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Evaluation of procedural pain for neonates in a neonatal intensive care unit: a single-centre study

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ABSTRACT

Background To evaluate the procedural pain experienced by neonates in a neonatal intensive care unit (NICU) setting and determine the corresponding pain grades.

Methods Two experienced nurses independently used the Neonatal Infant Pain Scale (NIPS) to evaluate the neonatal pain during procedures taking place in the tertiary NICU and two level-two neonatal care units in the Children's Hospital of Zhejiang University School of Medicine. The mean and distribution of NIPS pain scores and the corresponding pain grades of participants when experiencing clinical painful procedures were analysed.

Results A total of 957 neonates exposed to 15 common clinical painful procedures were included in the study. The clinical painful procedures experienced by 957 participants could be divided into three groups: severe pain (NIPS score 5–7: peripheral intravenous cannulation, arterial catheterisation, arterial blood sampling, peripherally inserted central catheter placement and nasopharyngeal suctioning), mild to moderate pain (NIPS score 3–4: finger prick, intramuscular injection, adhesive removal, endotracheal intubation suctioning, heel prick, lumbar puncture and subcutaneous injection) and no pain to mild pain (NIPS score 0–2: gastric tube insertion, enema and intravenous injection).

Conclusions The neonatal pain response to clinical procedures in NICU had certain pattern and preintervention drug analgesia could be taken for painful procedures with clustered high NIPS pain scores. Meanwhile, full coverage non-drug pain relief measures could be taken for procedures that are with scattered pain scores, and real-time pain evaluation should be provided to determine whether further drug analgesia is required.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Neonates can experience pain, and that effective pain management is important for their short-term and long-term health. However, there are challenges in assessing and managing neonatal pain in clinical settings, and pain scales and neurophysiological indicators have limitations in their application.

WHAT THIS STUDY ADDS

⇒ Pain assessment in the neonatal intensive care unit can be effectively performed using the Neonatal Infant Pain Scale. Our study highlights the wide variation in pain experienced by neonates undergoing different procedures.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study encourages the regular assessment of pain in neonates in the intensive care setting. Additionally, it advocates for the use of appropriate analgesia to minimise the occurrence of painful procedures.

INTRODUCTION

International Association for the Study of Pain has revised its definition of pain[1] to include the fact that inability to communicate does not negate the possibility that a human experiences pain. Studies[2 3] have shown that the pain threshold of newborns is 30%–50% lower than that of adults, and the pain tolerance is lower than that of children of other ages, making the pain perception more intense, lasting and profound for neonates.

Neonatal pain can cause haemodynamic and behaviour changes, interruption of eating and sleeping, increased energy consumption, and changes in short-term hormone secretion, leading to related complications, unstable condition and prolonged hospitalisation time.[4 5] It can also cause long-term changes in pain sensitivity, nervous system remodelling, endocrine system changes, immune response imbalance, emotional cognition and behaviour disorders.[6 7] Unfortunately, newborns, especially premature infants, often experience pain due to required medical treatment and nursing for premature birth or disease in the early stage of life.[8–10] Clinical painful procedures, such as heel prick, arterial and venous puncture, and various injections, are the main sources of neonatal pain, and daily nursing procedures for premature infants, such as nappy changing and temperature measurement, are common painful stimuli as well.[11]

At present, there are two main categories of methods for neonatal pain assessment (NPA). The first type of methods are based on the monitoring of neurohormonal and neurophysiological indicators, such as skin conductance,[12 13] salivary cortisol,[14 15] heart rate variability,[16] neonatal parasympathetic nerve assessment,[17] near infrared spectroscopy[18] and electroencephalogram.[19] While these indicators have been proved to be meaningful in the evaluation of neonatal pain, they are mainly used in research situations rather than complex clinical environments, limiting their applications in neonatal pain evaluation.

