The effectiveness of technology-based interventions compared to other non-pharmacological interventions for relieving procedural pain in hospitalized neonates: a protocol for a systematic review

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Conflicts of interest

There is no conflict of interest in this project.

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Abstract

Objective: The objective of this review is to evaluate the effectiveness of technology-based interventions in relieving procedural pain in hospitalized neonates compared to other non-pharmacological interventions.

Introduction: Neonates requiring hospital care often experience acute pain during medical procedures. The current best practice for relieving pain in neonates is the use of non-pharmacological interventions, such as oral solutions or intervention-based human touch. Technological solutions (such as games, eHealth applications, and mechanical vibrators) have become more commonplace in pediatric pain management over recent years. However, there is a knowledge gap about how effective technology-based interventions are at relieving pain in neonates.

Inclusion criteria: This review will consider experimental trials that include technology-based non-pharmacological interventions for relieving procedural pain in hospitalized neonates. Primary outcomes of interest include pain response to a procedure measured by a validated pain assessment scale for neonates, behavioral indicators and/or changes in physiological indicators.

Methods: MEDLINE (Ovid), CINAHL (EBSCO), Scopus (Elsevier), Cochrane Central Register of Controlled Trials, and the Medic databases will be searched for studies published in English, Finnish, and Swedish. Critical appraisal and data extraction will be conducted by two independent researchers following JBI methodology. Quantitative data will be pooled in statistical meta-analyses. If statistical analysis is not possible, the findings will be reported narratively.

Systematic review registration: PROSPERO CRD42021254218

Keywords: acute pain; device; neonate; non-pharmacological

Introduction

Neonates experience procedural pain (eg, vitamin K injections, immunizations, and heel sticks for screening tests) as a part of routine neonatal care during the first days of life.[1] A considerable share of newborns require hospital treatment immediately after birth due to medical conditions, such as infection, congenital anomaly, respiratory failure, low birth weight[2] and premature birth before the 37th gestational week.[3] Prematurity is also the most common reason for admission to the neonatal intensive care unit,[3] where painful medical and nursing procedures are part of the required care.[4,5]

Several studies have quantified the painful procedures performed on hospitalized neonates. The most common painful procedures in neonates are heel lance, intramuscular injection, and venipuncture. The heel lance is an equally common procedure in both pre- and full-term neonates,[6] but the exposure to pain varies between neonates. It has been observed that neonates experience a median of 16 painful procedures every day during the first 14 days of hospitalization, but the youngest newborns – as well as those with the most severe problems – experience up to 62 procedures per day.

Providing neonates with effective pain management is a priority from both an ethical perspective as well as to guard against the potential adverse effects of pain.[7] Repeated procedural pain without sufficient pain alleviation during neonatal care has been shown to have adverse short- and long-term effects on physical, cognitive, and brain development in neonates born before the 32nd gestational week. Frequent procedural pain is associated with delayed early postnatal body and head growth,[8] and with slower head circumference growth at six- and 12-months corrected age.[9] The number of skin-breaking procedures a neonate has experienced is negatively correlated with cognitive outcome at 18-months corrected age,[10] while further research has shown that skin-breaking procedures contribute to abnormalities in the white matter microstructure of the brain and a lower intelligent quotient at school age.[11]

Despite evidence that pain during the neonatal period can cause long-term consequences, procedural pain appears to be undertreated.[7] The current knowledge base indicates that non-pharmacological interventions, such as oral sucrose, skin-to-skin contact (SSC), containment/facilitated tucking, non-nutritive sucking and breastfeeding are suitable for alleviating the pain caused by small procedures.[7] Using oral sucrose alone or with non-nutritive sucking is the most frequently studied non-pharmacological method for procedural pain management in neonates. Sucrose is effective at alleviating the procedural pain related to skin-

breaking procedures (eg, heel lance, venepuncture, and intramuscular injection) in full- and pre-term infants.[12]

Skin-to-skin contact, during which a naked, diaper-dressed infant is placed on the caregiver's bare chest, provides a natural opportunity for the baby's parents to participate in pain management. There is empirical evidence that SSC reduces the pain caused by heel lance and intramuscular injection.[13] The effectiveness of SSC appears to be unaffected by whether the provider is the mother or another person, and no side effects have been reported for this method.[13] Facilitated tucking also allows parents to be involved in relieving their baby's pain.[14] During endotracheal suctioning, the facilitated tucking position – relative to routine care – is effective at managing pain in preterm neonates, yet does not demonstrate a significant advantage over oral glucose or opioids when used during heel stick.[14]

However, non-pharmacological pain relief methods also have certain limitations. For example, there is currently insufficient evidence that oral sucrose is effective at reducing the pain caused by some procedures, such as arterial puncture and nasogastric tube insertion.[12] It is also possible that repeated doses of sucrose in very preterm neonates may not be safe.[15] The appropriate dose of SSC, its effects over repeated use, and suitability for neonates of different gestational ages remain unclear due to the heterogeneity of previous studies.[13] In summary, there is not enough evidence to deem one of the aforementioned non-pharmacological interventions as the superior technique for pain management. Each of these methods provides some pain relief for neonates, but is not completely effective.[16]

