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Résumé de l'article

Introduction : La douleur répétée et non traitée peut entraîner des conséquences à long terme chez les nouveau-nés prématurés, comme une hypersensibilité à la douleur, une altération des développements moteur et intellectuel. Les interventions pharmacologiques et non pharmacologiques pour le soulagement de la douleur chez les nouveau-nés prématurés sont limitées. Objectif : Évaluer la faisabilité, l'acceptabilité et les effets préliminaires d'une intervention de stimulation olfactive avec du lait maternel pour la douleur procédurale des prématurés. Méthodes : Une étude pilote a été menée auprès de mères, d'infirmières et de nouveau-nés prématurés. Douze nouveau-nés prématurés ont été familiarisés avec l'odeur du lait de leur mère durant 9 heures. Pendant le prélèvement sanguin au talon, l'odeur du lait maternel était combinée avec les soins standards. La douleur a été mesurée à l'aide de l'outil Preterm Infant Pain Profile-Revised. Les mères (n=11) et les infirmières (n=20) ont rempli des questionnaires d'acceptabilité et de faisabilité. Résultats : Plus de 80% des mères et des infirmières ont déclaré que l'intervention était faisable et acceptable. Le temps nécessaire pour que le rythme cardiaque et la saturation en oxygène des nouveau-nés prématurés reviennent à la normale a été réduit et les scores de douleur étaient plus faibles lorsque la compresse imbibée de lait maternel était placée à 1 millimètre (mm) du nez du nouveau-né. Discussion et conclusion : L'intervention de stimulation olfactive est faisable et acceptable pour les infirmières et les mères. Les effets préliminaires suggèrent qu'une compresse imbibée de lait maternel placée à 1 mm du nez du nouveau-né prématuré réduirait sa douleur. Un essai clinique randomisé devrait être mené pour évaluer l'efficacité de cette intervention.

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Management of procedural pain in preterm infants through olfactive stimulation with mothers' milk: A pilot study

Prise en charge de la douleur procédurale des nouveau-nés prématurés par une intervention de stimulation olfactive avec du lait maternel : une étude pilote

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Keywords

pain; infant;
odor;
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Abstract

Introduction: Repeated and untreated pain can lead to long-term consequences in preterm infants, such as pain hypersensitivity and impaired motor and intellectual development. Studies on pharmacological and non-pharmacological interventions for pain management in preterm infants are limited. Thus, we piloted an intervention based on olfactive stimulation with mothers' milk. **Objective**: To assess the feasibility, acceptability, and preliminary effects of an olfactive stimulation intervention with mothers' milk for procedural pain in preterm infants. **Methods**: A pilot study was conducted with mothers, nurses, and preterm infants. Twelve preterm infants were familiarized to the odor of their mother's milk 9 hours before heel prick. During heel prick, mothers' milk odor was combined with standard care by placing a pad saturated with mothers' milk beneath the infant's nose. Pain was measured using Preterm Infant Pain Profile-Revised tool. Mothers (n=11) and nurses (n=20) completed questionnaires regarding feasibility and acceptability. **Results**: More than 80% of mothers and nurses reported that the olfactive stimulation intervention was feasible and acceptable. Time taken for preterm infants' heart rate and oxygen saturation to return to the baseline was reduced and pain scores were lower when the mothers' milk pad was placed at 1 millimeter (mm) of the infant's nose. **Discussion and conclusion**: The olfactive stimulation intervention is feasible and acceptable for nurses and mothers. The observed preliminary effects suggest that a pad saturated in mother's milk placed 1 mm from the preterm infants' nose could reduce the pain response. A randomized clinical trial should be conducted to assess the effectiveness of this intervention.

Mots-clés

douleur;
nouveau-né;
odeur; lait maternel;
prélèvement sanguin

Résumé

Introduction : La douleur répétée et non traitée peut entraîner des conséquences à long terme chez les nouveau-nés prématurés, comme une hypersensibilité à la douleur, une altération des développements moteur et intellectuel. Les interventions pharmacologiques et non pharmacologiques pour le soulagement de la douleur chez les nouveau-nés prématurés sont limitées. **Objectif** : Évaluer la faisabilité, l'acceptabilité et les effets préliminaires d'une intervention de stimulation olfactive avec du lait maternel pour la douleur procédurale des prématurés. **Méthodes** : Une étude pilote a été menée auprès de mères, d'infirmières et de nouveau-nés prématurés. Douze nouveau-nés prématurés ont été familiarisés avec l'odeur du lait de leur mère durant 9 heures. Pendant le prélèvement sanguin au talon, l'odeur du lait maternel était combinée avec les soins standards. La douleur a été mesurée à l'aide de l'outil *Preterm Infant Pain Profile-Revised*. Les mères (n=11) et les infirmières (n=20) ont rempli des questionnaires d'acceptabilité et de faisabilité. **Résultats** : Plus de 80% des mères et des infirmières ont déclaré que l'intervention était faisable et acceptable. Le temps nécessaire pour que le rythme cardiaque et la saturation en oxygène des nouveau-nés prématurés reviennent à la normale a été réduit et les scores de douleur étaient plus faibles lorsque la compresse imbibée de lait maternel était placée à 1 millimètre (mm) du nez du nouveau-né. **Discussion et conclusion** : L'intervention de stimulation olfactive est faisable et acceptable pour les infirmières et les mères. Les effets préliminaires suggèrent qu'une compresse imbibée de lait maternel placée à 1 mm du nez du nouveau-né prématuré réduirait sa douleur. Un essai clinique randomisé devrait être mené pour évaluer l'efficacité de cette intervention.

