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Original Article

The Effect of Endotracheal Suctioning Using the Four-handed Care on Physiological Criteria and Behavioral Responses of the Preterm Infants: Randomized Crossover Clinical Trial

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Abstract

Introduction: Endotracheal suctioning is one of the procedures that can cause pain and stress for infants admitted to neonatal intensive care units (NICUs). Pain and stress can be manifested with physiological and behavioral responses. This study is a crossover randomized clinical trial design that aimed to investigate the effect of endotracheal suctioning, using four-handed care on the physiological criteria and behavioral responses of preterm infants.

Methods: In this study, 40 infants were randomly divided into two groups of 20, one group was first suctioned by the routine method (two hands) and then with the four-handed method. The other group was first suctioned by the four-handed method and then with the routine one. The ALPS-Neo (Astrid Lindgren Children's Hospital Pain Scale Neonates) was used to evaluate pain and stress in infants. One camera recorded facial expressions and body movements, and physiological data were recorded from the monitor simultaneously.

Results: Repeated measures analysis of variance (ANOVA) showed no statistically significant difference in changes in arterial saturation, heart rate and behavioral response scores between the two methods, but there was a significant difference in the mean heart rate of infants during and two minutes after suctioning in four-handed method using independent *t* test. Data were analyzed using SPSS version 13.

Conclusion: Four-handed suctioning method can prevent an increase in the heart rate during and two minutes after suctioning, but it does not seem to affect behavioral responses and oxygen saturation of the infants. Since one of the symptoms of pain and stress in infants is the change of vital signs, especially the heart rate, we recommend four-handed method for suctioning of endotracheal tube.

Introduction

Extremely preterm infants are admitted to the neonatal intensive care unit (NICU) for weeks and months, where they undergo an average of painful procedures per day.[1] Before the 1980s, infants were thought to have no perception of pain or to have less understanding of pain than other age groups.[2] Although current studies have clearly shown that infants are able to perceive pain, many painful medical procedures are still performed in NICUs without the use of analgesic procedures.[3] Infants experience a great deal of pain and stress not only as a result of the disease process, but also through invasive procedures during hospitalization in the intensive care units, such as blood sampling, venipuncture, insertion of gastro-enteric feeding tube, endotracheal tube and suctioning. Infants in intensive care units may need ventilators and are frequently subjected to invasive and painful processes such as endotracheal suctioning.[4-6] Suction is performed frequently to eliminate excessive secretions and reduce possible airway obstruction, and although necessary, it is a harmful stimulant. Pain-induced behavioral and physiological changes have been observed in infants during suctioning. On the other hand, these vulnerable infants are at the risk of complications from suctioning, including hypoxia, bradycardia, tachycardia, and behavioral responses (such as face-twisted, limb abduction, or finger opening).[7,8]

Pain control is an important component of care of preterm infants, as the American pain association has defined the term "pain: the fifth vital sign" to emphasize its importance and raise awareness of the health care providers about pain control.[9,10] Untreated pain may have

many negative effects on the infant.[11] These negative effects include decreased oxygenation, hemodynamic instability, and increased intracranial pressure, and they may lead to anxiety, increased sensitivity to pain, emotional effects, hyperactivity and inattention in the child in the future. The release of stress hormones due to lack of pain control can delay wound healing, cause infection, increase hospitalization, and even cause neonatal mortalities.[12]

