



Scientific evidences for managing pain in the neonatal population

Evidências científicas no controle da dor no período neonatal

Evidencias científicas en el control del dolor en el periodo neonatal

Mariana Bueno¹, Amélia Fumiko Kimura², Carmen Simone Grilo Diniz³

ABSTRACT

Objective: To critically analyze the systematic reviews on neonatal pain management published in the Cochrane library database. **Methods:** The keywords “pain” and “neonate” were used to search the database. **Results:** Six systematic reviews were retrieved. The main themes addressed by these systematic reviews were the following: pain related to therapeutic procedures (one review), non-pharmacological approaches for pain management (two reviews), and pharmacological approaches for pain management (three reviews). **Conclusion:** The systematic reviews suggested the need for other clinical studies with a larger sample size and a stronger research design. These studies would provide further evidence regarding the best approaches for adequate pain management in the neonatal population.

Keywords: Pain/prevention & control; Infant, newborn; Evidence-based medicine

RESUMO

Objetivo: Identificar as revisões sistemáticas referentes ao controle da dor no neonato, catalogadas na Biblioteca Cochrane. **Métodos:** Utilizou-se os descritores *pain e neonate*. **Resultados:** Identificou-se seis publicações. Os temas abordados foram: dor resultante de procedimentos (uma revisão); métodos não-farmacológicos para o alívio da dor (duas) e métodos farmacológicos para analgesia (três). **Conclusões:** As revisões, de modo geral, apontam para a necessidade de condução de novos estudos clínicos, com amostras significativas e delineamentos adequados, para que mais evidências permitam instituir adequado controle da dor neonatal na prática clínica.

Descritores: Dor/prevenção & controle; Recém-nascido; Medicina baseada em evidências

RESUMEN

Objetivo: Identificar las revisiones sistemáticas relacionadas con el control del dolor en el neonato, catalogadas en la Biblioteca Cochrane. **Métodos:** Se utilizaron las palabras clave *pain y neonate*. **Resultados:** Se identificaron seis publicaciones. Los temas abordados fueron: dolor resultante de procedimientos (una revisión); métodos no-farmacológicos para el alivio del dolor (dos) y métodos farmacológicos para analgesia (tres). **Conclusiones:** Las revisiones, de modo general, apuntan para la necesidad de conducir nuevos estudios clínicos, con muestras significativas y delineamientos adecuados, para que nuevas evidencias permitan instituir un adecuado control del dolor neonatal en la práctica clínica.

Descriptores: Dolor/prevenición & control; Recién nacido; Medicina basada en evidencia

¹ Ph.D. candidate at the Escola de Enfermagem da Universidade de São Paulo – USP – São Paulo (SP), Brazil. FAPESP Doctoral Fellowship (process # 2008/52891-8).

² Ph.D. Professor at the Maternal-Children and Psychiatric Nursing Department at the Escola de Enfermagem da Universidade de São Paulo – USP – São Paulo (SP), Brazil.

³ Ph.D. Professor at the Department of Maternal and Child Health at Faculdade de Saúde Pública da Universidade de São Paulo – USP – São Paulo (SP), Brazil.

INTRODUCTION

For many years health professionals have assumed that newborns (NB) could not feel pain⁽¹⁾. This was generally attributed to the immaturity of the central nervous system and to the absence of memory for pain. Furthermore, the contraindication of the use of opioids in neonates was justified by the high risk of respiratory depression⁽²⁾. Thus, hospitalized NB have undergone painful procedures, even surgical ones, without any type of analgesia for many years.

Currently, clinical research has contributed to understand the painful phenomena in neonates, as well as to make professionals aware of pain and the need for pain assessment and control in order to prevent or treat pain in this population^(1,3). Thus, as of the 90's in the 20th century, pain occurrence started to be considered important in neonatal care.

