Trial of Music, Sucrose, and Combination Therapy for Pain Relief during Heel Prick Procedures in Neonates

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Objective To compare the effectiveness of music, oral sucrose, and combination therapy for pain relief in neonates undergoing a heel prick procedure.

Study design This randomized, controlled, blinded crossover clinical trial included stable neonates >32 weeks of postmenstrual age. Each neonate crossed over to all 3 interventions in random order during consecutive heel pricks. A video camera on mute mode recorded facial expressions, starting 2 minutes before until 7 minutes after the heel prick. The videos were later analyzed using the Premature Infant Pain Profile—Revised (PIPP-R) scale once per minute by 2 independent assessors, blinded to the intervention. The PIPP-R scores were compared between treatment groups using Friedman test.

Results For the 35 participants, the postmenstrual age was 35 weeks (SD, 2.3) with an average weight of 2210 g (SD, 710). The overall median PIPP-R scores following heel prick over 6 minutes were 4 (IQR 0-6), 3 (IQR 0-6), and 1 (IQR 0-3) for the music, sucrose, and combination therapy interventions, respectively. The PIPP-R scores were significantly lower at all time points after combination therapy compared with the groups given music or sucrose alone. There was no difference in PIPP-R scores between the music and sucrose groups.

Conclusions In relatively stable and mature neonates, the combination of music therapy with sucrose provided better pain relief during heel prick than when sucrose or music was used alone. Recorded music in isolation had a similar effect to the current gold standard of oral sucrose. *(J Pediatr 2017;190:153-8).*

Trial registration www.anzctr.org.au ACTRN12615000271505.

Although survival for preterm neonates has improved over the past 5 decades,[1] neonates regularly encounter a number of painful procedures, including blood sampling.[2-6] Heel prick is one of the most commonly performed painful procedures in the neonatal intensive care unit (NICU)[7] and pain relief is often provided using oral sucrose.[8-10] A recent Cochrane review deemed sucrose as safe and effective for procedural pain from a single event, but further research on pain management is warranted. Sucrose has not been shown to prevent the development of remote hyperalgesia.[11] There is uncertainty about the effect of repeated dosages and the effects in combination with other nonpharmacologic and pharmacologic interventions.[10,12,13] A few recent studies have raised concerns about the use of sucrose for pain relief in neonates and questioned its effectiveness as an analgesic.[14-17]

Music therapy can be used as a "structured intervention delivering music with the purpose of achieving specific therapeutic goals."[18] Music may modulate pain perception, cause distraction, and block pain pathways by causing sensorial saturation.[19] There is building evidence that carefully selected music in consultation with a trained music therapist may be beneficial in relieving procedural pain in both full-term and physiologically mature late preterm infants.[20,21] One of the major drawbacks of the studies conducted so far is comparison of music therapy with a control group of no pain relief and the lack of direct assessment with the current gold standard of sucrose. It is not known if music therapy and the combination of music therapy with sucrose can provide similar or better analgesia compared with oral sucrose.

The primary objective of the present study was to compare the effectiveness of sucrose with recorded music therapy (selected in consultation with a trained music therapist) and combination therapy for pain relief during heel prick. The secondary objective was to compare the effect of the 3 interventions on heart rate and oxygen saturation.

Methods

This randomized, controlled, blinded, crossover clinical trial was conducted in a level III perinatal center in Australia, caring for high-risk preterm and term neonates requiring intensive care. The NICU does not care for neonates undergoing surgery other than laser therapy for the treatment of retinopathy of prematurity.

NICU	Neonatal intensive care unit
PIPP-R	Premature Infant Pain Profile—Revised

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The authors declare no conflict of interest.

0022-3476/$ - see front matter.
https://doi.org10.1016/j.jpeds.2017.08.003

Heel pricks are performed by registered nurses trained in the procedure. They are used for minor blood collections up to 0.5 mL, using a spring-loaded device (BD Quickheel Preemie lancet; Becton, Dickinson and Company, East Rutherford, NJ). Sucrose is used for pain relief during heel prick, as a nurse-initiated medication.

A physiologically mature group of neonates was the primary target of the current study. Neonates admitted to the NICU were included if they were >32 weeks postmenstrual age at recruitment, not needing invasive ventilation, positive pressure or high-flow support, and were receiving a minimum of 60 mL/kg/day of feeds with an anticipated need for repeat heel pricks. Exclusion criteria were the presence of a major congenital abnormality, proven or suspected sepsis, necrotizing enterocolitis, major intraventricular hemorrhage (grade III or IV), seizures, and encephalopathy.