Inadequate pain management in preterm infants may lead to permanent changes in the process of organizing the brain and the emergence of maladaptive behaviors.[13,14] Pain may also have detrimental effects on child's future abilities to learn and remember new information. Nurses need to know how to control pain with pharmacological and non-pharmacological approaches.[15] The use of medications to manage pain in infants is unacceptable for many physicians because their regular use can have many side effects.[16] In addition to pharmacological approaches, non-pharmacological pain management techniques are important and safe interventions especially for mild/ moderate pain in the NICUs. Swaddling, kangaroo care (skin-to-skin contact), facilitated tucking, breastfeeding, non-nutritional sucking and use sucrose are good examples of non-pharmacological pain management techniques in the NICUs.[17-19] In NICUs, endotracheal suctioning is performed by a single caregiver who is usually a nurse.[20] Although some NICUs use the four-handed approach instead of the routine endotracheal suctioning, in many cases, there is no stable practical training. In the four-handed care, another person, in addition to the nurse, provides the infant with a gentle touch before suctioning, causes support and comfort for the infant and can help the nurse during the suctioning process.[21] Gentle human touch is a skin-to-skin touch contact technique designed specifically for physiologically fragile infants.[22] Facilitated tucking is a strategy whereby a caregiver places his/ her hands gently to contain the infant's head and extremities in a flexed position. But in four-handed care, it is not necessary to change the neonatal position. The focus of four-handed care is on the needs of the infant and the caregiver, the goal is to provide support for both parties during the procedure. Because the infant is positioned supine for proper suctioning, positioning/turning during the four-handed care is usually not performed.[23] During routine endotracheal suctioning, the heart rate increases, arterial oxygen saturation decreases and behavioral responses show pain including facial changes (such as raising eyebrows, squeezing the eyes, folding the naso-labial groove, limb abduction).[24] Behavioral responses are the only way for the infant to express his/ her needs to parents or caregivers. The main dimensions of the neonatal behavior include sleep, wakefulness, and activity such as crying, positioning, muscle tone, and movement patterns, especially in the face. Sleep and wakefulness are associated with evolutionary outcomes in addition to affecting the infant's immediate response to stimulation because of the reflection of the central nervous system function. Specialists use neonatal behaviors to determine pain and respond to interventions that improve neonatal care.[25] Peyrovi et al showed that the use of facilitated tucking position during endotracheal suctioning in preterm infants reduced heart rate as a physiological response compared to the normal position but it had no effect on arterial blood oxygen saturation and stress.[26] Similarly, Fatollahzade et al studied the effect of gentle human touch during endotracheal suctioning on procedural pain response in preterm infants admitted to NICUs. They found that the mean scores of pain and severe pain were significantly lower in preterm infants with gentle human touch during endotracheal suctioning.[15] Extensive reviews of internal and external studies have found limited studies on the effect of four-handed care during endotracheal suctioning on behavioral responses, with most studies examining only physiological responses.[21] Also, given the more favorable suctioning of the infant in a supine position, it seems that the four-handed care is more appropriate without positioning the infant (our mean from four-handed care is just supporting infant in her desire position). Since the routine endotracheal suctioning is used in most parts of Iran and the control of neonatal pain and stress is one of the goals of desirable nursing care, the current study aimed to investigate the effect of endotracheal suctioning, using four handed care on the physiological criteria and behavioral responses of premature infants admitted to NICUs.

Materials and Methods

In the present study, the researcher performed the study after obtaining permission from the ethics committee of Tehran University of Medical Sciences, registering the study at the Iranian Registry of Clinical Trials (IRCT(website (identifier: IRCT20180121038461N1) and coordinating with the authorities of the research center. First, the researcher met the NICU physician, head nurse, and nurses and provided a brief explanation of the study purpose and procedure, as well as video recording of the infant. Before sampling, the researcher explained to parents how the infants would be involved in the study, the voluntary nature of the study, and the possibility of withdrawing from the study. The parents were ensured that their withdrawal would have no impact on the quality of care and treatment of their infants. The researcher started sampling after obtaining the approval of physicians, the head nurse and nurses and written consent from the infants' parents. The parents completed the informed consent form for video recording and the goals and procedures were explained to them.

The inclusion criteria were infants aged between 29 and 37 gestational weeks and postnatal age below one week, birth weight ≥1000 g, having an endotracheal tube, absence of congenital anomalies, and having consumed no opioids or sedatives four hours before suctioning.

Then, the infants who needed suctioning and met the inclusion criteria were selected by convenience sampling. The researcher completed the demographic information questionnaire, using the neonatal medical record. This was a clinical trial study with a crossover design, in which the participants randomly received a sequence of either «suctioning with intervention- suctioning without intervention» or «suctioning without intervention- suctioning with intervention».

The sample size was calculated, using the maximum error of the first type 5%, the maximum error of the second type 20% and the standard deviation of 3.6 from the Jabraeili et al[27] study ($1-\alpha/2=1.96$, $1-\beta=1.64$, $SD=3.6$, $d=2$) and finally, 40 samples were calculated. The samples were randomly divided into two groups of 20. Randomization was performed using closed letters. Accordingly, one of the letters was randomly selected and the infants were assigned to one of the two groups. One group was first suctioned by the routine method and then, by the four-handed method. The other group was first suctioned by the four-handed method and then, by the routine method with infants serving as their own controls. The time interval between the two suctions per infant was a minimum of 2 and a maximum of 4 hours (because the endotracheal suctioning is a Pro re nata (PRN) procedure if infants didn't need suction, they were excluded from the study),[26] and also both were performed on the same day for each infant. Sampling was often done in the morning and evening shifts. First, the researcher made sure that the pulse oximeter probe was connected to the infant's foot to record physiological information (heart rate and arterial oxygen saturation). The camera was also adjusted so that the monitor screen and physiological responses were recorded simultaneously.

