Original Article

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Quick Response Code:

Website:
www.jehp.net

DOI:
10.4103/jehp.jehp_1042_24

Frequency and pain intensity of painful procedures in premature infants hospitalized in the neonatal intensive care unit

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Received: 04-06-2024
Accepted: 22-07-2024
Published: 28-12-2024

Abstract:

BACKGROUND: Various painful therapeutic and diagnostic procedures are performed daily for hospitalized infants. These procedures are very effective in their growth and recovery process. This study was conducted to determine "the frequency and pain intensity of painful procedures in premature infants hospitalized in NICU."

MATERIALS AND METHODS: This cross-sectional study was conducted from February 10, 2023 to April 10, 2023 on all infants who met the inclusion criteria and were admitted to NICU. The data collection tool was a multi-part questionnaire including demographic data, types of painful procedures, and NIPS pain scale. After collecting the data, it was entered into SPSS23 software and analyzed at a significance level of less than 0.05.

RESULTS: The highest frequency of painful procedures in each of the neonates during hospitalization, respectively, was related to orogastric tube insertion (24.43 ± 20.17), venipuncture (3.81 ± 1.03), IV cannula removal (3.74 ± 0.90) and intravenous insertion (3.72 ± 1.10). Pain intensity was moderate in 62.1% and severe in 36.2% of procedures. Endotracheal intubation, eye examination, nasogastric tube insertion, heel lance, oral suction, intramuscular injection, nasal suction, intravenous insertion, and venipuncture had the highest intensity of pain, respectively. Pain intensity was significantly higher in infants weighing more than 1500 g ($P = 0.007$) and gestational age more than 32 weeks ($P = 0.031$).

CONCLUSION: Premature infants admitted to the NICU frequently undergo painful procedures with moderate or severe pain intensity. Therefore, it is recommended to use appropriate pain management to increase growth and development, maintain and promote health in infants.

Keywords:

Intensive care units, pain, pain management, premature infants, procedures

Introduction

WHO estimated that approximately 10.6% of all live births in the world are preterm.[1] Iran is one of the regions with a high prevalence of premature births.[2] The prevalence of premature birth in Iran is about 9.2%.[3]

During the hospitalization of a premature neonate in the neonatal intensive care unit (NICU), many painful procedures are performed as part of routine medical care. There are also obstacles in the NICU that make effective pain management a challenge.[2]

This is a concern because many studies have shown that infants are capable of perceiving pain, and other studies have shown that even premature infants are more sensitive to pain than term infants, in addition, repeated

How to cite this article: Barzegari AA, Akbarian_rad Z, Nikbakht HA, Qanbari Qalehsari M, Jafarian_amiri SR, Zabihi A, *et al*. Frequency and pain intensity of painful procedures in premature infants hospitalized in the neonatal intensive care unit. J Edu Health Promot 2024;13:467.

pain in infants causes Cognitive and motor function impairment and brain development disorder, thus it is necessary to prevent or treat pain in infants.[4]

The results of a study showed that neonates with a gestational age of 42–25 weeks endure an average of 14 painful procedures in the first two weeks of life.[5] In another study, an average of 4.2 ± 1.05 painful procedures were performed on infants in the first 24 h of hospitalization.[6] Infants are more exposed to negative side effects caused by pain compared to children and adults.[7]

Infants admitted to the NICU are exposed to a large number of painful procedures, including orogastric tube insertion, lumbar puncture, routine injections, catheterization, tape removal, naso/oropharyngeal suction, heel lance, venipuncture, and stressful interventions such as moving and manipulating them[8] which can cause behavioral changes, including: decreased sensitivity to pain, increased anxiety disorders, stress, attention deficit disorder and self-destructive behaviors in the future.[9]

Considering the importance of pain in infants and the importance of untreated pain in the NICU, various studies have been conducted to investigate this issue. Some of these studies have addressed the issue of the frequency of painful procedures in infants along with the appropriate treatment measures.[10-12] In some other studies, only the frequency and types of painful procedures were investigated but pain intensity was not considered.[11] There are few studies in which the frequency of painful procedures and the pain score have been investigated at the same time, and all of these studies are related to foreign countries, and no study with this title was found in Iran. Pain monitoring and measurement in all kinds of painful procedures are not done systematically and routinely in the NICU. Considering the significant birth of premature infants, the frequency of painful procedures in NICU and the importance of pain management in infants, this study was conducted to investigate the frequency of painful procedures and the intensity of pain in premature infants hospitalized in the NICU.

