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REVIEW

25% GLUCOSE IN PAIN RELIEF IN NEWBORNS DURING ARTERIAL AND VENOUS PUNCTURE: A SCOPING REVIEW

GLICOSE 25% NO ALÍVIO DA DOR DE RECÉM-NASCIDOS DURANTE PUNÇÃO ARTERIAL E VENOSA: UMA REVISÃO DE ESCOPO

GLUCOSA 25% EN EL ALIVIO DEL DOLOR DEL RECIÉN NACIDO DURANTE LA PUNCIÓN ARTERIAL Y VENOSA: UNA REVISIÓN DEL ALCANCE

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ABSTRACT

The objective was to map knowledge about the use of a 25% glucose solution in pain relief in newborns during arterial and venous puncture. This is a scoping review. It was conducted during August 2020 in eight data sources (Cumulative Index to Nursing and Allied Health Literature, *Literatura Latino-Americana e do Caribe em Ciências da Saúde*, Medical Literature Analysis and Retrieval System Online, SciVerse Scopus, Web of Science, Scientific Electronic Library Online, Cochrane Library, and Theses and Dissertations Catalog), as well as in an electronic search engine. Eleven studies were selected, which corroborate the use of 25% glucose as a non-pharmacological measure to reduce pain in Newborns, evidencing its analgesic effect from the reduction of the scores in the scales that assess pain. Regarding use, it was noticed that most employed 2 mL of this solution, via oral route, two minutes before the procedure. The non-pharmacological measures are low-cost and easy to use. The 25% glucose solution is seen as a gold-standard method for pain relief in Newborns. This study provided additional scientific basis by showing that the use of a 25% glucose solution is beneficial in relieving pain in newborns during arterial and venous puncture, especially when associated with other techniques. The study elucidates the health actions for the management of neonatal pain and contributes to fostering scientific visibility and relevance regarding the theme.

Keywords: Pain Management; Analgesia; Blood Gas Analysis; Infant, Newborn.

RESUMO

O objetivo foi mapear o conhecimento sobre o uso da solução de glicose 25% no alívio da dor de recém-nascidos durante a punção arterial e venosa. Trata-se de uma revisão de escopo. Realizada busca em oito fontes de dados (Cumulative Index to Nursing and Allied Health Literature, Literatura Latino-Americana e do Caribe em Ciências da Saúde, Medical Literature Analysis and Retrieval System Online, SciVerse Scopus, Web of Science, Scientific Electronic Library Online, Cochrane Library, Catálogo de Teses e Dissertações) e em buscador eletrônico no mês de agosto de 2020. Foram selecionados 11 estudos, que corroboram a utilização da glicose 25% como medida não farmacológica para redução da dor em Recém-nascidos, evidenciando seu efeito analgésico a partir da redução da pontuação nas escalas que avaliam a dor. Quanto à utilização, notou-se que a maioria utilizou 2 mL dessa solução, por via oral, dois minutos antes do procedimento. As medidas não farmacológicas são de fácil uso e baixo custo. A glicose 25% é vista como um método padrão-ouro para o alívio da dor de Recém-nascidos. Este estudo possibilitou mais embasamento científico ao mostrar que o uso da solução de glicose 25% é benéfico no alívio da dor de recém-nascidos durante a punção arterial e venosa, principalmente quando associada a outras técnicas. O estudo elucida as ações de saúde para o manejo da dor neonatal e contribui para o fomento da visibilidade e relevância científica ao tema.

Palavras-chave: *Manejo da Dor; Analgesia; Gasometria; Recém-Nascido.*

RESUMEN

El objetivo fue mapear el conocimiento sobre el uso de una solución de glucosa al 25% para el alivio del dolor en recién nacidos durante punciones arteriales y venosas. Esta es una revisión de alcance. En agosto de 2020, se realizaron búsquedas en ocho fuentes de datos (Cumulative Index to Nursing and Allied Health Literature, Literatura Latino-Americana e do Caribe em Ciências da Saúde, Medical Literature Analysis and Retrieval System Online, SciVerse Scopus, Web of Science, Scientific Electronic Library Online, Cochrane Library, Catálogo de Tesis y Disertaciones) y en un buscador electrónico. Se seleccionaron once estudios, que corroboran el uso de glucosa al 25% como medida no farmacológica para reducir el dolor en Recién Nacidos, lo que demuestra su efecto analgésico a partir de la reducción de puntuaciones en escalas que evalúan el dolor. En cuanto al uso, se notó que la mayoría utilizó 2 mL de esta solución, por vía oral, dos minutos antes del procedimiento. Las medidas no farmacológicas son fáciles de usar y económicas. La glucosa al 25% se considera un método de referencia para el alivio del dolor en Recién Nacidos. Este estudio proporcionó mayor base científica al demostrar que el uso de una solución de glucosa al 25% es beneficioso para aliviar el dolor en recién nacidos durante punciones arteriales y venosas, especialmente cuando se asocia con otras técnicas. El estudio dilucida acciones de salud para el manejo del dolor neonatal y contribuye a promover la visibilidad y relevancia científica del tema.