In the routine suctioning (two- handed suctioning), the video camera (Power Shot A 1400 Digital Canon) was set up to fit the baby's entire body into the filming field, then video recording began two minutes before suctioning. The suctioning was performed by the corresponding nurse trained in the field. First, the nurse washed her hands and manually ventilated the infant to maintain the necessary pulmonary volume during suctioning.[28] She adjusted the pressure of the suction device between 60 and 100 mmHg, then measured the length of the suction catheter, inserted the catheter into the endotracheal tube, performed the suction according to the amount of discharge, and noted that the total suction duration did not exceed 10 seconds. If the discharge did not come out with one suction, the suction might be repeated up to 3 times. The time interval was 30 seconds. According to the pain instrument used, each infant was evaluated for 10 minutes, so video recording continued up to 8 minutes after suctioning. Finally, the video was reviewed by two people (researcher and research supervisor). Neonatal physiological behaviors and responses were assessed, using the (Astrid Lindgren Children's Hospital Pain Scale Neonates) ALPS-Neo checklist for 30 seconds two minutes before suctioning. Then, the evaluation was done for 30 seconds and then two minutes at the beginning of suctioning as well as 30 seconds after suctioning. It was repeated every two minutes for three more times. In total, the infant was evaluated 5 times from the start of suctioning[21] (Figure 1).

In four-handed suctioning, it started two minutes before the video-recording began. The researcher began to support the infant with washed and warm hands after two minutes and continued until the suction began. The neonatal support and touch stopped with suctioning.[29] The suctioning was performed by the responsible nurse trained in the field. First, the nurse washed her hands and manually ventilated the infant for two minutes to maintain the necessary pulmonary volume during suctioning. She adjusted the pressure of the suction device between 60 and 100 mm Hg, then measured the length of the suction catheter, inserted the catheter into the endotracheal tube, performed the suction according to the amount of discharge, and noted that the total suction duration did not exceed 10 seconds.[30] If the discharge did not come out with one suction, the suction might be repeated up to 3 times. The time interval was 30 seconds.

The researcher was also present and supported the infants during suctioning, with touch him, improve his position and paying attention to the infant's needs during suctioning. She also helped the nurses during the suction and assisting them, if needed, during the process. For example, if the nurse needed a device, she/he would provide it for her. In both groups, the suctioning was performed by same nurse, and the support care was performed by researcher. Physiological responses were also 135 recorded simultaneously. Recording continued for eight minutes after suctioning. Finally, two individuals independently observed and assessed the physiological responses and behavioral status of the infants as well as the recorded videos using the ALPS-Neo tool.

At first, the ALPS-Neo scale was confirmed by Lundqvist and colleagues in 2014.[31] The ALPS-Neo has five parts that estimate (1) the facial expression, (2) the pattern of respiration, (3) the tone of the organs, (4) the activity of the hands and feet, and 5- the level of activity. Each item is scored between 0 and 2. Therefore, the total score ranges from 0 to 10. Scores lower than 5 show no pain, 5-7 show moderate pain, and scores of 8-10 show severe pain.

In the video observations, physiological and behavioral responses were recorded for 30 seconds two minutes before the suctioning. Physiological and behavioral responses were recorded for 30 seconds at the start of the neonatal touch. They were also recorded for 30 seconds during suctioning. Physiological and behavioral responses were recorded and evaluated after suction, every two minutes for 30 seconds (4 times).[21] In total, neonatal physiological and behavioral responses were observed and recorded 5 times, using the ALPS-Neo.[31] The reliability for the coders