Materials and Methods

Study design and setting

This cross-sectional study was conducted in 2023 on 60 infants hospitalized in the NICU of Rouhani Hospital in Babol (northern of Iran) who met the inclusion criteria.

Study participants and sampling

We used census sampling and selected all the infants who were hospitalized in the NICU of Rouhani Hospital from February 10, 2023 to April 10, 2023 according to the inclusion criteria.

Inclusion criteria were included: (1) Cardiorespiratory physiological stability (oxygen saturation above 90%, heart rate between 120 and 160, breathing rate between 40 and 60 per minute). (2) The absence of congenital or genetic abnormalities. (3) Non-use of narcotics, antidepressants, and anticonvulsants by the mother during pregnancy. (4) Not using anesthetics. Exclusion criteria were included: (1) Infants who needed surgery during hospitalization. (2) Infants who experienced intra-ventricular bleeding more than grade II during the study. The infants were enrolled in the study after being examined by a neonatologist.

Data collection tolls and technique

The instrument used to collect data was a three-part checklist. Part one was related to the demographic and clinical information of the infants, the second was related to the types of painful procedures and their pain intensity, and the third part was related to pain management (use of pharmacological or non-pharmacological pain control methods), related to the types of procedures performed. Data was gathered by the researcher 24 h a day.

The intensity of pain was measured based on the score of the NIPS pain measurement tool, by the researcher using a video of the infant, up to 2 min after the procedures. From the moment the procedure started until 2 min after its end, only the infant's face was filmed in a closed view with the camera.[13] Then the videos were coded. The interpretation of the film was done by the researcher.

The questionnaire of demographic and clinical characteristics included questions such as: gender, birth weight, gestational age, age of the infant at hospitalization, duration of hospitalization, type of delivery, first and fifth minute Apgar, type of disease, or reason for hospitalization.

All kinds of painful procedures including venipuncture, arterial blood sampling, heel lance, intravenous insertion, nasogastric tube insertion, bladder catheterization, oral and nasal suction, intramuscular injection, eye examination, sampling of spinal fluid, etc., were investigated in this study.

A checklist was prepared for each infant and it included all procedures, their pain score, as well as pharmaceutical and non-pharmacological care performed in the relevant procedure. The Neonatal Infant Pain Scale (NIPS) examines five behavioral items (facial expression, crying, arms, legs, and state of arousal) and one physiologic indicator (breathing pattern). Each of the scale's items, except for crying, gets a score of one or zero, and three

states are considered for crying, so that not crying is given a score of zero, quiet crying is given a score of one, and severe crying is given a score of two. The final score of NIPS is between 0 and 7. A score of 0 to 2 indicates that the procedure is painless or mild pain, a score between 3 and 4 indicates mild to moderate pain that may require non-pharmacological interventions to relieve the pain, and a score above 4 indicates severe pain that requires pharmacological interventions to relieve.[14] This scale has recently been used in many studies to measure pain for both groups of term and preterm infants.[15] The validity and reliability of this tool were investigated and confirmed in the studies of Obiedat and Al-Maaitah ($r = 0.93$)[16] and Xie *et al*. ($r = 0.82$).[15] In addition, the number of pharmacological and non-pharmacological pain management used related to each procedure was recorded.

Statistical analysis

Data was entered into SPSS23 software and evaluated by statistical tests at a significance level of less than 0.05. Demographic variables were described using descriptive statistics (median or mean and standard deviation). Independent Samples *t*-test was used to compare the equality of two means between qualitative variables with the assumption of equality of variances, and if the assumptions were not established, the Mann–Whitney test was used. Also, to compare the means of variables with more than two categories of qualitative variables, an ANOVA test (one-way ANOVA) was used. The Chi-square test was used to check the relationship between two qualitative variables, and if the conditions of the Chi-square test were not met, Fisher's exact test was used.

