

#### Non-pharmacological methods for pain relief in premature neonates

Métodos no farmacológicos para el alivio del dolor en recién nacidos prematuros Métodos não farmacológicos no alívio da dor em neonatos prematuros

#### Abstract

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Submission: 03-10-2022 Approval: 04-30-2022 The aim was to know the non-pharmacological methods of pain relief in premature newborns admitted to the Neonatal Intensive Care Unit produced in the scientific literature on the subject. This is an integrative review. The following descriptors were used: "premature newborn", "pain management", "premature baby" and "pain". The following databases were used: Medical Literature Analysis and Retrieval System Online, Latin American and Caribbean Literature in Health Sciences, Nursing Database, Bibliographic Index Español en Ciencias de la Salud and Bibliografía Nacional en Ciencias de la Salud Argentina being found 275 articles. In the studies found that composed the sample (36 articles), it was possible to observe the following non-pharmacological techniques for pain relief: sucrose, breast milk, facilitated containment, skin-to-skin care, oral glucose 25%, non-nutritive sucking, kangaroo method, lullabies, winding up, kangaroo mother care, white noise, breastfeeding, pacifier, etc. It is noteworthy that 16.17% of the studies refer to the analgesia potential with sucrose, both alone and in combination with some other method. It is observed that some pain relief strategies that can be used and applied by the team responsible for care in the neonatal intensive care unit, expanding the view that simple alternatives can be effective to bring comfort to these babies.

Descriptors: Newborn Premature; Pain Management; Baby Prematuro; Pain; Child Health.

#### Resumén

El objetivo fue conocer los métodos no farmacológicos de alivio del dolor en recién nacidos prematuros ingresados en la Unidad de Cuidados Intensivos Neonatales producidos en la literatura científica sobre el tema. Esta es una revisión integradora. Se utilizaron los siguientes descriptores: "recién nacido prematuro", "manejo del dolor", "bebé prematuro" y "dolor". Se utilizaron las siguientes bases de datos: Medical Literature Analysis and Retrieval System Online, Latin American and Caribbean Literature in Health Sciences, Nursing Database, Bibliographic Index Español en Ciencias de la Salud y Bibliografía Nacional en Ciencias de la Salud Argentina encontrando 275 artículos. En los estudios encontrados que componían la muestra (36 artículos), fue posible observar las siguientes técnicas no farmacológicas para el alivio del dolor: sacarosa, leche materna, contención facilitada, contacto piel con piel, glucosa oral 25%, no Succión nutritiva, método canguro, canciones de cuna, liquidación, método madre canguro, ruido blanco, lactancia materna, chupete, etc. Llama la atención que el 16,17% de los estudios hacen referencia al potencial analgésico con sacarosa, tanto sola como en combinación con algún otro método. Se observa que algunas estrategias de alivio del dolor pueden ser utilizadas y aplicadas por el equipo responsable por el cuidado en la unidad de cuidados intensivos neonatales, ampliando la visión de que alternativas simples pueden ser efectivas para llevar bienestar a estos bebés.

Descriptores: Recién Nacido Prematuro; Manejo del Dolor; Bebé Prematuro; Dolor; Salud de los Niños.

#### Resumo

Objetivou-se conhecer os métodos não farmacológicos no alívio da dor nos recém-nascidos prematuros internados na Unidade de Terapia Intensiva Neonatal produzidos na literatura científica sobre o tema. Tratase de uma revisão integrativa. Utilizou-se os seguintes descritores: "recém-nascido prematuro", "manejo da dor" "bebê prematuro" e "dor". Utilizou-se as bases de dados: *Medical Literature Analysis and Retrieval System Online*, Literatura Latino-Americana e do Caribe em Ciências da Saúde, Base de Dados de Enfermagem, *Índice Bibliográfico Español en Ciencias de la Salud e Bibliografía Nacional en Ciencias de la Salud Argentina*, sendo encontrados 275 artigos. Nos estudos encontrados que compuseram a amostra (36 artigos), foi possível observar as seguintes técnicas não farmacológicas para alívio de dor: sacarose, leite materno, contenção facilitada, cuidado pele a pele, glicose oral 25%, sucção não nutritiva, método canguru, canções de ninar, enrolamento, método mãe-canguru, ruído branco, amamentação, chupeta etc. Destaca-se que 16,17% dos estudos referem-se ao potencial de analgesia com sacarose, tanto isoladamente quanto em combinação com algum outro método. Observa-se que algumas estratégias de alívio da dor que podem ser utilizadas e aplicadas pela equipe responsável pelos cuidados na unidade de terapia intensiva neonatal, ampliando a visão de que alternativas simples podem ser eficazes para trazer conforto a esses bebês.

Descritores: Recém-Nascido Prematuro; Manejo da Dor; Bebê Prematuro; Dor; Saúde da Criança.



#### Introduction

About 15 million premature babies are born all over the world and indicate a need for quality intervention through specialized or intensive care, with the aim of providing them with better living conditions. Premature neonates have a higher risk of death or disability. In 2017, approximately 2.5 million newborns died in the first 28 days in the world, with 80% of these newborns having low birth weight and two thirds being premature<sup>1,2</sup>.

Thus, the birth of premature newborns represents a public health problem that requires special attention and specific measures in order to promote an improvement in the quality of life of this population. The trajectory of the premature neonate is painful and quite uncomfortable, starting with hospitalization, which can last for long periods. During the hospitalization period, the premature newborn is subjected to different situations, invasive procedures and repeated manipulations, which the full-term baby does not need to experience, as he/she is born healthy. In addition, they are also exposed to various painful stimuli and the intensive environment, such as excessive lighting and noise, during their stay in the NICU<sup>3,4</sup>.

Pain, when not treated, can cause long-term damage to the neonate, especially in premature infants, as their brain nerve pathways are in the development phase, in intrauterine life. At just seven weeks of gestational age, the conceptus has perioral sensory receptors and, at 20 weeks of gestational age, the receptors are distributed throughout the mucocutaneous surface. Nociceptive stimuli received by these receptors are directed by incompletely myelinated fibers (a-delta fibers) or unmyelinated fibers (c fibers) to the spinal cord and, subsequently, to the basal ganglia and cerebral cortex<sup>5</sup>.

Thalamocortical synapses, connecting the basal ganglia to higher cortical processing centers, are evident from 24 weeks of gestational age. The entire afference of the nociceptive stimulus, from the periphery to the cerebral cortex, can travel, from the point of view of neuroanatomy, early in fetal life. The modulation of this nociceptive afference is carried out by means of neurochemical substances, of which tachykinins, endogenous opioids (endorphins and enkephalin, among others) stand out and, significantly from childhood, by the adrenergic and serotonergic systems. Such substances are responsible for the transmission, amplification, attenuation or inhibition of the nociceptive stimulus. With the exception of the adrenergic and serotonergic systems, which are responsible for regulating descending pain inhibitory pathways, all other neurotransmitters are present and functional at birth<sup>5</sup>.

Thus, pain can trigger some consequences, such as delay in postnatal growth, changes in brain development, cognitive and motor impairment, among others<sup>6</sup>.

In view of the exposed present, the research question of the study was defined as: What are the nonpharmacological methods for pain relief used in the performance of invasive procedures in premature newborns admitted to the NICU described in the literature?

In view of the importance of identifying nonpharmacological methods, the present research aimed, in Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM general, to know the non-pharmacological methods for pain relief in premature newborns admitted to the NICU produced in the scientific literature on the subject. Specifically, it aimed to investigate which nonpharmacological methods are recognized for pain relief in premature newborns admitted to the NICU. Due to the high number of painful invasive procedures performed with premature newborns hospitalized in BUs, the study becomes relevant because the use of non-pharmacological methods for pain relief makes it possible to reduce the potential of unfavorable consequences of early exposure to pain and promotes results positives. With the expansion of these practices in the BUs, premature newborns along with their families will benefit.

The present study contributes to better care at the NICU, enabling the health team to update nonpharmacological techniques for pain relief, in the search for a better quality of care in favor of reducing the pain experienced by premature newborns during the hospitalization. For professional training, by making it possible to expand the field of view of academics on the nonpharmacological methods used and effective in relieving the pain and suffering of premature newborns.