Palabras clave: *Manejo del Dolor; Analgesia; Análisis de los Gases de la Sangre; Recién Nacido.*

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INTRODUCTION

Advances in technological development in neonatal intensive care have been increasing but, although sophistication of the therapeutic resources has improved and increased the survival of newborns (NBs), they continue to be exposed to a range of painful procedures and exams that generate a high degree of stress, namely: Guthrie test, collection of specimens for laboratory tests, aspiration of the orotracheal tube, gastric tubing and introduction of peripherally inserted central catheter, among others.[1,2] It is estimated that, throughout the hospitalization in the neonatal intensive care unit (NICU), preterm NBs undergo many painful procedures, necessary for diagnostic and therapeutic implementation, which generate immediate changes in their physiological parameters.[3]

Pain management in NBs through non-pharmacological measures includes several care modalities, some of which are as follows: breastfeeding, non-nutritive sucking, skin-to-skin contact, massage and use of glucose solution, among others.[1] A number of studies show the benefit of this technique by observing that the physiological and behavioral changes caused by pain in NBs are mitigated or restored when these analgesic methods are used, providing physical and psychological comfort to the NB and reducing the pain scores.[4]

Recognized as the fifth vital sign, pain is described as a set of subjective sensations, which can be concomitant with situations of real or not tissue damage and, therefore, should be considered in the clinical practice. It was believed that NBs were not able to perceive sensory stimuli due to immaturity of the nervous system. However, from the 20th gestational week, fetuses have a functional nervous system and are already able to respond to painful perceptions.[5]

When left untreated, pain can be associated with increased morbidity and mortality and hinder recovery from surgical or clinical procedures, in addition to generating reorganization in the functional and permanent structure of the nociceptors, which will result in hypersensitivity to painful and non-painful stimuli.[5]

Non-pharmacological treatment for pain relief in newborns is considered a non-invasive technique to reduce aggressive stimuli from the environment, which guarantees qualified and humanized care, avoiding possible harms due to prolonged exposure to pain.[6] Among the advantages, the following stand out: low or no cost, ease of administration, almost immediate analgesic effect and low or no risk of complications.[4] Also in this perspective, the use of sweetened substances has been adopted as analgesic measures, especially 25% glucose and sucrose.[7]

Faced with painful stimuli, NBs present changes in their physiological (elevated heart rate, respiratory frequency and blood pressure) and behavioral (changes in facial movements, crying and irregular sleep pattern) reactions that are used as parameters to check and analyze pain in these NBs. Among these invasive procedures is blood collection with an emphasis on arterial puncture, a test routinely performed to alleviate respiratory disorders.[6,8]

A number of studies show that administering a 25% glucose solution in the NB's oral cavity before (for two minutes) or during invasive procedures considerably attenuates the effect of pain, in addition to releasing endorphins that also reduce the NB's heart rate, crying and facial movements and prevent a drop in oxygen saturation. Decrease in the respiratory frequency and reduction of the vagal tone stimulation are added to this.[8,9]

Along with this, it is necessary for nurses to develop knowledge and skills to take care of the child, their family and themselves, since these professionals deal with challenging emotional situations.[10]

Thus, the study is justified by the need and importance of a subject matter that reflects better care for newborns exposed to a large number of invasive procedures, specifically arterial and venous puncture. This is because, when pain does not stop, the negative implications such as increased morbidity and mortality, slower recovery of the NB and other issues, can be accentuated and thus interfere with later child development. Its due relevance in the public health context is added to the aforementioned, tracing courses of action for pain reduction in these NBs, taking into account their vulnerability degree. The objective of this study is to map knowledge about the use of a 25% glucose solution in pain relief in newborns (both preterm and full-term) during arterial and venous puncture.