Ethical consideration

This study was conducted after obtaining permission from the ethics committee with the code of IR.MUBABOL.REC.1400.114 and informed consent from the parents of hospitalized infants.

Results

In this study, 60 premature infants were evaluated. The gestational age of 50% of infants was less than 33 (30, 35) weeks. The birth weight of 50% of infants was less than 1695.01 (1232.50, 2053.75) grams. The mean and standard deviation of the length of hospitalization was 17.55 ± 13.41 days. An average of 24.66 ± 16.68 painful procedures were performed for each of the infants during hospitalization, and an average of 2.97 ± 2.11 procedures were recorded daily for each infant. The main reason for hospitalization of infants (71.7%) was prematurity. Pain intensity was moderate in 62.1% of procedures and severe in 36.2% of procedures.

The highest frequency of painful procedures in each of the infants during hospitalization was related to orogastric tube insertion (24.43 ± 20.17), venipuncture (3.81 ± 1.03), IV cannula removal (3.74 ± 0.90), and intravenous insertion (3.72.10 ± 1.10).

Endotracheal intubation, eye examination, nasogastric tube insertion, heel lance, oral suction, intramuscular injection, nasal suction, intravenous insertion, and venipuncture had the highest pain intensity, respectively. In total, in 54% of the procedures, non-pharmacological pain management and in 1.83% of them, pharmaceutical pain management was used. Non-pharmacological pain management was often used in venipuncture, heel lance, intravenous insertion, orogastric tube insertion, intramuscular injection, oral suction, tape removal, and IV cannula removal, the most common of which was the use of sucrose. Implementation of heel lance, intravenous insertion, endotracheal intubation, and IV cannula removal was combined with pharmacological pain management interventions, and in the endotracheal intubation procedure, more pharmacological pain management was used than other procedures. The most common pharmacological pain management during endotracheal intubation was the use of acetaminophen followed by fentanyl [Table 1].

The intensity of pain in the procedures of tape removal, chest physiotherapy, extubation, intramuscular injection, and IV cannula removal respectively, was significantly lower than in other procedures [Table 2].

The results after the *post hoc* analysis showed that the group of infants weighing less than 1000 g had significantly different pain intensity than the group weighing more than 1500 g. Also, the pain intensity of infants with a gestational age of more than 32 weeks was significantly high [Table 3].

Infants who had heel lance procedures, orogastric tube insertion, intramuscular injection, oral suction, nasal suction, endotracheal intubation, and eye examination had a significantly longer hospitalization period [Table 4].

Boys experienced more heel lance procedures, nasal suction, and chest physiotherapy compared to girls. Also, the number of umbilical venous line procedures was more frequent in infants weighing less than 1500 g. The frequency of performing umbilical venous line and endotracheal intubation procedures was higher in infants with a gestational age of less than 32 weeks.

Discussion

A mean of 2.97 ± 2.11 procedures daily and 24.66 ± 16.68 procedures during hospitalization were recorded for

Table 1: Frequency and pain intensity of the painful procedures in each of the infants during NICU hospitalization

Frequency and Pain intensity Procedures	Mean±SD	Median (min-max)	Pain intensity Mean±SD
Venipuncture (*n*=60)	1.03±3.81	4 (2–8)	4.29±0.72
Heel lance (*n*=56)	1.59±0.89	1 (1–5)	4.11±0.3
Intravenous insertion (*n*=50)	3.72±1.10	4 (1–5)	4.26±0.69
Orogastric tube insertion (*n*=49)	24.43±20.17	15 (1–80)	4.08±0.75
Nasogastric tube insertion (*n*=3)	4±1	4 (3–10)	4.01±0.22
Intramuscular injection (*n*=45)	1.38±0.48	1 (1–2)	3.95±0.42
Oral suction (*n*=48)	2.73±1.08	0 (1–10)	4.31±0.62
Nasal suction (*n*=29)	1.55±1.15	2 (1–8)	4.13±0.51
Tape removal (*n*=54)	3.52±0.78	3 (2–5)	3.46±0.73
Umbilical venous line (*n*=6)	1.67±1.03	1 (1–3)	3.38±0.27
Endotracheal intubation (*n*=24)	1.08±0.28	1 (1–2)	4.41±0.50
Eye examination (*n*=26)	1.73±0.77	1 (1–3)	4.19±0.49
Chest Physiotherapy (*n*=7)	1.86±0.69	2 (1–3)	3.71±0.48
Iv cannula removal (*n*=43)	3.74±0.90	3 (1–5)	4.00±0.43
Extubation (*n*=22)	1.04±0.20	1 (1–2)	3.81±0.39
Finger lance (*n*=1)	1	1 (1–1)	3
Body physiotherapy (*n*=1)	2	2 (2–2)	3.5
Nasal CPAP insertion (*n*=26)	2.12±0.81	2 (1–4)	3.84±0.44
Bladder catheterisation (*n*=1)	1	0 (1–1)	4.07±0.62

