Journal of Taibah University Medical Sciences (2022) 17(2), 311–319

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com

Original Article

The effect of sensory stimulation on apnea of prematurity

Asmaa S.A. Abdel Mageed, M.Sc. [a,*], Khaled A. Olama, Ph.D [b], Samia A. Abdel Rahman, Ph.D [b] and Hamouda E. El-Gazzar, M.D [a,c]

[a] *Department of Physical Therapy, Damanhour Medical National Institute, Beheira, Egypt*
[b] *Department of Pediatric Physical Therapy, Faculty of Physical Therapy, Cairo University, Giza, Egypt*
[c] *Department of Pediatrics, Medical National Institute, Beheira, Egypt*

Received 29 June 2021; revised 22 October 2021; accepted 25 October 2021; Available online 10 December 2021

الملخص

أهداف البحث: هدفت هذه الدراسة إلى تقييم تأثير التنبيه الحسي على انقطاع النفس الخداجي.

طرق البحث: شملت هذه الدراسة العشوائية المستقبلية ثلاثين من الخدج في العمر الحملي بين٣٢ و٣٤ أسبوعا وذوي وزن منخفض عند الولادة وملائم لعمر الحمل من ١٢٠٠ إلى ٢٠٠٠ جرام، تم تقسيمهم إلى مجموعتين متساويتين: تلقت مجموعة التحكم الرعاية المعتادة بما في ذلك الأكسجين الأنفي (واحد لتر/دقيقة) وسيترات الكافيين وتلقت مجموعة الدراسة نفس الرعاية بالإضافة إلى التحفيز الحسي (لمسي، حسي، حركي). وتم قياس معدل ضربات القلب، تشبع الأكسجين ووتيرة انقطاع النفس بواسطة التأكسج- النبضي من قبل فريق وحدة العناية المركزة لحديثي الولادة. كان وقت جلسة التحفيز الحسي ١٠ دقائق، بواقع ٣ مرات في اليوم بإجمالي ٣٠ دقيقة لمدة ٧ أيام متواصلة.

النتائج: بعد العلاج، كان هناك انخفاض ذو دلالة إحصائية في معدل ضربات القلب لكلا المجموعتين بالمقارنة مع قيمته المقابلة قبل العلاج، مع عدم وجود فروق ذات دلالة إحصائية بين المجموعتين. بعد العلاج، لم يوجد فرق واضح في تشبع الأكسجين داخل المجموعتين مقارنة بقيمته قبل العلاج مع عدم وجود فروق ذات دلالة إحصائية بين المجموعتين. أما قبل العلاج فكان هناك انخفاض واضح في معدل انقطاع النفس بين المجموعتين. وبعد العلاج، كان هناك انخفاض واضح في معدل انقطاع النفس في مجموعة الدراسة مقارنة بالمجموعة الضابطة.

الاستنتاجات: تطبيق التحفيز الحسي مع الرعاية التنفسية يمكن أن يخفض من تكرار انقطاع النفس الخداجي.

الكلمات المفتاحية: انقطاع النفس؛ رضيع؛ وزن منخفض عند الولادة؛ العمر الحملي؛ معدل ضربات القلب؛ التحفيز الحسي.

Abstract

Objectives: The study aims to assess the effect of sensory stimulation on apnoea among premature newborns.

Methods: Thirty preterm newborns that were diagnosed with apnoea of prematurity, had a gestational age between 32 and 34 weeks, had low birth weight, and were appropriate for gestational age from 1200 to 2000 g were included in this prospective randomized study. Subjects were divided into two equivalent groups: a control group that received the standard care including nasal oxygen (one litre per minute) and caffeine citrate, and a study group that received the same care plus sensory stimulation (tactile, proprioceptive, and kinaesthetic). Participants' heart rate, oxygen saturation, and apnoea frequency were measured by the neonatal intensive care unit team using a pulse-oximeter. The sensory stimulation sessions were 10 min, 3 times per day, totalling 30 min over a 7 day period.