Evidences have been published regarding the development of the nervous system during the fetal life. It starts at six weeks of pregnancy when the development and increase on number of sensory fibers and interneurons in the posterior horn of spinal cord occurs; during the seventh week of gestation, sensitive-cutaneous receptors are observed in the fetus' perioral area⁽⁴⁾. Not only anatomical development continues through the pregnancy, but the production of endogenous substances involved in the process of painful information also occurs. In the twentieth week of pregnancy, the ascending nociceptive pathways become functional⁽⁵⁾, meaning that the fetus is ready to perceive painful stimuli. Thus, all hospitalizes neonates, either presenting low, medium or high risk, can feel pain. It is important to stress that the necessary pathways for pain modulation and inhibition both in term and preterm NB are immature at birth⁽⁶⁻⁷⁾. Thus, exposure to the painful stimulus is not followed by efficient endogenous inhibition of pain, leaving NB more vulnerable to pain.

Pain in neonates results in several adverse events in short and long term. The following can be highlighted: changes in metabolism and catabolism, energy expenditure to control pain instead of using energy reserves for growth and clinical reestablishment, future changes in behavioral, emotional, and cognitive aspects regarding subsequent painful episodes, changes in sensibility and anatomic structures^(4,8-9). Therefore, there is the need for pain control in neonatal units.

The number of scientific publications referring to "pain in the neonatal period" is significant, requiring a critical analysis. This analysis allows the assessment of the quality of available data and can guide decision making in clinical practice. Thus, it is possible to seek for evidences to be introduced in the clinical setting, related either to assessment and diagnoses of neonatal pain or to effective interventions for pain relief, contributing to establish programs on

prevention, evaluation and treatment of neonatal pain.

Evidence-based practice does not take intuition, non-systematized observations, or pathological principles into account⁽¹⁰⁾, but rather the levels of scientific evidences presented on publications. Studies can be classified in the following levels⁽¹¹⁾: level 1, considered as strong evidence, it includes at least one systematic review of several well designed randomized controlled studies; level 2, strong evidence, it includes at least one well designed randomized controlled trial with adequate sample size; level 3 includes non-randomized well designed trials, pre and post-cohort trials, temporal series or paired case control; at level 4, non-experimental studies developed in one or more center or research group are included; at level 5, the experiences of authorities and experts, the clinical practice, and the descriptive studies are considered.

Systematic reviews are classified as the best level of evidence for practical application of scientific information. Its purpose is to investigate scientific data in order to answer specific questions⁽¹²⁾. To answer questions on interventions, systematic reviews and randomized clinical trials are the best study design⁽¹³⁾.

It is challenging to be updated on the knowledge produced in neonatology. In this sense, a systematic review of the Cochrane database is an excellent resource for professionals to have access to clinical trials and systematic reviews. With these reviews, health professionals can learn about interventions and therapeutic practices and the best available evidences can be implemented to guide clinical decisions or to change old practices and routines⁽¹⁾.

The present study aimed to identify systematic reviews about pain in the neonatal period catalogued by the Cochrane Library.

METHODS

The search was carried out in Cochrane Library, in February 2008, using pain and neonate as descriptors, identified in the words of the text. Seventy three complete systematic reviews were retrieved and sex reviews on neonatal pain were included. The 67 excluded publications refer to several themes such as analgesia during labor and delivery, medication for pre-eclampsia, neonate sepsis, gastroesophageal reflux, pain relief during pregnancy, vaccines, among others.

The following variables were extracted from the reviews: objectives of the review, number of studies assessed and number of included and excluded studies, total number of neonates studied, and conclusions and recommendations to authors.

RESULTS

Six systematic reviews have been assessed. Among the

publications included, the thematic identified refers to: acute procedural pain in neonates (one review), strategies to control pain either through non-pharmacological interventions (two reviews) or pharmacological interventions (three reviews). Therefore, results have been organized according to these themes.

Neonatal pain resulting from procedures

Only one (16.7%) of the reviews assessed deals with the issue of pain resulting from potentially painful procedures. To verify which procedure for blood collection, venepuncture or heel lance, is more painful in term NB was the objective of a systematic review carried out by Shah and Ohlsson⁽¹⁴⁾. The analysis of five studies, resulting in a total sample of 347 neonates concluded that venepunctures performed by experienced professionals are less painful than heel lances for blood collection in term NB.