Table 2: Comparison of painful procedures according to their pain intensity in infants hospitalized in NICU

Pain intensity procedures	Mean±SD	Mean difference	Degrees of freedom (df)	*P*
Venipuncture* (*n*=60)	4.29±0.72	0	59	1
Heel lance (*n*=56)	4.11±0.37	0.185	55	0.140
Intravenous insertion (*n*=50)	4.26±0.69	0.060	49	0.650
Orogastric tube insertion (*n*=49)	4.08±0.75	0.224	48	0.070
Intramuscular injection (*n*=45)	3.95±0.42	0.133	44	0.008
Oral suction (*n*=48)	4.31±0.62	0.041	47	0.730
Nasal suction (*n*=29)	4.13±0.51	0.137	28	0.250
Tape removal (*n*=54)	3.46±0.73	0.648	53	0.001
Endotracheal intubation (*n*=24)	4.41±0.50	-0.166	23	0.290
Eye exam (*n*=26)	4.19±0.49	0.153	25	0.420
Chest physiotherapy (*n*=7)	3.71±0.48	0.571	6	0.100
Iv cannula removal (*n*=43)	4.00±0.43	0.348	42	0.002
Extubation (*n*=22)	3.81±0.39	0.363	21	0.008
Nasal CPAP insertion (*n*=26)	4.07±0.62	0.076	25	0.664

*The pain intensity of other procedures was compared with the pain intensity of venipuncture

each infant in this study. The most frequent painful procedures were related to orogastric tube insertion, venipuncture, IV cannula removal, Intravenous insertion, and tape removal, respectively.

In the study of Assefa *et al*.,[6] which examined painful procedures in the first 24 h of hospitalization, a mean of 4.2 ± 1.05 painful procedures were performed on infants daily. This difference may be because in the first 24 hour of hospitalization, the infant's condition is more acute and serious, and most painful procedures are performed in the first hours of hospitalization. In the study of Kyololo *et al*.,[17] a mean of 1.6 ± 1.1 procedures were performed for each infant. In these studies, less painful procedures were investigated than in the present study. And this difference in average daily painful procedures may be for this reason. In addition, the most common procedure performed in the Assefa study was the heel lance,[6] and it was venipuncture and intramuscular injection in Kyololo study,[17] while in our study, orogastric tube insertion was the most common procedure. In our study, in more than 60% of cases, heel lance was done once. Since heel lance is usually done for screening and diagnosis of diseases in the first days of an infant's birth.

In a study, Ramos *et al*.[10] showed that the most common painful procedures were needling, such as venipuncture, heel lance, and arterial blood sampling. In our study, after the orogastric tube insertion procedure, venipuncture and intravenous insertion were more common than the rest of the procedures. It seems that the results of venipuncture in our study and the above study were almost the same, but in the case of the orogastric tube

Table 3: Pain intensity in infants during painful procedures according to demographic and clinical variables