Results: There was a significant decrease in heart rate within both groups after receiving treatment from before treatment ($p < 0.05$), with no significant differences between the two groups. Furthermore, there was no significant difference in oxygen saturation within the groups after treatment compared with the levels before treatment, with no significant differences between the two groups ($p > 0.05$). Before treatment, there was a non-significant difference in the apnoea rate between both groups ($p = 0.464$), whereas there was a significant decrease in the apnoea rate of the study group after treatment compared with the control group ($p = 0.031$).

Conclusion: Sensory stimulation applied with standard respiratory care can decrease the frequency of apnoea of prematurity.

* Corresponding address: Cairo University, 7 Ahmed Alzayate ST, Been Alsarayat, 12662, Giza, Egypt.
E-mail: dr.asmaa.elshehawy@gmail.com (A.S.A. Abdel Mageed)

Peer review under responsibility of Taibah University.

Production and hosting by Elsevier

 https://doi.org/10.1016/j.jtumed.2021.10.016

Keywords: Apnoea; Gestational age; Heart rate; Infant; Low birth weight; Sensory stimulation

Introduction

Preterm birth may be a serious factor in neonates' morbidity, mortality, and other long-term health concerns. Preterm infants have higher degrees of learning disabilities, sensory deficits, cerebral palsy, and respiration diseases than full-term infants. The morbidity related to prematurity tends to persist in later life, often resulting in great psychological, physical, and economic costs.[1–3] Furthermore, preterm neonates face difficulties with regulation of temperature, oral feeding skills, and normal breathing control. Apnoea cessation and acquiring a normal respiration pattern is a milestone of normal development for many preterm infants. Apnoea of prematurity (AOP) refers to respiration stopping for a period of time (≥10–20 s), or associated with oxygen desaturation ($SpO_2 \leq 80\%$ for ≥4 s) and bradycardia (heart rate <2/3 of baseline for ≥4 s) in preterm infants (<37 gestational weeks).[4,5] Intermittent hypoxia, cardiovascular sequelae, retinopathy, and neurodevelopmental diseases are commonly associated with AOP.[6,7] Clinically significant apnoeas are apnoeas that persist more than 20 s, or that are associated with bradycardia and desaturations. However, stopping breathing for even 5–10 s can be accompanied by bradycardia or a decline in oxygen saturation (SpO_2). Repeated intermittent hypoxic spells and bradycardia that happen with apnoea may lead to changes in neural development, which result in an elevated rate of death or abnormal neurodevelopment such as blindness at 3 years of age or cerebral palsy.[8,9]

Nasal intermittent positive pressure ventilation (NIPPV), continuous positive airway pressure (CPAP), and prone positioning are among the typical treatments used for AOP to avoid pharyngeal collapse and alveolar atelectasis. Also, methylxanthine therapy (caffeine and theophylline), which blocks adenosine receptors (the backbone of central apnoea intervention), is often used as a treatment.[10] In most Neonatal Intensive Care Units (NICUs), pharmacotherapy is used in addition to respiratory care to treat apnoea of prematurity; however, most preterm infants still develop apnoea, which calls for the caregiver to provide more support. Apnoea termination can be achieved using sensory stimulation (tactile), which is usually provided in addition to oxygen support or the use of ventilators (bag or mask).[11–14] Sensory stimulants, including tactile stimulation, may be beneficial in the care or avoidance of AOP. Tactile stimulation works by producing excitatory, nonspecific neuronal action in the brainstem centre, which in turn promotes respiratory work.[15] Using vibration on the soles of the feet or palms of the hand can stimulate joints proprioceptors, thereby supporting respiration by producing an inherent reflexive coupling between the respiratory rate and motion of the limbs.[16] The synchronization of breathing patterns and leg movements has been documented in humans, which allows us to conclude that limb motion can increase breathing. The moving limbs have proprioceptive afferents that generate coordination between locomotion and respiratory rhythm in humans.[17,18] In order to adjust the environment of preterm neonates, NICUs focus on massages that apply moderate pressure to physiologically stable preterm neonates and stroking with firm or moderate pressure, thus avoiding many complications associated with premature births.[19] Even during sleep, the rate of breathing and ventilation directly increases with passive limb movements. This benefit has been noticed in congenital central hypoventilation syndrome (CCHS) within which children demonstrate sustained apnoea during sleep, instead of the standard episodic breathing characteristic of AOP; however, hypoventilation is still common in both situations.[20]