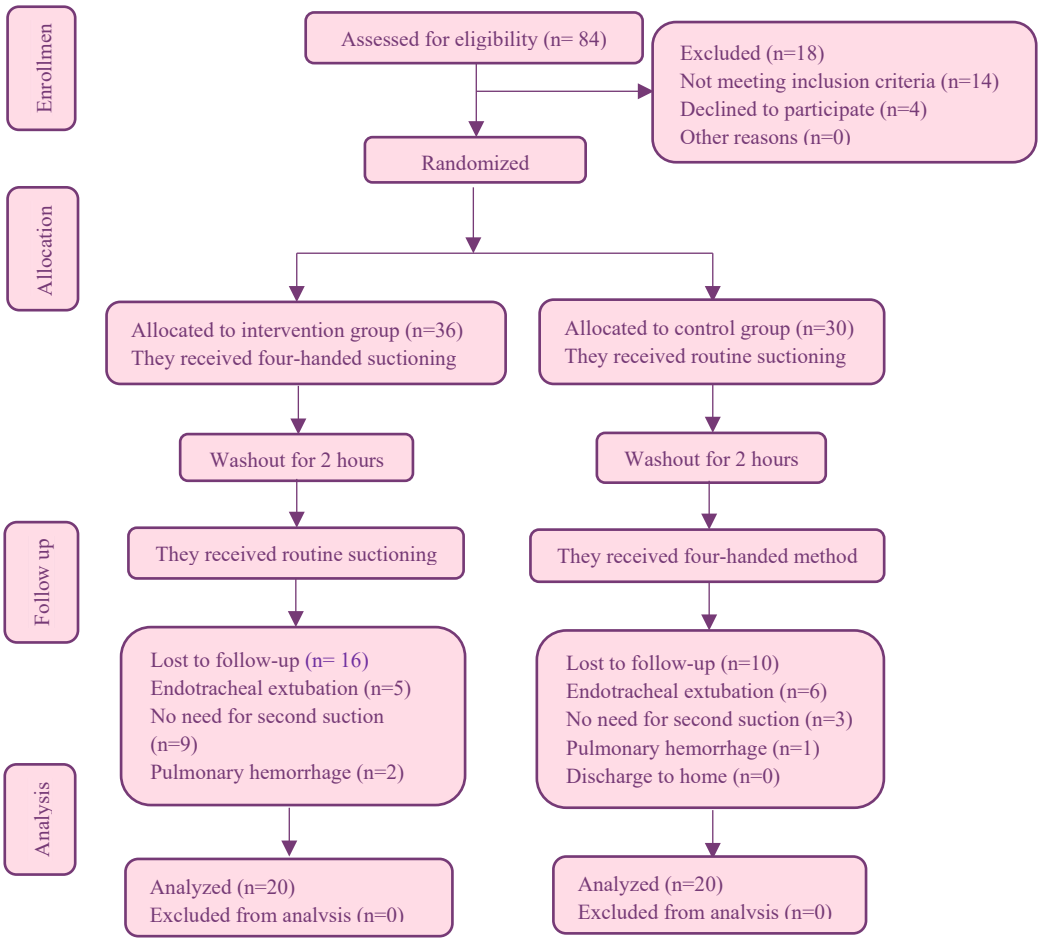

Figure 1. Flow chart of the study.

was obtained from scoring 25 samples simultaneously in a pilot form. The correlation between their scoring methods was examined by the Kappa coefficient, which was acceptable (90.48%) and they continued the evaluations after ensuring acceptable correlation.

Results

The collected data were analyzed by descriptive and analytical statistics, using SPSS 13 software so as to achieve the objectives of the study, and physiological indices (heart rate and arterial oxygen saturation percentage) and behavioral responses were measured using the ALPS-Neo.

Based on the results of the study in the routine (11 girls and 9 boys) and four-handed groups (13 girls and 7 boys), the chi-square test showed no significant difference between the two groups in terms of sex. Independent t-test also showed that infants in both groups were similar in weight and sex (Table 1).

Based on the results of Table 2, the repeated measures analysis of variance (ANOVA) test showed no significant difference in neonatal heart rate variations between the two methods, but there was a significant difference during and two minutes after suctioning as revealed by independent *t* test. The mean neonatal heart rate increased greatly in the routine method during the suctioning and it was significantly higher two minutes after the suctioning compared to the four-handed method. Although the heart rate was slightly higher in the four-handed method at the end of the two minutes, this difference was not statistically significant at the fourth, sixth and eighth minutes.

Based on the results of Table 3, repeated measures ANOVA showed no significant difference in neonatal arterial saturation changes between the two methods. The mean neonatal arterial saturation was not significantly different from one method to the other as revealed by an independent *t* test. Based on the results of Table 4, the repeated measures ANOVA test showed no significant difference in changes in neonatal behavioral response scores between the two methods. Infants' pain and stress were assessed with all AlPS-Neo scale items at intervals as shown in the table below. The mean scores of neonatal behavioral responses were not significantly different at any time between the two methods 170 using independent *t* test.

Discussion

The aim of this study was to examine the effect of endotracheal suctioning using the four-handed care on physiological criteria and behavioral responses of the preterm infants. The results of the current study showed

Table 1. Characteristics of infants

Variable	Mean (SD)		*P* value
	Routine suction	Four-handed suction	
Gender (male)	9	7	0.74[a]
Sex (female)	11	13	0.63[a]
Gestational age	31.7 (2.67)	33.50 (1.63)	0.01[b*]
Weight	1882 (498.57)	2102 (289.33)	0.09[b]

[a] Chi-square test, [b] *t* test, * Statistically significant.