The use of technology-based interventions in the treatment of pediatric pain has increased over the past years; for example, two recent systematic reviews investigated the effectiveness of vibratory stimulation for needle-related procedural pain management in children.[17,18] The reviews revealed that the vibrator device was able to significantly reduce self-,[17,18] parent-,[17] and observer-reported procedural pain.[17,18] There is also some evidence that virtual reality distraction is effective at relieving pain among children. Studies have found that virtual reality interventions can relieve needle-related pain,[19] pain related to burn wound cleaning,[20] and dental treatment.[21] Nevertheless, there remains limited empirical evidence on how effective virtual reality is at relieving pain among children.[22] Humanoid robots represent the latest technology for procedural pain management in children.[23-25]

In summary, previous systematic reviews that have evaluated whether technology-based interventions are effective for pain management in pediatric patients have focused on children and/or adolescents aged 0-18 years.[17,18,22,24] Of these reviews, neonates were only covered by the work of Ueki et al.,[18] with one of the included randomized controlled studies evaluating the effectiveness of vibratory stimulation in alleviating pain among neonates during heel stick. It is important to note that technology is becoming increasingly prevalent in neonatal care[26]; as such, it would be useful to investigate the effectiveness of technology-based methods in neonatal pain management. A preliminary search of PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews, and *JBI Evidence Synthesis* was conducted, with no current or in-progress systematic reviews on the topic identified.

Review question

What is the effectiveness of technology-based interventions at relieving procedural pain in hospitalized neonates compared to other non-pharmacological interventions?

Inclusion criteria

This review will consider studies that include both hospitalized full-term neonates (> 37 completed weeks postmenstrual age) and pre-term neonates (< 37 completed weeks postmenstrual age) to a maximum postpartum age of one month or with a corrected age who are undergoing a procedure that may cause pain

Interventions

This review will consider technology-based, non-pharmacological intervention studies that evaluate how effective a certain intervention is at managing procedural pain in hospitalized neonates. In the context of this review, technology refers to an electronic device or computer technology. Several examples of technological interventions that can be considered include: mechanical vibration or vibrator, transcutaneous electrical nerve stimulation, games, audio intervention, virtual reality, and robots.

Comparators

This review will consider studies that compare a technology-based intervention to alternative non-pharmacological intervention including for example breastfeeding, facilitated tucking, holding, live music, non-nutritive sucking, rocking, sensorial saturation, skin-to-skin contact, swaddling, sweet solution and combinations of non-pharmacological interventions. The review will not include studies comparing technology-based intervention with other technology-based interventions.

Outcomes

To understand whether technology-based interventions are effective at alleviating pain in neonates following a painful procedure, this review will consider studies that describe the outcome of procedural pain, that is, the response to a painful procedure as measured by at least one of the following:

Primary outcomes

- Pain scores measured using a validated pain assessment scales for neonates (eg, COMFORT[27]; Neonatal Infant Pain Scale [NIPS][28]; Neonatal Pain, Agitation and Sedation Scale [N-PASS][29]; Premature Infant pain profile [PIPP][30]; or Premature Infant Pain Profile-Revised [PIPP-R][31]);
- Behavioral indicators (eg, cry duration, facial expressions);
- Changes in physiological indicators (eg, changes in heart rate, respiratory rate, oxygen saturation, near-infrared spectroscopy).

Secondary outcomes

- Recovery from the procedure (time during which the measured pain indicator returns to the baseline value);
- Adverse effects of the intervention (eg, apnea, bradycardia, desaturation).

These indicators will be categorized as "yes" or "no."

Types of studies

This review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, and randomized cross-over trials.

Methods

This systematic review will be conducted in accordance with JBI methodology for systematic reviews of effectiveness evidence.[32] This protocol is registered in PROSPERO CRD42021254218.

Search strategy

The search strategy will aim to identify both published and unpublished studies**.** In accordance with the JBI methodology for systematic reviews, a three-step search strategy will be used for this review.[32] An initial, limited search of the MEDLINE (Ovid) and CINAHL (EBSCO) databases will be undertaken to identify articles on the topic, followed by an analysis of words in the titles and abstracts of potentially relevant articles, along with the search terms used to describe the articles. A second search, including all of the identified keywords and index terms relevant to the use of technological interventions for procedural pain relief in newborns will then be performed in all of the included databases. The search strategy developed for MEDLINE (Ovid; see Appendix I) will be adapted for each separate database and/or information source. In the third step of the search, the reference lists of all included sources of evidence will be screened for additional studies that may

have been missed during the first two searches. Studies published in English, Swedish, and Finnish will be included. There will be no restrictions regarding the date of publication.

MEDLINE (Ovid), CINAHL (EBSCO), and Scopus (Elsevier) databases, along with the Cochrane Central Register of Controlled Trials and the Finnish database Medic, will be searched. In-progress and recently completed studies will be identified from clinical trial registers, and MedNar and ProQuest Dissertations and Thesis Global will be searched for unpublished studies.