METHOD

This study is a scoping review, which aims at mapping and categorizing the main concepts of a given knowledge area and to examine the extent, scope and nature of the research, select these studies, extract the data, summarize and disseminate the research data, and identify existing research gaps in the literature.[11]

In order to track and identify other scoping reviews or protocols similar to the objective of this paper, a search was conducted in May 2020 in the following study platforms: International Prospective Register of Systematic Reviews (PROSPERO), Open Science Framework (OSF), The Cochrane Library, JBI Clinical Online Network of Evidence for Care and Therapeutics (COnNECT+) and Database of Abstracts of Reviews of Effects (DARE). The results indicated non-existence of scoping research studies similar to the objective of this study.

This research was developed in accordance with the recommendations of the Joanna Briggs Institute Reviewer's Manual,[11] and used the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) protocol.[12] It was registered on the OSF platform for the registration of scientific papers (https://osf.io/dc8yg).[13]

The population, concept and context (PCC) strategy was used as a research strategy, with "P" being newborns, "C" being the use of 25% glucose as non-pharmacological therapy for pain relief, and "C" being the neonatal unit. Consequently, the following research guiding question was elaborated: "Which is the current knowledge about the use of a 25% glucose solution in pain relief in newborns during arterial and venous puncture?"

Eight data sources were accessed by means of the federated academic community in the Journals Portal of the Coordination for the Improvement of Higher Level Personnel (*Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*, CAPES), namely: Cumulative Index to Nursing and Allied Health Literature (CINAHL), *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE), SciVerse Scopus, Web of Science, Scientific Electronic Library Online (SciELO), Cochrane Library and Theses and Dissertations Catalog (CAPES). The controlled descriptors from the Medical Subject Headings (MeSH) were "Pain management", "Analgesia", "Blood gas analysis", "Infant, Newborn" and "Glucose", together with the keyword "Arterial puncture". Crossings of the descriptors and keywords were made through Boolean operators *AND* and *OR*. Table 1 addresses the research syntax adopted according to the data sources used.

The search strategy was carried out in August 2020 and, for the purposes of this review, scientific articles available online in full and in Open Access format, in any language and in the time frame between 2016 and 2020, were adopted as inclusion criteria. Scientific articles that did not answer the research guiding question were excluded, as well as abstracts, congress annals and letters to the editor.

Table 1 - Research syntax in the data sources. *Natal*, RN, Brazil, 2020

DATA SOURCE	SINTAX
LILACS†	*recém-nascidos [Palavras] AND glicose [Palavras] AND gasometria [Palavras] AND recém-nascidos [Palavras] AND analgesia [Palavras] AND gasometria [Palavras] AND recém-nascidos [Palavras] AND glicose [Palavras] AND manejo da dor [Palavras]*
Scopus‡	*TITLE-ABS-KEY (infant,newborn) AND TITLE-ABS-KEY (glucose OR pain AND management) AND TITLE-ABS-KEY (blood AND gas AND analysis AND arterial AND puncture)) AND (TITLE-ABS-KEY (infant,newborn) AND TITLE-ABS-KEY (analgesia AND glucose) AND TITLE-ABS-KEY (blood AND gas AND analysis AND arterial AND puncture)*
MEDLINE§	*Infant, Newborn AND (Analgesia OR pain) AND (Blood Gas Analysis OR arterial puncture) AND (Analgesia OR pain) AND (glucose AND arterial puncture) AND Infant, Newborn AND Infant, Newborn AND (Arterial Puncture OR Blood Gas Analysis) AND (Glucose AND Pain Management)*
CINAHL||	*Infant, newborn AND glucose AND arterial puncture AND infant, newborn AND analgesia AND blood gas analysis AND infant, newborn AND glucose AND pain management*
Cochrane Library†	*Infant, Newborn in Title Abstract Keyword AND Analgesia OR glucose OR Pain Management in Title Abstract Keyword AND arterial puncture OR Blood Gas Analysis in Title Abstract Keyword AND Infant, Newborn in Title Abstract Keyword AND Analgesia OR glucose OR Pain Management in Title Abstract Keyword*
Web Of Science¶¶	*TOPIC: (Infant, Newborn) AND TOPIC: (Analgesia OR glucose OR Pain Management) AND TOPIC: (arterial puncture OR Blood Gas Analysis) AND TOPIC: (Infant, Newborn) AND TOPIC: (Pain Management OR Glucose OR Analgesia)*
SciELO**	*(*Infant, Newborn) AND (Analgesia OR glucose) AND (arterial puncture OR Blood Gas Analysis) AND (*Infant, Newborn) AND (Arterial Puncture) AND (Pain Management OR Analgesia)*
Theses and Dissertations Catalog (CAPES)¶	*(Recém-nascidos AND Dor) OR (Gasometria AND Dor) (Glicose AND Analgesia) AND (Recém-nascidos AND Dor AND Glicose)*