INTRODUCTION

Preterm infants feel pain (Anand & Hickey, 1987) but express it differently than full-term infants. Pain is expressed by preterm infants through various observable signs such as crying, physiological responses (i.e. heart rate, oxygen saturation) and behavioural responses including motor responses and facial expressions (Gibbins et al., 2014). Preterm infants are particularly vulnerable to the consequences of untreated pain (Grunau, Holsti, & Peters, 2006). Indeed, repeated and untreated pain can lead to hypersensitivity to pain (Valeri et al., 2016), as well as neurological impairment (Brummelte et al., 2012; Grunau et al., 2009; Ranger et al., 2013; Ranger et al., 2015). Thus, repeated painful procedure in preterm infants leads to a decrease in white and grey subcortical brain matter as early as 40 weeks of corrected age (Brummelte et al., 2012). In addition, mental and psychomotor development indices are significantly lower in preterm than for full-term neonates at the age of 8 and 18 months (Grunau et al., 2009). Moreover, repeated painful procedures would result in a decrease in brain volume at seven years of life (Ranger et al., 2013; Ranger et al., 2015). The number of painful procedures in Canadian neonatal intensive care units (NICU) has declined from 14 per week in 1997 (Johnston, Collinge, Henderson, & Anand, 1997) to 5.8 per week in 2011 (Johnston, Barrington, Taddio, Carbajal, & Filion, 2011). Only half of preterm infants undergoing a heel prick received any pharmacological or non-pharmacological pain management intervention (Johnston et al., 2011). Several studies have evaluated the effectiveness of interventions to manage and prevent consequences of pain in preterm infants (Anand & Scalzo, 2000; Johnston et al., 2017; Pillai Riddell et al., 2015; Ranger & Grunau, 2014; Stevens, Yamada, Ohlsson, Haliburton, & Shorkey, 2016). However, pain management in NICUs is still suboptimal (Pillai Riddell et al., 2015).

The use of pharmacological pain management interventions, such as local anesthetics, are not effective for preterm infants during heel prick (American Academy of Pediatrics, 2016), leading nurses to consider non-pharmacological interventions. Some interventions, such as skin-to-skin contact (Johnston et al., 2017), sucrose with non-nutritive sucking (NNS) (Pillai Riddell et al., 2015; Stevens et al., 2016) and swaddling or tucking (Pillai Riddell et al., 2015) are effective for preterm infants during a heel prick. However, these interventions are not always possible; skin-to-skin contact, for instance, requires the presence of a parent, while the combination of sucrose and NNS is reported to be ineffective on some components of pain during a heel prick (Stevens et al., 2016). In addition, the combined use of non-pharmacological pain management interventions is recommended by the American Academy of Pediatrics (2016) to manage procedural pain more effectively in preterm infants, such as sucrose associated with NNS. Thus, olfactive interventions could be combined with other effective interventions, such as sucrose associated with NNS, to improve pain management.

Pain management is a part of developmental care interventions, which include family centered care as well (Lavallée et al., 2019). Thus, pain management interventions involving parents are most appropriate for the preterm infant because it accentuates parent-infant proximity (Axelin et al., 2015). For example, their care implication is essential as skin-to-skin is an effective intervention to manage pain in preterm infants (Johnston et al., 2017). However, many barriers to parental presence exist, including contextual factors such as communication, partnership and organizational resources (Marfurt-Russenberger, Axelin, Kesselring, Franck, Cignacco, 2016) as well as barriers related to parents for instance having other children at home, living far away from the hospital, having work responsibilities or having household responsibilities (Forest, 2016). In this context, it is essential to evaluate innovative intervention to encompass parents' absence and still ensure a collaboration with them int the pain management of their infant.

There are only three studies evaluating olfactive stimulation interventions in preterm infants (Badiee, Asghari, & Mohammadizadeh, 2013; Goubet, Rattaz, Pierrat, Bullinger, & Lequien, 2003; Jebreili et al., 2015). In these studies, the olfactive intervention consisted of putting a pad with a natural (Badiee et al., 2013; Jebreili et al., 2015) or artificial odor (Goubet et al., 2003) in proximity of the infant during a painful procedure. Olfactive stimulation intervention appeared more effective when the infants were familiarized to the

odor a few hours before the painful procedure. This familiarization has been tested only with full-term infants (Goubet et al., 2007; Sadathosseini et al., 2013). To our knowledge, no study has evaluated the effect of mothers' milk odor with familiarization on preterm infants' pain response during heel prick. Thus, we have designed a pilot study to address this research question (Sidani & Braden, 2011).