Study selection

Following the search, all identified citations will be collated and uploaded into Covidence (Veritas Health Innovation, Melbourne, Australia) systematic review software, after which duplicates will be removed. Following a pilot test, titles and abstracts will then be screened by two independent reviewers against the inclusion criteria for the review. The full-text versions of potentially relevant studies will then be retrieved and imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia). Full-text articles will then be assessed in detail against the inclusion criteria by two or more independent reviewers, and reasons for exclusion will be recorded and reported in the systematic review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion or via an additional reviewer. The results of the search and the study inclusion process will be reported in full in the final systematic review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.[33]

Assessment of methodological quality

All of the eligible studies will be critically appraised for methodological quality by two independent reviewers using standardized critical appraisal instruments from JBI for experimental and quasi-experimental studies.[32] Where data are missing or additional information is needed for clarification, the authors of the paper will be contacted. Any disagreements that arise will be resolved through discussion or, if this is not possible, by including a third reviewer. The results of the critical appraisal will be reported in narrative form and in a table.

All studies, regardless of the results of their methodological quality, will undergo data extraction and synthesis where possible. The quality of the studies will be considered in the interpretation of results.

Data extraction

Data will be extracted from studies included in the review by two independent reviewers using the standardized data extraction tool in JBI SUMARI.

The extracted data will include specific details about the participants (eg, gestational age, postpartum age, condition of health), study methods, interventions (eg, type of technology-based intervention, type of comparison), and outcomes (eg, score on a pain scale). Any disagreements that arise between the reviewers will be resolved through discussion or, if this is not possible, by including a third reviewer. Attempts will be made to contact the research team if any data are missing from a certain study.

Data synthesis

Studies will, whenever possible, be pooled in a statistical meta-analysis using JBI SUMARI. Effect sizes will be expressed as odds ratios (for dichotomous data) and weighted (or standardized) final post-intervention mean differences (for continuous data). The corresponding 95% confidence intervals will also be calculated and presented. Heterogeneity will be statistically assessed using the standard χ^2 and I^2 tests, and subgroup analysis divided full-term and preterm infant will be considered. Statistical analyses will be performed using fixed-effects or random-effects models for meta-analysis based on the guidance by Tufanaru et al.[34] Experimental data concerning each distinct outcome (eg, PIPP score after procedure, heart rate after procedure) will be synthesized in separate meta-analyses. Sensitivity analyses will be carried out to test whether the methodological quality or heterogeneity of the studies impacts the results. Where statistical pooling is not possible, the findings will be presented in narrative form, including tables and figures to aid in data presentation Whenever 10 or more studies are included in a meta-analysis, a funnel plot will be generated to assess publication bias. Statistical tests for funnel plot asymmetry (Egger test, Begg test, Harbord test) will then be performed.

Assessing certainty in the findings

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach will be used to assess confidence in the quality of evidence.[35] The results of this assessment will be shown in a Summary of Findings table (SoF) created using GRADEPro software (McMaster University, ON, Canada). The SoF will present absolute risks for treatment and control, estimates of relative risk, along with a ranking of the quality of evidence based on study limitations (risk of bias), indirectness, inconsistency, imprecision, and publication bias. The outcomes reported in the Summary of Findings will be: pain score during procedure, pain score after procedure, changes in physiological indicators during procedure, physiological indicators following procedure, duration of cry following procedure and duration of recovery after procedure.

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Appendix I: Search strategy

MEDLINE (Ovid)

Search conducted on November 11, 2020

Records retrieved: 617

Language limits: English, Finnish, Swedish

#1 (infant*[Abstract, Title] or newborn*[Abstract, Title] or baby [Abstract, Title] or neonate*[Abstract, Title] or "premature infant"[Abstract, Title] or preemie*[Abstract, Title])

Result: 579,014

#2 Infant [MeSH, Explode]

Result: 1,147,346

#3 #1 OR #2

Result: 1,346,665

#4 ("pain management"[Abstract, Title] or "pain care"[Abstract, Title] or "pain treatment" [Abstract, Title] or "pain alleviation" [Abstract, Title] or "pain relief" [Abstract, Title])

Result: 56,723

#5 Pain Management [MeSH, Explode]

Result: 4827

#6 ("procedural pain" [Abstract, Title])

Result: 1132

#7 #4 or #5 or #6

Result: 81,435

#8 Technology [MeSH, Explode]

Result: 418,797

#9 ("technology-based" [Abstract, Title] or technolog* [Abstract, Title] or vibrat*[Abstract, Title] or buzzy [Abstract, Title] or TENS[Abstract, Title] or player*[Abstract, Title] or record*[Abstract, Title] or headset*[Abstract, Title] or computer [Abstract, Title] or mobile [Abstract, Title] or virtual*[Abstract, Title] or robot*[Abstract, Title] or video*[Abstract, Title] or device*[Abstract, Title] or mechanic*[Abstract, Title])

Result: 2,694,839

#10 #8 or #9

Result: 2,994,099

#11 #3 and #7 and #10

Result: 617