

NON-PHARMACOLOGICAL METHODS FOR NEONATAL PAIN MANAGEMENT: AN INTEGRATIVE REVIEW

MÉTODOS NÃO FARMACOLÓGICOS PARA MANEJO DA DOR NEONATAL: UMA REVISÃO INTEGRATIVA

MÉTODOS NO FARMACOLÓGICOS PARA EL TRATAMIENTO DEL DOLOR NEONATAL: UNA REVISIÓN INTEGRATIVA

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Objective: to identify non-pharmacological methods used as pain management in newborns described in the literature. **Method:** an integrative literature review conducted in the Virtual Health Library, Cochrane, Embase, PubMed and Scopus databases from February to May 2023. The sample consisted of 32 studies. **Results:** there are several strategies applied for neonatal pain relief, such as oral administration of sweet solution, skin-to-skin contact, aromatherapy, laser acupuncture, music therapy and regional massage. The evaluation of pain scales, chronometer and cardiac monitor showed that most of the interventions were effective in the management of pain in the newborn. **Final considerations:** there are several non-pharmacological therapies described in the literature and the importance of their applicability is highlighted in order to reduce the negative impacts caused by frequent exposure to pain in the newborn.

Descriptors: Infant. Newborn. Complementary Therapies. Pain Management. Pain. Neonatology.

Objetivo: identificar os métodos não farmacológicos utilizados como manejo da dor em recém-nascidos descritos em literatura. **Método:** revisão integrativa da literatura realizada nas bases de dados Biblioteca Virtual em Saúde, Cochrane, Embase, PubMed e Scopus nos meses de fevereiro a maio de 2023. **A amostra foi composta por 32 estudos.**

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Resultados: há diversas estratégias aplicadas para o alívio da dor neonatal, como administração oral de solução adocicada, contato pele a pele, aromaterapia, acupuntura a laser, musicoterapia e massagem regional. Mediante a avaliação de escalas de dor, cronômetro e monitor cardíaco, notou-se que a maior parte das intervenções foram eficazes no manejo da dor no recém-nascido. Considerações finais: há diversas terapias não farmacológicas descritas em literatura e destaca-se a importância de sua aplicabilidade, a fim de reduzir os impactos negativos provocados pela frequente exposição à dor no recém-nascido.

Descritores: Recém-nascido. Terapias complementares. Manejo da Dor. Dor. Neonatologia.

Objetivo: identificar los métodos no farmacológicos utilizados como manejo del dolor en recién nacidos descritos en literatura. Método: revisión integrativa de la literatura realizada en las bases de datos Biblioteca Virtual en Salud, Cochrane, Embase, PubMed y Scopus en los meses de febrero a mayo de 2023. La muestra consta de 32 estudios. Resultados: hay diversas estrategias aplicadas para el alivio del dolor neonatal, como administración oral de solución endulzada, contacto piel a piel, aromaterapia, acupuntura láser, musicoterapia y masaje regional. Mediante la evaluación de escalas de dolor, cronómetro y monitor cardíaco, se notó que la mayor parte de las intervenciones fueron eficaces en el manejo del dolor en el recién nacido. Consideraciones finales: hay diversas terapias no farmacológicas descritas en literatura y se destaca la importancia de su aplicabilidad, a fin de reducir los impactos negativos provocados por la frecuente exposición al dolor en el recién nacido.

Descriptores: Recién Nacido. Terapias Complementarias. Manejo del Dolor. Dolor. Neonatología.

Introduction

According to the International Association for the Study of Pain (IASP), pain is “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”^(1:14). Thus, neonatal pain is when this bad sensation occurs in an individual with a maximum age of 27 days⁽²⁾.

Until the mid-1980s, due to the precariousness of scientific knowledge in neonatology, it was believed that newborns (NBs) were unable to perceive pain due to the immature nervous system of this public⁽³⁾. In view of this, invasive procedures, although considered painful, were performed without any analgesic intervention, including some surgeries⁽⁴⁾. However, with the advancement of scientific studies, the existence of neonatal pain was perceived through physiological, behavioral and hormonal changes in the newborn⁽⁵⁾.

With scientific progress, it has become possible to discover negative impacts on human development due to the accumulation of neonatal pain⁽⁶⁾. These consequences can immediately affect the NB, through the regulation of body temperature and the sleep-wake cycle or, subsequently, through cognition, emotions and the physiological structure of the individual⁽⁴⁾.

That said, it is necessary to previously identify all painful procedures and promote effective treatment

during their applicability, aiming to reduce negative impacts on human development⁽⁴⁾. Studies indicate that, due to physiological immaturity and altered metabolism, pharmacological treatments for pain management during small painful interventions in the NB are not recommended⁽⁷⁾. Therefore, non-pharmacological methods and complementary therapies are major allies in these situations⁽⁸⁾.

Within this context, the World Health Organization⁽⁹⁾ defines traditional, complementary and integrative medicine (TCIM) as the sum total of knowledge, skills and practices based on theories, beliefs and different cultures, that are not part of the current conventional medicine. It is used as a pillar or complement in the provision of health services, including pain management, in almost all countries. Although some elements are similar, each State has autonomy to develop its own nomenclatures, classifications and practices⁽⁹⁾.

Since then, in 2019, our country has implemented TCIM in the public health system, adding 29 Integrative and Complementary Health Practices (IChP) to Law 8080, of September 19, 1990⁽¹⁰⁾. However, in addition to IChP, there are other non-pharmacological economic strategies with easy application indicated as adjuvants or even substitutes for some analgesic medications, such as breastfeeding, skin-to-skin contact, non-nutritive

sucking, among others. Therefore, it is recommended that each health service establish the most effective method according to its reality⁽²⁾.

It is known that nurses are extremely active in the care of the health of the NB and that, within their professional practice, they guarantee the patient a safe environment, identify neonatal pain and execute strategies for its management⁽¹¹⁾. In addition, nurses are responsible for promoting team and family members frequent health education, strengthening the implementation of non-pharmacological strategies for pain management in health services and also at home⁽¹²⁾.