OBJECTIVE

To assess the feasibility, acceptability, and preliminary effects of an olfactive stimulation intervention using mothers' milk to manage preterm infants' pain during heel prick. The specific objectives were the following: a) assess the feasibility of the pilot study's recruitment and data collection, b) assess the feasibility and the acceptability of the olfactive stimulation intervention by mothers, c) assess the feasibility and the acceptability of the olfactive stimulation intervention by nurses, d) observe the preliminary effects of the olfactive stimulation intervention on preterm infants' pain during a heel prick procedure.

METHODS

DESIGN

The design was a pilot study. The inclusion of only one group (and no control group) was based on the recommendation to not compare the effects of an intervention as the main variable between groups in a pilot study, but to focus on acceptability and feasibility of the intervention (Feeley et al., 2009).

SAMPLE

This study was conducted in April 2017, in a level-III NICU where approximately 130 preterm and full-term infants are hospitalized every year. Sucrose is considered the standard care for painful procedures performed in this NICU. Ethics approval was obtained from the Ethics Review Board of this hospital.

A total of 12 mother-preterm infant dyads and 20 nurses caring for them were recruited to participate in the study, after having signed a consent form. Mothers were included if they were; a) 18 years of age or older, b) fluent in English or French, and c) producing milk. Mothers who had any pathology preventing the use of their milk (HIV, drugs, etc.) were excluded. Preterm infants were included if they were born between 28 and 36 weeks of gestation. Exclusion criteria for preterm infants included any conditions that might have modified their pain response; a) congenital disease, such as Trisomy 21, b) intraventricular hemorrhage > grade II, c) leukomalacia, d) surgery in the first days of life, e) intubated, under Continuous Positive Airway Pressure or nasal oxygen, and (f) an APGAR[1] < 6 at 5 minutes of life (score to assess baby's health at birth). Other preterm infant exclusion criteria were also considered at the time of data collection; a) sedation or pharmacologic treatment for pain within 48 hours prior to heel prick, and b) being under phototherapy treatment. Nurses were included if they had at least six months experience in neonatology.

PAINFUL PROCEDURE

The painful procedure selected for this study was a heel prick as it is the most common painful procedure performed in NICUs (Carbajal et al., 2008). This procedure was done in five steps by a nurse; 1) moving the preterm infant into a supine position, 2) disinfecting the site with an antiseptic, 3) pricking the infant's heel (needle insertion) followed by blood collection, 4) placing a bandage onto the site of insertion, and 5) repositioning the infant into their original position. The time to return to baseline is the time needed for the heart rate to return to its baseline rate (evaluated 1 minute before the painful procedure). The time to return to baseline was calculated for a maximum of 5 minutes after the painful procedure, as instructed by previous studies (Cook et al., 2017; Johnston et al., 2003). The entire procedure was videotaped to assess the feasibility of using the Premature Infant Pain Profile-Revised (PIPP-R) during the heel prick (Stevens et al., 2014). The procedure, carried out by a nurse, was done for the purpose of collecting the weekly blood sample.

OLFACTIVE STIMULATION INTERVENTION

The olfactive stimulation intervention consisted of two stages: a familiarization stage, in which infants were familiarized with the odor of their mothers' milk for 9 hours before heel prick,

and the exposure stage, in which infants were exposed to the odor during heel prick. To our knowledge, no scientific data established the quantity of milk necessary for our experimentation. We estimated, after testing in the neonatal units, that 20 milliliters (ml) of milk would be the total quantity needed. Four ml of milk was used on a sterile pad, changed three times during the 9 hours of the familiarization stage, following the recommendations of the infection control department, and 4 ml of milk was used for the heel prick stage. In addition, 4 ml of milk was stored in case more milk was needed.

The intervention was carried out only when mother's lactation was well established, after the third day postpartum. The day before the prescribed heel prick, the mother expressed her milk so that the nurses could carry out the familiarization during the evening and night shifts. The milk was stored in the NICU lactarium. In this NICU, the heel prick was scheduled at 6 AM, so familiarization began at 9 PM. Nurses did the familiarization by immersing a pad with 4 ml of the preterm infants' mothers' milk, which was then placed 10 centimeters (cm) from their nose infant inside the incubator, as recommended in previous studies (Goubet et al., 2003; Goubet et al., 2007; Neshat et al., 2015; Nishitani et al., 2009; Razaghi et al., 2015; Sadathosseini et al., 2013). The pad was put into a small sterile plastic container that was laid on the mattress and was changed every 3 hours (for hygiene and infection control). Before the heel prick, a new pad saturated with mothers' milk was placed 3 cm from the preterm infant's nose 5 minutes before the painful procedure (Jebreilli et al., 2015; Sadathosseini et al., 2013). The odor was sustained for a maximum of 5 minutes after the end of the heel prick or until the heart rate and oxygen saturation had returned to baseline. Only fresh milk was used because the odor of the milk can change when frozen.