Other methods are based on pain scales, for example, the Neonatal Infant Pain Scale (NIPS), which are most commonly adopted in medical institutions.[20] However, there are quite a few problems in the application of pain scales, such as differences in the evaluation dimensions and scopes of application among the scales, the limited technical level and willingness of medical staff to assess and interpret pain, significant differences in pain evaluation based on scales,[21–23] the standardisation and continuity in scale usage[24 25] and strong subjectivity.[26] In recent years, scholars[27] have also attempted to use artificial intelligence technology to address the issue of clinical manual scoring with promising results.

This study intends to provide a basis for the management of expected procedural pain by quantifying and grading pain experience of commonly performed painful procedures according to the NIPS pain score and pain grade, so that medical staff could adopt early interventions conveniently and precisely when performing specific necessary procedures on newborns.

METHODS

Study design and setting

This is a single-centre cross-sectional study of the extent of pain in neonates caused by routine clinical painful procedures. The study was conducted at a tertiary neonatal intensive care unit (NICU) and two level-two neonatal care units in the Children's Hospital of Zhejiang University School of Medicine from 1 July 2018 to 30 June 2019.

Eligibility criteria

Figure 1 shows the flow of participants in our study. A total of 957 neonates admitted to the neonatal ward of our hospital were enrolled in the collection of clinical data after obtaining informed consent from the guardians of the neonatal patients. The detailed information of the subjects is presented in table 1. All procedures in this study were conducted in accordance with the relevant guidelines and regulations.

Exclusion criteria: Neonates with severe birth trauma, severe asphyxia, shock, metabolic encephalopathy, moderate severe hypoxic-ischaemic encephalopathy and severe cardiopulmonary disease were excluded from the study. Additionally, neonates with major congenital malformations, facial dysmorphisms, facial nerve injuries, facial surgery and other conditions affecting facial pain evaluation.

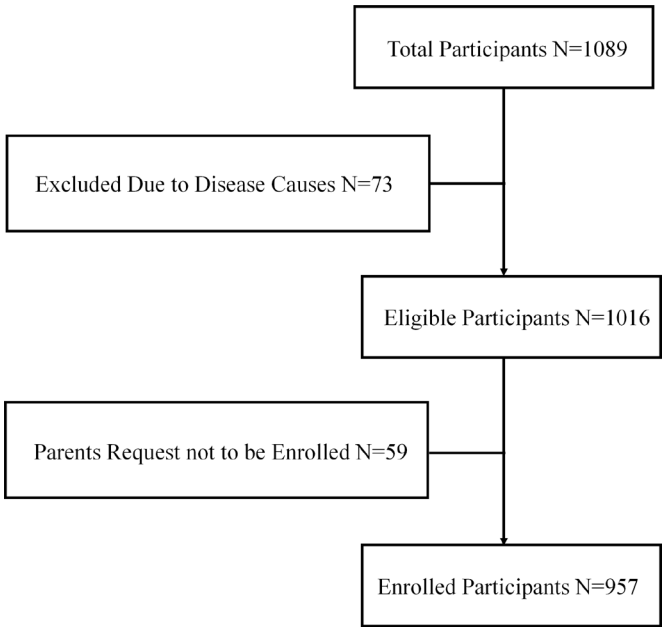

Figure 1 Flow chart of participant screening.

Neonates who had received medications were excluded to ensure that the study focused on the natural pain responses and to avoid confounding effects of prior analgesia or sedation. Analgesic medications included opioids (such as morphine and fentanyl) and non-opioid medications (such as acetaminophen and ibuprofen). Meanwhile, sedative medications included benzodiazepines (such as midazolam) and other sedative agents (such as propofol and dexmedetomidine). Furthermore, endotracheal intubation, retinopathy of prematurity fundus examination, thoracentesis and wound treatment were not included as painful procedures due to the use of premedication before elective endotracheal intubation.