Although there are several studies that address neonatal pain, its consequences on the development of the child and the importance of its treatment, underreporting and subtraction of this pain still occurs in our country⁽⁴⁾. Therefore, knowing that in addition to the ICHP established in law, there are other non-pharmacological practices that, when performed, can guarantee a significant reduction in the negative impacts resulting from the accumulation of neonatal pain, thus the following research question was elaborated: What are the non-pharmacological methods used for pain management in newborns described in the literature?

This research aimed to identify the non-pharmacological methods used as pain management in newborns described in the literature.

Method

This is an integrative review (IR), based on the five stages proposed by Cooper⁽¹³⁾. This methodology consists of grouping the results obtained in primary research on the same subject, with distinct designs, aiming to synthesize and analyze the data collected, in order to develop a more comprehensive explanation of a specific phenomenon⁽¹³⁾.

The formulation of the problem⁽¹³⁾ was constituted by the guiding question: What are the non-pharmacological methods used for pain management in newborns described in the literature?

Evidence-Based Practice (EBP) provides methodologies to identify evidence and effectiveness

of a specific phenomenon or treatment, strategies for critical evaluation of the quality of studies found and mechanisms for the implementation of these phenomena in care⁽¹⁴⁾.

Within the EBP⁽¹⁴⁾, there are four components that are fundamental in the construction of the research question with interventions for a satisfactory bibliographic search and that can be organized through the acronym PICO, being considered: P = target population, I= intervention, C= comparator and O= Outcome. Thus, when applying this strategy in the research question of this study, we obtain: P= newborns, I= not applicable, C= not applicable, O= non-pharmacological methods used for pain management in newborns described in the literature.

The second stage defined the criteria used to search for the selected studies to compose this integrative review. The databases listed for the search and selection of materials related to the theme were: Virtual Health Library (VHL), Cochrane Library, Embase, PubMed and Scopus.

The descriptors used to search for the materials were extracted from the Health Science Descriptors (DeCS/MeSH), in English and Portuguese, aiming to find as many documents as possible to answer the research question. Then, the following descriptors were selected: *recém-nascido* (infant newborn), *terapias complementares* (complementary therapies), *manejo da dor* (pain management), *dor* (pain) and *neonatologia* (neonatology), using the Boolean operators "AND" and "OR" for crossing these descriptors.

The inclusion criteria for the selection of studies were articles available in full, in English, Spanish and Portuguese, published between 2018 and April 2023, which presented as target population newborns, regardless of their gestational age at birth. Materials such as review article, study protocols, studies conducted with children aged 28 days or older and studies that exclusively addressed pharmacological methods for pain relief were excluded. Data collection occurred between February and April 2023.

During this process, a collection instrument was developed in order to organize and

obtain better visualization of the extracted data. Subsequently, only the documents related to the theme were included, as well as answering the guiding question of the research. This collection instrument was constructed and structured containing the following information: title, year of publication, country of origin, author, journal, area, objective, type of publication, methodology, level of evidence, definition of population and sample, results and considerations of the authors.

The selected articles were classified by the level of evidence⁽¹³⁾, namely: level 1 – systematic review, meta-analysis of multiple studies, or from guidelines of all Randomized Controlled Trials; level 2 – well-designed randomized controlled trials; level 3 – well-designed, non-randomized trials; level 4 – case-control or cohort studies; level 5 – systematic reviews of descriptive and qualitative studies; level 6 – descriptive or qualitative studies; level 7 – evidence of the opinion of experts and/or reports arising from expert committees.

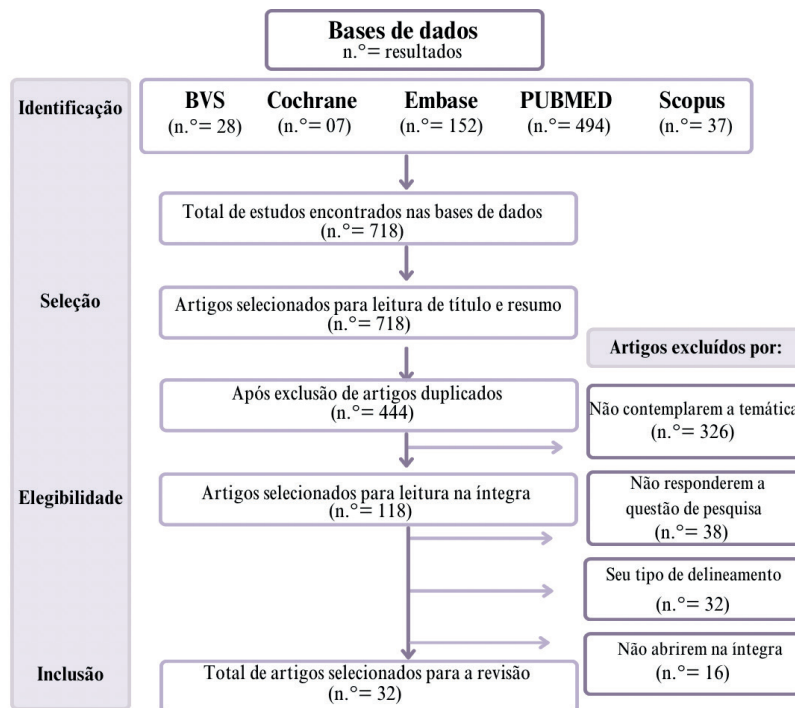
For data analysis and interpretation, the various information of the selected studies contained in the data collection instrument were synthesized and recorded in a synoptic chart to group and compare points relevant to the objective of the study, facilitating the process of data interpretation.

This IR was carried out considering the ethical aspects, maintaining the legitimacy of the information and the authenticity of ideas, concepts and definitions, as dealt with Law N. 9.610, of February 19, 1998.