OUTCOMES MEASURES

Mothers' feasibility and acceptability. The mothers' feasibility and acceptability of the olfactive stimulation intervention were evaluated with self-administered questionnaires. Mothers completed a five-item questionnaire after their preterm infants' heel prick was done (see Table 1). The Likert scale had five levels from totally disagree to totally agree. Expected rates of feasibility and acceptability of the olfactive stimulation intervention were 80% for mothers (addition of agree and totally agree scores). Also, mothers completed six demographic questions.

Nurses' feasibility and acceptability. The nurses' feasibility and acceptability of the olfactive stimulation intervention were evaluated with self-administered questionnaires. Nurses completed an eight-item questionnaire to assess the acceptability of the intervention; three items related to familiarization and five items to the odor exposure during heel prick (see Table 1). Nurses that worked 12 hours' shifts (n = 2) conducted both stages of the intervention. Nurses (n = 9) who worked only in the evening (4 PM to 12 AM) installed the first pad at 9 PM at the beginning of the familiarization stage and night nurses (n = 11) completed the familiarization stage by installing a new pad with mother's milk at 12 AM and 3 AM. Night nurses also administered the heel prick at 6 AM. A different questionnaire was administered to the nurses who worked evenings (without items about the heel-prick). This questionnaire included a Likert scale, dichotomic questions and open questions (see Table 1). The Likert scale had five levels from totally disagree to totally agree. Expected rates of acceptability and feasibility were the same for nurses as mothers: 80% (agree and totally agree).

Feasibility of data collection for pain measurement. The feasibility of data collection to measure pain was also evaluated. The standardized PIPP-R tool was selected to measure pain because it is a reliable and validated tool to use with preterm infants aged between 28 and 36 weeks of gestation (Stevens, Johnston, Petryshen, & Taddio, 1996; Stevens et al., 2014). The PIPP-R contains four parts: gestational age, state of sleep-awake, physiological parameters, and behavioural parameters. Physiological parameters include heart rate and oxygen saturation, coded by ordinal numbers. Physiological parameters were collected with the cardiorespiratory monitor (Philips Intellivue MX800). Behavioural parameters (i.e. facial expressions) include brow bulge, eye squeeze, and naso-labial furrow, which are measured in seconds (sec). Behavioural parameters were videotaped during the heel prick.

Table 1

Acceptability and feasibility items for mothers and for nurses

Acceptability and feasibility for mothers	
Five-points Likert scale: from totally disagree to totally agree	▪ I would like to be present during the pricks done to my baby. ▪ I agree to use the equivalent of 2 tablespoons of my milk for a research that may help to relieve my baby's pain during a heel prick. ▪ I found it was feasible to come to in the neonatal unit to express my milk the evening preceding my baby's heel prick. ▪ I believe that my milk odor can help to reduce my baby's pain. ▪ Expressing milk in the neonatal unit to relieve my baby's pain was easy.
Acceptability and feasibility for nurses	
Five-points Likert scale: from totally disagree to totally agree	▪ In my opinion, the use of the mother milk odor helped to reduce the pain of the preterm infants during heel prick. ▪ It makes sense to use the mother milk odor to relieve pain of preterm infants during heel prick. ▪ The mother milk's odor is appropriate to relieve pain of preterm infants during heel prick. ▪ The use of mother's milk odor for pain management of preterm infants is an easy and possible intervention. ▪ I would like to do this intervention again during preterm infants' heel pricks. ▪ According to me, the 9 hours of familiarization helped to diminish the preterm infant's pain during the heel prick. ▪ Familiarization with mother milk odor is appropriate to relieve pain of preterm infants. ▪ I would like to do again the familiarization before preterm infants' heel pricks.
Dichotomic questions	▪ Did placing a pad at the desired distance from the preterm infant's head during my shift interfered with my care? ▪ During heel prick, was the pad with mother milk maintained at the desired distance from the preterm infant's nose?
Open questions	▪ During your working, how many times did you change the pad with mother milk? ▪ Do you have any suggestions to help you remember to change the pad with the mother milk every three hours? ▪ Was the quantity of the mothers' milk enough to soak five pads? ▪ What are the main difficulties you encountered in performing this intervention during heel prick?