Table 1 Demographic information

Types of clinical painful procedures	No
Gender	
Male	594 (62.07%)
Female	363 (37.93%)
Delivery mode	
Vaginal delivery	431 (45.04%)
Caesarean section	526 (54.96%)
Gestational age	34.75±4.53 weeks
Weight	2.37±1.01 kg
Types of procedures	
Blood sampling	565 (59.04%)
Injection	65 (6.79%)
Catheterisation	146 (15.26%)
Other	181 (18.91%)

Table 2 Clinical painful procedures in this study

Types of clinical painful procedures	No	Proportion (%)
Blood sampling	**565**	**59.04**
Arterial blood sampling	252	26.33
Heel prick	208	21.74
Finger prick	105	10.97
Injection	**65**	**6.79**
Intramuscular injection	24	2.51
Subcutaneous injection	21	2.19
Intravenous injection	20	2.09
Catheterisation	**146**	**15.26**
Peripheral intravenous cannulation	63	6.58
Peripherally inserted central catheter placement	29	3.03
Arterial catheterisation	23	2.41
Gastric tube insertion	31	3.24
Other	**181**	**18.91**
Lumbar puncture	24	2.51
Endotracheal intubation suctioning	27	2.82
Nasopharyngeal suctioning	45	4.70
Enema	26	2.72
Adhesive removal	59	6.16

The bold values are the numbers and proportions of the four distinct categories.

Parents were allowed to request withdrawal from the study at any time.

Clinical painful procedures

The research conducted a classification of 15 types of painful procedures[28] into 4 distinct categories: blood sampling, injection, catheterisation and others. Table 2 provides a comprehensive overview of the procedure types and their composition.

Neonatal pain evaluation

This study used the NIPS to quantify neonatal pain. NIPS, which takes facial expression, crying, limb activity, arousal state and respiratory physiological indicators into account (as shown in table 3), is suitable for assessing newborns with gestational age between 28 and 38 weeks, and is particularly useful for acute pain evaluation such as venipuncture, heel prick and postoperative pain.[29] The score range of NIPS is 0–7 points, with 0–2 points indicating no pain or mild pain, 3–4 points indicating mild to moderate pain and 5–7 points indicating severe pain. One painful procedure was selected per patient to avoid duplicate calculations and ensure the accuracy of the data. Each patient contributed data for only one painful procedure, and multiple procedures from the same patient were not included in the analysis. This approach allowed us to maintain consistency in the number of procedures and participants throughout the study.

The pain scores were assessed independently by two experienced nurses for each painful procedure. The nurses evaluated the neonate's pain using the NIPS at the same time, but independently of each other. This was done to ensure consistency and accuracy in the pain assessment. After each nurse assessed the neonate's pain, they recorded their scores separately on a standardised data collection form. The two scores were then compared, and in cases where there was a discrepancy of more than two points, the nurses discussed the pain assessment and reached a consensus score.

Non-pharmacological pain relief measures, such as kangaroo care, swaddling and sucrose administration, are commonly employed in NICUs to alleviate pain and enhance comfort during painful procedures.[30] Although our study did not specifically assess or include data on these measures, we acknowledge their potential use in NICU settings.

At the same time, since parental presence during procedures is encouraged and supported in many NICUs due to positive effects on both the infants and the parents,[31] we acknowledge the possibility of parental presence during the procedures in NICUs and its potential impact on the outcomes.

Table 3 The parameters of the Neonatal Infant Pain Scale

Parameters	0 point	1 point	2 points
Facial expression	Relaxed	Grimace	N/A
Cry	No cry	Whimper	Vigorous crying
Breathing pattern	Relaxed	Change in breathing	N/A
Arms	Relaxed	Flexed/extended	N/A
Legs	Relaxed	Flexed/extended	N/A
State of arousal	Sleeping/awake	Fussy	N/A

Pain level: 0–2 points=no pain, 3–4 points=moderate pain, >4 points=severe pain.
N/A, not available.

Table 4 Distribution of Neonatal Infant Pain Scale pain scores for different clinical painful procedures