Table 2. Comparison of the mean and standard deviation of the neonatal heart rate at different times between two groups of the routine and four-handed suctions

Time	Mean (SD)		*P* value[a]
	Routine suction	Four-handed suction	
Two min before suction	154.5(17.7)	153.3(17.58)	0.76
During suction	158.9(15.4)	155.1(17.12)	0.29
Two min after suction	161.3(15.3)	152.9(17.55)	0.02*
Four min after suction	157.9(14.6)	152.3(17.47)	0.12
Six min after suction	157.6(16.2)	151.8(18.31)	0.13
Eight min after suction	157.8(16.0)	152.2(18.15)	0.14
P value[b]	0.16		-

[a] *t* test, [b] Repeated measures ANOVA, *Statistically significantly.

Table 3. Comparison of the mean (SD) of neonatal blood arterial oxygen saturation between the two groups of routine and four-handed suctions at different times

Time	Mean (SD)		*P* value[a]
	Routine suction	Four-handed suction	
Two min before suction	95.2 (3.55)	96.3 (2.93)	0.14
During suction	93.5 (4.19)	93.8 (4.13)	0.70
Two min after suction	93.9 (4.18)	93.1 (5.76)	0.48
Four min after suction	94.6 (3.99)	94.8 (4.27)	0.80
Six min after suction	95.5 (2.99)	94.9 (4.91)	0.52
Eight min after suction	95.5 (3.45)	95.9 (2.71)	0.56
P value[b]	0.86		-

[a] *t* test, [b] Repeated measures ANOVA.

Table 4. Comparison of the mean (SD) of neonatal behavioral responses between two groups of routine and four-handed methods at different times

Time	Mean (SD)		*P* value[a]
	Routine suction	Four-handed suction	
Two min before suction	0.22 (0.42)	0.30 (0.46)	0.45
During suction	3.30 (1.92)	3.15 (1.68)	0.71
Two min after suction	1.52 (1.53)	1.35 (1.38)	0.59
Four min after suction	0.57 (1.10)	0.42 (0.54)	0.44
Six min after suction	0.35 (0.57)	0.35 (0.73)	0.99
Eight min after suction	0.27 (0.59)	0.12 (0.33)	0.17
P value[b]	0.49		-

[a] *t* test, [b] Repeated measures ANOVA.

that the four-handed suctioning had no significant difference in behavioral responses of the preterm infants admitted to NICUs, but could prevent the heart rate increase during and two minutes after suction.

Salmani et al studied the effect of facilitated tucking created with simulated hands on physiological pain indicators during venipuncture in premature infants. They reported no significant difference between the intervention and control groups in arterial blood oxygen saturation level and the heart. Their findings seem to be consistent with those of the present study.[32] The results of our study showed that Four-handed suctioning method was able to prevent an increase in the heart rate during and two minutes after suctioning but it did not affect behavioral responses and oxygen saturation of the preterm infants admitted to NICUs. The probable cause of such difference between these results might be attributable to human touch and simulated hands touch that can be important in calming infants.

Also, the comparison of changes in behavioral responses before, after and during suctioning in the two groups of routine and four-handed suctioning showed that there was no significant difference between the methods in the changes of infants' behavioral responses. The mean scores of neonatal behavioral responses were not significantly different at any time between the two methods as shown by the independent *t* test. Fatollahzade et al studied the effect of gentle human touch during endotracheal suctioning on procedural pain response in preterm infants admitted to NICUs. The study aimed to examine the effect of gentle human touch during endotracheal suctioning on procedural pain response in preterm infants admitted to NICUs. The study was performed on 34 preterm infants that randomly received a sequence of suctioning with/without or suctioning without/with gentle human touch. The study had a crossover design. The results of that study showed that the pain due to suctioning procedure is considerably reduced by applying gentle human touch. This study results showed that human touching can reduce neonatal pain during endotracheal suctioning.[15] Their results are inconsistent with the results of the present study because, in the current study, the four-handed suctioning had no effect on coping with stress and behavioral responses of the preterm infants. This may be due to the fact that in our study we just support infants in his position and no intervention was actually used for them.