Intermittent hypoxic episodes in human neonates lead to early and late morbidities, including impaired growth, retinopathy of prematurity and bronchopulmonary dysplasia, cardiovascular dysregulation, neurodevelopmental disabilities, and disordered breathing in sleep.[21–24]

It is important to find various methods that can reduce apnoeic episodes, and to lower the number of accompanying bradycardic events, thereby preventing the dangerous complications of AOP and the hazards of traditional treatments. Low-cost limb stimulation procedures have the potential to provide a non-invasive intervention to reduce apnoea, bradycardia, and intermittent hypoxia in premature neonates. It was hypothesized that sensory stimulation has no effect on apnoea of prematurity. Therefore, this study's purpose was to examine the effect of sensory stimulation in the form of tactile stimulation, vibration, and passive movements on heart rate (HR) and the frequency of apnoea in premature infants with AOP.

Materials and Methods

Study design

This study is a prospective randomized study that was conducted at the neonatal intensive care units of Damanhur Medical National Institute, Dmesna Paediatric Hospital, and Abu Hommos Local Hospital.

Participants were randomly divided into two equal groups using a sealed envelope method; the control group received the standard care given in such cases (close monitoring, adequate thermal environment, proper nutrition, adequate circulatory support, nasal oxygen, and caffeine citrate), while the study group received the same standard care in addition to sensory stimulation.

Sampling method and venue

Convenience sampling of preterm newborns with AOP were recruited from the NICU at Damanhur Medical National Institute, Dmesna Paediatric Hospital, and Abu Hommos Local Hospital. The program was also conducted in the NICU at Damanhur Medical National Institute, Dmesna Paediatric Hospital, and Abu Hommos Local Hospital.

Sample size

Based on a pilot study, the sample size was calculated according to the insignificant difference in the value of mean difference (pre-treatments − posttreatment values) of the HR of the control group (8.14 ± 5.67) and the study group (6.57 ± 4.38) in an unpaired *t*-test, with $\alpha = 0.05$, a power of 80%, and an effect size of 0.78. Therefore, a sample size of 15 patients per group was required, and this figure was increased to 18 patients to allow for a 20% dropout rate (GPower 301 http: www.psycho.uni-duesseldorf.de).

Participants

Thirty preterm newborns that were diagnosed with AOP were included in this study. Subjects were recruited by referral from the primary care team according to the following inclusion criteria: gestational age between 32 and 34 weeks, infants with AOP, and infants with low birth weight and appropriate for gestational age from 1200 to 2000 grams. Infants who had any of the following exclusion criteria: major congenital anomalies or malformations, respiratory distress syndrome (RDS), respiratory depression from medications, obstructive apnea (wrong position and/or secretions), history of hypoxic-ischemic encephalopathy, intra-ventricular hemorrhage, sepsis, hypothermia, anemia, hypoglycemia or low APGAR score at birth, were not included in the study. Participants were divided into two equal groups: a control group that received the standard care given in such cases (close monitoring, adequate thermal environment, proper nutrition, adequate circulatory support, nasal oxygen, and caffeine citrate), and a study group that received the same standard care in addition to sensory stimulation.

Instrumentation

A pulse-oximeter (DIXION, Patient Monitor, model: Storm DS-5, Power: 100−220 V, 50−60 Hz, 1.7−0.8 A) was used to measure the HR in both groups before and after intervention. In the case of the study group, a small vibratory device was also used (Beurer GmbH, model: MG40, soflingerstr. 218, 89077 Ulm, GERMANY, 220−240 V, 50−60 Hz, 12 W).[16]

Procedures

Subject recruitment

After collecting the consent forms, the name, gender, date of birth, age, and date of examination of each infant were recorded. Infants were recruited by referral from the primary care team and by self-selection. Each infant was examined by the researcher and the NICU physicians to ensure that they met the eligibility criteria. Eligible infants were then selected and divided into two equal groups.

