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## Factors related to use of systemic analgesia in neonatology

Fatores relacionados ao uso de analgesia sistêmica em neonatologia

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#### **ABSTRACT**

The purpose of this paper was to carry out a review of literature on the history and current stage of the knowledge of systemic analgesia in neonatology and the factors influencing its use. A search for scientific articles was made in the MEDLINE, SciELO and LILACS databases using the keywords: analgesia, systemic analgesics, pain, neonatology, newborn, intensive care units and neonatal intensive care units. Additional research was made on dissertations and thesis databanks as well as text books. Literature consulted disclosed that, in general, analgesia is not

a routine practice in neonatal intensive care units, despite the numerous studies demonstrating its importance. Although pain relief is a basic principle of medicine, involving ethic and humanitarian issues and despite the current availability of a number of practical guidelines and consensus regarding pain management in newborns at risk, findings of the present study fall far short of current recommendations. Urgent intervention is required to redress this situation.

**Keywords** Analgesia/methods, Pain; Infant, newborn; Neonatal intensive care units

#### INTRODUCTION

Studies have shown that repetitive or prolonged pain stimulus in early life may lead to changes in the central nervous system with consequences during childhood and possible adult life. (1,2) As such, prolonged or repetitive persistent pain would induce physiological and hormonal changes that would alter the molecular neurobiological mechanisms. Therefore, it is suggested that the severely ill baby, by the senses will remember the pain, not necessarily with a cognitive register. Furthermore, changes in the neural connections might contribute to the "chronic pain syndrome" (1,3,4).

Starting from the conceptual model of use of systemic analgesics in neonatal intensive care units, shown in figure 1, a description of the variables related to the newborn, to the medical professional and to the services involved will be performed.

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#### VARIABLES RELATED TO THE PATIENTS

Occurrence of painful situations, capacity to feel and express pain and patient's biological profile

For the newborn in a neonatal intensive care unit there are many

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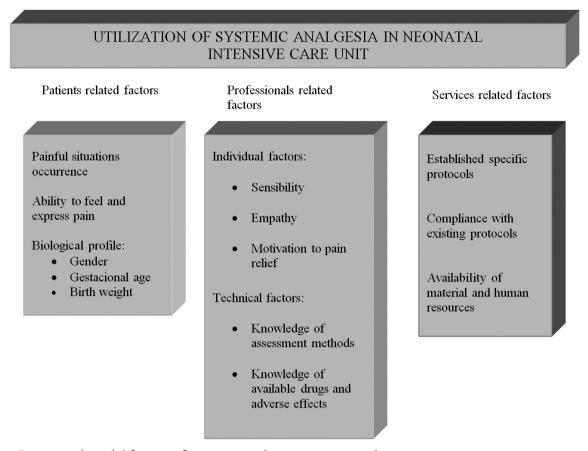


Figure 1 - Conceptual model for use of systemic analgesia in a neonatal intensive care unit.

causes of stress, including mechanical ventilation, inadequate nutrition, episodes of drop in oxygen saturation, intense lighting, constant noise and multiple procedures among others. It is known that the cochlea and sensorial organs develop about the 25th gestation week and that the capacity to hear noises of 40 decibels is present after the 28th week. Another factor is the development of a circadian rhythm occurring around the 32nd week which may be changed by variation of environmental lighting in a neonatal intensive care unit. (5)

That is why it is fundamental to try to minimize the aggression suffered by the newborn during stay in the neonatal unit by simple strategies such as positioning, adjustment of procedures and humanization of care. (6-8) Important non-pharmacological actions can be taken to minimize pain and stress during stay in the neonatal unit. (9,10)

With increasing knowledge about pain in the neonatal period, research has been developed to identify the capacity to perceive pain in intra-uterine life. (11,12). It is known that since the 16<sup>th</sup> week of gestation, trans-

mission of pain, based upon peripheral receptors to the cortex is possible and undergoes complete development after the 26<sup>th</sup> week. As such, the fetus is able to feel pain at this stage. However, it is noteworthy that inhibitory and pain modulatory mechanisms only develop after birth, so that the immature organism is even more sensitive to painful stimuli. (11-14)