Scores range from 0 to 21 where a higher score means more pain, a score less than 6 signifies an absence of pain, and a score greater than 12 indicates moderate to severe pain. The PIPP-R suggests two measurement times: an observation at least 15 sec before the painful procedure and 30 sec after the end of the blood collection (Stevens et al., 2014). Three measurement times were added in this study: at the needle insertion, 1 minute after the needle insertion, and when physiological parameters returned to baseline to have a better assessment of pain. Data related to pain confounding variables were also collected using a light meter (TES-1336A Digital light meter) and a sound meter (dB A-weighted scale sound meter: Sound Examiner SE-402), in addition to the medical records.

STUDY PROCESS

According to their schedule, nurses were recruited by the PI (principal investigator) for the study 16–48 hours prior to a prescribed heel prick. Nurses were encouraged to perform the standard of care (normally sucrose), but administration was not controlled to evaluate if standard care was really done (De Clifford, Aita, Le May, 2019). Five minutes before the beginning of the heel prick procedure, a

video camera, attached to the incubator, was installed and connected to a computer for recording purposes. Physiological parameters were reported manually at specific times: 15 sec before touching the preterm infant, at the needle insertion, 60 sec after the needle insertion, 30 sec after the bandage was applied, and when physiological parameters returned to baseline. Then, nurses completed questionnaires at the end of their evening or night shift to assess the feasibility and acceptability of the intervention. After the heel prick, the questionnaire was completed by mothers.

STATISTICAL ANALYSES

Descriptive statistical analyses were used to analyze feasibility, acceptability, and the observed preliminary effects of the intervention. Feasibility of data collection was evaluated through the codification of videotapes.

RESULTS

DEMOGRAPHICS

Tables 2, 3 and 4 present the characteristics of the participants recruited in this pilot study: the preterm infants (n = 12), mothers (n = 11), and nurses (n = 20).

Table 2

Preterm infants' Demographic Characteristics (n = 12)

Preterm infant	Mean (x)	Standard deviation (SD)	Min – Max
Birth weight (g)	1554	±1120.43	870 – 2250
Gestational age at birth (in weeks + days)	31+1	± 1 w. + 4 days (11 days)	29 – 34
Number of days of life at the time of heel prick	24	± 12	6 – 45
Adjusted gestational age (in weeks + days)	34+6	± 1 w. + 4 days (11 days)	32+2 – 36+3

Table 3

Mothers' Demographic Characteristics (n = 11)

Mothers	N	Percentage
First infant	4	36 %
First preterm infant	11	100 %
Mothers of twins	4	36 %
Breasfeeding of previous children	6	55 %
Wish to breastfeed after infant discharge	11	100 %
Language		
French	10	91 %
English	1	9 %

Table 4

Nurses' Demographic Characteristics (n = 20)

Nurses	Mean (x)	Standard deviation (SD)	Min – Max
Experience in the NICU (years)	6.3	± 1.42	5 – 10

CHANGES IN THE OLFACTIVE STIMULATION INTERVENTION

Three important changes to the protocol were carried out over the course of this pilot study to enhance the feasibility of the intervention:

1. Quantity of milk. Initially, the use of 20 ml of milk was planned, only 4 ml per pad was needed to achieve the intervention (including familiarization stage and heel prick stage) for a total of 16 ml (4 ml additional if needed). According to the majority of nurses (90%, n = 18/20) this volume of 4 ml could be decreased to 3 ml, for a total of 12 ml. This quantity of 20 ml was diminished after the second preterm infant enrolled and was maintained for the remainder of the study. The milk not used for the intervention was conserved by the NICU lactarium and given for feeding.

2. Distance. The distance between the pad and the preterm infant's nose was changed to assess the feasibility of different distances. The PI quickly observed, during data collection, that the initial distance of 10 cm for familiarization and 3 cm for heel prick seemed to be too far from the infant's

nose to observe an effect. Therefore, the pad distance was decreased to 3 cm, and then further decreased to 1 mm during the two stages of the intervention. Regardless, all nurses thought that distance had no influence on the feasibility of keeping the pad to the set distance during the familiarization and heel prick stages. At the time of the heel prick, 82% (9/11) of nurses found it was feasible to keep the pad at the desired distance. This rate remained stable despite the methodological changes made during the pilot study.

3. Method of odor dissemination. Initially, the pad immersed with mothers' milk was put in a sterile plastic container at a distance of 3 cm from the preterm infants' nose for the heel prick stage. When the distance was reduced, nurses expressed difficulties with the use of the sterile plastic container. So, the pad immersed with mothers' milk (measuring 2 X 2 cm) was put on two dry pads (each measuring 4 X 4 cm) rather than in the plastic container, allowing the pad to be closer to the preterm infant's nose. According to the nurses, it was easier to place a 2 X 2 cm pad immersed with mothers' milk on a 4 X 4 cm dry pad instead of placing it in a sterile plastic container. This change allowed us to keep the mothers' milk odor 1 mm from the preterm infant's nose for the duration of the familiarization stage without interfering with the care provided by nurses.