Results

In order to present the report of this integrative review in a coherent and organized manner, the PRISMA flowchart was applied (Figure 1), which aims to help authors in qualifying the reports of their scientific works, systematic reviews, meta-analyses or integrative reviews⁽¹⁵⁾.

Figure 1 – PRISMA Flowchart



Source: created by authors.

Figure translation: From top to bottom - Databases n=results. Identification. VHL (n=28); Cochrane (n=07); Embase (n=152); PUBMED (n=494); Scopus (n=37). Selection. Total of studies found in the databases (n=718). Articles selected to read title and abstract (n=718). Articles excluded due to: Not meeting the theme (n=326); Not answering the research question (n=38); Type of design (n=32); Incomplete (n=16). Eligibility. After exclusion of duplicated articles (n=444). Articles selected for full reading (n=118). Inclusion. Total of articles selected for review (n=32).

There were studies compatible with the subject from 14 different countries, with India and Turkey being the countries with the highest number of publications, totaling 5 articles each, 31.25% of the total selected documents. Then Brazil, Iran and Switzerland with 4 publications each (37.5%); Spain with 2 studies published (6.25%); and with a single publication: Austria, China, United States, Indonesia, Italy, Nigeria, Pakistan and Sweden (25%). Regarding the language, 93.75% of the articles were in English, 6.25% in Portuguese and none in Spanish.

Regarding the design, 96.88% were clinical, controlled, randomized and only 3.12% were observational, prospective clinical studies. As for the level of evidence, the highest found was level 2 in 31 articles, and only one level 3.

It is important to emphasize that some studies applied more than one non-pharmacological method during the research, seeking to compare and/or unite different interventions, aiming at

validating their effectiveness. Ten of the studies used breast milk as a multisensory factor, that is, both taste and odor were tested. In addition to breast milk, 14 studies addressed different types of sweetened nutritional solutions, such as glucose⁽⁵⁾, sucrose⁽⁵⁾, dextrose⁽³⁾ and melatonin⁽¹⁾. However, non-nutritive suction was also exposed in 3 published articles.

In addition, some other non-pharmacological treatments were used, such as Yakson⁽²⁾, gentle human touch⁽¹⁾, regional massage⁽¹⁾, reflexology⁽¹⁾ and sensory saturation⁽¹⁾. Other care was also applied, such as bandage⁽²⁾, facilitated fold⁽²⁾, reduced luminosity⁽²⁾, ear protection⁽¹⁾, skin-to-skin contact⁽¹⁾ and net⁽¹⁾. However, only 9 non-pharmacological methods can be considered, according to the Brazilian Law of Integrative and Complementary Health Practices: music therapy⁽⁵⁾, essential oils⁽³⁾ and acupuncture⁽¹⁾. For better understanding, the articles were numbered in sequential order, then (A1, A2, A3...) (Chart 1).

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A1	Laser acupuncture versus oral glucose administration for pain prevention in term neonates: an observer-blinded non-inferiority randomized controlled clinical trial. Stadler J, Avian A, Pichler G, Posch K, Urlesberger B, Raith W ⁽¹⁶⁾ . 2021	Quantitative research: controlled, randomized clinical trial with a blinded observer. (Level 2).	To investigate the effect of laser acupuncture on LI4 compared to oral glucose solution on pain in neonates undergoing routine calcaneal puncture.	The mean Premature Infant Pain Profile (PIPP) in both groups was 12, with an interquartile range of 10 to 14 in GA and 9 to 14 in GG (p = 0.981). Therefore, acupuncture cannot be considered inferior to the use of glucose in the management of neonatal pain.
A2	Analgesic effect of direct breastfeeding during bcg Vaccination in healthy neonates. Dar JY, Goheer L, Shah, AS ⁽¹⁷⁾ . 2019	Quantitative research: controlled and randomized study. (Level 2).	To observe whether breastfeeding is a good analgesic method for babies during BCG vaccination.	No pain scale was applied during the study. There was a significant reduction in crying time in the experimental group compared to the control group.

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A3	The effect of regional massage performed before blood collection on pain and vital signs in newborns. Küçüktepe A, Şahiner NC ⁽¹⁸⁾ . 2023	Quantitative research: experimental, randomized and controlled study. (Level 2).	To examine the effects of regional massage performed before the procedure on pain and vital signs in full-term newborns.	The experimental group, based on the NIPS scale, had a lower level of pain, higher oxygen saturation and its average respiratory rate was lower than in the control group.
A4	Pain Control with Lavender Oil in Premature Infants: A Double-Blind Randomized Controlled Study. Usta C, Tanyeri-Bayraktar B, Bayraktar S ⁽¹⁹⁾ . 2021	Quantitative research: clinical, randomized, controlled and double-blind study. (Level 2).	Attribute the effect of lavender oil scent in relieving pain in premature infants during calcaneal puncture.	There was a significant difference between the two groups in relation to PIPP-R scores during and after the procedure (p=0.008 and p=0.03). Therefore, lavender aroma is effective in controlling pain in premature infants during calcaneal puncture.
A5	Effect of music combined with swaddling on pain in full-term newborns: randomized clinical trial. Melo GM, Cardoso MV, Almeida PC, Rodrigues EC ⁽²⁰⁾ . 2021	Quantitative research: factorial, randomized and triple-blind trial. (Level 2).	To evaluate the effect of music associated with swaddling on the pain response and physiological response in newborns before and during venipuncture.	Based on the Neonatal Facial Coding System (NFCS) assessment, it was determined that 15 minutes of lullaby combined with swaddling was more effective when compared to 10 minutes of music and swaddling, due to the greater absence of pain-related facial movements.
A6	Comparison of the analgesic effect of inhaled lavender vs vanilla essential oil for neonatal frenotomy: a randomized clinical trial. Maya-Enero S, Fàbregas-Mitjans M, Llufríu-Marquès RM, Candel-Pau J, Garcia-Garcia J, López-Vílchez MA ⁽²¹⁾ . 2022	Quantitative research: randomized, blind clinical trial. (Level 2).	Discover whether vanilla essential oil is more effective in reducing neonatal pain during frenotomy than inhaling lavender oil.	Based on the NIPS scale, no significant difference was observed between the two groups. Therefore, it cannot be concluded which of them was more effective in managing pain in neonates undergoing frenotomy.