During the neonatal period there is a rapid growth and cerebral development so that pain and repeated stress at this time, may lead to an altered development of the pain system, associated to a decrease of its threshold, in addition to an alteration in the respiratory, cardiovascular and metabolic stability. (1,3,9,12,14-17)

Newborn exposed to noxious stimuli present immediate hormone and physiological changes. However, premature and full-term babies have a different response to pain. The premature may present with a reduced initial response to pain, which does not mean that they do not feel it. (8,18) It is noted that heavier infants and those with more gestation age at birth, present with a greater chance of receiving analgesia. (19)

#### VARIABLES RELATED TO PROFESSIONALS

Despite the increasing availability of therapeutic resources and evaluation, the limited use of analgesics is still noted in neonatal intensive care units. (19-22) Management of newborn pain is not adequate, due to lack of knowledge of the mechanisms of nociception and incorrect application of available information. (23) According to Castro et al., (19) difficulties in adequate treatment of pain in the newborn are not only due to lack of diagnostic and therapeutic options, but on how health professionals make use of the scientific knowledge about presence, diagnosis and treatment of pain in their daily practice.

#### **Individual factors**

Among the factors that interfere in perception of the other's pain and in motivation for relief of the patient's pain, is the physician patient relationship, interpersonal relationship in which are found: identification (psychological process by which an individual assimilates an aspect, an attribute of the other and is transformed according to this person's model), transference (the array of phenomena that constitute the relationships among persons) and the countertransference (array of the physician's unconscious reactions to the person of the patient). From the physical suffering of the patient, the interpersonal relationship is in play, that is to say the physician reactivates and personalizes various feelings in addition to the events experienced at another time, at former stages of his/her life. Thus, perception and intervention in a symptom may be severely compromised in their care and understanding. (24)

Furthermore, by means of a cognitive restructuring, a mechanism of psychological defense of the professional who performs the invasive procedures as a routine can be detected making them more skeptical in relation to subjective response to pain and stress shown by patients in intensive care. As a consequence, a disinterest in the actions to reduce stress and pain in the baby may be noted. (19) Although professionals acknowledge that the newborn feels pain, they have difficulty in defining and dealing with it. (6)

#### Knowledge of the assessment methods

Because pain is a subjective occurrence, it is difficulty to evaluate, mainly in individuals unable to verbalize it, especially newborn. This leads to an adult's need to recognize and decode signs of pain emitted by the preverbal patient, relying therefore on a knowl-

edge about pain at this age bracket, of the sensibility and attention for perception of these signs. (19,21,22) According to Silva et a., "pain must be appraised as the fifth vital sign and assessed systematically even in the newborn". (25)

Currently various physiological and behavioral parameters are available, in addition to multidimensional scales for assessment of presence and intensity of pain in the newborn. (9,19,21,23,26-28) Among these physiological parameters are included: cardiac rate, respiratory rate, arterial pressure, oxygen saturation, transcutaneous oxygen and carbon dioxide tension and hormone dosage. Among the main behavioral parameters used were: crying, motor activity and facial expression of pain.

Crying is a form of communication and manifestation of the baby and is much used by mothers and caretakers. Although crying is considered an important parameters for assessment of pain the American Academy of Pediatrics and the Canadian Paediatric Society, in 2000, when discussing prevention and management of pain as well as stress in newborn, called attention to absence of behavioral responses, including crying and movement which are not necessarily indicative of the absence of pain. Crying is not very specific but seems to be a useful instrument when associated with other measurements of pain assessment. (6,16,29)

Isolated motor activity also seems to be a sensitive method to assess pain in premature and full-term newborn but, when analyzed with the other physiological and behavioral variables it becomes safer. (16) A specific method for the assessment of pain is the observation of facial expression. (30)