†*Literatura Latino-Americana e do Caribe em Ciências da Saúde*, ‡Elsevier's SCOPUS, §Medical Literature Analysis and Retrieval System Online, ||Cumulative Index of Nursing and Allied Health, †Cochrane Library, ¶¶Web Of Science, **Scientific Electronic Library Online, ¶Theses and Dissertations Catalog (CAPES).
Source: Research Data.

Articles in the *Open Access* format were used, since this format allows unrestricted, direct, permanent and free access to the full texts of the scientific and research literature through the Internet. This presupposes free leverage of the scientific information, provided that authorship is duly acknowledged. In addition, many studies need to be paid for and this makes it impossible to access information without prior purchase of material or subscriptions to scientific journals by those seeking information, thus restricting the use of an important source of knowledge about this theme of great value for health care.

Screening of the articles included in the study was performed by the three reviewers independently and blinded, who made their reviews on the same day and at the same time through different electronic devices, based on the information available in the titles and abstracts. Final sample selection was performed by two independent reviewers, with full-reading of the texts. In case of disagreement about the inclusion of any article in the final list, the reviewers analyzed the papers' full versions until reaching consensus.

RESULTS

The initial search conducted in the eight data sources resulted in a total of 1,378 studies and an additional record identified in another source (Google Scholar). After excluding duplicate citations, the titles of 1,367 studies were read to verify if they met the inclusion criteria. Of these, 25 were assessed for eligibility by reading their full texts. Thus, the final selection consisted in 11 articles, as shown in Figure 1.