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A7	<p>Analgésico effect of inhaled lavender essential oil for frenotomy in healthy neonates: a randomized clinical trial.</p> <p>Maya-Enero S, Fàbregas-Mitjans M, Llufríu-Marquès RM, Candel-Pau J, García-García J, López-Vílchez MA⁽²²⁾. 2022</p>	<p>Quantitative research: randomized, single-blind clinical trial. (Level 2).</p>	<p>Demonstrate that inhaling lavender essential oil is effective in reducing pain during frenotomy.</p>	<p>The experimental group's NIPS scores were significantly lower, as was the crying time.</p>
A8	<p>Oral dextrose reduced procedural pain without altering cellular ATP metabolism in preterm neonates: a prospective randomized trial.</p> <p>Angeles DM, Boskovic DS, Tan JC, Shih W, Hoch E, Forde D, et al⁽²³⁾. 2020</p>	<p>Quantitative research: prospective and randomized study. (Level 2).</p>	<p>To examine the effects of 30% oral dextrose in relation to pain, stress and degradation of adenosine triphosphate in premature newborns undergoing plantar puncture.</p>	<p>There were no differences in PIPP-R scores regarding pain in response to calcaneal puncture between the three groups. This indicates that 30% dextrose is an effective analgesic for preterm infants compared to other interventions containing fructose, such as sucrose.</p>
A9	<p>Skin-to-Skin Care by Mother vs. Father for Preterm Neonatal Pain: A Randomized Control Trial.</p> <p>Shukla VV, Chaudhari AJ, Nimbalkar SM, Phatak AG, Patel DV, Nimbalkar AS⁽²⁴⁾. 2021</p>	<p>Quantitative research: blind, randomized control study. (Level 2).</p>	<p>To compare the effectiveness of skin-to-skin contact with the mother and father for the management of neonatal pain.</p>	<p>The father's skin-to-skin care proved to be as effective as the mother's for pain management. The PIPP score at 0, 1 and 5 minutes in the two groups did not show significant differences.</p>
A10	<p>Evaluation of the Effect of Nutritive Versus Non-nutritive Pacifiers as Adjuncts to Local Anaesthesia in Male Neonatal Circumcision Using the Plastibell Technique – A Prospective Randomised Controlled Study.</p> <p>Ihediwa C, Bode C, Alakaloko F, Elebute O, Seyi-Olajide J, Ladipo-Ajayi O, et al⁽²⁵⁾. 2022</p>	<p>Quantitative research: prospective, randomized and controlled study. (Level 2).</p>	<p>To compare nutritive versus non-nutritive pacifiers as adjuncts to local anesthesia in neonatal male circumcision using the Plastibell technique.</p>	<p>According to NIPS, the control group had the highest average pain score compared to the other groups. The nutritious pacifier group had significantly higher pain scores and reduced crying time.</p>

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A11	Effectiveness of Hammock Positioning in Reducing Pain and Improving Sleep-Wakefulness State in Preterm Infants. Ribas, Ribas CG, Andreazza MG, Neves VC, Valderramas S ⁽²⁶⁾ . 2019	Quantitative research: randomized, controlled clinical trial. (Level 2).	To evaluate the effectiveness of hammock positioning compared to traditional positioning in reducing pain in premature infants.	Based on analysis of PIPP and NFCS scores, babies positioned in a hammock had significantly less pain and better sleep-wake status than those positioned traditionally.
A12	Effect of eye shield and ear muffs on pain intensity during venous blood sampling in premature infants: a clinical trial study. Shykhveisi F, Amiri RJ, Zabihi A, Mojaveri MH, Arzani A, Chejrazi M, et al ⁽²⁷⁾ . 2023	Quantitative research: clinical and randomized trial. (Level 2).	To investigate the effect of using ear and eye protectors on premature babies in reducing pain during blood collection.	Based on the NIPS assessment, the trend of pain changes in the eye protector + ear protectors group was lower than in the other groups.
A13	Effect of glucose and non-nutritive sucking on puncture pain in premature infants: a crossover clinical trial. Silveira ALD, Christofell MM, Velarde LGC, Rodrigues EC, Magesti BN, Souza RO ⁽²⁸⁾ . 2020	Quantitative research: randomized crossover clinical trial. (Level 2).	Compare the effect of non-nutritive sucking, 25% oral glucose and 25% oral glucose + non-nutritive sucking on pain relief in newborns undergoing calcaneal puncture.	Comparison between the three groups showed that. When interventions are offered in combination, premature newborns are able to return to their baseline state more quickly, that is, there is a reduction in the duration of pain sensation.
A14	Effect of Music on Outcomes of Birth Asphyxia: A Randomized Controlled Trial. Konar MC, Islam K, Sil A, Nayek K, Barik K ⁽²⁹⁾ . 2021	Quantitative research: clinical and randomized study. (Level 2).	Determine the effects of music therapy on birth asphyxia outcomes.	Based on the Neonatal Pain Agitation and Sedation Scale (N-PASS) analysis, pain and heart rate were lower in groups exposed to music therapy.
A15	Prevention of Pain During Screening for Retinopathy of Prematurity: A Randomized Control Trial Comparing Breast Milk, 10% Dextrose and Sterile Water. Nayak R, Nagaraj KN, Gururaj G ⁽³⁰⁾ . 2020	Quantitative research: controlled, randomized and double-blind study. (Level 2).	To compare the effectiveness of oral administration of 10% dextrose, breast milk and sterile water in preventing pain during ROP examination in premature neonates.	The 10% dextrose group had a lower mean PIPP score. However, these considerations were statistically insignificant. The breast milk group had a lower mean heart rate value.