RECRUITMENT FEASIBILITY

Eighty-one preterm infants were evaluated for eligibility (see Figure 1). Among these, 67 were excluded because they did not meet the eligibility criteria. Twelve mothers were invited to participate in the study and all agreed to participate. One dyad preterm-mother was transferred before the heel prick was prescribed, and so did not receive the intervention. Eleven mothers completed the questionnaire. Two of the mothers had twins, so the total number of preterm infants was 13. One preterm infant had to be removed from the analysis because of a technical problem with the videotape recorder. Therefore, the final sample was composed of 12 preterm infants. Recruitment was completed within four weeks, with more than two infants recruited per week. In addition, all nurses invited agreed to participate in the study (n= 20). Among the 20 nurses, nine were evening nurses (start the intervention at 9 PM to 11 PM) and 11 were night nurses (11 PM to 6 AM the next day for the heel prick).

FEASIBILITY OF DATA COLLECTION PROCESS

Videotaping the infant's face during the heel prick and transcribing the physiological parameters to measure pain response were all completed by the PI. Coding of videotapes for behavioural responses was feasible because the filming went as planned for 92.3% (12/13) of the preterm infants. All physiological parameters were reported as expected.

ACCEPTABILITY AND FEASIBILITY OF THE INTERVENTION BY MOTHERS

The intervention was evaluated as acceptable by mothers and 91% (n = 10) thought that the odor of their milk could help relieve their baby's pain during painful procedures. All mothers found that the procedure of giving 20 ml of milk was easy. All mothers were able to arrive at the NICU the day before heel prick to express their milk. All mothers were invited to be present during heel prick. Six mothers (55%) responded that they wanted to be present during the painful procedures conducted on their infant. However, no parents attended the heel prick.

ACCEPTABILITY AND FEASIBILITY OF THE INTERVENTION BY NURSES

Acceptability of the intervention by night and evening nurses (n= 20) ranged between 70% and 100% for all items, with an overall average of 82.6%. Regarding the familiarization process to mothers' milk odor, 82% of the night nurses (9/11) answered that they would do it again. Seventy-three percent (8/11) perceived that the familiarization to mothers' milk odor helped to reduce the preterm infants' pain during the heel prick. Similar results were found for the olfactive stimulation intervention during the heel prick. All nurses (n= 20) thought it was logical to use mothers' milk odor as an intervention to manage procedural pain in preterm infants, and 90% (18/20) found that it was appropriate to use mothers' milk odor to decrease preterm infants' pain. According to 80% (16/20) of the nurses, mothers' milk odor helped manage preterm infants' pain during the heel prick. Seventy percent (14/20) of nurses would use this intervention again, during a

heel prick, for pain management. A majority of nurses (70%, 14/20) found that the olfactive stimulation intervention was easily achievable. The other 30% of nurses commented the first method of odor dissemination, i.e., some nurses found difficult using the sterile plastic container at a distance up to 1 mm. More than 80% (17/20) of the nurses responded that it was feasible to change the pad saturated with mothers' milk every 3 hours, and 90% (18/20) of the nurses said it was feasible to achieve the intervention with the quantity of milk (12 ml). Over 80% (17/20) of nurses answered that it was feasible to keep the pad at the determined distance from the preterm infants' nose during the familiarization and heel prick stages. It was feasible for 82% (9/11) of the night nurses to change the pad immersed with mothers' milk every 3 hours. More than half of the night nurses (64%, 7/11) reported that it was easy to remember to change the pad because it coincided with their routine care.

During the familiarization stage, a distance of 10 cm between the pad and the preterm infant's nose was planned, as established in previous studies (Goubet et al., 2003; Sadathosseini et al., 2013). Eighty-two percent (9 out of 11) percent of night nurses said that it was feasible to keep the pad immersed by mothers' milk close to the preterm infants' nose for 9 hours. Only 18% (2 out of 11) found that the pad, during the familiarization stage, interfered with their care (they had to replace the pad).

