phenikaa University Hospital (Approval No. 12/HDDD-BVHP). Parents or legal guardians will receive study information and provide written informed consent before their infant's participation, including consent for video recording. Refusal to participate or withdrawal from study will not affect the infant's usual care.

DISCUSSION

This protocol is designed to evaluate the effectiveness of white noise in reducing procedural pain in term neonates while addressing a key gap in intervention standardization. Recent synthesized evidence suggests that white noise may reduce pain scores and crying duration and may support stabilization of certain physiological indicators in neonates. However, findings from individual trials remain inconsistent ²⁻⁵. Previous studies have used heterogeneous sound levels, speaker distances, intervention durations, and outcome assessment procedures. The present protocol seeks to improve reproducibility through a standardized intervention manual, documented sound-exposure measurements, predefined outcome assessment windows, and consistent usual-care procedures. Co-design with healthcare professionals and parents/legal guardians is intended to refine these procedures for the local clinical context. Nevertheless, these measures do not eliminate all sources of bias or establish the clinical effectiveness of the intervention ⁶.

NIPS was selected as the primary outcome because it is appropriate for neonates and reflects behavioral manifestations of pain ⁷. Nevertheless, NIPS alone may not fully capture the physiological pain response. Therefore, this protocol combines NIPS with heart rate, SpO₂, and crying duration. Predefining assessment times, defining the peak-pain time point, and specifying the method for recording crying duration are intended to reduce measurement variability.

Co-design is a key feature of this study. Involving physicians, nurses, and parents/legal guardians may make the protocol more compatible with clinical workflow, safety

requirements, and acceptability within the neonatal unit ⁸. Specific outputs, including an intervention checklist, sound-volume-control procedures, equipment-cleaning procedures, and video-coding processes, may support intervention fidelity and facilitate translation into clinical practice.

The randomized design, allocation concealment, blinded assessment of coded video recordings, and planned intention-to-treat analysis are measures intended to minimize bias. However, blinding of intervention providers is not feasible. The study will also be conducted at a single center and is limited to term neonates; therefore, generalizability to preterm infants or other facilities may be limited. Standardization or stratification by procedure type is important because pain intensity may differ substantially between procedures.

If the intervention is effective and feasible, white noise may represent a simple, low-cost, and easily integrated adjunctive non-pharmacological pain-relief option alongside routine care. Study findings will provide a basis for multicenter research, evaluation among preterm infants, and studies combining white noise with other non-pharmacological interventions.

CONCLUSION

This protocol describes a co-design phase followed by a randomized controlled trial to evaluate white noise as an adjunct to usual care for procedural pain management in term neonates. The study is intended to generate evidence on its effects on procedural pain and related outcomes, as well as its feasibility in the study setting. No conclusions regarding effectiveness, feasibility, or acceptability can be drawn until the study has been completed and the findings analyzed.

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