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A16	Comparison of the Effect of Yakson Touch and Oral Glucose on the Severity of Phlebotomy Pain in Preterm Infants. Dehghani K, Ahmadabadi AB, Fallahzade H, Salimi T ⁽³¹⁾ . 2019	Quantitative research: randomized clinical trial. (Level 2).	To compare the effect of Yakson's touch and oral glucose in relation to phlebotomy pain in premature newborns.	The mean pain severity scores, according to the NIPS scale, after phlebotomy, had significant differences when comparing group 1 and also group 2 with the control group.
A17	Comparison between oral melatonin and 24% sucrose for pain management during retinopathy of prematurity screening: a randomized controlled trial. Behura SS, Dhanawat A, Nayak B, Panda SK ⁽³²⁾ . 2022	Quantitative research: prospective, non-blind, randomized and controlled study. (Level 2).	To explore the analgesic effect of oral melatonin and compare its effectiveness with the use of 24% sucrose.	The median PIPP was lower in the melatonin group when compared to the 24% sucrose group 1 minute after the procedure, but there was no difference after 5 minutes.
A18	Breastmilk as a Multisensory Intervention for Relieving Pain during Newborn Screening Procedures: A Randomized Control Trial. Lan HY, Yang L, Lin CH, Hsieh KH, Chang YC, Yin T ⁽³³⁾ . 2021	Quantitative research: controlled, randomized and blind study. (Level 2).	To combine several sensory stimuli and examine their effects in relation to pain during calcaneal puncture.	Group 3 (breast milk odor + gentle touch + verbal comfort) had the significantly lower NIPS scores during the calcaneal stick and recovery phases.
A19	A Randomized Comparative Effectiveness Study of Reflexology, Sucrose, and Other Treatments for Needle Procedures in Newborns. Us MC, Saran MG, Cebeci B, Akkuş E, Şeker E, Aybar ŞŞŞ ⁽³⁴⁾ . 2023	Quantitative research: randomized clinical trial. (Level 2).	To determine the effect of reflexology compared to other non-pharmacological methods in relation to pain and physiological changes.	All methods significantly reduced pain averages during procedures, but the routine care group had the highest NIPS scores. Sucrose 24%, followed by reflexology, was the most effective method for reducing pain.

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A20	The effect of inhaling mother's breast milk odor on the behavioral responses to pain caused by hepatitis B vaccine in preterm infants: a randomized clinical trial. Rad ZA, Aziznejadroshan P, Amiri AS, Ahangar HG, Valizadehchari Z ⁽³⁵⁾ . 2021	Quantitative research: randomized, single-blind clinical trial. (Level 2).	To investigate the effect of inhaling human milk on behavioral pain responses caused by the Hepatitis B vaccine in premature babies.	The mean pain score assessed from the PIPP was considerably lower in group A when compared to the other groups, that is, the odor of breast milk proved to be more effective in reducing pain in premature infants.
A21	Effect analysis of embracing breast milk sucking to relieve pain of neonatal calcaneal blood sampling: a randomized controlled trial. Wu H, Zhang J, Ding Q, Wang S, Li J ⁽³⁶⁾ . 2021	Quantitative research: controlled and randomized study (Level 2).	To determine whether sucking breast milk reduces pain associated with calcaneal stick.	Blood collection, crying and bleeding times were shorter, while the NIPS score was higher in the intervention group, when compared to the control group.
A22	Oral Glucose and Listening to Lullaby to Decrease Pain in Preterm Infants Supported with NCPAP: A Randomized Controlled Trial. Tekgündüz KŞ, Polat S, Gürol A, Apay SE ⁽³⁷⁾ . 2018	Quantitative research: double-blind, controlled and randomized study (Level 2).	To investigate whether oral glucose and listening to lullabies have an analgesic effect during the removal and reinsertion of tracheal tubes and oronasopharyngeal aspiration.	The NIPS scale indicated that 82.9% of babies exposed to the lullaby had mild pain, 11.4% moderate pain and 5.7% severe pain after the intervention, and 100% of the glucose group had mild pain. PIPP scores were higher in the control group than those in the song and glucose groups.
A23	Role of OPRM1, clinical and anthropometric variants in neonatal pain reduction. Erbi I, Ciantelli M, Farinella R, Tuoni C, Gentiluomo M, Moscuza F, et al ⁽³⁸⁾ . 2020	Quantitative research: controlled and randomized study. (Level 2).	To investigate the genetic variability of the OPRM1 gene in relation to the non-pharmacological method for pain relief in neonates.	Based on ABC and PIPP analysis, the administration of 33% dextrose was effective in managing pain in 966 newborns. Therefore, it was observed that the type of feeding significantly interferes with neonatal pain.