Gomes Neto et al in the Brazil studied the effect of facilitated tucking position during painful procedure in pain management of preterm infants in NICU. The study aimed to investigate the effects of facilitated tucking position during painful procedure in pain management of preterm infants. Fifteen studies met the eligibility criteria, including 664 preterm infants. The meta-analyses showed a significant reduction in pain during endotracheal suctioning for the participants in the facilitated tucking position group compared with routine care group. The results also showed that different behavioral interventions

performed in the NICUs increased the infant's ability to cope with stress.[33] The results of our study are different from those of Gomes Neto et al study, and the four-handed suction did not affect neonatal stress and behavioral responses compared to the routine one. This difference can be due to the use of different tools and methodology.

Based on Välitalo et al study results, (Pain and distress caused by endotracheal suctioning in neonates is better quantified by behavioral than physiological items: a comparison based on item response theory modeling), that compared behavioral and physiological items in predicting pain. Finally they found behavioral items are better in indicated pain,[7] but our study showed that physiological items are more sensitive in expressing neonatal pain. It can due to using two strong pain scales in their study that are capable of assessing neonatal behavioral than physiological items.

Peyrovi et al in Iran studied the effect of facilitated tucking position on physiological responses and coping with stress in preterm infants during endotracheal suctioning and concluded that there was no difference between facilitated tucking position and the routine care in coping with stress in infants. In the same study, they reported the effective role of facilitated tucking position in neonatal pain during endotracheal suctioning. The interventions that reduce pain may decrease behavioral responses in infants.[26] The present study is in agreement with that study in terms of decreasing behavioral responses and has no effect on coping with stress and behavioral responses of preterm infants but it is different in terms of the effect on physiological responses because in our study, the heart rate increase in the four-handed suction was lower than that in the routine suction and the heart rate decreased two minutes after the four-handed suctioning compared to the routine suctioning. Heart rate variations during medical examinations are important as the indicators of pain assessment. Studies have reported the heart rate increase as physiological symptoms of pain, and the results have also shown that premature infants use physiological symptoms more, especially the heart rate and that full-term infants use behavioral symptoms more such as crying and facial changes to express pain.[34,35] Therefore, according to the results of the present study, lower fluctuations in neonatal heart rate during the four-handed suctioning can cause less pain and stress in the infants admitted to intensive care units and reduce short-term and long-term complications of the pain and stress induced by tracheal suction. As for the limitations of the study, it has to be mentioned that the collected data, a few number of infants in the ward needed tracheal suctioning, which extended the sampling time.

Conclusion

The results of the current study showed that the four-handed suctioning had no statistically significant difference in behavioral responses of the preterm infants admitted to the NICUs but could prevent the heart rate increase during and two minutes after suction. Since one of the methods of neonatal pain assessment is physiological criteria, especially heart rate, reduction of heart rate fluctuations by the four-handed care during endotracheal suctioning can control neonatal pain and stress. Therefore, it is recommended the four-handed care be used during endotracheal suctioning to control neonatal pain and stress. Based on the results of this study and other studies confirming these results, it is recommended to assess the effect of four-handed Care on other invasive procedures in next studies.

Research Highlights

What is the current knowledge?

Pain and stress manifest with physiological and behavioral responses in infants and stable vital signs during painful procedures can be an indication of the effectiveness of pain relief method in invasive procedures such as suctioning.

What is new here?

Four-handed suctioning method can prevent an increase in heart rate during and after suctioning. Since one of the symptoms of pain and stress in infants is the change of vital signs, especially the heart rate.

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Authors' Contributions

SSN, BP, JM: Study conception and design; SSN, BP, JM: Data collection; SSN, BP, HR, ASF: Data analysis and interpretation; BP, AS, SSN: Drafting of the article; ASF, BP, HR: Critical revision of the article. All authors have read and agreed to the published version of the manuscript.

Ethical Issues

The study protocol was approved by Tehran University of Medical Sciences committee of ethics in research (IR.TUMS.FNM.REC.1397.022); 11 April 2018. Ethical considerations include parental consent and ensuring the confidentiality of information, as well as being free to leave the study at any stage.

Conflicts of Interest

The authors declared no potential conflicts of interest.