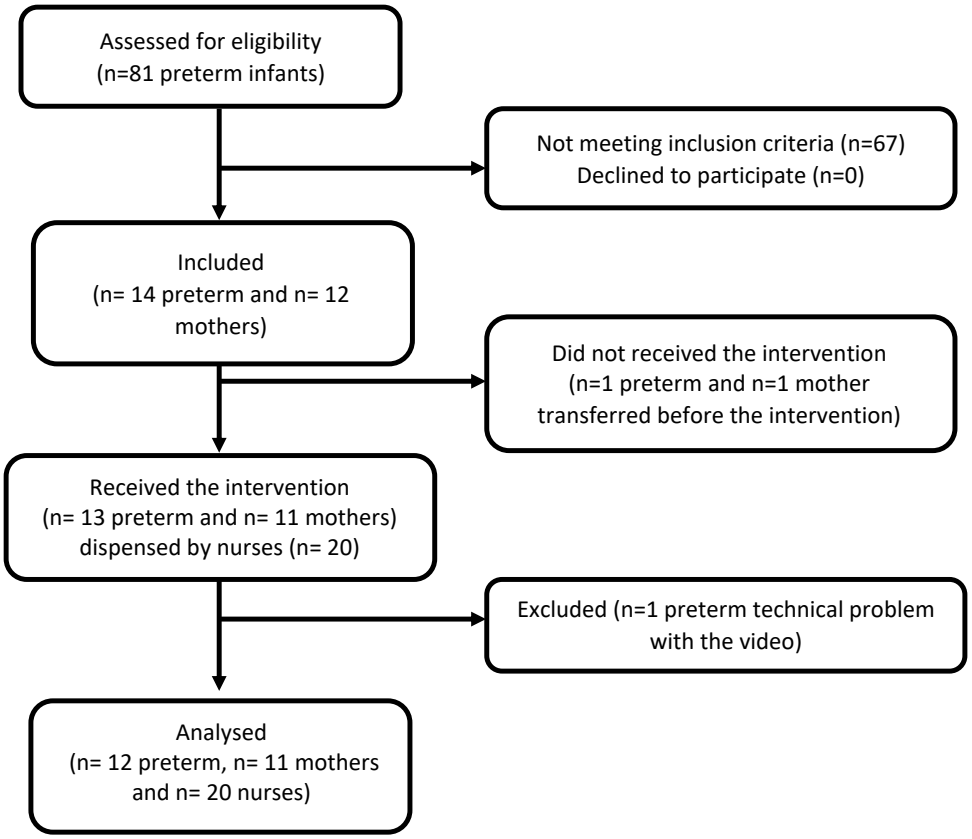

Figure 1. Flow Diagram

PRELIMINARY EFFECTS

Pain response, including time taken for physiological parameters to return to baseline, was evaluated in relation to the different distances the pad was placed from the preterm infants' nose: 10 cm, 3 cm, 1 cm, then 1 mm. For the heel prick, the planned distance was 3 cm, but some nurses put the pad at 10 cm instead of 3 cm because the use of a sterile plastic container hindered them from putting it closer. The use of two dry pads (measuring 4 X 4 cm), in place of the container, solved this problem. Other adjustments were made during the pilot study (diminution of the distance: 1 cm and then 1 mm) to observe if there was a difference in preterm infants' reactions during heel prick. To evaluate the effect of distance, preterm infants were distributed into three groups of four infants, according to the distances: group A (3 cm to 10 cm), group B (1 cm to 3 cm) and group C (1 mm). No adverse effects were reported by nurses or seen by the PI during familiarization or heel prick.

Table 5

Time taken for the preterm infants' physiological parameters to return to baseline, according to the distance of the pad from their nose

Group[a] A, B, C	Preterm infants	Distance	Time to return to baseline	
Group A 3 to 10 cm	1	10 cm	240 sec	Mean at 270 sec
	2	10 cm	>300 sec	
	3	3 cm	>300 sec	
	4	3 cm	240 sec	
Group B 1 to 1.5 cm	5	1.5 cm	120 sec	Mean at 81 sec
	6	1 cm	60 sec	
	7	1cm	70 sec	
	8	1 cm	75 sec	
Group C 1 mm	9	1 mm	70 sec	Mean at 50 sec
	10	1 mm	50 sec	
	11	1 mm	40 sec	
	12	1 mm	40 sec	

[a] n = 4 in each group

The time needed for the preterm infants to return to their baseline heart rate and oxygen saturation, as well as their PIPP-R scores, was compared. Although the sample was small (n = 12), it was possible to observe a difference in the distances the pad was placed from the preterm infant's nose (see Table 5). A clear difference was observed for the time taken for the preterm infants' heart rate and oxygen saturation to return to baseline after the heel prick between the three groups. It was easily observable that the proximity of the pad to the preterm infant's nose facilitated their return to baseline (Table 5). The average time to return to baseline for group A was 270 sec, whereas this decreased to 81 sec for the group B, then down to 50 sec for group C. Table 6 shows results on pain scores obtained with the PIPP-R (Gibbins et al., 2014). Regarding pain response, there seemed to be differences in the pain score at the time of the needle insertion as well as 30 sec after the bandage. Still, for all groups, pain levels remained high during heel prick at the time of the needle insertion and 1 minute after the start of heel prick (see Table 6).

Table 6

Preterm Infants' Pain scores (PIPP-R) according to the distance of the pad from their nose (n = 12)

Distance	PIPP-R at needle insertion	PIPP-R at 1 min	PIPP-R 30 sec after the blood collection
3 to 10 cm	11.67	10.33	4.67
1 to 1.5 cm	10.25	11.00	3.25
1 mm	8.75	9.75	1.50

PIPP-R score can range from 0 to 21, where a higher score means more pain and a score fewer than 6 signify an absence of pain. Preterm infants received different pain management interventions as standard of care.