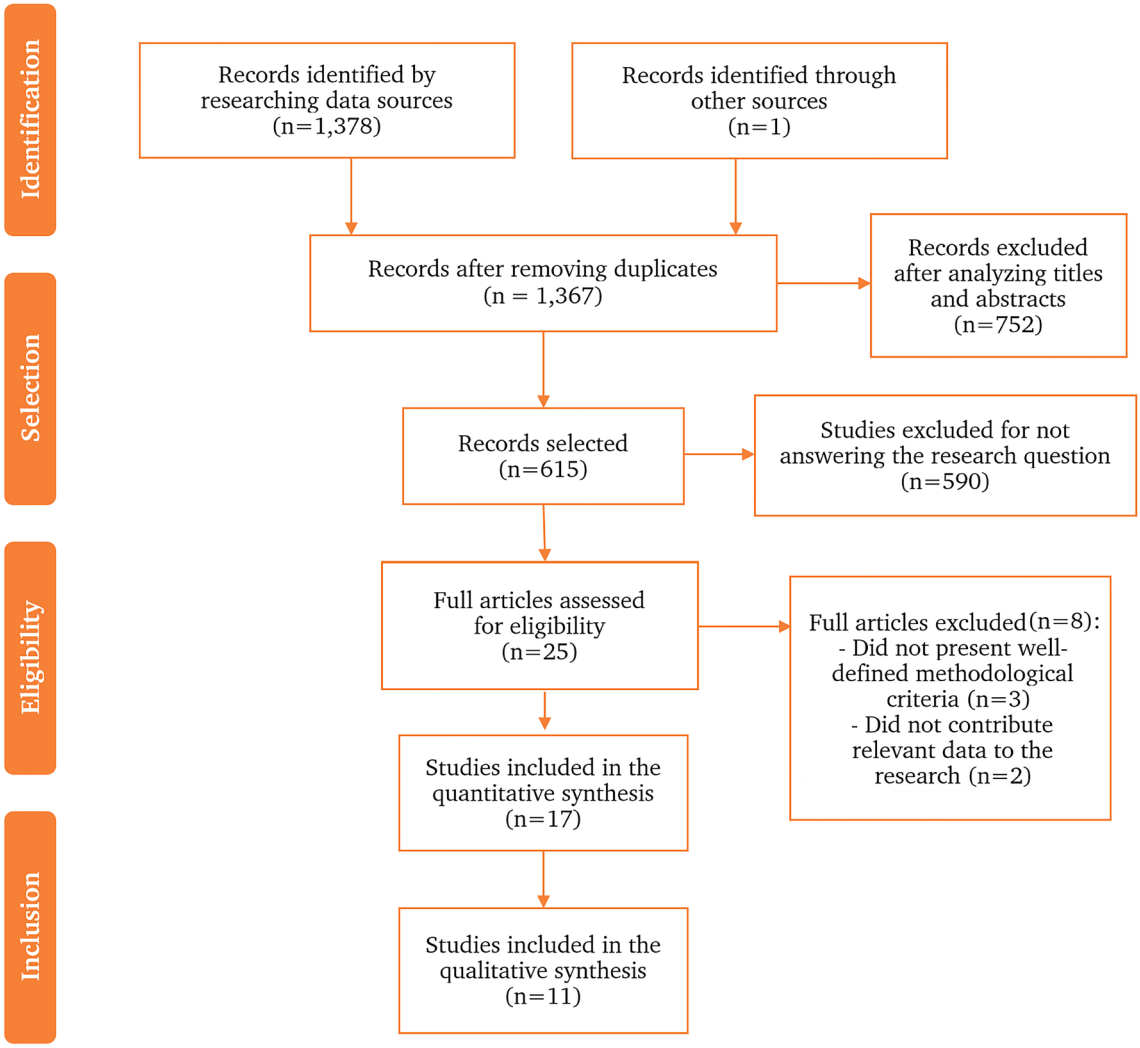

Figure 1 - Flowchart corresponding to the search and selection of the scoping review articles. Natal, RN, Brazil, 2020.
Source: Research Data.

The 11 selected studies met the inclusion criteria previously established for this review, since they addressed the use of 25% glucose as a non-pharmacological therapy in NBs during arterial or venous puncture. Table 2 presents the description of the articles included in the review, organized by study, year of publication, country and objective.

An increase is observed in the number of articles published about the non-pharmacological measures in neonatal pain relief throughout the years. In this review, there was prevalence of studies conducted in Brazil (45.4%), followed by Canada, United States, Italy, India, Cameroon and Iran (9.09% each). The articles included in the study were published between 2016 and 2020.

Table 3 characterizes the publications according to the degree of recommendation/level of evidence,[14] population and main results of the studies included in the scoping review.

According to Table 3, it is concluded that most of the studies have a high degree of recommendation and level of evidence (81.8% are articles with degree of recommendation A and level of evidence 1B), showing the quality and reliability of the data presented in this study. It was observed that many studies proved the benefit of oral glucose on neonatal pain relief during arterial and venous puncture.

Table 2 - Characterization of the study about the use of glucose in pain relief in newborns during arterial/venous puncture, according to year of publication, country and objective (n=11). *Natal*, RN, Brazil, 2020

STUDY	YEAR	COUNTRY	OBJECTIVE
E 2	2016	Brazil	To describe the practices of the Nursing team in pain management in newborns who received a peripherally inserted central catheter (PICC) in a neonatal intensive care unit (NICU)
E 8	2017	Brazil	To compare the pain response in preterm newborns subjected to arterial puncture who received a musical intervention with that of those who received the 25% glucose intervention
E 15	2016	Brazil	To know how the Nursing team uses the non-pharmacological measures for neonatal pain relief
E 16	2017	Canada	To review all the trials that assess sweet solutions for analgesia in NBs and to perform cumulative meta-analyses (CMAs) on pain behavioral results
E 17	2020	United States of America	To examine the effects of 30% oral dextrose on the biochemical markers of pain, adenosine triphosphate (ATP) degradation and oxidative stress in preterm NBs with clinically necessary heel puncture
E 18	2018	Italy	To evaluate the relative analgesic effect of oral solutions (glucose and expressed breast milk) with and without the mother-infant relationship (mother holding and mother breastfeeding) on the cortical and clinical responses to a minor painful procedure (heel puncture)
E 19	2017	India	To study the analgesic effect of oral 25% glucose when compared to oral 24% sucrose during heel puncture in preterm NBs
E 20	2016	Brazil	To compare the analgesic effect of 25% glucose and of non-nutritive suction in newborns subjected to vaccination against Hepatitis B
E 21	2016	Cameroon	To compare the analgesic effect of breastfeeding and of 30% glucose on induced pain in full-term newborns during a single painful procedure
E 22	2020	Iran	To compare the effect of oral dextrose and facilitated tucking in reducing pain during heel puncture in preterm infants and to assess the benefit and feasibility for use in emergency settings
E 23	2018	Brazil	To evaluate the analgesic effect of expressed fresh oral breast milk (experimental group) when compared to 25% glucose (control group) on pain relief in preterm newborns under oxygen therapy, subjected to the arterial blood gas collection procedure

Source: Research data.