Once subjectivity that involves this subject and the need to perceive the models to establish presence of pain, was taken into account, various scales have been developed for assessment. Those most studied are: *Neonatal Facial Coding Scale* (NFCS); *Neonatal Infant Pain Scale* (NIPS) and the *Premature Infant Pain Profile* (PIPP). (31-33)

NFCS is a unidimensional scale widely used in research, accepted and validated for assessment of acute pain. NIPS evaluates parameters before and after invasive procedures in full- term and premature newborn. In addition, it assesses the baby's response to potentially painful procedures. In the patient under mechanical ventilation, the score of facial expression is doubled, without assessing the parameter of crying (intubated patient). (34) PIPP is the more indicated scale for prematures because it considers alterations pertaining to this

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group of patients.

A gold standard is still not available for the assessment of pain in the newborn and the currently available tools are not able to objectively measure pain intensity. However, given the importance of the correct evaluation of situations to adopt the correct conduct, each case must be individually analyzed for use of the best suited instrument.

### Knowledge about drugs available and adverse effects

There is no consensus about the best pharmaceutical protocol for treatment of pain in critically ill patients. Even with the possible explanations for the poor use of analgesia in a neonatal intensive care unit already reported, adverse effects of drugs, reported as "fearful" by some professionals must be remembered. Noteworthy among these are: respiratory depression, rigidity of the thoracic wall, tolerance, abstinence and dependence. (16,34-38) The following drugs are more frequently used in neonatal intensive care units. (9,39)

#### Non-opioid analgesics

Among the drugs in this group only paracetamol is released for use in the neonatal period, however, in Brazil, it is not produced for parenteral use, restricting utilization in neonatal intensive care units. (16,40) The recommended dose is 10 to 15 mg/kg for full-term newborn and 10 mg/kg for premature, every six hours. It is not indicated for bearers of G6PD deficiency. (16)

#### **Opioid** analgesics

In neonatal intensive care, these are the most important tool for pain treatment. (10) Among the undesirable effects, common to all opioids, are: respiratory depression, sedation, paralytic ileus, urine retention, nausea, vomit and physical dependence. (41)

- Morphine: recommended doses are, intermittent administration of 0.05 to 0.2 mg/kg/ up to every four hours, intravenous. For continuous administration in full term newborn from 5 to  $20\mu g/kg/hour$  and for premature from 2 to  $10\mu g/kg/hour$ .
- Fentanyl: has almost immediate onset of action and shorter duration than morphine with hemodynamic stability and is often used in neonatology. Recommended doses for intermittent, intravenous administration from 1 to 4 $\mu$ g/kg, every 2 to 4 hours. For continuous administration in full- term newborn from 0.5 to 3 $\mu$ g/kg/hour and for premature from 0.5 to 2 $\mu$ g/kg/hour. The tolerance effect is a disadvantage of con-

tinuous infusion.(16)

- Remifentanil: synthetic opioid that has all the pharmacodynamic characteristics of its class, however with rapid recovery from effects (five to tem minutes), with direct correlation between doses, blood levels and response. Doses vary according to the desired objective, and are recommended for infusion in bolus for intubation of 1 to 3µg/kg and for continued infusion of 0.1 to 5µg/kg/minute. (42)

#### VARIABLES RELATED TO SERVICES

With the increasing complexity of care (indiscriminate use of technology and more and more sophisticated procedures), there has been more work and research to assess the quality of medical care. With this focus, various studies have been undertaken in different countries to verify professional practice related to pain management in the neonatal period, but there are few services that have written routines for management of acute pain and prolonged pain control. (7,43) A gap is found between scientific evidence and clinical practice (20,44) so that all units must establish their norms and routines for neonatal analgesia, since it is difficult and time consuming to transform evidence into practice. (45)

#### **CONCLUSIONS**

It is known that pain relief is one of the basic principles of medicine, in addition to involve ethical and humanitarian issues; nevertheless analgesia is not a routine practice in neonatal intensive care units. Currently a series of practical guidelines and consensus on the management of pain in newborns at risk are available. (10,16,46,47)

Therefore, an effort to redress current shortcomings in neonatal intensive care is required, through new research on the subject, including safer drugs, addition to the formal curriculum of disciplines related to strategies for patient's wellbeing, organization of the service to detect shortcomings in the assistance and establishment of specific routines for management of pain in the newborn as well as the updating and increased awareness of professionals taking care of babies.