Pain intensity Demographic and clinical variables		Mean±SD	*P*
Gender	Male	4.40±0.71	0.190
	Female	4.15±0.73	
Birth weight	<1000	3.72±0.90	*0.007
	1500-1000	4.26±0.59	
	≤1500	4.50±0.62	
Gestation age	<32	4.07±0.78	0.031
	≥32	4.84±0.62	
Type of delivery	Vaginal delivery	4.55±0.52	0.253
	Cesarean section	4.25±0.75	
Cause of hospitalization	Prematurity	4.22±0.74	0.446
	Respiratory disorder	4.60±0.54	
	Other disease	4.44±0.72	
First minute apgar	<7	4.23±0.56	0.700
	>7	4.31±0.78	

*After post hoc analysis between the group of infants weighing less than 1000 g and the group weighing more than 1500 g

Table 4: Painful procedures according to the duration of hospitalization of infants in NICU

Hospitalization time Painful procedure		Duration of hospitalization Mean±SD	*P*
Heel lance	No	3.40±6.75	0.022*
	yes	18.33±13.54	
Orogastric tube insertion	No	10.8±18.19	0.026*
	yes	19.06±13.94	
Intramuscular injection	No	13.91±20.35	0.002*
	yes	18.45±11.16	
Oral suction	No	10.83±14.56	0.001*
	yes	19.22±12.72	
Nasal suction	No	16.12±16.50	0.008*
	yes	19.06±9.10	
Endotracheal intubation	No	16.22±15.74	0.009*
	yes	19.54±8.80	
Eye examination	No	13.29±8.93	0.007*
	yes	23.11±16.20	

*Independent *t*-test

insertion, which was the most common procedure in our study, was not included in other studies.

The results of our study showed that most of the painful procedures in infants had moderate (62.1%) to severe (36.2%) pain intensity, which requires proper planning for palliative interventions in most procedures in the NICU. Poorly treated pain in neonates may lead to lifelong consequences, including altered neurobehavioral development.[18]

In a study conducted by Laudiano-Dray *et al*.,[8] infants were exposed to 17 types of painful procedures in the NICU, of which the procedure of heel lance and tape removal was the most painful. In the study of Merter and Bolişik, heel lance was more painful for infants than venipuncture.[19] In our study, heel lance had high pain intensity. In another study conducted by Luo *et al*.,[20] the most painful procedure were peripheral intravenous cannulation, arterial catheterization, arterial blood sampling, peripherally inserted central catheter placement, and nasopharyngeal suctioning. While in our study, the most painful procedure was endotracheal intubation. It seems that the pain intensity score in different procedures depends on the way the procedures are performed and the type of needles used, which probably caused the difference between the results of the present study and other studies.

In the study of Laudiano and Larsson, heel lance,[8] but in our study, the endotracheal intubation procedure was the most painful. The reason for this difference may be due to the use of needles with a larger diameter in blood sampling in the studied centers or failure to take precautions and pain management in this regard. It is possible that the use of smaller diameter needles and non-pharmacological palliative measures in our study caused less pain.

The results of our study showed that the pain intensity of intramuscular injection, tape removal, IV cannula removal, and extubation was significantly lower than other procedures. The results of the study by Luo *et al*.[20] showed that the gastric tube insertion, enema, and intravenous injection were significantly less painful than other procedures.

The present study showed that performing heel lance, nasal suction, and chest physiotherapy were more frequent in male infants compared to female infants. Similar to our study, in Bonutti *et al*.'s study,[21] there were more painful procedures in male infants. However, in other studies, the sex of the infants did not have a significant relationship with the frequency of painful procedures.[11,22]

The number of umbilical vein catheterizations was more in infants weighing less than 1500 g and intrauterine age less than 32 weeks. This may be due to the difficulty in accessing the peripheral vessels for this procedure in these infants.

In this study, the mean number of painful procedures was significantly more in infants under 28 weeks of gestation. In Wang *et al*.'s study,[23] the age and length of hospitalization of infants were influential factors in the frequency of painful procedures, and the results of this study and our study were consistent in this case. Kassab *et al*.'s study[11] also showed that the number of painful procedures was inversely related to gestational age and birth weight, which results were similar to our study. In the study of Kyololo *et al*.,[17] gestational age

and birth weight did not affect the number of painful interventions. Contrary to our study, in the study of Assefa *et al*.,[6] infants at a younger gestational age were exposed to fewer procedures. Overall, it seems that in most studies, birth weight and gestational age were inversely related to the frequency of painful procedures, which was the same in our study. The higher frequency of painful procedures in infants with lower gestational age and birth weight may be due to more medical issues and problems of these infants.