For research, the study aims to broaden the view of different non-pharmacological pain relief methods that can be used in premature newborns during intensive care at the NU and thus enable the expansion of their use in the routine of the units. With this knowledge on the subject, it is easier to evaluate correctly and develop effective techniques in the management of the painful sensation. As justification for the study, it is considered that premature babies are those born before the 37th week of gestation, being classified as: extremely premature newborns with less than 28 weeks of gestation, very premature newborns with gestational age at birth between 28 and 32 weeks and moderate to late preterm when the premature baby is between 32 and 37 weeks of gestation<sup>3</sup>.

Extremely premature newborns with extremely low birth weight go through difficult times in the Neonatal Unit (NU) involving resuscitation and other procedures. This is necessary because these neonates are not yet prepared to independently deal with extrauterine life. Thus, to keep them alive, stable and ensure a satisfactory recovery, they need to be exposed to numerous painful and unpleasant procedures that trigger overstimulation of all sensory modalities compared to stimuli previously received in utero<sup>7</sup>.

In their first two weeks of life, premature babies admitted to the NICU undergo an average of 34 procedures, making these first days of life deeply uncomfortable<sup>1</sup>.

Among the painful procedures that are most frequently seen in BUs are: venipunctures, arterial punctures, heel punctures, and intramuscular injections. Pain is a sensation that involves psychological and sensory aspects of the individual. This sensation begins in intrauterine life, where the fetus is already able to respond to pain in the 20th – 24th week of pregnancy. It is known that the anatomical, neurophysiological and hormonal development required to sense pain is complete and that neurotransmitter functions are highly developed in fetuses



in late pregnancy. It is understood that premature babies remember recurrent painful stimuli that occur in the initial period, and that they manifest an excessive response to these stimuli in later moments. In preterm infants, repeated exposure to neonatal pain-related stress has been associated with altered brain microstructure, modified stress hormone levels, and worse cognitive, motor, and behavioral development. Thus, adequate pain management in BUs is essential, since when pain is poorly managed it can lead to medium and long-term harm for these babies<sup>8-10</sup>.

Given the above, it is necessary to investigate nonpharmacological pain relief methods, as their advantages are evident, such as low cost, no adverse effects and no drug interaction. Even if it is difficult to completely eliminate pain, knowledge of these methods is fundamental to be able to reduce its intensity and quantity, as well as encourage the search for more humanized and less invasive interventions in the search to provide comfort and well-being to Non-pharmacological methods for pain relief in premature neonates Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM premature<sup>6</sup>.

#### Methodology

This is an integrative literature review study. The integrative review is a method that aims to summarize the results obtained through research on a given subject. It is called integrative, as it provides broader information on a particular topic or subject<sup>11</sup>.

The search for articles was carried out from July 13 to July 21, 2020, with the question - What nonpharmacological methods for pain relief are used in performing invasive procedures? - For the construction of the appropriate question for the researched clinical question, the PICo strategy was used where the acronym "P" corresponds to the patient (premature newborns); "I" corresponds to the intervention (non-pharmacological methods); "Co" corresponds to the context (providing comfort to premature newborns)<sup>12</sup>.

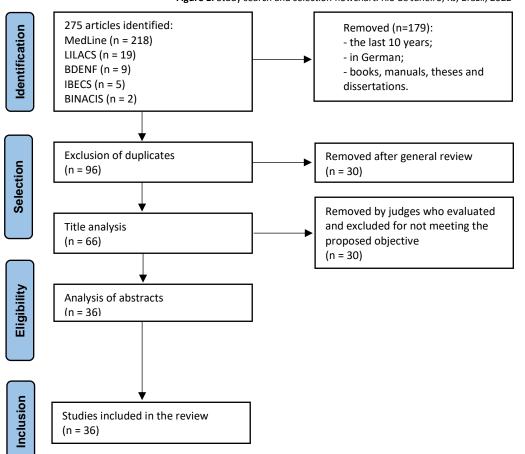


Figure 1. Study search and selection flowchart. Rio de Janeiro, RJ, Brazil, 2022

The searches were carried out using the Virtual Health Library (BVS), a platform that gathers bibliographic data in health sciences, which have articles and scientific documents, as well as databases such as the Catalog of Scientific Journals and Health Sciences Descriptors (DeCS). The selected databases were: Medical Literature Analysis and Retrieval System Online (MEDLINE), Latin American and Caribbean Literature in Health Sciences (LILACS), Nursing Database (BDENF), Bibliographic Index Español en Ciencias de la Salud (IBECS) and Bibliografía Nacional en Ciencias de

la Salud Argentina (BINACIS).

The study inclusion criteria were articles published between 2016 and 2020, which addressed premature newborns as study participants, whose setting comprised the NU and covered invasive procedures. Studies that focused on other themes, books, manuals, theses, master's and doctoral dissertations were excluded.

The searches were carried out using the association of the following descriptors through the Boolean operators "AND" - "premature newborn", "pain management", "pain



management", "manejo del pain". Also located appropriate controlled MeSH vocabulary "premature baby", "premature infant", "premature born newborn", "dor", "pain", "dolor".

After the searches, a table was made with all the articles found and forwarded to three judges, who judged according to the PICo question, which articles would remain in the study and which would be excluded.

A flowchart was constructed according to the PRISMA checklist, which enables the presentation of all selected articles in a synthetic way for a broader view. The flowchart shows a more general analysis of the article search and selection process, from identification in the respective databases to the choice of selected articles.

Data analysis was performed using thematic content analysis. Thus, content analysis comprises investigation procedures that allow the systematization, description of messages and attitudes linked to the enunciation situation, as well as inferences about the collected data<sup>13</sup>.

# Results

A total sample of 36 articles collected from the databases was obtained after applying previously defined inclusion and exclusion criteria. Of the studies included in this review, it was possible to identify the largest number of publications in the year 2018 (n= 14; 38.88%), followed by publications from 2015 (n=8; 22.22%), after publications from 2017 ( n=6; 16.66%), after 2016 (n=5; 13.88%) and, at the end of 2019 (n=3; 8.33%). The studies were selected according to the year of publication, title, objective, abstract and result.

According to the articles, the non-pharmacological methods of sucrose, breast milk, facilitated containment, skin-to-skin care, oral glucose, non-nutritive sucking, kangaroo method, lullabies, swaddling, kangaroo mother method and white noise were the most used , the rest appearing only once.

Among the countries where the research was carried out, it was identified that the predominance was in the United States with 7 works carried out, followed by Turkey with 5, Brazil with 4, China with 4, India with 4, Canada with 3, Asia with 2 works performed. Countries such as South Korea, Spain, France, Indonesia, Lebanon, Malaysia and Sweden appear with only one study each, demonstrating a limited number of studies on the subject.

Regarding the design of the studies, twenty-one were randomized controlled clinical trials with a narrow confidence interval, being classified as level of evidence I, five trials systematic review of randomized controlled clinical trials, with level of evidence I, five observations of therapeutic results (outcomes research), with level of evidence II, three cohort studies (including lower quality randomized clinical trial), with level of evidence II, a systematic review of case-control study, with level of evidence III, one case-control study , with level of evidence III.

The studies were empirically grouped, based on non-pharmacological interventions performed to relieve pain in premature newborns, being defined based on the

#### Non-pharmacological methods for pain relief in premature neonates

Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM similarity between the methods, four thematic categories: Category 1 – Oral Stimuli; Category 2- Organization and Comfort Stimuli; Category 3 - Auditory Stimuli and Category 4 - Kangaroo Method.

Painful procedures are common throughout the care of premature newborns in the NU, and the administration of analgesic drugs is something very necessary, but which should not be prioritized due to its side effects. In this sense, non-pharmacological pain relief methods are acceptable options to provide analgesia and comfort during these procedures<sup>14</sup>.

These methods use strategies associated with one or more senses, such as: vision, hearing, smell, touch and taste as a way to reduce pain during painful procedures in premature babies<sup>9</sup>.