Procedures	Distribution of Neonatal Infant Pain Scale pain scores for procedures							
	0	1	2	3	4	5	6	7
Peripheral IV cannulation	0.0%	1.6%	1.6%	1.6%	1.6%	14.3%	25.4%	54.0%
Arterial catheterisation	0.0%	0.0%	0.0%	0.0%	8.7%	21.7%	17.4%	52.2%
Arterial blood sampling	1.2%	1.2%	1.6%	3.2%	4.4%	12.7%	28.2%	47.6%
Nasopharyngeal suctioning	0.0%	0.0%	4.4%	15.6%	17.8%	4.4%	28.9%	28.9%
Peripherally inserted central catheter placement	0.0%	0.0%	0.0%	0.0%	6.9%	51.7%	24.1%	17.2%
Intravenous injection	50.0%	25.0%	5.0%	10.0%	5.0%	5.0%	0.0%	0.0%
Enema	30.8%	26.9%	38.5%	3.8%	0.0%	0.0%	0.0%	0.0%
Gastric tube insertion	16.1%	16.1%	35.5%	32.3%	0.0%	0.0%	0.0%	0.0%
Finger prick	1.9%	1.0%	9.5%	5.7%	16.2%	36.2%	18.1%	11.4%
Intramuscular injection	0.0%	0.0%	12.5%	12.5%	16.7%	29.2%	20.8%	8.3%
Lumbar puncture	0.0%	4.2%	12.5%	29.2%	29.2%	12.5%	12.5%	0.0%
Endotracheal intubation suctioning	0.0%	3.7%	7.4%	7.4%	48.1%	25.9%	3.7%	3.7%
Subcutaneous injection	14.3%	0.0%	14.3%	9.5%	47.6%	0.0%	14.3%	0.0%
Adhesive removal	20.3%	6.8%	1.7%	3.4%	8.5%	11.9%	25.4%	22.0%
Heel prick	11.5%	11.5%	11.5%	10.1%	9.1%	11.1%	21.6%	13.5%

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Distribution of NIPS pain scores for each procedure

As shown in table 4, the distribution of NIPS pain scores was clustered for peripheral intravenous cannulation, arterial catheterisation, arterial blood sampling and peripherally inserted central catheter (PICC) placement and dispersed for adhesive removal, subcutaneous injection and heel prick. For those clinical painful procedures with aggregated pain scores, they could be further divided into three categories according to the NIPS pain grades. The procedures with pain scores gathered in the severe pain grade are peripheral IV cannulation, arterial catheterisation, arterial blood sampling, nasopharyngeal suctioning, PICC placement. The procedures whose pain scores fall in the mild to moderate pain grade are finger prick, intramuscular injection, lumbar puncture and endotracheal intubation suctioning. The pain scores of intravenous injection, enema and gastric tube insertion are gathered in the no pain or mild pain grade.

Meanwhile, the pain scores for procedures such as subcutaneous injection, adhesive removal and heel prick are relatively scattered, indicating a variability in pain experience among neonates. These procedures have discrete scores, with more factors affecting pain during such procedures. For instance, subcutaneous injections may cause pain due to the depth of the injection, the type of medication being delivered, injection temperature and skin tension, etc. Adhesive removal can also cause discomfort due to the adhesive properties of the tape and the sensitivity of the neonate's skin. Similarly, heel prick procedures may be affected by factors such as the size of the lancet used, the depth of the puncture and the neonate's skin thickness. The detailed proportion of pain grades of each procedure is shown in figure 2.

According to the pain levels of NIPS, the average pain scores for each clinical painful procedure are divided into three levels, as shown in table 5.

DISCUSSION

Neglect of neonatal pain

As pointed out in the updated definition of pain, although pain is a subjective feeling, it cannot be denied that tissue damage is often a significant factor in the experience of pain. For patients with nonverbal expressive skills who

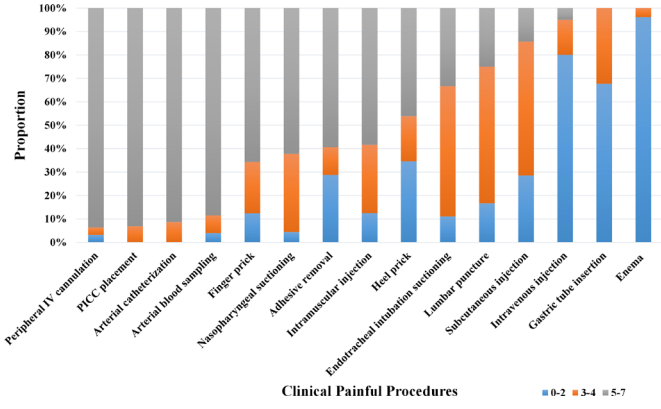

Figure 2 Proportion of pain grades for different clinical painful procedures. PICC, peripherally inserted central catheter.