#### **RESUMO**

O objetivo desse trabalho foi **r**ealizar uma revisão da literatura sobre o histórico e o estágio atual de conhecimento sobre a analgesia sistêmica em neonatologia e os fatores que influenciam

a sua utilização. Foi realizada busca de artigos científicos através das bases dados do MEDLINE, SciELO e LILACS com as palavras chave: analgesia, analgésicos sistêmicos, dor, neonatologia, recém-nascido, unidade de terapia intensiva e unidade de terapia intensiva neonatal, além de pesquisa adicional em bancos de dados de dissertações, teses e livros texto. A literatura consultada revela que a analgesia não é uma prática rotineira nas unidades de terapia intensiva neonatal, de uma forma geral, apesar dos inúmeros estudos demonstrando a importância do tema. Apesar

de ser o alívio da dor um dos princípios básicos da medicina, de envolver questões éticas e humanitárias, e de estarem disponíveis atualmente vários guias práticos e consensos a respeito do manejo da dor no neonato de risco, os resultados encontrados no presente estudo estão muito aquém das recomendações atuais, tornando-se necessária uma intervenção urgente para reverter a situação observada.

**Descritores:** Analgesia/métodos; Dor; Recém-nascido; Unidades de terapia intensiva neonatal

#### REFERENCES

- Guinsburg R. A dor que não fala [tese livre docência]. São Paulo: Universidade Federal de São Paulo. Escola Paulista de Medicina; 2001.
- Porter FL, Grunau RE, Anand KJ. Long-term effects of pain in infants. J Dev Behav Pediatr. 1999;20(4):253-61. Review.
- 3. Wolf AR. Pain, nociception and the developing infant. Paediatr Anaesth. 1999;9(1):7-17.
- 4. Marcus DA. A review of perinatal acute pain: treating perinatal pain to reduce adult chronic pain. J Headache Pain. 2006;7(1):3-8.
- 5. Hall RW, Anand KJS. Physiology of pain and stress in the newborn. NeoReviews. 2005;6(2):e61-8.
- Gaíva MAM, Dias NS. Dor no recém-nascido: percepção de profissionais de saúde de um hospital universitário. Rev Paul Enferm. 2002;21(3):234-9.
- Hennig MAS, Gomes MASM, Gianini NOM. Conhecimentos e práticas dos profissionais de saúde sobre a "atenção humanizada ao recém-nascido de baixo peso método canguru". Rev Bras Saúde Matern Infant. 2006;6(4):427-36.
- 8. Guideline statement: management of procedure-related pain in neonates. J Paediatr Child Health. 2006;42 Suppl 1:S31-9. Review.
- Silva YP, Silva JF, Barbosa SMM. História da dor em pediatria a situação do Brasil. In: Silva YP, Silva JF, organizadores. Dor em pediatria. Rio de Janeiro: Guanabara Koogan; 2006.p.3-7.
- Silva YP, Gomez RS, Máximo TA, Silva ACS. Sedação e analgesia em neonatologia. Rev Bras Anestesiol. 2007;57(5):575-87.
- 11. Glover V, Fisk NM. Fetal pain: implications for research and practice. Br J Obstet Gynaecol. 1999;106(9):881-6.
- 12. Van de Velde M, Jani J, De Buck F, Deprest J. Fetal pain perception and pain management. Semin Fetal Neonatal Med. 2006;11(4):232-6.
- 13. Lee SJ, Ralston HJ, Drey EA, Partridge JC, Rosen MA. Fetal pain: a systematic multidisciplinary review