Table 3 - Characterization of the studies on the use of glucose to relieve pain in newborns during arterial/venous puncture, according to: degree of recommendation/level of evidence, population and results (n=11). *Natal*, RN, Brazil, 2020

STUDY	DEGREE OF RECOMMENDATION/ LEVEL OF EVIDENCE	POPULATION	MAIN RESULTS
E 2	C/4	11 interviews with five nurses and 6 Nursing technicians	Positive results were evidenced with the use of the glycated solution at 25% (1 mL), orally, nearly 1-2 minutes before the painful procedure in full-term and preterm NBs. A reduction in the scores of the *Premature Infant Pain Profile* (PIPP) scale was observed, regarding the incidence and duration of crying.
E 8	A/1B	48 preterm NBs in the experimental (music for 10 minutes, n=26) and control (25% glucose two minutes before puncture, n=22) groups	There were similitudes between the groups at the baseline, and recovery 1 and 2 moments. Both measures produce beneficial therapeutic effects on pain reduction. During treatment, a statistically significant difference was observed between the experimental and control groups ($p = 0.014$). At the painful moment, there was a statistically significant difference ($p = 0.029$) between the two groups, with the weighted mean of the *Neonatal Facial Coding System* (NFCS) of the experimental group (music) being higher than that of the control group (25% glucose). In group 1, pain was more prevalent (≥ 3) and, in group 2, there was absence of pain (< 3), according to NFCS.
E 15	A/1B	26 professionals from the NICU Nursing team	The Nursing professionals use 25% glucose and positioning of the NB (full-term and preterm) as most common strategies for pain relief. Some professionals place the 25% solution on a soaked gauze before the procedure; other do so on the glove's finger, around 4 drops of the sweetened solution. The number of drops depends on the NB size.
E 16	A/1A	168 studies included	Significant reduction in the mean time of NB crying (full-term and preterm) for sweet solutions when compared to placebo for almost 30 seconds. In the final test, the mean difference in the time of crying was -23.18 seconds in favor of the sweet solutions. A significant reduction in the standardized pain scores was evident in the second trial. The final cumulative result showed a standardized mean difference of -0.90 in favor of the sweet solutions in relation to control or placebo.
E 17	A/1B	169 preterm NBs were randomized to receive (1) 30% oral dextrose, (2) facilitated tucking or (3) 30% oral dextrose and facilitated tucking 2 minutes before heel puncture	During heel puncture, the median PIPP-R score of the individuals in the dextrose only group was 7 (min-max: 0.15); the median PIPP-R score of the individuals in the facilitated tucking only group was 8 (min-max: 0.17); and the median PIPP-R score of the individuals in the combined dextrose and facilitated tucking group was 8 (min-max: 0.16), $p = 0.783$). Oral dextrose with and without facilitated tucking did not increase the plasma markers of ATP metabolism and active stress oxidation.
E 18	A/1B	80 full-term NBs, assigned to 4 parallel groups (20 infants per group): glucose, expressed breast milk, glucose offered in the mother's arms, breastfeeding	Oral glucose alone or combined with maternal tucking was associated with no cortical activation during heel puncture. Expressed breast milk was associated with localized bilateral activation of the somatosensory and motor cortices ($p<0.01$). Breastfeeding was associated with extensive bilateral activation of the somatomotor, somatosensory, and right parietal cortices ($p<0.01$). The expression of pain was lower with the mother-infant relationship ($p = 0.007$)
E 19	A/1B	94 preterm NBs (47 in the 24% sucrose group and 47 in the 25% glucose group)	PIPP scores, crying and adverse event rate between the glucose and sucrose groups did not differ statistically, indicating similar analgesia provided by both solutions during heel puncture.

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Tabela 3 - Caracterização dos estudos acerca do uso da glicose no alívio da dor de recém-nascidos durante punção arterial/venosa, segundo: grau de recomendação/nível de evidência, população e resultados (n=11). *Natal*, RN, Brasil, 2020