References

1. Tremblay S, Ranger M, Chau CMY, Ellegood J, Lerch JP, Holsti L, et al. Repeated exposure to sucrose for procedural pain in mouse pups leads to long-term widespread brain

alterations. Pain. 2017; 158(8): 1586-98. doi: 10.1097/j.pain.0000000000000961
2. Anand KJS. Discovering pain in newborn infants. Anesthesiology. 2019; 131(2): 392-5. doi: 10.1097/aln.0000000000002810
3. Cruz MD, Fernandes AM, Oliveira CR. Epidemiology of painful procedures performed in neonates: a systematic review of observational studies. Eur J Pain. 2016; 20(4): 489-98. doi: 10.1002/ejp.757
4. Şener Taplak A, Erdem E. A comparison of breast milk and sucrose in reducing neonatal pain during eye exam for retinopathy of prematurity. Breastfeed Med. 2017; 12: 305-10. doi: 10.1089/bfm.2016.0122
5. Schiavenato M, Holsti L. Defining procedural distress in the NICU and what can be done about it. Neonatal Netw. 2017; 36(1): 12-7. doi: 10.1891/0730-0832.36.1.12
6. Mirlashari J, Holsti L, Begjani J, Roohipoor R, Kasaeian A, Safaiee Fakhr A. Comparison of breast milk and sucrose in neonatal pain relief and coping with stress of ROP examination using ALPS-Neo. Iran J Neonatol IJN. 2021; 12(2): 46-55. doi: 10.22038/ijn.2021.49621.1866
7. Välitalo PAJ, van Dijk M, Krekels EHJ, Gibbins S, Simons SHP, Tibboel D, et al. Pain and distress caused by endotracheal suctioning in neonates is better quantified by behavioural than physiological items: a comparison based on item response theory modelling. Pain. 2016; 157(8): 1611-7. doi: 10.1097/j.pain.0000000000000485
8. Khalili Z, Molavi Vardanjani M, Bashiri S, Khalili A. The relationship between pain score and change in physiological indices of premature neonates under ventilation. Scientific Journal of Nursing, Midwifery and Paramedical Faculty. 2018; 3(3): 1-7. doi: 10.29252/sjnmp.3.3.1
9. Barros MM, Luiz BV, Mathias CV. Pain as the fifth vital sign: nurse's practices and challenges in a neonatal intensive unit care. BrJP. 2019; 2(3): 232-6. doi: 10.5935/2595-0118.20190041
10. Lynch M. Pain as the fifth vital sign. J Intraven Nurs. 2001; 24(2): 85-94.
11. Wallace H, Jones T. Managing procedural pain on the neonatal unit: do inconsistencies still exist in practice? J Neonatal Nurs. 2017; 23(3): 119-26. doi: 10.1016/j.jnn.2016.10.004
12. Kaspar A, Rubarth LB. Neuroprotection of the preterm infant. Neonatal Netw. 2016; 35(6): 391-6. doi: 10.1891/0730-0832.35.6.391
13. Anderson DE, Patel AD. Infants born preterm, stress, and neurodevelopment in the neonatal intensive care unit: might music have an impact? Dev Med Child Neurol. 2018; 60(3): 256-66. doi: 10.1111/dmcn.13663
14. Knudsen K, McGill G, Ann Waitzman K, Powell J, Carlson M, Shaffer G, et al. Collaboration to improve neuroprotection and neuropromotion in the NICU: team education and family engagement. Neonatal Netw. 2021; 40(4): 212-23. doi: 10.1891/11-t-680
15. Fatollahzade M, Parvizi S, Kashaki M, Haghani H, Alinejad-Naeini M. The effect of gentle human touch during endotracheal suctioning on procedural pain response in preterm infant admitted to neonatal intensive care units: a randomized controlled crossover study. J Matern Fetal Neonatal Med. 2020: 1-7. doi: 10.1080/14767058.2020.1755649
16. Liaw JJ, Yang L, Katherine Wang KW, Chen CM, Chang YC, Yin T. Non-nutritive sucking and facilitated tucking relieve preterm infant pain during heel-stick procedures: a prospective, randomised controlled crossover trial. Int J Nurs Stud. 2012; 49(3): 300-9. doi: 10.1016/j.ijnurstu.2011.09.017
17. Mangat AK, Oei JL, Chen K, Quah-Smith I, Schmölzer GM. A review of non-pharmacological treatments for pain management in newborn infants. Children (Basel). 2018; 5(10): 130. doi: 10.3390/children5100130
18. Hatfield LA, Murphy N, Karp K, Polomano RC. A systematic review of behavioral and environmental interventions for procedural pain management in preterm infants. J Pediatr Nurs. 2019; 44: 22-30. doi: 10.1016/j.pedn.2018.10.004
19. Pirlotte S, Beeckman K, Ooms I, Van Rompaey B, Cools F. Pharmacological interventions for the prevention of pain during endotracheal suctioning in ventilated neonates. Cochrane Database Syst Rev. 2019; 2019(6): CD013355. doi: 10.1002/14651858.CD013355
20. Mooney-Leber SM, Brummelte S. Neonatal pain and reduced maternal care: early-life stressors interacting to impact brain and behavioral development. Neuroscience. 2017; 342: 21-36. doi: 10.1016/j.neuroscience.2016.05.001
21. Cone S, Pickler RH, Grap MJ, McGrath J, Wiley PM. Endotracheal suctioning in preterm infants using four-handed versus routine care. J Obstet Gynecol Neonatal Nurs. 2013; 42(1): 92-104. doi: 10.1111/1552-6909.12004
22. Smith JR. Comforting touch in the very preterm hospitalized infant: an integrative review. Adv Neonatal Care. 2012; 12(6): 349-65. doi: 10.1097/ANC.0b013e31826093ee
23. Lan HY, Yang L, Hsieh KH, Yin T, Chang YC, Liaw JJ. Effects of a supportive care bundle on sleep variables of preterm infants during hospitalization. Res Nurs Health. 2018; 41(3): 281-91. doi: 10.1002/nur.21865
24. Pouraboli B, Rayyani M, Dehghan Anari M, Hosseini F, Loghmani L. Lullaby effect with mother's voice on respiratory rate and the speed of its return to the pre-suction state in intubated preterm infants, during tracheal tube suction Kerman, Afzalipour hospital 2016. Electron J Gen Med. 2019; 16(1): em106. doi: 10.29333/ejgm/93471
25. Im H, Kim E. Effect of Yakson and Gentle Human Touch versus usual care on urine stress hormones and behaviors in preterm infants: a quasi-experimental study. Int J Nurs Stud. 2009; 46(4): 450-8. doi: 10.1016/j.ijnurstu.2008.01.009
26. Peyrovi H, Alinejad-Naeini M, Mohagheghi P, Mehran A. The effect of facilitated tucking position during endotracheal suctioning on physiological responses and coping with stress in premature infants: a randomized controlled crossover study. J Matern Fetal Neonatal Med. 2014; 27(15): 1555-9. doi: 10.3109/14767058.2013.868429
27. Jabraeili M, Eskandari S, Bagher Hosseini M, Rahmani P. The effect of body position on pain due to nasal continuous positive airway pressure (CPAP) in premature neonates: a cross-over clinical trial study. Int J Pediatr. 2018; 6(1): 6861-71. doi: 10.22038/ijp.2017.26364.2258
28. Green AD. Mechanical Ventilation: Pediatric Pressure Mode (Respiratory Therapy). Elsevier; 2020.
29. Alinejad-Naeini M, Mohagheghi P, Peyrovi H, Mehran A. The effect of facilitated tucking during endotracheal suctioning on procedural pain in preterm neonates: a randomized controlled crossover study. Glob J Health Sci. 2014; 6(4): 278-84. doi: 10.5539/gjhs.v6n4p278
30. Bruschettini M, Zappettini S, Moja L, Calevo MG. Frequency of endotracheal suctioning for the prevention of respiratory morbidity in ventilated newborns. Cochrane Database Syst Rev. 2016; 3: CD011493. doi: 10.1002/14651858.CD011493.pub2
31. Lundqvist P, Kleberg A, Edberg AK, Larsson BA, Hellström-