Assessment procedures

Gestational age, birth weight, gender, mode of delivery, apnoea frequency, and HR were measured for each infant by the NICU team. In general, the HR was continuously measured in the NICU over a 24-h period using a pulse oximeter, but only documented every three hours or with any new event such as bradycardia, tachycardia, or arrhythmia. The mean value of these eight daily readings was taken and recorded for our study, rather than the absolute value of the HR during apnoeic spells.

Treatment procedures

Infants in both groups received supplemental oxygen via nasal cannula, as well as a loading dose of caffeine citrate (20 mg/kg). They then continued on a maintenance dose 5 mg/kg/day until they reached 34 weeks or went a total of 7 days free of apnoea. Additionally, infants in the study group received sensory stimulation. Kesavan et al. (2016) used a small low voltage vibratory device (0.3 g/128 HZ) on the palms and soles of preterm neonates to stimulate proprioceptive sensations as neuromodulators to decrease apnoea rate.[16]

Preparation for the session

The session was conducted in a quiet and warm environment when the infants were awake and not having an apnoeic spell. Pain was avoided by observing the infants' facial expressions in response to the stimuli. The therapist was wearing full personal protective equipment for the safety of the neonate and to avoid contamination, since the study was conducted during the COVID-19 pandemic. During the session, infants lay in a comfortable supine position to avoid any trauma or tube detachment (pulse-oximeter, feeding tube or nasogastric tube), and vibratory stimuli did not exceed 50 Hz to avoid any harmful or annoying effects because of the fragile nature of preterm infants.

The sensory stimulation procedures were selected in the following way, based on the work of Cramer et al. (2018)[25]:

1) Tactile stimulation: applied for five minutes in the form of rubbing and flicking the palms of infants' hands and the soles of their feet (both sides) for three minutes, as well as a gentle massage of the palms and soles (both sides) by the researcher's thumb for a total of two minutes.
2) Proprioceptive stimulation: applied in the form of vibration of the palms of the hands and the soles of the feet (both sides) in a circular motion using the vibratory device for a total duration of three minutes.
3) Kinaesthetic stimulation: applied in the form of passive movements of all four extremities using repetitive flexion and extensions for a total duration of two minutes.

The sessions were supervised by attending physicians or residents in the NICU, and the infants were also continuously monitored.

The time of sensory stimulation session was 10 min,[26] three times per day for a total of 30 min daily for 7 consecutive days. All outcome measures were measured before and after 7 days of intervention for both groups. The primary outcome was apnoea frequency (number of episodes per 24 h), and the secondary outcome was the HR.

We used short periods of stimulation to avoid any harmful impact on the babies such as interruption of their sleep/wake homeostasis. A limited number of sessions were conducted per day to avoid interference with their daily care, feeding, and treatments. The longest possible period was used to improve the observation levels.

Statistical analysis

The results were expressed as a mean ± standard deviation, median (minimum−maximum), and number (percentage). The Kolmogorov−Smirnov test of normality was used to measure the distribution of data pre-treatment. A comparison between the categorical data [number (%)] was performed using a chi-square test, and the Fisher exact test instead if the cell count was less than 5. An analysis of covariance (ANCOVA) test was used to compare the after-treatment values of the two groups after controlling for the effect of the value before treatment. A paired *t*-test was used to compare the differences between groups. For non-normally distributed data, the Mann−Whitney test was used to compare the variables between the two groups. Within the same group, the Wilcoxon Sign Ranks test was used to compare pre- and post-treatment data. The data analysis was performed using a statistical Package for the Social Sciences (SPSS) computer program (version 19 windows). *P*-values of ≤ 0.05 were considered significant.

Results

The general characteristics of the participants are illustrated in Table 1. There was no statistically significant difference between the two groups in terms of gestational age, chronological age, gender, mode of delivery, and birth weight ($p > 0.05$).