STUDY	DEGREE OF RECOMMENDATION/ LEVEL OF EVIDENCE	POPULATION	MAIN RESULTS
E 20	A/1B	78 preterm healthy NBs; 40 in the 25% glucose group and 38 in the non-nutritive suction group	The NBs who received 25% glucose presented lower scores in the NIPS scale when compared to those who received non-nutritive suction [mean (SD), 3.3 (2.1) *vs*. 5.6 (1.6), p < 0.001]. The group that received 25% glucose presented no change in SpO_2, only 20% of those who received the solution had vigorous crying and 35% changed their breathing during the procedure. And 82% of the patients who received non-nutritive suction presented changes in the respiratory pattern.
E 21	A/1B	100 preterm healthy NBs with at least 24 hours of life	The analgesic effect of breastfeeding proved to be more beneficial in relation to the 30% glycated solution. The individuals in the breastfeeding group obtained a baseline median score (IQR) for pain of 0 (0.5–0.5) and 0 (0–0) in the 30% glucose solution group. The median pain score presented in the 30% glucose group was 1.5 times higher in relation to the breastfeeding group.
E 22	A/1B	60 preterm infants hospitalized in a NICU: 23 (38.34%) girls and 37 (61.66%) boys	Oral dextrose was superior in relation to facilitated tucking. After the use of oral dextrose (3.58 ± 0.34) during puncture, there was a reduction in the scores when compared to facilitated tucking (5.58 ± 0.53). The application of oral dextrose was considered beneficial when administered in facilitated tucking and is a method capable of significantly reducing pain.
E 23	A/1B	35 preterm NBs in the experimental group (expressed oral breast milk) and 35 in the control group (25% glucose)	It was not possible to assert pain relief in either group that underwent the intervention, as heart rate was increased after the arterial blood gas test for both groups; however, oxygen saturation remained stable,

Source: Research data.

DISCUSSION

There is complexity in the process that involves newborns regarding their hospitalization in neonatal units and the common use of pain-generating invasive procedures. Consequently, the issue represents a global health problem; therefore, it is necessary to reduce pain intensity in NBs for the treatment to be satisfactory. With this, national and international studies were found.

Among the techniques most frequently performed in neonatal units, it is noticed that venous and arterial puncture are some of the procedures that generate pain in NBs. This painful sensation can generate potentially harmful physiological responses for the NBs as a result of the prematurity of their organic systems.[24,25]

That said, non-pharmacological measures are constantly being indicated as a care strategy for pain relief, and oral administration of glucose, considered the gold standard, is the most widespread measure in health systems today, mainly because of its low cost, ease of application and expressive results.[24,25]

With regard to the population addressed, most of the studies carried out their research with preterm[8,17] and full-term NBs[18] admitted to NICUs, and only one study administered 25% glucose in healthy NBs. Based on the results previously presented by the studies, it was possible to verify that the NBs who received the 25% glucose solution had a significant reduction in pain, as well as a reduction in crying time, lower scores in the PIPP scale, reduction in heart rate and SpO_2 stabilization.[2,15-10]

Although the biochemical effects of glucose are not yet fully proven in human NBs, a research study carried out in the laboratory with animals attested that the analgesic effects driven by the sweet taste are capable of causing sensations in the body similar to those generated by opiates, encouraging the release of endorphins and dopamine.[26]

In relation to the method's benefit, the application of sweetened solutions presents benefits in the reduction of physiological pain indicators, such as decreased cortisol concentration, reduced heart rate and oxygen saturation, as well as reduced agitation and crying.[15-20]

Regarding the scales used in the studies to analyze pain, the following stand out: PIPP,[2,17,22] which measures the behavior of the NB in pain, mainly evaluating physiological indicators (such as heart rate, oxygen saturation and gestational age); NFCS,[8] which presents responses in a more specific way than the values observed by physiological parameters;[8] and NIPS, which uses behavioral as well as physiological signals (among them: facial expression, crying, limb movements and breathing pattern) to identify pain.[15,16,18-21]

Regarding the administration of the sweetened solution, the most efficient way found was from 0.5 to 2 mL in gauze soaked with 25% glucose, with a significant reduction in the pain scale.[15-20,24] It is noteworthy that there is no ideal amount of solution that applies to all cases, as the dose should vary according to the NB's gestational age, disease severity and procedure to be performed.[26]

Regarding the comparative studies between glucose and other non-pharmacological measures for neonatal pain relief, such as: breastfeeding, non-nutritive sucking, skin-to-skin contact, massage and music, it was found that oral glucose was more beneficial, evidenced by the reduction in the scores of scales that assess pain. These articles addressed the following non-pharmacological methods: music, non-nutritive sucking, sucrose, facilitated tucking, expressed breast milk and breastfeeding.[8,16-20,22] In contrast, another study reveals that breastfeeding during painful procedures is as beneficial in reducing neonatal pain as glucose, as it was associated with decreased pain responses, reduced heart rate and shorter crying time in full-term NBs.[26]