Thus, non-nutritive sucking with and without sucrose, swaddling/kangaroo care, music therapy and multisensory stimulation are examples of some of the non-pharmacological pain relief measures used through stimulation of the baby's senses. These measures possibly have a modulating effect on pain in premature neonates by activating their attention, thereby distracting them from pain and, therefore, modifying their perception of pain. There is also the possibility of stimulating more than one of the senses, that is, the combination of two or more non-pharmacological interventions used in the same painful procedure, which can become even more useful, varying from baby to baby<sup>15</sup>.

# Oral stimulation

This category comprises studies that investigated the management of non-nutritive sucking technique, use of oral sucrose and use of breast milk alone or in combination with the purpose of pain relief.

# <u>Sucrose</u>

In a study<sup>16</sup> the neurobehavioral responses of newborns subjected to repeated painful procedures under the effect of analgesia with sucrose were evaluated. 93 newborns participated in the study, where 47 were on sucrose and 46 on the placebo group. No significant difference was observed in the assessment at 40 weeks of gestational age, between the groups in the domains of motor development and vigor, as well as alertness and orientation, nor difference in adverse effects such as a drop in heart rate or oxygen saturation. Thus, it was concluded that both oral analgesia with sucrose and distilled water as a placebo did not present poor neurobehavioral results in preterm infants when evaluated using the Neurobehavioral Assessment of Preterm Infant (NAPI) scale during 40 weeks. The use of sucrose for pain during the seven-day procedure period appeared to be free of long-term adverse effects.

Another study<sup>17</sup> evaluated the main and interactive effects of neonatal clinical risk and intervention with sucrose as a routine for acute pain relief, evaluating the baby's behavior during pain and its response to recovery. The 104 very low birth weight infants (104) were placed into low and high clinical risk groups according to the Clinical Risk Index for Babies (CRIB). One group received sucrose solution (25%,



0.5ml/Kg) two minutes before the procedure and the control group received standard care. Pain reactivity and recovery was evaluated according to the Neonatal Facial Coding System (NFCS) scale, sleep-wake state scale, crying time and heart rate divided into five phases (baseline, antisepsis, puncture, recovery and rest). Regardless of the Neonatal Clinical Risk (NCR) level, sucrose had an effect on pain response and crying time during the puncture and on recovery and rest. Regardless of the NCR or sucrose routine intervention, all neonates were active in the puncture and decreased behavioral response in the recovery and rest phase. All neonates showed physiological recovery ten minutes after the puncture.

#### Non-nutritive sucking associated with sucrose

In a study<sup>10</sup>, The effectiveness of sucrose and nonnutritive sucking alone and in combination on repeated pain during the heel stick procedure was evaluated. Premature infants were allocated before the heel-prick procedure by a nurse using a computer-generated random table into four groups: routine group, non-nutritive sucking group, oral sucrose group, and oral sucrose combined with non-nutritive sucking group. All premature babies wore only diapers, were placed in prone or lateral decubitus and remained undisturbed for 30 minutes in the incubator. In the routine care group, the premature baby received only comfort through touch after the heel-prick procedure. In the nonnutritive sucking group, a pacifier was given to stimulate sucking two minutes before and during the recovery phase of the heel puncture. The sucrose group received 20% sucrose (0.2 ml/kg) administered into the preterm infant's mouth by a 1 ml syringe, two minutes before the heel stick procedure. In the group that received oral sucrose associated with non-nutritive sucking, 20% sucrose (0.2 ml/kg) was administered into the baby's mouth by a 1 ml syringe, two minutes before the heel puncture procedure, and then a pacifier was given. to stimulate suction until the heel puncture recovery phase. Thus, pain was measured by the PIPP scale, which identified that in the initial phase there was no significant difference in heart rate, oxygen saturation and crying time between groups.

Regarding pain parameters during the collection phase and recovery phase, regarding the PIPP score, the group that received oral sucrose associated with nonnutritive sucking was significantly lower than the other three groups, the sucrose group as well as the group non-nutritive sucking had lower pain parameters than the routine care group. Regarding heart rate and oxygen saturation, the sucrose and non-nutritive sucking combination group achieved a significant improvement in relation to the other groups.

Regarding the percentage of crying, the combination group was significantly lower, the routine care group was higher, and the non-nutritive sucking group was significantly similar to the sucrose group. It is concluded that both sucrose and non-nutritive sucking have an analgesic effect on premature babies with repeated pain during heel puncture, but the combination of the two shows better efficacy. Thus, when sucrose and non-nutritive sucking can Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM be offered, the combination of the two can be recommended as an analgesic measure for repeated exposure in premature pain.

#### Breast milk combined in pain relief

A study<sup>18</sup> evaluated the analgesic effects of expressed breast milk and 24% oral sucrose in preterm neonates during venipuncture. 66 premature babies participated in the study, being randomly divided into two groups. They received expressed breast milk or sucrose two minutes before venipuncture, along with suction and swaddling. Pain was measured with the PIPP scale and crying was also measured. There was no statistically significant difference between groups.

PIPP scores were seven with breast milk and six with sucrose. The 11 babies born less than 28 weeks of age had the highest scores of nine for breast milk and four for sucrose. The conclusion is that expressed breast milk and sucrose 24% had the same analgesic effect during venipuncture in most preterm neonates, but sucrose worked better in extremely preterm infants.

In a study<sup>19</sup>, was investigated whether instillation of breast milk or dextrose water into the oral cavity could reduce pain in the heel puncture procedure in premature infants. Twenty premature newborns participated in the study. Each baby in the study received a heel stick 4 times. Breast milk, 10% dextrose water, distilled water (placebo) and nothing (control group) were administered one after the other in random order to the same patient before heel puncture. The PIPP scale was used to assess pain scores. The whole process consisted of 4 sections, with a baseline period of 1 minute, heel puncture period of 20 seconds and recovery period of 5 seconds. The primary outcome is to compare the PIPP scores in the 4 groups. The conclusion of the study is that offering something with flavor such as breast milk or 10% dextrose is safe and effective in reducing pain during a heel puncture procedure in preterm infants, with breast milk being the first recommended option. Thus, the two safe methods.

Study<sup>20</sup> compared the effect of the combination of sucking and breast milk; suckling, breastmilk, and restraint; and, routine care of preterm infant pain during and after heel-prick procedures. Pain was measured by watching video recordings of infants undergoing heel-trick procedures and scoring pain at one-minute intervals with the PIPP. Data were collected over eight phases.

In phase 1, the babies remained ten minutes without being stimulated before the heel puncture, phases 2 and 3 comprise the heel puncture phase and, finally, the recovery phases of the neonates, which occurred 10 minutes after the puncture (comprises the phase from 4-8). For infants receiving both suckling and breastmilk, changes in pain score from baseline at stages 2-8 were units lower than corresponding changes in pain score for infants receiving routine care (all values <0. 05 except for phases 6 and 7).

Similarly for infants who received suckling, breastmilk, and restraint, pain score changes from baseline were lower than corresponding pain changes in routine care infants at stages 2-8 (all p values <0.05 except for phase 4).



After receiving sucking, breastmilk plus containment, and sucking plus breastmilk, the infant's risk of mild pain (pain score >6) decreased significantly, 67% and 70.1% respectively, compared to infants receiving nursing care. routine. After receiving suckling, breastmilk plus containment, and suckling plus breastmilk, an infant's risk of moderate to severe pain (pain score >12) decreases by 87.4% and 95.7%, respectively, compared with infants receiving routine care.

The conclusion of the study is that the combined use of sucking, breastmilk plus restraint, and sucking plus breastmilk effectively reduced the preterm infant's mild pain and moderate and severe pain during the heel stick procedure. Adding the facilitated restraint helped the babies recover from pain in eight stages of heel stick procedures. The findings increase knowledge about the effects of the combination of expressed breast milk, sucking and restraint on procedural pain in premature babies admitted to the NICU.

# Organization and coziness stimuli

This category comprises methods of positioning on the hammock, winding up, facilitated containment, and wrapped bathing alone or associated with pain relief.