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A24	<p>Efficacy of Breast Milk Olfactory and Gustatory Interventions on Neonates' Biobehavioral Responses to Pain during Calcaneal Prick Procedures.</p> <p>Lin CH, Liaw JJ, Chen YT, Yin T, Yang L, Lan HY⁽³⁹⁾. 2022</p>	<p>Quantitative research: double-blind, randomized and controlled trial. (Level 2).</p>	<p>To compare the effects of three interventions on biobehavioral responses after calcaneal prick for neonatal screening.</p>	<p>Pain was assessed based on crying time. As a result, the averages for groups 1, 2 and 3 were 200, 130 and 80 seconds, respectively, proving the effectiveness of olfactory and gustatory interventions with breast milk.</p>
A25	<p>Painful procedures and pain management in newborns admitted to an intensive care unit.</p> <p>Rocha VA, Silva IA, Cruz-Machado SD, Bueno M⁽⁴⁰⁾. 2021</p>	<p>Quantitative research: primary, observational and prospective clinical study. (Level 3).</p>	<p>To determine the number of painful procedures, vital signs, pain scores, pharmacological and non-pharmacological pain relief measures, from admission to the 3rd day of hospitalization.</p>	<p>Between D0 and D3, newborns were subjected to 2,732 painful procedures. The most used procedure, non-pharmacological and pharmacological method were, respectively, calcaneal lancing, light reduction and continuous fentanyl.</p>
A26	<p>Evaluation of Methods to Minimize Pain in Newborns during Capillary Blood Sampling for Screening: A Randomized Clinical Trial.</p> <p>Napiórkowska-Orkisz M, Gutysz-Wojnicka A, Tanajewska M, Sadowska-Krawczenko I⁽⁴¹⁾. 2022</p>	<p>Quantitative research: randomized and pragmatic clinical trial. (Level 2).</p>	<p>To evaluate the intensity of pain after applying a non-pharmacological method during a calcaneal prick for neonatal screening.</p>	<p>According to the NIPS scale, most newborns felt no pain or only felt mild discomfort after the intervention and during the painful procedure.</p>
A27	<p>The effect of Yakson and Gentle Human Touch methods on pain and physiological parameters in preterm infants during calcaneal lancing.</p> <p>Dur Ş, Çağlar S, Yıldız NU, Doğan P, Güney Varal İ⁽⁴²⁾. 2020</p>	<p>Quantitative research: randomized and controlled study. (Level 2).</p>	<p>To determine the effects of the Yakson and Gentle Human Touch (GHT) methods on pain and physiological parameters during neonatal screening.</p>	<p>According to NIPS, pain levels in the GHT and Yakson groups were statistically lower before, during and after calcaneal puncture.</p>

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (continued)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A28	Oral sweet solution to prevent pain during neonatal hip examination: a randomised controlled trial. Olsson E, Pettersson M, Eriksson M, Ohlin A ⁽⁴³⁾ . 2018.	Quantitative research: randomized and controlled study. (Level 2).	To determine whether oral glucose has a pain-relieving effect during examinations in newborns.	According to Lund Children's Hospital Pain and Stress Assessment Scale (ALPS-Neo) and Visual Analogue Scale (VAS), newborns in the intervention group had a lower level of pain.
A29	Pain Control Interventions in Preterm Neonates: A Randomized Controlled Trial. Shukla VV, Bansal S, Nimbalkar A, Chapla A, Phatak A, Patel D, et al ⁽⁴⁴⁾ . 2018	Quantitative research: controlled and randomized study. (Level 2).	To compare the individual effectiveness and additive effects of pain control interventions in preterm infants.	Based on the PIPP score, kangaroo mother care with and without music therapy significantly reduces procedural pain compared to expressed breast milk alone.
A30	The effect of concurrent use of swaddle and sucrose on the intensity of pain during venous blood sampling in neonate: a clinical trial study. Talebi M, Amiri SR, Roshan PA, Zabihi A, Zahedpasha Y, Chehrazi M ⁽⁴⁵⁾ . 2022	Quantitative research: clinical and randomized study (Level 2).	To investigate the analgesic effect of the combined use of swaddles and sucrose tasting during neonatal venous blood collection.	Based on the PIPP score, non-pharmacological interventions led to a reduction in heart rate and pain perception in the intervention groups compared to the control group.
A31	Pain responses in preterm infants and parental stress over repeated painful procedures: a randomized pilot trial. Eissler AB, Stoffel L, Nelle M, Hahn S, Zwakhalen S ⁽⁴⁶⁾ . 2023	Quantitative research: randomized pilot study (Level 2).	To determine whether parental involvement in pain management, or their passive observation, interferes with neonatal pain and parental stress.	According to the Bernese Pain Scale for Neonates (BPSN), facilitated folding proved to be a good method for involving parents in measures to reduce their baby's pain. However, no differences were found between the groups in relation to parental stress and neonatal pain.

Chart 1 – Characterization of studies included in the integrative review according to article title, author, year, type of study, objectives and results (conclusion)

N.	Title, author(s) and year	Design and level of evidence	Objectives	Results
A32	Modified Sensory Stimulation Using Breastmilk for Reducing Pain Intensity in Neonates in Indonesia: A Randomized Controlled Trial. Friti SY, Lusmilasari L, Juffrie M, Bellieni CV ⁽⁴⁷⁾ . 2020	Quantitative research: controlled and randomized study. (Level 2).	To compare the analgesic effect of sensory saturation, 24% sucrose and breast milk in premature infants undergoing venipuncture.	Based on NIPS, the average pain intensity in newborns submitted to sensory saturation + breast milk was the lowest, while the average in those who received only 24% sucrose was the highest ($p = 0.001$).

Source: created by the authors.

Discussion

Lavender essential oil⁽²¹⁾ is the most studied aroma by health professionals and, in addition, does not present adverse effects in newborns relaxation and analgesia through its sedative properties and its direct interaction with the glutaminergic and cholinergic systems⁽¹⁹⁾.

A study published in 2021⁽¹⁹⁾ points out that after intervention with lavender essential oil and evaluation of the PIPP score, this method can be considered effective for pain relief and reduction of crying time in premature infants during small painful interventions. Moreover, by comparing lavender and vanilla essential oils, the study carried out in 2022⁽²¹⁾ determined, through the NIPS scale, stopwatch and cardiac monitor, that vanilla essential oil is as effective as lavender oil during the frenotomy procedure in relation to pain, crying time and variations in arterial oxygen saturation (SaO₂) and heart rate (HR) values.

A clinical trial⁽⁵⁵⁾ applied the comparison of olfactory interventions between the smell of breast milk and the smell of another mother's milk. The study showed that, although no statistically significant differences were found in SaO₂, systolic blood pressure (SBP) or diastolic blood pressure (DBP) between the groups, stimulation with the mother's own milk presented lower values for HR and PIPP score, characterizing the reduction of neonatal pain.