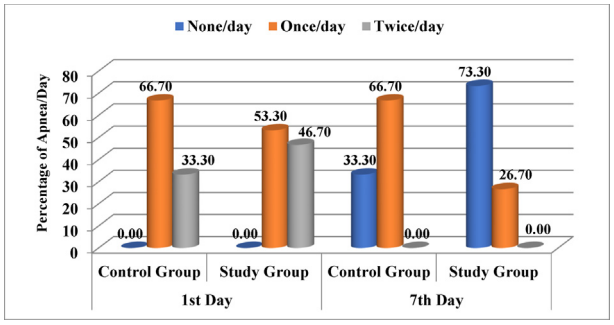

Figure 1: Percentage of apnea rate/day in the two groups measured before and after treatment.

The results revealed a statistically significant decrease in the mean value of HR after treatment compared with its corresponding value before treatment in both the control and study groups ($p < 0.05$), with percentage decreases of 7.74% and 5.50% for the control and study groups, respectively. However, there was no statistically significant difference in the mean value of the HR between the control

Table 1: General characteristics of the participants.

	Control Group (n = 15)	Study Group (n = 15)	t-value	P-value
Gestational Age (wks.)	32.40 ± 0.51	32.33 ± 0.49	0.367	0.716 (NS)
Chronological Age (days)	3.60 ± 0.73	3.53 ± 0.74	0.247	0.807 (NS)
Birth Weight (kg.)	1.32 ± 0.08	1.34 ± 0.06	−0.831	0.413 (NS)
Gender (F:M)	8 (53.3%): 7(46.7%)	6 (40.0%): 9 (60.0%)	$\chi^2 = 0.536$	0.464 (NS)
Mode of delivery (CS: NVD)	14 (93.3%): 1(6.7%)	15 (100%): 0 (0.0%)	$\chi^2 = 1.034$	0.309 (NS)

Data are expressed as mean ± standard deviation or number (%). n: Number. F: female. M: male. P: Probability value. t: Unpaired t-test. χ^2: Chi square test. Kg: Kilogram. NS = non-significant.

Table 2: Intra and inter-group comparison regarding heart rate measured before and after treatment.

Day of Measure	Control Group (n = 15)	Study Group (n = 15)	F-value	P-value
Before treatment	138.60 ± 9.61	133.20 ± 9.59	2.373	0.135 (NS)
After treatment	127.87 ± 6.79	125.87 ± 3.46	0.569	0.457 (NS)
Mean difference	10.73	7.33		
% change	7.74 ↓↓	5.50 ↓↓		
t-value	3.803	2.950		
p-value	0.002 (S)	0.011 (S)		

Data are expressed as mean ± standard deviation. %: Percentage. n: Number. t: Paired t-test. F-value = ANCOVA test. P: Probability value. NS: Non-significant. S: Significant.

Table 3: Intra and inter-group comparison regarding oxygen saturation measured before and after treatment.

Day of Measure	Control group (n = 15)	Study group (n = 15)	F-value	P-value
Before treatment	94.20 ± 1.97	93.80 ± 1.70	0.354	0.556 (NS)
After treatment	94.47 ± 1.30	94.67 ± 1.40	0.084	0.775 (NS)
Mean difference	0.27	0.87		
% change	0.29 ↑↑	0.93 ↑↑		
t-value	−0.385	−1.483		
p-value	0.706 (NS)	0.160 (NS)		

Data are expressed as mean ± standard deviation. %: Percentage. n: Number. t: Paired t-test. F-value = ANCOVA test. p: Probability value. NS: Non-significant. S: Significant.

Table 4: Within and between-group comparison regarding apnea rate/day measured before and after treatment.

Day of Measure	Control Group (n = 15)	Study Group (n = 15)	Z-value	p-value
Before treatment	1.0 (1.0–2.0)	1.0 (1.0–2.0)	−0.733	0.464 (NS)
After treatment	1.0 (0.0–1.0)	0.0 (0.0–1.0)	−2.159	0.031 (S)
Median difference	1.0 (0.0–2.0)	1.0 (0.0–2.0)	−2.104	0.035 (S)
Z-value	−2.887	−3.286		
p-value	0.004 (S)	0.001 (S)		

Data are expressed as median (minimum–maximum). n: Number. Z: Wilcoxon signed ranks test. P: Probability value. S: Significant. NS: Non-significant.

and the study groups before or after treatment ($p > 0.05$) (Table 2).