Table 5 Mean Neonatal Infant Pain Scale (NIPS) pain scores and severity for each procedure

Severity of pain procedure	NIPS pain score*
Severe pain	
Peripheral intravenous cannulation	6.17±1.24
Arterial catheterisation	6.13±1.06
Arterial blood sampling	5.97±1.43
Peripherally inserted central catheter placement	5.52±0.87
Nasopharyngeal suctioning	5.24±1.63
Mild to moderate pain	
Finger prick	4.71±1.57
Intramuscular injection	4.58±1.50
Adhesive removal	4.20±2.68
Endotracheal intubation suctioning	4.11±1.22
Heel prick	3.81±2.37
Lumbar puncture	3.71±1.33
Subcutaneous injection	3.33±1.80
No pain or mild pain	
Gastric tube insertion	1.84±1.06
Enema	1.15±0.92
Intravenous injection	1.10±1.52

*Data are presented as mean±SD.

endure tissue injury, proper evaluation of the pain experience is an important basis for adopting pain intervention strategies in the clinic. If the patient has definite tissue injury or the pain is definitely intolerable, it is necessary to give corresponding intervention before the pain occurs. However, there are still major deficiencies and even lacks in NPA and management in actual clinical practice.

Sposito *et al*[32] found less than 4% of the total procedures were scored as pain in the NICU, where only 32.5% of pain records employed pharmacological or non-pharmacological interventions for pain relief. Kyololo *et al*[33] studied 404 invasive procedures experienced within 24 hours of admission on 95 neonates, only 1 procedure was rated as severe pain yet no form of analgesia was performed. Additionally, a prospective study from 243 NICUs in 18 European countries found that only 10% of 6648 infants underwent daily pain evaluation using scales.[34]

To explore the reasons, on the one hand, most of clinical painful procedures were short term, and the path of 'procedure-evaluation-intervention' was not suitable for short-term procedures. However, the fact that clinical painful procedures are highly frequent in the NICU makes these short-term procedures become frequent events that newborns often experience. On the other hand, it may also indicate a failure or difficulty in implementing or applying the pain scale.

Suppose we change the pain management pathway to assessing the pain grade of a procedure, applying preintervention and starting the procedure, it would help avoid or relieve most of the procedural pain experienced in the NICU. Therefore, the quantitative evaluation of procedural pain for neonates to support precise and effective pain management is essential for the healthy growth of the newborn,[20 35] especially in high frequency painful stimulation environments such as the NICU.

Quantification of neonatal procedural pain severity

In clinical practice, the association between pain and tissue damage is often still considered, and the degree of tissue damage is often used as a basis for assessing pain severity. However, it is important to note that clinical procedures can vary greatly in their nature and may have different impacts on the overall pain burden experienced by an individual baby. Simply classifying pain based on tissue damage may shift the pain grade down and cause pain interventions to be easily ignored for those high frequency procedures with low tissue damage. For example, tissue damage is not serious for those procedures characterised by local tissue puncture, such as arterial catheterisation, arterial blood sampling and finger prick.

In Laudiano-Dray's study,[36] the authors aimed to estimate the pain severity of common NICU procedures using published pain scores. They extracted pain scores using 59 randomised controlled trials for 15 different procedures and conducted hierarchical cluster analysis of average pain scores, resulting in 5 discrete severity groups. Compared with our study, despite variations in the specific procedures and pain assessment tools used, there is consistency in the categorisation of pain levels.

These research findings have important implications for clinical practice. They provide healthcare professionals with valuable insights into the pain experienced by neonates during different procedures in an NICU setting. The identification of different pain severity groups allows for more accurate assessment and tailored interventions to manage neonatal pain effectively.