# Winding and pacifier

An article<sup>21</sup> aimed to evaluate the effectiveness of pacifiers and windings on pain scores, heart rate and oxygen saturation in premature babies during invasive procedures. This randomized trial involved 30 preterm infants who were randomly assigned to control (n=15) and intervention (n=15) groups. Babies in the intervention group were given a pacifier and swaddled when undergoing painful procedures. Two-day outcome indicators were pain score, heart rate, and oxygen saturation. The PIPP was used in this study to measure the pain of babies. The study concluded that providing a pacifier and swaddling can prevent the increase in pain and heart rate of premature babies during invasive procedures, therefore it can be implemented as an alternative for the treatment.

## Sponge bath - Rolled bath

A study<sup>22</sup> determined the effects of sponge baths and wrap baths on premature infants' vital signs, oxygen saturation levels, crying time, and stress levels. The Newborn Stress Scale, created by the authors of the study, was used to assess stress in premature babies. This study was a randomized trial with a crossover design. The study included 35 preterm infants born at 33-37 weeks of gestation with birth weight <1500 g. Two bathing methods were applied at 3-day intervals. Vital signs and oxygen saturation levels were measured before and at 1, 5, 15, and 30 minutes after bathing. Baby bathing was videotaped to assess pain and stress behavior. The infants' pain and stress behavior was assessed by independent observers. A significance level of 0.05 was used for all statistical analyses. There were statistically differences between bathing methods in vital signs, oxygen saturation levels, and crying. Stress and pain levels according to the type of bath were significantly higher

#### Facilitated containment

A study<sup>23</sup> aimed to investigate the effect of facilitated restraint on neonatal pain during heel-prick blood sampling. This is a crossover clinical trial that was performed on 40 preterm infants. During blood sampling, newborns were placed in a facilitated position or facilitated routine at random and the PIPP was completed for each newborn. At the time of the next sampling, the positions were changed and the process was repeated. Data were analyzed using descriptive statistics. The results showed that the mean intensity of pain in each position was increased during sampling (p=0.0001) and after that it was significantly decreased (0.001), but before, during and after sampling there was no significant difference between the two positions. (p>0.05). The conclusion shows that comparing the two positions there was no significant difference in their intensity and pain. These results show that there is not much research in this area. There is a need to deepen and investigate this subject.

A study<sup>24</sup> determined the effectiveness of facilitated restraint in reducing pain when venipuncture is being performed in premature infants. The study was conducted by a cohort study of preterm infants, with 42 participating infants divided into 21 in the control group and 21 in the treatment group to determine the effect of facilitated restraint on pain relief during venipuncture of preterm infants in the NICU. Pain intensity was measured using the PIPP score. The primary outcome was reduction in pain profile pain scores in preterm infants. Pain profile scores in preterm infants for the treatment group were significantly lower (M = 662, SD = 2598) than for the control group (p<0.005). The study found that facilitated restraint reduced PIPP scores.

In a review<sup>25</sup>, the studies were identified in the PubMed database, being a systematic review of the literature, which had as inclusion criteria: experimental studies such as randomized clinical trial and articles from the last 5 years. The Cochrane database of systematic reviews was also used. The study demonstrates that facilitated restraint reduces the expression of pain in premature babies. As a whole, the research supports the use of facilitated restraint for infants from 23 weeks of gestational age during painful procedures including: heel stick, endotracheal suction, and venipuncture. The study came to the conclusion that pain management interventions are needed to lessen the unfavorable consequences of early exposure to pain and to promote positive outcomes. Additional research is indicated to discover the effects of non-pharmacological interventions in neonates with severe illness, congenital anomalies and/or assisted breathing.

An article<sup>26</sup> compared the effectiveness of facilitated restraint in combination with non-nutritive sucking (intervention group) with non-nutritive sucking alone (control group) in reducing pain during procedures in preterm infants. Premature infants (gestational age between 28 and 32 weeks) were randomly assigned by a computer program to the intervention or control group during heel-



prick in the first 48 hours of life. 60 premature babies participated, in both groups they were placed in an asymmetrical position on a pillow, noise and light were limited after routine care. The heel puncture was performed first, in the care sequence. In the intervention group, facilitated restraint was performed by a nurse or nursing assistant. The procedure was recorded in 15 seconds before the procedure until three minutes after the end of the procedure. Pain was evaluated by two specialist nurses in the subject.

The primary outcome was pain score assessed 15 seconds before the procedure and 30 seconds immediately after by PIPP. The secondary outcome was the pain score assessed between T-15 seconds T+3 min by the DAN scale, a French neonatal pain assessment scale. The conclusion of the study was that the combined use of facilitated restraint and non-nutritive sucking did not significantly relieve pain during the heel puncture procedure. However, the addition of facilitated restraint enabled a faster recovery from pain after heel puncture procedure.

# Containment facilitated - sucrose - winding

An article<sup>27</sup> aimed to survey the interventions of neonatal nurses for the management of pain in premature newborns. Twenty nurses were recruited for this pilot observational research study. Standard pain management interventions used by nurses were assessed using a questionnaire. In addition, 11 of the 20 nurses were observed during the research to assess how the interventions were carried out. All infants received at least one pain management intervention during the survey. For 95% of the nurses, sucrose is a standard intervention reported in the survey, but observations have shown that it is not always applied (64%). Positioning is used more (64%) by nurses than reported in the survey (45%). Facilitated restraint was reported as a standard intervention by 45% of nurses, but it does not seem to be adequately performed (36%). According to the results, it would be essential to review nurses' knowledge and skills regarding standard pain management interventions during painful procedures, since the quality of these practices is questionable.

## Network positioning

A study<sup>28</sup> used the positioning in the hammock, because the position of the hammock simulates the position that the baby is in the mother's uterus. In this study, newborns are placed in a rectangular piece of cloth that is attached to the end of the incubator. Twenty-six spontaneously breathing newborns who were clinically stable at 30 to 37 weeks' gestational age were randomly assigned to two groups: hammock placement group (n=13) in which newborns were placed in hammocks in the lateral position and a traditional positioning group (n=13) in which they were also kept in the lateral position. The following variables were assessed at baseline and at the end of treatment: pain with the PIPP and NFCS, sleep-wake status with the Brazelton Neonatal Behavioral Assessment Scale (BNBAS), heart rate, respiratory rate and oxygen saturation. The study concluded that hammock positioning was an

Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM effective treatment option to minimize pain and improve sleep and wakefulness. Mesh placement was a simple and inexpensive option for effective treatment to reduce pain, being a non-pharmacological method option. It also helped to reduce heart rate and respiratory rate, and increase peripheral SpO2, which made it a treatment option for preterm infants.

# Auditory stimuli

The third thematic category, called auditory stimuli, comprises methods such as: listening to a lullaby, recorded mother's voice, music therapy and white noise.

Musical stimulation is one of the interventions that have been researched to reduce the stress of premature babies admitted to the NICU and favor an ideal neurobehavioral function. It is believed that music is a noninvasive tool for effective sensory stimulation and that it does not cause harm in relieving pain by promoting feelings of familiarity and security in the neonate<sup>29</sup>.

By receiving effective auditory stimulation, the baby is distracted and the pain is controlled. This is a cognitive tactic to reduce the pain response. Thus, rhythmic and smooth music provides several positive effects on the baby, such as: changing the focus of pain, release of natural endorphins in the brain, reduction of adrenocorticotropic hormone (ACTH) levels, increase in phenylethylamine secretion and relaxation of muscle tone, as well as release of body tension by activating the autonomic nervous system<sup>9,29</sup>.

There is also the use of white noise, with sounds that resemble the sounds of the uterus and the mother's heartbeat. The subsequent contact with these familiar sounds and rhythms after birth generates a calming experience about the baby<sup>29</sup>.

In this category of studies, seven articles were selected that used methods related to white noise/music therapy/lullaby/recorded maternal voice, in order to assess their effectiveness as a measure of pain relief.

Already in a study<sup>30</sup>, the combination of white noise and glucose was used to reduce pain during screening for retinopathy in premature babies. 396 premature babies participated in the study. These babies were divided into 4 groups, namely: control group (without any intervention), white noise group, glucose group and white noise group associated with glucose. PIPP scale was used to determine pain score and all groups were evaluated in terms of PIPP score before and after screening for retinopathy. The results showed that there was no significant difference between the four groups in the PIPP score, heart rate and oxygen saturation in the three minutes before the screening. In the first and fifth minutes after screening, the groups: white noise, glucose and white noise associated with glucose had heart rate and PIPP score significantly lower than the control group; oxygen saturation in these three groups was significantly higher than in the control group. The white noise group associated with glucose had heart rate and PIPP score significantly lower than the groups: white noise and glucose; oxygen saturation was significantly higher than the groups: white noise and glucose. The study concluded that



the combination of white noise and glucose can reduce pain in retinopathy screening, as well as maintain stable vital signs in preterm infants.