Nevertheless, in addition to agreeing that the smell of breast milk is able to reduce the average heart rate during the bite on the calcaneal of the neonate, it was pointed out that the junction between the odor and taste of breast milk reflects, in addition to the above, in higher values of SaO₂ and in the reduction of crying time⁽³⁹⁾. However, in the absence of the application of recognized scales, neonatal pain was not evaluated in this study.

That said, authors⁽³⁹⁾ present that, according to the NIPS pain scale, newborns submitted to calcaneal puncture and exposed to odor union with the taste of breast milk, when compared to NBs that received only the olfactory intervention, pain during the puncture and recovery phases of the procedure. In view of this, the authors consider breastfeeding a safe and economical method for the management of neonatal pain⁽¹⁷⁾.

In another study⁽³⁶⁾, the following combined intervention was used: mother's embrace plus breastfeeding. The hug aims to convey security to the newborn, while breastfeeding aims at pain relief during blood collection in the calcaneal. Through the analysis of NIPS, cardiac monitor and stopwatch, it was possible to detect significantly different values in the group that received the intervention when compared to the control, being able to interpret that breastfeeding, together with the maternal hug, reduces the time of calcaneal bleeding, HR, crying time and pain.

Breastfeeding is a set of mechanisms that have an analgesic effect, such as the release of endorphins due to sweet taste, sucking reflex and skin-to-skin contact combined with rocking movements⁽⁴⁸⁾. This multisensory stimulation of breastfeeding promotes cortical activation, reducing pain perception, while the administration of sweetened solutions has no significant effects on the cortical level⁽¹⁷⁾.

There were no significant differences⁽⁴⁸⁾ in the means of the NIPS scale between the groups of breastfeeding and oral administration of glucose 20%, however, heart rate values were lower in newborns submitted to sweetened solution⁽⁴⁸⁾. When comparing the interventions: 1) milk milked 2) dextrose 10%, there were higher results of SaO₂ and lower HR in neonates allocated in group 1, while NBs in group 2 have lower PIPP scores. Nevertheless, it is worth noting that the results of this study were not statistically significant, that is, the effects of milked milk and 10% dextrose on the screening of retinopathy of prematurity are similar⁽³⁰⁾.

Another study conducted in newborns during ROP screening points out that sensory saturation (junction of visual, auditory, gustatory, olfactory and tactile stimuli), combined with oral administration of sucrose 24%, has greater pain relief than the sweetened solution alone. In contrast, the lowest averages for the NIPS scale, but statistically insignificant, are NBs submitted to sensory saturation with breast milk. Therefore, the combination of sensory saturation with both breast milk and 24% sucrose can be considered an effective strategy in the management of neonatal pain⁽⁴⁷⁾.

The mean PIPP⁽³²⁾ score in the first minute after ROP screening was lower in neonates who used melatonin orally instead of sucrose 24%. However, in the fifth minute after the procedure, the differences between the two groups were insignificant. Therefore, both solutions can be an effective alternative for neonatal pain control. In a study conducted during the calcaneal puncture, according to the NIPS scale, the oral administration of sucrose 24% stood out compared to the other non-pharmacological treatments applied, such as reflexology, kangaroo method and music therapy⁽⁴⁹⁾.

The combination of 24% sucrose and swaddle was satisfactory for pain management during venous blood collection in newborns, due to the low value in the PIPP score⁽⁴⁵⁾. It should be noted that the oral use of sucrose 24% reduces the level of pain, however, this substance tends to significantly increase the mean heart rate and biochemical markers of ATP degradation in the neonatal public⁽²³⁾. Therefore, in the search for an effective intervention in both pain reduction and other exposed factors, the authors considered 30% oral dextrose an efficient practice to reduce pain before a clinically necessary calcaneal puncture⁽²³⁾.

Although treatment with dextrose 30% is successful as pain management, not all newborns obtain analgesic effect during painful interventions with this method. When investigating the relationship of the OPRM1 gene with the response to non-pharmacological treatment for neonatal pain relief, based on the ABC and PIPP scales, it was associated with feeding the NBs the best analgesic result, that is, babies who receive daily diet with breast milk are subject to greater chances of efficacy in non-pharmacological methods for pain relief⁽³⁸⁾.

Currently, oral glucose has been widely used because it has greater availability, in the form of ampoules, within health services, and effects similar to other sweetened solutions in the management of neonatal pain⁽²⁸⁾. When comparing its analgesic efficacy with that of lullabies during removal and reinsertion of tracheal tubes and oronasopharyngeal aspiration, it was observed that preterm infants exposed to glucose obtained lower scores on the NIPS pain scale⁽³⁷⁾.

The oral use of glucose, based on the evaluations of ALPS-Neo and VAS, was efficient in reducing pain in RNs during routine hip exams⁽⁴³⁾ and also during phlebotomy procedures, according to the NIPS score⁽³¹⁾. In addition, oral administration of glucose 30% does not present adverse reactions and has satisfactory effects on crying time and mean PIPP score in relation to small painful interventions in NBs⁽¹⁶⁾.

Sweet substances are great practices for the relief of neonatal pain, however, they expose that, in addition to these, non-nutritive sucking is

also an effective and well-established strategy⁽²⁸⁾. Nevertheless, higher heart rate values were found in newborns who used pacifiers during capillary blood sampling, when compared to babies who received oral administration of glucose at 20%⁽⁴⁸⁾. Therefore, the use of oral glucose combined with non-nutritive suction is recommended, since this union favors the return of premature infants to the baseline pain parameter in just 90 seconds after small painful interventions.

Based on the analysis of the PIPP⁽²⁵⁾ score, the use of pacifiers significantly assists pharmacological treatment in pain management after the male circumcision procedure in neonates. However, pacifier sucking together with sucrose, in addition to being more effective in relieving pain, results in shorter crying time and lower heart rate values in the NBs submitted to this painful procedure.