- of the evidence. JAMA. 2005;294(8):947-54. Comment in: JAMA. 2006;295(2):159; author reply 160-1. JAMA. 2006;295(2):159; author reply 160-1. JAMA. 2006;295(2):160; author reply 160-1.
- 14. Simons SH, Tibboel D. Pain perception development and maturation. Semin Fetal Neonatal Med. 2006;11(4):227-31.
- 15. Gaspardo CM, Linhares MBM, Martinez FE. A eficácia da sacarose no alívio da dor em neonatos: revisão sistemática da literatura. J Pediatr (Rio J). 2005;81(6): 435-42.
- 16. Guinsbug R. Avaliação e tratamento da dor no recém-nascido. J Pediatr (Rio J). 1999;75(3):149-60.
- 17. Grunau RE, Holsti L, Peters JW. Long-term consequences of pain in human neonates. Semin Fetal Neonatal Med. 2006;11(4):268-75.
- 18. Peters JW, Schouw R, Anand KJ, van Dijk M, Duivenvoorden HJ, Tibboel D. Does neonatal surgery lead to increasead pain sensitivity in later childhood? Pain. 2005;114(3):444-54.
- Castro MCFZ, Guinsburg R, Almeida MFB, Peres CA, Yanaguibashi G, Kopelman BI. Perfil da indicação de analgésicos opióides em recém-nascidos em ventilação pulmonar mecânica. J Pediatr (Rio J). 2003;79(1):41-8.
- 20. Carbajal R, Rousset A, Danan C, Coquery S, Nolent P, Ducrocq S, et al. Epidemiology and treatment of painful procedures in neonates in intensive care units. JAMA. 2008;300(1):60-70.
- Guinsburg R, Balda RCX, Berenguel RC, Almeida MFB, Tonelloto J, Santos AMN, Kopelman BI. Aplicação das escalas comportamentais para avaliação da dor em recémnascidos. J Pediatr (Rio J). 1997;73(6):411-8.
- 22. Prestes ACY, Guinsburg R, Balda RCX, Marba STM, Rugolo LMSS, Pachi PR, Bentlin MR. Freqüência do emprego de analgésicos em unidades de terapia intensiva neonatal universitárias. J Pediatr (Rio J). 2005;81(5):405-10.
- 23. Guinsburg R, Kopelman BI, Almeida MFB, MiyoshiMH. A dor no recém-nascido prematuro submetido a ventilação mecânica através de cânula traqueal. J Pediatr (Rio J). 1994;70(2):82-90.
- 24. Pires ALS. Fatores que afetam a percepção da dor em crian-

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- ças. In: Silva YP, Silva JF, organizadores. Dor em pediatria. Rio de Janeiro: Guanabara Koogan; 2006.p.21-8.
- 25. Silva YP, Gomez RS, Máximo TA, Silva ACS. Avaliação da dor em neonatologia. Rev Bras Anestesiol. 2007;57(5):565-74.
- 26. Suraseranivongse S, Kaosaard R, Intakong P, Pornsiriprasert S, Karnchana Y, Kaopinpruck J, Sangjeen K. A comparison of postoperative pain scales in neonates. Br J Anaesth. 2006;97(4):540-4.
- 27. Grunau RE, Oberlander T, Holsti L, Whitfield MF. Bedside application of the Neonatal Facial Coding System in pain assessment of premature neonates. Pain. 1998; 76(3):277-86.
- 28. Guinsburg R, de Almeida MF, de Araújo Peres C, Shinzato AR, Kopelman BI. Reliability of two behavioral tools to assess pain in preterm neonates. Sao Paulo Med J. 2003;121(2):72-6.
- 29. Prevention and management of pain and stress in the neonate. American Academy of Pediatrics. Committee on Fetus and Newborn. Committee on Drugs. Section on Anesthesiology. Section on Surgery. Canadian Paediatric Society. Fetus and Newborn Committee. Pediatrics. 2000;105(2):454-61.
- Boyle EM, Freer Y, Wong CM, McIntosh N, Anand KJ. Assessment of persistent pain or distress and adequacy of analgesia in preterm ventilated infants. Pain. 2006;124(1-2):87-91.
- 31. Grunau RV, Craig KD. Pain expression in neonates: facial action and cry. Pain. 1987;28(3):395-410.
- 32. Lawrence J, Alcock D, McGrath P, Kay J, MacMurray SB, Dulberg C. The development of a tool to assess neonatal pain. Neonatal Netw. 1993;12(6):59-66.
- 33. Stevens B, Johnston C, Petryshen P, Taddio A. Premature Infant Pain Profile: development and initial validation. Clin J Pain. 1996;12(1):13-22.
- 34. Chermont AG, Guinsburg R, Balda RCX, Kopelman BI. O que os pediatras conhecem sobre avaliação e tratamento da dor no recém-nascido? J Pediatr (Rio J). 2003;79(3):265-72.
- 35. Bartolomé SM, Cid JLH, Freddi N. Sedação e analgesia em crianças: uma abordagem prática para as situações mais freqüentes. J Pediatr (Rio J). 2007;83(2 Suppl):S71-82.
- 36. Simons P, Anand KJ. Pain control: opioid dosing, popula-