Westas L, Norman E. Development and psychometric properties of the Swedish ALPS-Neo pain and stress assessment scale for newborn infants. Acta Paediatr. 2014; 103(8): 833-9. doi: 10.1111/apa.12672

32. Salmani N, Karjoo Z, Dehghani K, Sadeghnia A. Effect of facilitated tucking created with simulated hands on physiological pain indicators during venipuncture in premature infants. Iran J Neonatol IJN. 2017; 8(4): 7-12. doi: 10.22038/ijn.2017.21562.1247
33. Gomes Neto M, da Silva Lopes IA, Araujo A, Oliveira LS, Saquetto MB. The effect of facilitated tucking position during painful procedure in pain management of preterm infants in neonatal intensive care unit: a systematic review and meta-analysis. Eur J Pediatr. 2020; 179(5): 699-709. doi: 10.1007/s00431-020-03640-5
34. Quiram PA, Capone A, Jr. Current understanding and management of retinopathy of prematurity. Curr Opin Ophthalmol. 2007; 18(3): 228-34. doi: 10.1097/ICU.0b013e3281107fd3
35. Manzotti A, Cerritelli F, Lombardi E, La Rocca S, Chiera M, Galli M, et al. Effects of osteopathic treatment versus static touch on heart rate and oxygen saturation in premature babies: a randomized controlled trial. Complement Ther Clin Pract. 2020; 39: 101116. doi: 10.1016/j.ctcp.2020.101116