A randomized controlled trial<sup>31</sup> sought to analyze whether oral glucose and listening to lullabies provided some pain relief during painful tracheal tube removal and reinsertion procedures, as well as oronasopharyngeal sucking in premature infants who received continuous nasal airway pressure application. Participating babies were divided into intervention and control groups. Assessments of responses to pain were performed using the Neonatal Infant Pain Scale and PIPP. The lullaby and oral glucose groups had less pain compared to the control group that experienced more pain. The study showed that pain can be significantly reduced in premature babies through the interventions presented, but further studies are needed.

Another randomized clinical trial<sup>29</sup> sought to evaluate the effect of the recorded maternal voice, the odor of breast milk and the cover of the incubator on the pain and comfort of premature babies during the painful procedure of peripheral cannulation. 136 premature babies participated in the study and they were divided into different groups, namely: maternal voice group (which used a recorded maternal voice), breast milk odor group (which was exposed to the odor of breast milk) and coverage group of the incubator (which was covered using an incubator cover before, during and after the procedure in the babies of the experimental group). It was found that before the procedure, there was no difference between groups in terms of total PIPP scores. In the moments during and after the procedure, there was a significant difference between the PIPP scores. The three methods were recommended because they are simple, safe and beneficial in controlling pain.

A comparative study<sup>32</sup> evaluated pain in premature newborns and, based on the total scores of the NFCS of preterm newborns, compared neonatal variables (gender, type of delivery, birth weight, corrected gestational age, chronological age in days, period length of stay in days, Apgar scores 1' and 5', head circumference and chest circumference) and therapies (type of oxygen therapy, place of hospitalization and puncture site) in neonates submitted to arterial puncture exposed to music and 25% oral glucose. Forty-eight premature newborns participated in the study. Of these, 26 were part of the music group and 22 of the 25% glucose group. The groups did not show significant difference in variables and pain scores. At the end of the study, it was found that there were no differences when comparing the music group with the 25% glucose group, nor in the variables studied.

Authors<sup>15</sup> investigated the impact and mechanism of the Combined Music and Touch Intervention (CMTI) on pain response in preterm infants. About sixty-two preterm infants participated in the study. One part stayed in the experimental group, where they underwent painful procedures with CMTI, and the other part in the control group, where they also underwent painful procedures, but without CMTI. Blood samples were collected from all participants at baseline and 2 weeks later to assess cortisol Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM and  $\beta$ -endorphin concentrations. PIPP scores after 2 weeks were significantly higher in the control group than in the experimental group. There was no significant difference in cortisol concentration between the two groups at the beginning of hospitalization or 2 weeks later. However, the experimental group had a higher serum concentration of  $\beta$ endorphin than the control group, both at the beginning of hospitalization and 2 weeks later. The study concluded that CMTI can help decrease pain in premature babies, significantly improving the concentration of  $\beta$ -endorphin, but not the concentration of cortisol in the blood.

A research<sup>29</sup> sought to observe the occurrence of impact on pain in premature babies (through physiological and behavioral parameters) when listening to the same music that their mothers listened to during pregnancy, when exposed to the heel puncture procedure. Forty-two preterm infants participated in the study. These babies were divided into groups, namely: the music group that their mothers listened to during pregnancy, the recorded lullabies group, and the group without any music. All three groups were evaluated before, during and after the heel puncture. The Neonatal Pain, Agitation and Sedation Scale (N-PASS) was used to measure pain responses, and a nurse blinded to the intervention recorded physiological and behavioral responses. N-PASS pain scores were lower in the music group their mothers listened to during pregnancy compared to the other two groups. Physiological parameters were not significantly different between groups. In the music group that their mothers listened to during pregnancy, the babies spent more time in a state of silent alertness, with a significant decrease in their respiratory rates. It was concluded that the music that mothers listened to during pregnancy was more favorable to preterm infants, as it reduced pain and improved behavioral states during a heel puncture.

In an experimental study<sup>9</sup>, the effect of white noise for pain relief in premature babies during vaccination was evaluated. Seventy-five premature babies participated in the study and were divided into a study group and a control group. In the study group, premature babies were exposed to white noise for one minute before vaccination, and the noise continued until one minute after vaccination. The control group did not receive the intervention. Data collection for the study took place through the Premature Baby Information Form, Intervention Follow-up Form and PIPP. It was found that the pain level of the control group was significantly higher than that of the study group. It was also found that 67.6% of the babies in the study group had moderate pain during vaccination and 2.9% had severe pain. In the control group, 82.5% had severe pain and 17.5% had moderate pain. In this study, white noise was considered effective for the researched sample.

#### Kangaroo Method

The fourth thematic category called kangaroo method, comprises: kangaroo care, kangaroo mother method and skin-to-skin contact.

The Kangaroo position consists of positioning the baby, with only a diaper on the parents' bare chest to remain



there for brief or longer periods. This position favors better temperature regulation, weight gain for the child, increased production of mother's breast milk, approximation between the baby and the parents, blocking the perception of pain due to the different stimuli offered, which include tactile stimuli through the skin-to-skin contact, auditory and olfactory stimuli<sup>8,14,33</sup>.

In this category of studies, ten articles were selected that used the kangaroo mother method/kangaroo care/skin-to-skin contact, in order to assess its effectiveness as a pain relief measure.

In a systematic review<sup>34</sup>, We analyzed findings from randomized controlled trials that tested the effects of behavioral and environmental procedural pain management interventions on behavioral pain response in preterm infants. The study found that across all age groups, methods such as: facilitated tucking, oral sucrose, and the kangaroo position only reduced the behavioral and physiological pain response in combination with other behavioral and environmental interventions. In conclusion, the study found that facilitated restraint, oral sucrose, and the kangaroo position significantly alleviate pain in the biobehavioral pain response related to painful procedures in preterm infants.

In a blinded randomized control trial<sup>35</sup>, methods were used: skin-to-skin contact and oral sucrose to compare the effectiveness in pain management in premature newborns. About 100 neonates who underwent the heelprick procedure were divided into two groups, half were part of the skin-to-skin contact group and the other half were part of the oral sucrose group. The skin-to-skin contact group used this method 10 minutes before the procedure. The second group received 0.2 ml of oral sucrose two minutes before the procedure. PIPP assessment was performed 30 seconds after the procedure. From the PIPP result, it was noticed that the score of the skin-to-skin contact group was lower than that of the oral sucrose group, but not significantly. The study came to the conclusion that both skin-to-skin contact and oral sucrose are similarly effective in controlling pain in premature babies.

Authors<sup>35</sup> compared individual efficacy and additive effects of pain management measures in preterm infants. Kangaroo mother care (kangaroo position offered by the mother), music therapy and expression of breast milk were used as non-pharmacological pain relief measures. The PIPP score was significantly lower in the kangaroo mothering group and in the kangaroo mothering with music therapy group compared to the control group. The study observed that kangaroo mother care with or without music therapy associated with expressed breast milk significantly reduces pain during the painful procedure of heel puncture when compared to the exclusive use of expressed breast milk. Thus, kangaroo mother care in conjunction with expressed breast milk should be the first option as a pain management measure in premature babies.