Nonpharmacological interventions for neonatal pain control

Nonpharmacological methods for pain relief in neonates were the objective of two systematic reviews available at the database assessed.

The objective of Shah et al's publication⁽¹⁵⁾ was to assess the effectiveness of breastfeeding in reducing procedural pain in neonates. Twelve studies were assessed, one was excluded and there were a total of 1,030 NB included. The main conclusions were the following: breastfeeding or breast milk reduces pain from isolated painful procedures when compared to placebo, positioning (swaddling or holding), or no intervention. The review indicates that other clinical studies are needed to assess the effectiveness and the safety of these interventions in repeatedly performed procedures, including preterm neonates.

Stevens et al⁽¹⁶⁾ published a systematic review with the objective of assessing the efficacy, the effect of doses, the administration methods, and the safety of sucrose orally given for procedural pain relief. Through the analysis of 44 studies, 21 were included, with a total sample of 1,616 neonates drawing the following conclusions: oral administration of sucrose is effective for pain control in isolated procedures in NB, with minimal or absent adverse events; oral use of 0.012 to 0.12 g (0.05 to 0.5 ml) of 24% sucrose solution is recommended for analgesia in neonates, two minutes before painful procedures such as heel lance and venepuncture.

However, because of a reduction of only 20% on pain scores observed in published data, the authors suggest the conduction of new studies associating other nonpharmacological methods (tactile stimulus and skin-to-skin contact) and pharmacological strategies (morphine and fentanyl citrate) to oral sucrose, which could increase

its effects and result in lower scores or even absence of pain.

Authors also recommend further studies with the inclusion of a proper number of neonates, to enable statistical analysis with greater significance, the use of reliable and validated outcomes for pain assessment, as well as the need to consider particularities on pain expression of neonates and the context in which pain is experienced. The use of sucrose solution must be assessed from a clinical standpoint, from the neonatal development, and the economic point of view. Oral use of sucrose should also be studied in low birth weight neonates, unstable NB and also in mechanically ventilated infants.

Pharmacological interventions for the control of neonatal pain

The analysis of pharmacological methods available for the use in neonates was approached in three of the reviews published at the Cochrane Library.

The review conducted by Taddio et al⁽¹⁷⁾ aimed to assess the efficacy and effectiveness of the eutectic mixture of lidocaine and prilocaine (EMLA®) as analgesic drug for circumcision in neonates and to offer evidence-based recommendations for clinical practice. Four papers were assessed, three were included and one was excluded. A total of 139 neonates were studied. The main conclusions were the following: the evidences are enough to recommend the use of EMLA® in units where there is no treatment or no standardized pain control strategies to be implemented during neonatal circumcision; to replace other treatments that are considered effective (such as dorsal penile nerve block with lidocaine) by topical application of the emulsion is not recommended. The use of EMLA® is considered safe when applied in isolated doses on the intact skin of NB with regard to methaemoglobinaemia occurrence.

Authors highlight the importance of studies to assess the effect of the emulsion in other painful procedures and in repeated doses. They also recommend further studies to assess other methods for pain relief in circumcision, to be used isolated or combined.

Brady-Fryer et al⁽¹⁸⁾ published a systematic review to assess the efficacy and safety of interventions for pain relief during circumcision in neonates. Through the analysis of 42 studies, the inclusion of 35 articles and exclusion of 7 papers, with a total of 1,997 neonates, authors concluded that: the best anesthesia options for the procedure are dorsal penile nerve block and ring block, both using subcutaneous lidocaine infiltration, EMLA®, and topical lidocaine; dorsal penile nerve block was the intervention presenting the best results for pain control; ring block was also effective compared to placebo and, furthermore, it is simpler and safer than dorsal penile

nerve block. Topical use of EMLA® and lidocaine is also effective when compared to the use of placebo, but the emulsions are difficult to apply and the EMLA® takes long to present anesthetic effect. Authors also highlight that interventions such as giving oral sucrose solutions or orally administered analgesic, and changes in the environment where the procedure is performed did not present consistent results of decreasing pain from circumcision.