The results of the present study showed that the intensity of pain caused by painful procedures in infants had a significant relationship with their birth weight, so the pain intensity increased significantly with increasing birth weight and gestational age of more than 32 weeks. In the study of Schenk *et al*.,[24] it was also shown that the pain score of infants had a positive relationship with gestational age, which was in line with our study. The increase in the pain score of infants with higher gestational age and weight may be due to neural development and greater ability to react to painful stimuli or may be pain is more difficult to assess in premature infants with lower gestational age and the score could be less than the reality.

The most common method of pain management in our study, similar to other studies, was non-pharmacological interventions. Non-pharmacological pain management was often used in the procedures of venipuncture, heel lance, intravenous insertion, orogastric tube insertion, intramuscular injection, oral suction, tape removal, and Iv cannula removal, most of which was the use of sucrose, and other non-pharmacological interventions were non-nutritive sucking, positioning, light dimming, sound dimming, and manipulation. Maciel *et al*.'s study[25] showed that most interventions and palliative strategies in infants were non-medicated and most of them (25%) were related to nesting. In the study of Sposito *et al*.,[12] the most common non-pharmacological intervention were, non-nutritive sucking, positioning, swaddling, touching, kangaroo care, etc., respectively. Also, in other studies, breastfeeding and olfactory stimulation with breast milk were recommended as effective methods to reduce pain in infants.[26,27] Since the early exposure of infants to uncontrolled pain is associated with multiple negative long-term outcomes such as pain sensitization, adverse psychological symptoms, and altered neurodevelopment. Thus, it emphasizes the critical role of pain management in neonatal care.[28]

In the present study, the implementation of heel lance, intravenous insertion, endotracheal intubation, and IV cannula removal were accompanied by pharmacological pain management interventions. The most common drug used for pain management during endotracheal intubation was acetaminophen, followed by fentanyl. In Bonutti *et al*.'s study,[21] the most common pharmacological palliative intervention was fentanyl and the most common non-pharmacological palliative intervention was oral sucrose. In another study conducted by Mangat *et al*.,[29] oral sucrose was the most common non-pharmacological relief intervention. In Maciel's study, the most common pharmacological interventions for pain management in the NICU were the use of fentanyl (56.1%), midazolam (31.8%), morphine (4.4%), and dipyrone (3.5%), respectively.[25] Mohamadamini *et al*.[30] suggested that for proper pain management in the NICU, a continuous education program and the use of skilled personnel should be considered.

Strengths, limitations, and recommendations

The strength of the current study is its comprehensiveness, which simultaneously examined all painful procedures, their pain intensity, and palliative interventions used in infants hospitalized in the NICU. Also, one of the important and unique results of this study is the determination of pain intensity in all types of painful procedures, so pain intensity was moderate in 62.1% of procedures and severe in 36.2%. The limitation of this study was the short study period and the small number of samples. Therefore, to more fully understand painful methods, pain intensity, and more appropriate management of pain in infants and to increase the generalizability of the results, more research in this field with a larger sample size and in multiple centers is recommended.

Conclusion

This study showed that the intensity of pain caused by painful procedures in premature infants was often moderate or severe. Therefore, it is recommended to use appropriate pain management in premature infants due to the significant prevalence of painful procedures and the consequences of uncontrolled pain. Considering the importance of the issue of pain in premature infants and its adverse effects on their growth and development, it should be considered seriously to maintain and promote their health. Also, educational interventions should be conducted for nurses to improve their knowledge and performance in the pharmacological and non-pharmacological management of pain in infants.

Abbreviations

NICU: Neonatal Intensive Care Unit, NIPS: Neonatal Infant Pain Scale, IV: Intravenous, CPAP: Continuous Positive Airway Pressure, WHO: World Health Organization.

Acknowledgments

We would like to thank the Vice-Chancellor for Research and Technology of Babol University of Medical Sciences

for supporting this research project and the staff of the NICU of Rohani Hospital of Babol for their cooperation in this research.

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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