The results revealed no statistically significant difference between the mean value of SpO2 before treatment and its corresponding value after treatment for the control and study groups, with a percentage increase in the mean value of SpO2 of 0.29% and 0.93%, respectively. However, there was no statistically significant difference in the mean value of SpO2 between the control and the study groups before or after treatment ($p > 0.05$) (Table 3).

When comparing the data before and after treatment, the results revealed a statistically significant decrease in apnoea rate/day in both groups ($p < 0.05$; Figure 1), which represents the percentage of apnoeic episodes per day based on the total episodes of apnoea in the group on that same day. The findings revealed a non-statistically significant difference of apnoea rate/day between the control and study groups before treatment ($p = 0.464$). However, there was a statistically significant decrease in apnoea rate/day in the study group in contrast to its corresponding value in the control group after treatment ($p = 0.031$; Table 4).

Discussion

The study results revealed a non-statistically significant difference in apnoea rate/day between the control and study groups before treatment. Studies of animals have shown that sensory stimulation has a great effect on respiratory onset soon after birth.[27,28] Although manual stimuli are considered to be very important in international or local resuscitation guidelines, their impact on breathing initiation has only recently been investigated in preterm infants.[29]

The results showed a statistically significant decrease in apnoea rate/day in the study group compared to its corresponding value in the control group after treatment. In the case of central apnoea, the best proven non-pharmacological management is gentle tactile stimulation of new-borns' body parts. Generally, this stimulation is enough for spontaneous breathing stabilization. The process starts with light stimulation, and if the parameters do not improve, more powerful stimulation can be used on the soles of the feet. The incidence and time of apnea of premaurity has been shown to be positively influenced by tactile stimulation.[25,30]

The study results revealed a statistically significant decrease in apnoea rate/day in both groups. In the guidelines, tactile stimulation (rubbing the soles of the feet or the back) has been suggested to motivate spontaneous breathing. Although it is permitted to be used in interventions, the effect of tactile stimulation is not yet certain. Experimental studies have shown that tactile stimulation has a positive effect on spontaneous breathing, yet there is not enough human data demonstrating this in preterm infants.[31–33]

Tactile stimulation can be used to alter the arousal condition of newborns and improve their breathing effort. The reaction on arousal is mainly conditional on motivated nerves site.[34]

Evidence reinforcing the positive outcomes of using massage in preterm neonates includes improved weight acquisition, enhanced growth and gastrointestinal function, enhanced body fat deposition, enhanced neurobehavioral consequences, pain reduction, a decline in infant stress and stress-related issues, a decrease in late-onset sepsis, enhanced immune systems, diminished jaundice, and enhanced pulse rate variability, in addition to a decrease in maternal depression and anxiety.[35–46]

The influence of mechanical stimulation on the centres of respiration depends on stimulated nerves. The skin has various sensation receptors, which are sensitive to a definite degree of stimulus. For example, rubbing with low ranges of frequency on the thorax region is supposed to excite intramuscular mechanoreceptors, including the Golgi tendon organs and muscle spindles. These outcomes indicate that the location of a stimulus can influence respiration, which depends on the presence of specific receptors.[47]

Chest wall vibration might also stimulate intrapulmonary receptors because it produces a vibration effect on the lung. The receptors of stretching within lungs are answerable to inspiration inhibition after lung volume increases. Additionally, these receptors are supposed to work on the tone of airways smooth muscles, systemic vascular resistance, and HR.[48,49]

Since the invasive use of caffeine is controversial, new non-invasive methods without chemical stimulants have been developed. Mechanical stimulation has been successful in this regard. The vibrators use various parameters including amplitude and frequency to excite various body parts (e.g., whole body, thorax, and feet).[50–52]