When comparing glucose and facilitated tucking during puncture in preterm newborns, the studies revealed that the NBs who received oral glucose obtained lower scores in the *Premature Infant Pain Profile* (PIPP) scale, lower energy expenditure (plasma markers of ATP metabolism) and less oxidative stress.[17, 22] Another study carried out with preterm NBs showed that the group that received glucose obtained lower scores in the NIPS scale when compared to the lullaby group, confirming its analgesic effect during painful procedures.[27]

A randomized clinical trial evaluated the cerebral cortical response and the pain level in 80 full-term newborns during the heel puncture procedure. These NBs were divided into four groups: oral glucose, expressed breast milk, glucose administered in the mother's lap and breastfeeding. Cortical activation in the parietal, temporal and frontal cortices was assessed by multichannel near-infrared spectroscopy and pain expression was assessed using the *Neonatal Infant Pain Scale* (NIPS). It was evidenced that oral glucose offered on the mother's lap (mother-infant interaction) presented the lowest median in the NIPS scale and had no cortical activation, emphasizing more benefits than expressed breast milk and oral glucose.[18]

Studies that used the NIPS scale to assess pain in 99 preterm NBs during a phlebotomy procedure in a NICU corroborate this information. The preterm NBs were divided in three groups: oral glucose (experimental), Yakson massage (experimental), and no intervention (control). The results of this study allowed concluding that both oral glucose and massage were able to reduce the NIPS scale score, highlighting its benefit in neonatal pain reduction.[28]

Another study used music and 25% glucose as an analgesic effect during arterial puncture, using facial expressions or mimicry as a parameter to assess pain in NBs. There was a significant reduction in the newborn's facial expression when both methods were used, which favored relaxation and accommodation of the facial reactions in the NBs. Therefore, each method proved to be effective in reducing pain intensity before painful procedures. However, when used in combination, pain intensity was even lower.[29]

The professionals in the NICU team recognize that venous puncture is a painful procedure and are able to identify the painful perception in the NBs through crying, for example. This behavioral factor was mentioned by the professionals as indicative of pain, as well as facial mimicry.[2]

In this sense, it was also emphasized that the non-pharmacological practices offer low cost, ease of administration and almost immediate analgesic effect. In addition to that, this study emphasized the benefit of sucking associated with glucose, which reported that neonates who suck the pacifier with glucose presented lesser pain responses when compared to those who do not use this analgesic practice. The nurses reported that the presence of a professional exclusively in charge of pain management would be ideal, while other professional would perform the venous or arterial access. However, there is often no possibility of this happening due to staff reduction.[2]

Another study, carried out in a teaching hospital in Maceió-AL, showed that nurses at the hospital in question used 25% glucose in soaked gauze before the procedure or placed around four drops of this sweetened substance on the finger of a glove, depending on the size of the newborn. This was the most used strategy by the Nursing professionals, followed by the positioning method (decubitus change, fetal position and coziness, through the formation of "small packages").[15]

Most of the studies reinforce the use of 25% glucose as a non-pharmacological measure to reduce pain intensity in NBs subjected to arterial or venous puncture. As for the way of using it, it was noted that the majority employed 2 mL of this solution, via the oral route, two minutes before the procedure. Finally, although this review intended to evaluate most of the existing literature, limitations may occur as there are research studies published in other indexing databases not included in this research or published more than five years ago.

CONCLUSION

It was possible to identify that the application of a sweetened 25% glucose solution was the most used in the studies, due to its potential to reduce pain intensity in newborns undergoing painful procedures such as arterial and venous puncture.

However, the selected studies presented few details on the best way to administer 25% glucose in the newborn population, making it difficult to fully analyze the quality of the practice under study. The need for new research studies in this area is highlighted to standardize the way in which the solution is administered and to delve deeper into other items, as a deficit in publications on this topic was noticed, especially in the case of arterial puncture.

It is noteworthy that there were papers that associated other non-pharmacological methods as a favorable tool for pain reduction, showing that both 25% glucose and/or music and/or breastfeeding had positive impacts on pain intensity. It is to be noted that, when associated, they have more benefits, as they are in line with other studies that used stimuli which simultaneously affect more than one sense.

The results of this study are useful for the development of future research studies in the neonatal area, for training, skills and competences in the process of training nurses and health professionals, in order to elucidate health actions for pain management in newborns and to contribute to promoting visibility and scientific relevance of the theme.

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