The study was approved by the ethics committee of the Local Health District. No changes to the trial methods, inclusion and exclusion criterion, or outcomes were made after study commencement. Informed written consent was obtained by the investigators before recruitment from parents or guardians. The study was prospectively registered with Australian New Zealand Clinical Trials Registry (ANZCTR), www.anzctr.org.au (Trial Id: ACTRN12615000271505).

Interventions

Each eligible neonate was crossed over to all 3 interventions in random order, using a computer-generated sequence, during consecutive heel pricks as clinically indicated. The computer allocation of intervention sequence was carried out immediately before the heel prick, by a research nurse. The interventions were administered by the trained medical officers and bedside nurse. There was a minimum 30 minutes of 'wash-out' period between successive interventions (**Figure 1**).

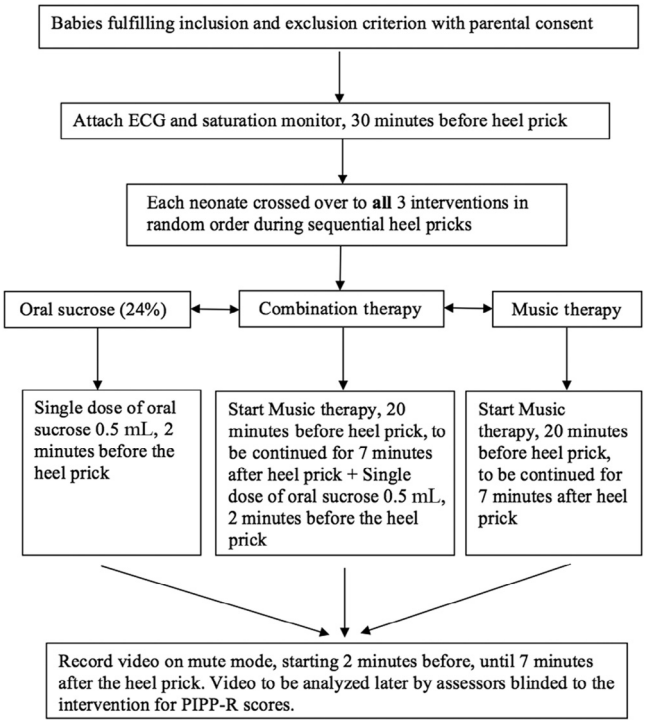

Figure 1. Study flow diagram. *ECG*, Electrocardiograph.

Intervention I: Recorded Music. In the music intervention, neonates were exposed to recorded music with sounds up to 60 A-weighted decibels,[22] starting 20 minutes before the heel prick, continuing for 7 minutes after the procedure. Music was administered using the "Deep Sleep" track from "Bedtime Mozart: Classical Lullabies for Babies" (2011), an instrumental lullaby music track chosen after discussion with a music therapist for stability, repeatability, and presence of minor tones. The piece of music was presented as a loop and was played back from a sound source using 2 high-quality portable speakers, placed equidistant from the head on each side. The sound levels at both ears were checked after speaker placement and the sound was gradually scaled up to the study limit of 60 A-weighted decibels. To maintain resemblance to a real-life scenario, the ambient noise was not modulated. However, the total auditory exposure was checked to ensure that it remained within the recommended limits at the ear level.[22]

Intervention II: Oral Sucrose Therapy. In the sucrose intervention, neonates received 0.5 mL of oral sucrose (24%) 2 minutes before the heel prick.

Intervention III: Combination Therapy. In the music-sucrose intervention the neonate received both recorded music and oral sucrose during heel prick as a combination of the previous 2 interventions.

All infants received similar standard nonpharmacologic methods of pain relief such as swaddling and comforting throughout the heel prick and blood collection procedure. Pacifiers were avoided to maintain consistency between the groups.

A Masimo Rad 5 pulse Oximeter (Masimo Corporation, Irvine, CA) was attached to the right wrist approximately 30 minutes before the heel prick to obtain readings of heart rate and oxygen saturation every 2 seconds. The monitor probe remained attached for 7 minutes after the procedure. The monitor data were downloaded immediately after the intervention.

A video camera on mute mode recorded facial expressions, starting 2 minutes before and continued until 7 minutes after the heel prick. No forms of patient identifiers were recorded and the videos were labelled with an allocated study number. Recorded facial expressions in the videos were later scored independently by 2 assessors, who were blinded to the intervention sequence, using the Premature Infant Pain Profile—Revised scale (PIPP-R).

The PIPP-R is a 7-item multidimensional (composite) measure of pain widely used to assess acute pain in preterm neonates. The scores obtained for the 7 items are summed to obtain a total pain intensity score. The maximum attainable PIPP score is 21 for preterm infants <28 weeks GA and 18 for full-term infants.[23,24] PIPP-R has been evaluated and validated for acute pain assessment in preterm neonates.[23,24]