DISCUSSION

We found that the olfactive stimulation intervention with mothers' milk for pain management in preterm infants is feasible and acceptable for both mothers and nurses. In addition, the intervention seems to have an effect on preterm infants' pain response and time taken for physiological parameters to return to baseline, following a heel prick, when the pad saturated with mothers' milk is placed 1 mm from their nose.

Although the recruitment of NICU participants for research is an issue widely discussed in the literature (Hoehn et al., 2005; Kraybill, 2004; McKechnie & Gill, 2006; Shilling et al., 2011), the recruitment of mother-infant dyads in this pilot study was feasible and timely. In addition, all mothers agreed to come to the NICU the day before the prescribed heel prick to express their milk, reflecting their interest in the proposed intervention. According to Cleveland (2008), the most important need of parents when their preterm infant is hospitalized in the NICU is to be involved in their care. However, even if mothers were invited to be present in the NICU and could sleep in their infant's room (single room), none were present during heel prick. Barriers related to parents such as having other children at home, living far away from the hospital, having work responsibilities or having household responsibilities might explain this result (Forest, 2016). The mothers' participation in this study allowed them to be involved in care and perhaps may have decreased their stress levels.

Despite the innovative aspect of the intervention and the changes made related to the distance between the pad and the nose, the intervention was still acceptable for all nurses. This finding also suggests that if the effectiveness of such an intervention on preterm infants' pain was confirmed, neonatal nurses would probably be inclined to perform it in their clinical practice during painful procedures.

Previous studies have also used different methods to expose the preterm infant to mothers' milk odor: immersing a pad or cotton (Neshat et al., 2015; Sadathosseini et al., 2013) using a diffuser (Brevaut-Malaty et al., 2015; Nishitani et al., 2009) or blotting paper with a few drops of milk placed at the bottom of a little bottle (Badiee et al., 2013). Distances from the preterm infants' nose also varied (1 mm to 10 cm) in previous studies in relation to the type of odor used. For instance, Neshat et al. (2015) placed an immersed pad with mothers' milk at 1 mm from the preterm infants' noses and obtained significant results on their physiological stability during venipuncture, similar to our results. This suggests that in a full-scale RCT, the preferable distance at which the pad saturated with mothers' milk should be placed is 1 mm. In addition, no adverse effects were reported by nurses when the pad was 1 mm from the preterm infants' nose. In the present study, familiarization to mothers' milk odor was established at 9 hours preceding the heel prick, based on previous studies (Goubet et al., 2003; Goubet et al., 2007; Sadathosseini et al., 2013). The 9 hours was an acceptable duration for nurses as well as for mothers who were able to express enough milk before the intervention, and to ensure that the pad would be changed with fresh milk every 3 three hours during the night. However, the optimal duration for familiarization to mothers' milk odor is still unknown, as no previous study evaluating an olfactive stimulation intervention with infants did a sequence of familiarization to mothers' milk odor or tested the effect of familiarization. This intermediate step seems important as it significantly reduced pain, according to previous studies (Goubet et al., 2003; Goubet et al., 2007; Sadathosseini et al., 2013). It would be interesting to assess whether familiarization and its duration, increases the effect of the intervention on preterm infants' pain response during a painful procedure.

LIMITATIONS

Olfactive stimulation intervention resulted in a shorter time taken to return to baseline, when the mothers' milk pad was placed at 1 mm of the infant's nose, meaning that the intervention might support preterm infant self-regulation. However, the results regarding pain response and the time taken to return to baseline after the heel prick should be interpreted with caution. First, videos were coded by the PI which can influence the assessment of preterm infant pain responses, particularly since the distance of the pad to the nose was observable on the videos. Then, during heel prick, any standard care in combination with the olfactive intervention was allowed. A significant heterogeneity in pain management interventions (sucrose, swaddling, positioning, NNS and others) was used by nurses in combination to the olfactive stimulation intervention during heel prick (De Clifford et al., 2019). These other pain management interventions differed by their nature and duration. Finally, many confounding variables could have influenced the preterm infants' pain response and their time taken to return to baseline, such as gestational age and postnatal age, duration of extracting blood during the procedure, number of previous heel pricks, frequency of skin-to-skin contact and breastfeeding,

and variability in the provision of standard care. Another limit is associated with the feasibility and acceptability of the intervention which were evaluated in only one NICU, limiting generalization of results to other NICUs.

CONCLUSION

Findings of this pilot study provided valuable information on the methodology necessary for a larger study. The use of mothers' milk odor as a non-pharmacological intervention to manage preterm infant pain is feasible and acceptable for nurses and mothers in addition to being innovative and inexpensive. This intervention enables mothers to be involved in the pain management of their preterm infants without requiring to be physically present during the procedure. Indeed, this intervention is underpinned by a partnership between the mothers and the nurses, where each one is engaged to reduce the pain response of preterm infants.

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[1]NOTE

Abbreviation: APGAR (score to assess baby's health at birth based on five items**:** Appearance, Pulse, Grimace, Activity and Respiration).

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