A research<sup>36</sup> sought to verify the effect of skin-toskin care on neonatal pain during painful medical and nursing procedures in neonates, in comparison with the application of no intervention, the application of sucrose or other analgesics, or the addition of rocking during skin-to-

#### Non-pharmacological methods for pain relief in premature neonates

Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM skin care . It also sought to determine the incidence of adverse effects of skin-to-skin care, in addition to comparing the effect of skin-to-skin care in different subgroups of children. Standard methods from the Cochrane Neonatal Collaborative Review Group were used. A total of twelve databases were searched. Of the nineteen studies included, 15 used heel sticks as a painful procedure; 1 combined venipuncture and heel puncture; 2 used intramuscular injection and 1 used vaccination. Eleven studies compared skin-to-skin care alone to an untreated control, all of which measured heart rate during painful procedures. Three studies that were not included in the meta-analysis found no difference in heart rate after the painful procedure. Two studies exposed variability in heart rate results, without significant differences. Five studies used PIPP as the primary outcome, which benefited skin-to-skin care at 30, 60 and 90 seconds, but at 120 seconds there was no difference. None of the studies provided findings on heart rate return to baseline, oxygen saturation, cortisol levels, crying duration, and facial actions that could be entered into the analysis. Eight studies compared skin-to-skin care with another intervention. Two crossover studies compared the mother with another provider on PIPP scores at 30, 60, 90, and 120 seconds, with no significant difference. One study compared kangaroo care with and without dextrose and found that the combination was more effective and that skin-to-skin care alone was more effective than dextrose alone. Another study showed that skin-to-skin care was more effective than oral glucose for heart rate but not for oxygen saturation. Skin-to-skin care combined with breastfeeding or alone was favored over an untreated control, but not different from breastfeeding.

In conclusion, the study revealed that skin-to-skin care appeared to be effective when measured by composite pain indicators and including physiological and behavioral parameters, in addition to being safe for a single painful procedure. It was observed that behavioral indicators tended to favor skin-to-skin care, despite the persistence of a questionable bias. The physiological ones, in general, did not show differences between the conditions. There were greater differences in studies with behavioral outcomes.

Authors<sup>37</sup> evaluated the effectiveness of kangaroo mother care and alternative kangaroo care provided by other mothers postpartum and swaddling for postprocedure pain relief in preterm infants. Fifty-one premature newborns were divided into: kangaroo mother care (kangaroo position offered by the mother), alternative female kangaroo care (kangaroo care provided by other mothers who agreed to act as alternative providers for the baby because the mothers were not in health conditions to care for the newborn and also because they did not receive support from female relatives) and swaddling (a procedure in which the babies were placed in the incubator in a prone position and wrapped in a blanket) for 30 minutes before the heel puncture. Outcomes included PIPP scores at 30 seconds and the time taken for heart rate to return to baseline. Mean PIPP scores were lower in the kangaroo mother care and alternative female kangaroo care groups, and heart rate normalization took less time in these same groups. Kangaroo



mother care fared better than kangaroo care for pain and heart rate. The study concluded that both providing kangaroo mother care and alternative female kangaroo care prior to heel puncture resulted in better pain relief compared to coiling.

A study<sup>8</sup> verified the effectiveness of the Kangaroo Method (care offered by the mother in which there is stimulation of touch through skin-to-skin contact, in addition to other stimuli such as auditory and olfactory) in relieving pain during neonatal heel puncture. Fifty-six neonates participated in the study, and they were divided into two groups: a group of neonates submitted to kangaroo care and a control group. The physiological responses of neonates were evaluated, including: heart rate, oxygen saturation, duration of crying and PIPP scores, before, during and one minute and two minutes after heel puncture. It was found that the heart rate in the group of newborns submitted to kangaroo care was lower in one and two minutes than in the control group. PIPP scores in the group of neonates undergoing kangaroo care were significantly lower during and after sampling. The duration of crying for neonates submitted to kangaroo care was around 10% of the duration of the control group. In this way, the study concluded that the kangaroo method can be an effective intervention in the relief of pain in premature neonates.

In a single-blind crossover study<sup>38</sup>, the effect of the Kangaroo Mother Care (it is a physiological intervention involving the parents) on the response to pain in preterm neonates was investigated. We also tried to determine the behavioral and physiological responses to painful stimuli in premature neonates. One hundred and forty neonates were enrolled and the pain stimulus was given by means of heel puncture before and after the execution of the method under study. Heart rate variability in the Kangaroo Mother Care group was statistically significant in preterm and very low birth weight infants. The mean drop in SpO2 from baseline was smaller in the Kangaroo Mother Mother group compared with the no-method group at 60 seconds and 120 seconds. Mean duration of crying and PIPP was significantly shorter in the Kangaroo Mother Care group compared to the non-Kangaroo Mother Care group. In the Kangaroo Mother Care group, it was significantly lower after heel puncture at 60 seconds. It was concluded that the Kangaroo Mother Care is a more physiological and beneficial intervention in pain control that can be implemented for physiological or behavioral stability in preterm infants.

Authors<sup>33</sup> investigated whether during venipuncture performed in premature babies, it would be possible for skin-to-skin contact to provide pain relief, measured with Near Infrared Spectroscopy (NIRS). Ten babies were analyzed during a venipuncture blood sampling procedure in two conditions: in skin-to-skin contact with their mother or lying in the incubator or crib. The NIRS device was used, and oxygen saturation and heart rate values were monitored by pulse oximetry. The baby's face and pulse oximetry values were recorded throughout the procedures for assessing pain using PIPP. There was a significantly smaller increase in oxygenated hemoglobin during venipuncture when skin-to-skin contact was applied

#### Non-pharmacological methods for pain relief in premature neonates

Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM compared to when babies were in the incubator or crib. Comparing venipuncture with a simulated procedure, oxygenated hemoglobin increased significantly more when they were in the incubator or crib than when in skin-to-skin contact. There was no significant difference in PIPP outcome between groups. The study found that skin-to-skin contact of premature babies with their mothers during venipuncture had an analgesic effect.

A study<sup>39</sup> investigated the effect of acupressure on the Kun Lun (UB60) and Taixi (K3) points for pain control in premature infants before heel puncture for blood collection. The babies were divided into two groups and the acupressure group received application for three minutes at points UB60 and K3 immediately before heel puncture. There were no significant differences between groups with regard to gestational age, birth weight, gender, type of delivery, age at procedure, weight at procedure, or PIPP score. The mean duration of both the procedure and crying were shorter in the acupressure group. The study showed that acupressure at points BL60 and K3 before heel puncture is associated with minor: procedure time and crying duration.

Authors<sup>10</sup> tested the effectiveness of the Kangaroo Mother Care on repeated heel pain in premature newborns. Eighty premature babies were divided into two groups, namely: incubator group and Kangaroo Mother group (defined by the author as the vertical position of the baby covered in diapers, skin-to-skin and chest-to-chest with an adult). Pain assessments took place during four routine heel puncture procedures. In the first puncture, babies in both groups did not receive any intervention (they remained in the incubator). In the next three punctures, babies in the Kangaroo Mother Care group received heel punctures with Kangaroo Mother Care; in contrast, babies in the incubator group received punctures in the incubator. The procedure for each puncture included three phases: baseline, blood collection, and recovery. Aspects such as crying, grimaces and heart rate in response to pain were assessed at each phase through four heel punctures. Comparison between the two groups showed that the heart rate of preterm infants was significantly lower, and the duration of crying and grimacing were significantly shorter in the Kangaroo Mother group than in the incubator group, from the blood collection phase to the recovery phase. during repeated heel punctures. There was no significant difference, for the Kangaroo Mother Care group, in heart rate between the initial phase and the recovery phase through repeated heel punctures. The incubator group achieved significant withingroup differences in heart rate between baseline and recovery across repeated heel sticks. Therefore, the study concluded that the effect of repeated analgesia in the Kangaroo Mother Care remains stable in premature babies during the performance of repeated painful procedures. Because the routine of these premature babies in the unit requires painful and invasive procedures, most mothers choose to provide relief and comfort for their babies during these procedures. The Kangaroo Mother Care can be a safe analgesic alternative for these babies.



# Discussion

By analyzing the objectives, results and conclusions of the articles included in the systematic review, it was possible to observe the variety of resources that can be used to relieve pain in premature newborns, the effectiveness of the methods, the benefits brought about by these practices, especially in the long term. in the baby's development, methods most commonly used in the units in contrast to others less applicable and known. The analysis of the studies made it possible to perceive how nursing care is given to premature newborns hospitalized in the NICU, in order to provide pain relief in the performance of different painful procedures and, therefore, in favoring the least possible discomfort during the stay of this clientele in the unit.