The use of different types of surgical instruments, Mogen and Gomco clamps in this case, showed that the procedure is performed more often with the use of Mogen clamp, reducing the total amount of time of pain exposure.

Authors stress that none of the studied interventions completely eliminated pain from circumcision in neonates. They also stated that further studies are needed to confirm the efficacy of analgesia and of combining two or more interventions to perform circumcision in neonates.

A review conducted by Bellù et al⁽⁹⁾ assessed the analgesic effects of opioids in painful episodes, in the duration of pulmonary mechanic ventilation, in mortality, in growth, and in neurological outcomes when compared to untreated neonates or those receiving placebo, non-opioid drugs or sedatives. The analysis of 16 studies, with later exclusion of three articles with a total of 1,505 NB included drew the following conclusions: the evidences for recommending the use of opioids for mechanically ventilated neonates are insufficient; it suggests the careful use of opioids in NB, based on clinical judgment and pain assessment. Morphine rather than midazolam is recommended for pain relief because of the less significant side effects presented by this opioid.

Authors also highlight that there is the need for further studies

with a different methodology; they also mention the importance of carrying out studies in NB that present pain during mechanic pulmonary ventilation, and proper pain assessment by using specific tools. The need for studies in preterm neonates and for surveys to assess the medium and long term effects of opioid use on the neurological development of this population is also considered important by authors.

CONCLUSIONS

Although there are a great number of publications available on neonatal pain in databases such as Pubmed, the number of randomized clinical trials with a suitable methodology and significant sample sizes is still small, hindering the performance of systematic reviews and meta-analysis with enough evidence to make clinical practice recommendations.

The results presented in this study confirm the following: scientific evidences regarding adequate pain

control in the neonatal period that can support the clinical practice are still lacking. Only one systematic review approached the issue of pain from procedures commonly conducted in inpatient units; two reviews focused on the use of nonpharmacological methods for procedural pain relief (breastfeeding or breast milk and oral sucrose solutions); three reviews assessed pharmacological treatment for pain (two for circumcision and one for mechanically ventilated NB).

FINAL CONSIDERATIONS

Evidences must be considered to support clinical decisions on diagnoses, interventions, and outcomes (20). Thus, care provided by nurses and other health professionals based on clinical evidences fosters not only a better quality of care but also greater safety to the patients cared for.

However, applying principles of evidence-based practice, especially in nursing, is not a reality since the field does not have enough studies with the features to support this practice (10). As for control of pain in the neonatal period, this is not a limitation restricted to the nursing area only; the number of good quality publications with an adequate level of evidence from the several fields involved with NB care is also scarce as showed by the previously presented results.

There are many other painful situations that have not been approached by systematic reviews, such as neonates undergoing chest drainage, venous or arterial catheterization, surgical procedures, dressing wounds changing, among others. Likewise, there are many other types of pharmacological and nonpharmacological methods described in the literature as useful for neonatal pain control that have not been completely studied in terms of their effectiveness and safety. The studies on nonpharmacological methods, such as breastfeeding, breast milk, and skin contact, isolated or together can be developed in the current scenario in Brazil, where kangaroo-mother care is encouraged in many hospitals.

Pain prevention and control in neonates are actions that should become part of the routine of inpatient units to avoid the short and long term deleterious effects from pain. The nursing staff should work with the evidences available up to date and change their practice according to the current recommendations. However, new evidences should be searched through clinical trials of intervention using adequate sample size and statistical analysis.

Last, it is important to mention that because this is a vulnerable population, there is a hindrance in the performance of clinical studies in neonates, especially studies referring to the use of analgesic drugs. Thus, methodological adjustment and following ethical principles of research should be considered as essential to carry out studies in this field.

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