Some of the advantages of tactile stimulation include it being non-invasive, low-cost, safe, and based on physiological steadiness, as well as not causing agitation/pain score changes among newborns who receive massage.[53]

Most of the neonates successfully accomplish a shift from the intrauterine to extrauterine environment; however, nearly 10% of neonates need support during this shift. HR is the most significant clinical indicator to assess the clinical condition of a neonate.[54]

The results revealed a statistically significant decrease in the mean value of HR after treatment compared with its

corresponding value before treatment. Whatever the type, apnoea frequently causes hypoxemia and/or bradycardia, which can cause long-term complications, such as neurodevelopmental impairment and retinopathy of prematurity. Therefore, massages have been recommended as a method of enhancing neonates' growth and development via its effects improving their HR, blood flow, immunity, and digestion.[43,55]

On the other hand, the results of this study contradicted Schmolzer et al.'s (2013) findings that the effect of tactile stimulation on breathing by arousal is not clear, since infants are exposed to other stimuli that might alter their arousal state (i.e. light, cold, and sound). Furthermore, most preterm infants receive respiratory support, which could also cause increased breathing effort. In contrast, it could be possible that during tactile stimulation, the focus is shifted away from other interventions during stabilization. In addition, vigorous stimulation could possibly lead to displacement of the face mask.[56]

However, other means of stimulation like the application of kinaesthetic stimulation have not been proven to be useful as a treatment for apnoea in the NICU.[57]

While tactile stimulation is a widespread practice, the style and intensity of tactile interventions have not been specified. Even though this intervention is often used to treat serious situations with potentially life-long harmful effects if left untreated, the treatment method is highly subjective. This indicates that it is unclear what methods and pressures are used by medical staff and if they differ in effectiveness. We assume that each medical staff member has a different internal thought about what is considered a gentle versus strong tactile stimulation. To date, no effort has been made to objectively determine the different pressure intensities that are used to treat central apnoea in premature infants. Additionally, there is no classification system of the different means of tactile foot stimulation.[58]

The environment of NICU for premature infants is characterized by body fixation due to the connections with different medical devices, difficulty of antigravity movement given immature physical development conditions, bright lighting, extreme noise, and contact with the firm floor and plastic walls of the incubator. This contrasts with the uterine environment, which provides proper sensory stimuli, such as tactile, vestibular, visual, and auditory sensations in contact with the amniotic fluid. These conditions provoke stress responses in premature infants, which may interfere with their growth due to raised intracranial pressure, apnoea, peripheral vasoconstriction, reduced gastrointestinal motility, and the secretion of stress hormones such as cortisol and catecholamines.[59]

The abnormal sensory stimuli received by premature neonates are likely to generate physiological instability, hinder behavioural and physiological reactions, and impede normal growth; therefore, interventions using normal sensory stimuli should be implemented instead. However, premature infants that obtain medical treatment for survival in a neonatal intensive care unit face difficulties in receiving proper sensory stimulation interventions due to their unstable physiological state. Furthermore, extreme sensory stimulation interventions may produce stress in premature infants, thereby accelerating abnormal posture, tension, and movement. In other words, even interventions that are thought to be gentle and harmless in other situations may have hazardous and irreversible consequences for premature infants in the NICU. Thus, when sensory stimulation interventions are employed for premature infants, caution should be applied in order to prevent premature infants, who are in a vulnerable and unbalanced situation, from experiencing stress by carefully monitoring the intensity and duration of intervention, taking the physiological state of the specific newborns into account.[60,61]

Tactile stimulation or massage therapy, which is sometimes associated with kinaesthetic stimulation, is sometimes used alongside the traditional clinical treatment. Tactile stimulation has been the focus of clinical studies since the 1960s, when it was first proposed as a method of promoting preterm infant growth and development. Additionally, new studies have shown that interventions such as tactile/kinaesthetic stimulation have the additional advantage of decreasing behavioural manifestations of stress.[37]