# **Oral stimulation**

In this category, six studies were found<sup>11,14-17,32</sup>. One study associates non-nutritive sucking with sucrose<sup>11</sup>, two studies used sucrose alone<sup>14,32</sup>. Another study associates sucrose with breast milk<sup>15</sup>. One study used breast milk or 10% dextrose16. One study compared the effect of a combination of sucking, breast milk, restraint and routine care<sup>17</sup>.

Of the six studies, each one obtained different results for painful procedures, namely: one article cites unspecified painful procedures<sup>32</sup>, four heel puncture articles<sup>11,12,17,18</sup> and a venipuncture article<sup>16</sup>.

As for pain assessment scales, one study used the NAPI scale<sup>32,</sup> one study used the NFCS scale, Clinical Risk Index for Babies and NCR<sup>14</sup> and four used the PIPP scale<sup>11,15-17</sup>.

Studies<sup>16,17</sup> evaluated the effect of sucrose alone. He came to the conclusion that sucrose alone was effective in relieving pain in premature newborn babies. The longterm use of sucrose appears to be free of adverse effects. A study<sup>10</sup> used non-nutritive sucking compared to sucrose in opposition to research<sup>16,17</sup>, as he states that the effect of sucrose is better combined with non-nutritive sucking than alone.

In line with the method of pain relief using sucrose, a study<sup>40</sup> mentions that oral sucrose acts by two mechanisms. The sweet sensation stimulates the palate to activate the cortical area related to pleasure. And the second is the action of endogenous opioids, occupying nociceptors and modulating the transmission of pain stimuli. This study found that sucrose used alone or combined with another method is effective with an analgesic effect in painful procedures.

In line with the relief method of non-nutritive sucking associated with sucrose, one study<sup>41</sup> mentions that non-nutritive sucking is used alone in a few studies, but combined with oral sucrose is more effective.

Studies<sup>18,19</sup> agree when using something with a sweet taste with breast milk, where the first study<sup>18</sup> uses sucrose with breast milk for pain relief during venipuncture and the second study<sup>19</sup> compared whether the administration of breast milk or 10% dextrose in the oral cavity could reduce heel puncture pain. Breastfeeding is preferred and 10% dextrose as a second option. Both are

Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM safe, however, on the other hand, the second study19 states that in extremely premature babies, sucrose alone works better.

A research<sup>20</sup> compares the effect of the combination of sucking, breast milk; containment and routine care about the baby's pain. It concludes that these methods in combination effectively reduce the heel puncture pain.

In line with the study, citing breast milk in pain relief, a research<sup>42</sup> demonstrates that breast milk has the advantage of being a low-cost method. The study points to the effectiveness of breast milk components such as tryptophan and melatonin, which elevates beta endorphins, helping in the pain process, providing an analgesic effect. Can be used alone or in combination.

#### Organization and coziness stimuli

Within this category, eight studies were found<sup>2, 3, 5, 8-10, 34, 36</sup>, where in one study, network positioning was used in comparison to traditional positioning<sup>2</sup>. One study used the pacifier and winding<sup>10</sup>. Four studies used facilitated restraint, and in three of these it was used alone and in one it was used in comparison with non-nutritive sucking<sup>5,8,34,36</sup>. A study<sup>9</sup> used facilitated containment, sucrose and wrapping, evaluating which methods are most used by nurses to relieve pain in premature newborns<sup>3</sup>. One study compared a sponge bath to a wrap bath.

Of the eight studies, different results were obtained for painful procedures, namely: One study investigated venous access and heel puncture, endotracheal aspiration and venipuncture. One study used invasive procedures that were not specified, one study used venipuncture, three studies used heel stick. One study did not use an invasive procedure<sup>2,3,5,8-10,34,36</sup>.

In this category, three studies used the PIPP scale to detect the level of pain. In addition to the PIPP scale, other scales were used. One study used PIPP and NFCS, Brazelton Neonatal Behavioral Assessment Scale, one study used the Newborn Stress Scale (NSS). One study used a questionnaire and observation of nurses in the use of non-pharmacological methods of pain relief in premature newborns, one study used the Cochrane database. One study used the DAN scale (French acronym for the Acute Pain Off Newborn)<sup>3,5,8,10,34,36</sup>.

A study<sup>21</sup> revealed that providing a pacifier and winding it up can prevent an increase in the baby's pain index and heart rate in invasive procedures.

In agreement with this study<sup>21</sup>, in which winding decreases the pain index, official document<sup>43</sup> mentions the importance of this method for the preterm baby because it acts on proprioceptive, tactile and thermal receptors, providing stimuli that can compete with pain and stress, bringing some benefits such as: quieting the baby, decreasing heart rate, reduce pain, decrease saturation drops, improve neuromuscular development in very low birth weight babies. It is most effective when performed before the painful procedure. The limbs and hips are kept flexed and the hands close to the face, and adequate thoracic excursion must be confirmed. It can be used in babies who are monitored and clinically stable.



In line with the pacifier pain relief method, research<sup>44</sup> brings the finding that the use of a pacifier in premature babies admitted to the NICU inhibits hyperactivity and reduces the discomfort of the newborn. It helps the child to organize himself after stressful stimuli, reducing the physiological and behavioral repercussions.

Authors<sup>22</sup> use the sponge bath and the wrap bath where there were significant differences between the bathing methods in vital signs, oxygen saturation levels and crying. Stress and pain levels according to the type of bath were significantly higher in the sponge bath.

In agreement with the given study<sup>22</sup>, which reports the difference between a wrap bath and a sponge bath, official document<sup>43</sup> mentions that bathing is characterized by excessive handling of the baby. Sponge bath in premature infants before and after was investigated. There was an increase in the number of heartbeats and a decrease in oxygen saturation. Thus, it is understood the need to respect the baby's behavioral state, ask the mother for help in the procedure, start the bath from the face and without using soap, use wrapping with the newborn immersed in water in a towel or diaper, being removed as you soap the newborn.

Studies<sup>24,25</sup> associated facilitated containment, determining its effect in reducing the pain of preterm infants in invasive procedures. Researches<sup>23,25</sup> identified that there is a need for investigation and deepening in relation to facilitated containment.

A research<sup>26</sup> associates facilitated containment with non-nutritive suction in opposition to the others, as he reports that the combined use of facilitated containment and non-nutritive suction does not significantly relieve pain during the heel puncture procedure. On the other hand, he says that the addition of facilitated containment enabled a quick recovery after heel puncture.

In accordance with the containment facilitated pain relief method, official document<sup>43</sup> mentions that it is a variation of positive touch, where it uses gentle motor restraint of flexed arms and legs, in lateral or supine decubitus. The very firm but elastic containment is responsible for sending stimuli to the central nervous system that compete with stimuli that are painful, modulating the perception of pain in painful procedures with less intensity.

Study<sup>27</sup> evaluated the knowledge of professionals regarding non-pharmacological methods of pain relief in premature newborns, concluding that it would be essential to review nurses' knowledge and skills regarding standard pain management interventions during painful procedures.

A study<sup>45</sup> recommends the need for nurses and technicians to have satisfactory knowledge and understanding to provide correct pain relief for the baby, according to their needs.

Research<sup>28</sup> reports that hammock positioning was an effective treatment option to minimize pain and improve sleep and wakefulness in premature newborns.

Authors<sup>46,47</sup> explain that positioning in the hammock consists of placing the premature newborn in a hammock inside the incubator. These hammocks are in sizes suitable for incubators, providing comfort to the baby without causing damage. Thus, they should be used in babies

Non-pharmacological methods for pain relief in premature neonates Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM who do not need respirators.

The same authors concluded that in the hammock, the premature baby can adhere to a more physiological posture, flexed and similar to the position he was in the mother's womb, reducing the baby's stress, bringing comfort, helping in sensory integration and protection<sup>46,47</sup>.

# Auditory stimuli

Of the seven studies<sup>1,6,12,21,23,25,27</sup> envolvendo esta categoria: dois usaram a glicose, um na comparison with white noise and another with listening to lullabies. One study evaluated the effect of recorded maternal voice, breast milk odor and incubator cover.