Our study also confirmed that the vast majority of newborns felt pain with more than moderate grades, with mean 6.13±1.06, 5.97±1.43 and 4.71±1.57, respectively. Therefore, it is important to take into account the actual pain experience of these high frequency low injury manipulations in order to avoid or relieve pain. The neglect of the actual pain experience of these high frequency low injury manipulations may also aggravate pain, and neurological immaturity and repeated exposure to pain in the neonatal period may lower pain thresholds and thus render infants more sensitive to subsequent pain events.[37] However, it is important to note that pain assessment should consider multiple factors, such as behavioural indicators, physiological measures and autonomic nervous system responses. Additionally, individual differences, including developmental level, pain

sensitivity and contextual factors, should be taken into account when assessing and managing neonatal pain.

The 15 procedures could be grouped into 2 main categories based on the distribution of pain scores, specifically as either score clustered, that is, the score aggregation in a specific score range exceeds the average, or score dispersed. This suggests that pain experiences are similar across much of the neonatal population, and suitable preprocedural administration of pharmacological or non-pharmacological interventions that match the pain grade have significant utility for the respective procedure.

Procedures with more than moderate pain should be managed with sedative analgesics or local anaesthetic before the procedure. However, due to the immaturity of drug metabolism in infants and drug-related side effects, such as hypotension[38] and respiratory depression,[39] the use of local or systemic pharmacological analgesia should be used with caution. Meanwhile, non-pharmacological interventions, such as oral sucrose, nonnutritive sucking, etc, should be taken as basic analgesic measures for reassurance and manipulation prior the procedures, regardless of the degree of pain.

As for procedures with pain score dispersed, they are not amenable to giving uniform interventions and should be based on the widespread adoption of non-pharmaceutical care strategies such as breast feeding and kangaroo care.[40 41] Further interventions were given after comprehensive evaluation based on clinical reality, newborns' pain experience and so on.

Strengths and limitations

Stepped pain control, including non-pharmacological and pharmacological interventions, is the fundamental of neonatal pain management. However, the implementation of NPA in present is still based on various scoring systems after the fact and are not available for prior pain management or preintervention for impending clinical painful procedures.

Our work is of great value as to accurately quantify and generalise pain experience across different procedures in a population context, providing a preintervention basis for expected clinical procedures. It is of great practical importance to optimise clinical pathways in current neonatal pain management.

Although we would like to truly reflect the neonatal pain state to the greatest extent, the pain is still affected by many factors, and our research still has many limitations. First of all, our study was conducted at a single centre, which may limit the generalisability of our findings to other settings. Additionally, our study only involved two examiners, which may have introduced bias in the pain assessments. We acknowledge that healthcare professionals' personal beliefs and professional experience may influence pain assessments, and future studies should aim to address this by involving a larger number of examiners from different backgrounds. Lastly, we excluded neurologically impaired and seriously ill newborns, which may limit the generalisability of our findings to these populations. We recognise that the severity of illness and neurological state may affect pain expression in neonates, and future studies should aim to include these populations.

Meanwhile, our study did not examine other factors that may influence pain expression in neonates, such as gestational age, environmental factors and sleep-wake state. Future studies should be proposed to collect more comprehensive data in order to analyse the impact of these factors on neonatal pain expression. This will help to provide a more complete understanding of the complex factors that could contribute to pain expression in neonates and guide more accurate assessment and management of neonatal pain.

CONCLUSION

This study provides evidence that pain response is similar across the studied neonatal population. As suitable preprocedural administration of pharmacological or non-pharmacological interventions that match the pain grade have significant utility for the respective procedure, it is important to take into account the actual pain experience of high frequency low injury manipulations in order to avoid or relieve pain. Neglect of the actual pain experience of these high frequency low injury manipulations may also aggravate pain, and neurological immaturity and repeated exposure to pain in the neonatal period may lower pain thresholds and thus render infants more sensitive to subsequent pain events. The findings of this study have important implications for the management of neonatal pain, and further research is needed to explore the optimal strategies for pain management in the neonatal period.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the study protocol was approved by the Institutional Review Board of the Children's Hospital, Zhejiang University School of Medicine (ethics number: 2018-IRB-051). Participants gave informed consent to participate in the study before taking part.

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