Massage is another non-pharmacological strategy for the relief of neonatal pain, economic and easy to apply, which can be used before, during and after painful procedures, such as calcaneal puncture for neonatal screening⁽¹⁸⁾. It acts on the newborn's body through touch, inhibiting the transmission of pain along the ascending fibers, reducing nociceptive transmission and activating endogenous opioid and non-opioid pathways⁽⁴⁹⁾. A study published in 2023⁽¹⁸⁾ stated that regional massage reflects higher SaO₂, shorter crying time and lower pain and HR levels.

Other tactile stimulations with neonatal pain-reducing effect are the Yakson and Gentle Human Touch methods. Although the two practices basically consist of gently caressing painful areas of the individual's body, each has a specific technique for their realization. By comparing both interventions during the calcaneal puncture procedure in preterm infants, they found that, according to NIPS, the group submitted to Yakson's stimulus obtained greater pain relief, while in the GHT group, NBs had lower values of heart rate and SaO₂. However, due to the proximity of the results between the two interventions, both can be considered effective in relation to pain treatment in neonates⁽⁴²⁾.

In agreement, the clinical trial⁽³¹⁾, published in 2019, corroborates that Yakson's touch is an excellent non-pharmacological treatment

for pain management during the phlebotomy procedure in newborns, because, compared to other strategies, it obtains lower NIPS scores. In 2022, authors⁽⁴⁹⁾ proved that reflexology, when compared with the kangaroo method, reduces the values in cardiac and respiratory frequencies during painful procedures in neonates.

Skin-to-skin contact has been one of the preferred treatments for pain control due to its wide range of benefits through multisensory stimulation. Thus, a study⁽²⁴⁾ analyzed the analgesic effect of skin-to-skin contact offered by the mother compared to skin-to-skin contact offered by the father during calcaneal puncture in premature infants. Based on the PIPP score, there were no significant differences between the two groups, that is, both mother and father are effective during this intervention. However, in 2018, it was presented that the kangaroo method has greater efficiency in pain control when combined with milked breast milk and music therapy⁽²⁴⁾.

In recent years, science has been examining the effects of music therapy in neonates and physiological and behavioral improvements have been observed. Authors⁽³⁷⁾ report that lullabies result in pain relief in premature infants during removal and reinsertion of the tracheal tube and or nasopharyngeal aspiration; however, this method is more effective when combined with oral administration of sweet solution. A study published in 2021⁽²⁹⁾ observed that music therapy reflects significantly on the reduction of hospital stay, oxygen dependence, incidence of apnea, and pain levels during painful procedures. Based on the Neonatal Facial Coding System evaluation in 2022, a study analyzed that music therapy combined with Swaddle, i.e., bandage, reduces the facial expressions of pain and HR in neonates submitted to calcaneal puncture⁽²⁰⁾.

On the other hand, authors⁽²⁷⁾ studied the effects of reduction of sound stimuli on pain intensity in NBs submitted to venous blood collection. The study points out that, although the use of ear protectors reflects directly on pain perception, joining this strategy to the use of eye protectors affects lower NIPS scores, that is, greater analgesic effect. A clinical, observational

and prospective study⁽⁴⁰⁾, conducted in 2021 in Brazil, observed, through analysis of medical records, the execution of considerable non-pharmacological methods for pain control within the neonatal intensive care unit (NICU). However, the reduction of luminosity was the strategy most frequently performed, followed by the method of nesting, in other words, coziness in the bed.

Another study developed in Brazil⁽²⁶⁾ points out that the positioning of hospitalized premature infants has consequences on the parameters of ventilation and pulmonary perfusion. That said, the research pointed out that the networked position is a simple, non-invasive method that stimulates flexion and promotes symmetry, reduces pain and improves the sleep-wake state of newborns. In addition, facilitated bending has been shown to be an effective position for pain management in newborns, which can be applied by both nurses and parents, considering that the executor of this method will not result in losses in the analgesic result⁽⁴⁶⁾.

A limitation of the study concerns that most of the studies were conducted in an intensive neonatal treatment environment and due to the higher incidence of hospitalization, 50% of the studies treated premature newborns. Therefore, the implementation of non-pharmacological interventions for neonatal pain control in other health services and at home is of paramount importance, given that neonatal pain is not restricted to the hospitalized public only.

The results are expected to contribute to expand the knowledge of nurses, because, for that, the diagnosis and management of pain with non-pharmacological methods are essential, and thus qualify the practice of care for the neonate's pain and reflect on a higher rate of training for parents and family members on the topic addressed.

Final Considerations:

This integrative review allowed the observation that frequent exposure to pain negatively affects the development of the neonate, causing

permanent consequences on the physiological and neurobehavioral responses of the individual. Considering that the use of analgesic medications is not recommended in newborns during small painful procedures, the early identification of neonatal pain and the immediate execution of a non-pharmacological treatment are fundamental in this situation.

Different interventions were presented in the literature as effective non-pharmacological methods in the management of neonatal pain, highlighting combinations of multisensory strategies, such as administration of sweet solution with massage techniques, acupuncture or music therapy, for example. All practices significantly affected the pain of the NB, and some of them also reflected in shorter crying time, lower HR values, higher SaO₂ rates, improvement in the sleep-wake process, among others.

Although there is a considerable number of publications on non-pharmacological strategies for the treatment of neonatal pain, some methods appear repeated in the studies. Therefore, it is necessary to develop randomized studies validating the effectiveness of other possible methods, as well as the publication of more research on the subject in other environments than Neonatal Intensive Care Unit.

Collaborations:

1 – conception and planning of the project: Rafaela Abrão and Camila Neves da Silva;

2 – analysis and interpretation of data: Rafaela Abrão;

3 – writing and/or critical review: Rafaela Abrão, Marcela Rosa da Silva, Joyce Mara Serafim Kollet, Maria da Graça Corso da Motta and Camila Neves da Silva;

4 – approval of the final version: Rafaela Abrão, Marcela Rosa da Silva, Joyce Mara Serafim Kollet, Maria da Graça Corso da Motta and Camila Neves da Silva.

Competing interests

There are no competing interests.

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