A study<sup>21</sup> compared neonatal and therapeutic variables in premature newborns exposed to music and 25% oral glucose. One study used the combined intervention of music and touch<sup>23</sup>. One study looked at physiological and behavioral parameters in premature babies when they listened to the same music their mothers listened to during pregnancy<sup>25</sup>. Another study used white noise<sup>27</sup>.

Of this total of seven articles, each one covered a different painful procedure. In addition, the evaluative methods of pain response used in neonates were different, prevailing, however, in five studies<sup>1,6,12,23,27</sup>, the PIPP scores.

A research<sup>30</sup>, in their conclusion, it shows that white noise combined with glucose reduces pain and keeps vital signs stable in premature babies. Corroborating this study, article<sup>48</sup> reveals that the odor of breast milk, the recorded mother's voice and the cover of the incubator are recommended interventions because they are simple, safe stimuli that lead to positive effects during painful procedures. The studies<sup>15,29</sup> also confirmed the improvement in pain response to painful stimuli through combined music and touch intervention and music that mothers listened to during pregnancy, respectively.

In contrast to the aforementioned studies, the articles<sup>9,31</sup>, despite revealing a reduction in pain in premature neonates from the use of interventions such as lullabies or glucose and white noise respectively, they emphasize the need for further studies on the subject to more accurately identify their benefits. An article<sup>32</sup> menciona que não houve diferença na comparação das interventions with music and 25% glucose, in addition to the other variables studied.

White noise was recommended in two studies for pain control<sup>1,27</sup>, glucose was recommended in three studies<sup>1,6,21</sup>, lullabies were recommended in one study<sup>6</sup>, recorded maternal voice was recommended in one study as well as the odor of breast milk and incubator cover<sup>12</sup>, music was recommended in one study<sup>25</sup>, as well as music combined with touch<sup>23</sup> and listening to the music mothers listened to during pregnancy<sup>25</sup>.

In the NICU environment, premature newborns are exposed to unexpected sensory stimuli in a period of rapid brain growth and differentiation, which may be related to the difficulty in responding to auditory stimuli not only during, but also after, hospitalization. The manual cites factors that differentiate the acoustic environment of a NICU from that of a gravid uterus, such as: air conduction; external



acoustic frequencies in general; loud to very loud sound; broad spectrum of non-salient signals, with no pattern, in the midst of highly competitive background noise; no or few discernible patterns and absence of circadian rhythms, related to chaotic daily experiences, factors that cause discomfort to preterm newborns because it is an atypical environment to which they were accustomed when accommodated in the womb. In addition, the manual mentions frequent problems related to noise in the units, such as alarms, crying babies, handling the incubator, among others, and at the same time presents some possible solutions for them, how to respond promptly to alarms and cries, be careful when handling all parts of the incubator, do not hit the incubator with your fingers, among others<sup>43,49</sup>.

In this way, it can be pointed out that a careful evaluation of the NICU space in general needs to be taken into account in the use of non-pharmacological methods for pain relief related to auditory stimuli, in order to provide comfort and a less negatively impacting stay to the patient. hospitalized newborn.

# **Kangaroo Method**

Of the ten articles<sup>4,7,13,22,24,29-31,33,35</sup> selected for this category: One study reviewed randomized controlled trials that tested the effects of behavioral (including kangaroo mother care) and environmental procedural pain management interventions on behavioral pain response in preterm infants<sup>4</sup>. Two studies compared skin-to-skin contact/kangaroo mother care with other interventions, namely: oral sucrose in one study<sup>7</sup> and, music therapy and breast milk expression in another<sup>13</sup>. One study sought to verify the effect of skin-to-skin contact alone on pain in painful procedures, compared to no intervention, sucrose or other analgesics, or addition to simple skin-to-skin care, such as rocking; in addition to determining the incidence of adverse effects from skin-to-skin contact and comparing the effect of this intervention in different subgroups of children<sup>22</sup>. Three studies evaluated the effectiveness of kangaroo mother care/kangaroo care in pain relief<sup>24, 29, 35</sup>. One study investigated the effect of kangaroo mother care on pain response in addition to assessing behavioral and physiological responses to painful stimuli in preterm infants<sup>30</sup>. One study used NIRS to investigate whether skinto-skin contact could provide pain relief during a painful procedure<sup>31</sup>. Another study investigated the effect of acupressure on the Kun Lun (UB60) and Taixi (K3) points for pain control in premature babies undergoing a painful procedure<sup>33</sup>.

Of the ten studies, each one encompassed one or more type(s) of painful procedure(s). In this category, among the different evaluation methods used, the PIPP prevailed, totaling eight studies<sup>7,13,22,24,29-31,33</sup> who used the same.

Researches<sup>34,37</sup> associated kangaroo care with other interventions such as facilitated folding and oral sucrose; and, alternative female kangaroo care respectively, where both revealed improvement in pain relief when performing painful procedures. Authors<sup>35</sup> compared skin-to-skin contact/kangaroo care with other interventions, namely: sucrose and music therapy (with expressed breast milk) Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM respectively, in which there was no difference in efficacy for skin-to-skin contact and sucrose, and kangaroo care with expressed breast milk was indicated as the best choice in pain control. Studies<sup>8,10,33,38</sup> também showed that kangaroo care is beneficial and favors pain relief in premature newborns.

In a research<sup>36</sup>, a counterpoint is revealed in relation to the others. Although the authors emphasize that skin-to-skin contact seems to be effective in controlling pain, there is a questionable bias in relation to the behavioral indicators evaluated to measure the response to pain, thus requiring further studies on the subject for better clarity.

Authors<sup>39</sup> revealed that acupressure at points BL60 and K3 was favorable in response to pain.

Studies have proven that kangaroo care is beneficial in relieving pain for neonates. Five studies used only one intervention<sup>29-33,35</sup>, one associated two interventions in the same painful procedure<sup>7</sup> and four compared different nonpharmacological interventions in pain relief<sup>4,13,22,24</sup>.

Study<sup>7</sup> discusses the paternal role in performing the kangaroo position for low birth weight newborns. The authors deal with the important and necessary participation of the father in the face of the hospitalization situation experienced by the child and the benefits arising from this practice that goes far beyond the improvement of the baby's clinical condition, generating above all a bond and appropriation of the father figure.

It is emphasized that the kangaroo method refers to the extremely important component in the development of the baby. Experience of containment, breastfeeding, development of security and bonding are some of the benefits obtained from skin-to-skin contact that favors not only the baby, but also the mother-baby binomial. The manual highlights that this care can be carried out both in the NICU and in the Intermediate Unit and can be experienced when the baby is stable from a clinical point of view and when the parents so wish<sup>43</sup>.

Therefore, given the advantages that the kangaroo position provides, adherence to this non-pharmacological method is valid whenever possible, since in addition to bringing mother and child closer, it helps in the development of the baby.

#### **Final Considerations**

Based on the data brought in the studies, it is clear that premature babies exposed to painful procedures during their hospitalization can and should receive pain relief interventions, favoring not only their stay and comfort in the passage through the NICU, but also mitigating the chances of harm. futures. It is up to professionals, including nurses, to assess the best possibilities on a case-by-case basis and provide the most appropriate interventions according to reality.

Care for premature newborns in the NICU requires special attention from professionals. Within this circumstance, it is necessary to emphasize the importance of the NB's pain sensitivity, as practices adopted within the NICU generate pain and stress for the hospitalized baby, bringing some consequences for its development and



complete recovery of health. By alleviating the pain of these preterm infants, it is possible to promote the improvement of their discomfort and provide a significant improvement in their health conditions.

The elaboration of the present study broadened the vision, making it possible to observe some strategies that not only can be adopted for pain relief, but should also be carried out by the team responsible for the care of newborns admitted to the NICU, thus providing a significant improvement in pain relief. pain through non-pharmacological practices.

# Non-pharmacological methods for pain relief in premature neonates

Pereira TS, Silva PF, Pacheco STA, Marta CB, Silva LJ, Araújo BBM The lack of knowledge regarding nonpharmacological methods before the multidisciplinary team is present, requiring training of the team so that the provision of humanized and quality assistance to these hospitalized babies occurs.

In view of the above, there is a need for further studies for the adoption and applicability of nonpharmacological methods in pain relief, so that there is an improvement in the quality of care and humanization in the assistance of this vulnerable population.

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