- tion kinetics and side-effects. Semin Fetal Neonatal Med. 2006;11(4):260-7.
- 37. Suresh S, Anand KJ. Opioid tolerance in neonates: a state-of-the-art review. Paediatr Anaesth. 2001;11(5):511-21.
- 38. Tibboel D, Anand KJ, van den Anker JN. The pharmacological treatment of neonatal pain. Semin Fetal Neonatal Med. 2005;10(2):195-205.
- Lago PM, Piva JP, Garcia PCR, Knight G, Ramelet AS, Duncan A. Analgesia e sedação em situações de emergência e unidades de tratamento intensivo pediátrico. J Pediatr (Rio J). 2003;79(Suppl 2):S223-30.
- 40. Jacqz-Aigrain E, Anderson BJ. Pain control: non-steroidal anti-inflammatory agents. Semin Fetal Neonatal Med. 2006;11(4):251-9.
- 41. Bellù R, de Waal KA, Zanini R. Opioids for neonates receiving mechanical ventilation. Cochrane Database Syst Rev. 2005;25(1):CD004212.Review.Update in: Cochrane Database Syst Rev. 2008;(1):CD004212.
- 42. Pereira e Silva Y, Gomez RS, Barbosa RF, Simóes e Silva AC. Remifentanil for sedation and analgesia in a preterm neonate with respiratory distress. Paediatr Anaesth. 2005;15(11):993-6. Comment in: Paediatr Anaesth. 2005;15(11):909-12.
- Gray PH, Trotter JA, Langbridge P, DohertyCV. Pain relief for neonates in Australian hospitals: a need to improve evidence-based practice. J Paediatr Child Health. 2006;42(1-2):10-3. Comment in: J Paediatr Child Health. 2006;42(1-2):2-3.
- 45. Heaton P, Herd D, Fernando A. Pain relief for simple procedures in New Zealand neonatal units: practice change over six years. J Paediatr Child Health. 2007;43(5):394-7.
- Anand KJ; International Evidence-Based Group for Neonatal Pain. Consensus statement for the prevention and management of pain in newborn. Arch Pediatr Adolesc Med. 2001;155(2):173-80.
- 47. American Academy of Pediatrics Committee on Fetus and Newborn; American Academy of Pediatrics Section on Surgery; Canadian Paediatric Society Fetus and Newborn Committee; Batton DG, Barrington KJ, Wallman C. Prevention and management of pain in the neonate: an update. Pediatrics. 2006;118(5):2231-41. Erratum in: Pediatrics. 2007 Feb;119(2):425. Comment in: Pediatrics. 2007 Feb;119(2):421-2. Republished in: Adv Neonatal Care. 2007 Jun;7(3):151-60.