Despite the fact that manual tactile stimulation is a widely used therapy, the exact neural pathways to the respiratory centre remain uncertain. It is assumed that tactile stimulation influences respiratory control by motivating the brainstem reticular formation that causes arousal. The magnitude of the respiratory response varies depending on sleep type and is highest during the rapid eye movement sleep. However, tactile stimuli can also encourage spinal and respiratory responses in infants without causing cortical arousal.[62,63]

The termination of apnoea is achieved by tactile intervention, which is often combined with extra oxygen and, if required, mask ventilation. The period of the apnoea and the associated hypoxia and/or bradycardia is then dependent on the reaction time of the tactile stimulation supplier. A heavy workload and alarm fatigue might have a negative effect on acceptable apnoea treatments. The longer the delay in response time, the longer the total period of apnoea, and the worse the peripheral oxygen saturation (SpO_2). Also, applying tactile stimulation aggravates the risks of infection due to cross-contamination and interrupts sleep, which can be hazardous for an infant's growth and development.[12,13,50,64–66]

Study limitations

The study's limitations included some neonates that had frequent apnoeic episodes, which calls for more oxygen support and continuous positive airway pressure (CPAP); these cases were excluded from the final sample of the study. Another limitation was that some neonates showed signs of neonatal sepsis (clinical and/or laboratory). Additionally, the study was conducted on a relatively small number of eligible neonates in a restricted geographic area; The study was also conducted for a short time period that allowed for observation and assessment to precisely evaluate the recurrence of apnoea after treatment.

Conclusions

Based on the scope and findings of this study, sensory stimulation that is applied in conjunction with standard care (close monitoring, adequate thermal environment, proper nutrition, adequate circulatory support, nasal oxygen, and caffeine citrate) could decrease apnoea frequency for infants with AOP.

Recommendations

Further research should be conducted to study the effect of sensory stimulation on AOP in younger gestational age groups (i.e. below 32 weeks). Additionally, other studies should be conducted to compare the effects of various sensory stimuli (tactile, vibratory, kinaesthetic, and proprioceptive) on AOP, as well as to clarify the safe limits of vibratory stimuli used in premature neonates. In order to verify the findings presented herein, future studies should also use a larger number of premature neonates with a wider geographical distribution. Post discharge studies over longer periods of time are needed to follow up and evaluate the recurrence rate of apnoea after treatment.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethical approval

a. Approval reference number and date. The study was conducted from March to September 2020. The clinical trial was not applicable in this case.
b. Patient Consent Declaration statement. The Ethical Committee of the Faculty of Physical Therapy, Cairo University, Egypt (No: P.T.REC/012/002512) approved this study at November 13th 2019. Children's participation was authorized by a signed written consent form with a parent or legal guardian's agreement before the study was initiated.

Authors contributions

ASAA and KAO made the study design, provided research conduction, selected research materials, and conducted the data collection and organization. SAA conducted the analysis and interpreted the data. HEE provided the initial and final draft of the article and gave logistic support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Acknowledgment

The authors would like to thank all the parents and guardians who consented to including their infants in this research.

References

1. Petrou S, Mehta Z, Hockley C, Cook-Mozaffari P, Henderson J, Goldacre M. The impact of preterm birth on hospital inpatient admissions and costs during the first 5 years of life. **J Pediatr 2003**; 112(6 part 1): 1290–1297.
2. Wang ML, Dorer DJ, Fleming MP, Catlin EA. Clinical outcomes of near-term infants. **J Pediatr 2004**; 114(2): 372–376.
3. Petrou S. The economic consequences of preterm birth during the first 10 years of life. **Int J Gynaecol Obstet 2005**; 112(1): 10–15.
4. Stokowski LA. A primer on Apnea of prematurity. **Adv Neonatal Care 2005**; 5(3): 155–170.
5. Moriette G, Lescure S, El Ayoubi M, Lopez E. Apnea of prematurity: what's new? **Arch Pediatr 2010**; 17(2): 186–190.
6. Di Fiore JM, Bloom JN, Orge F, Schutt A, Schluchter M, Cheruvu VK. A higher incidence of intermittent hypoxemic episodes is associated with severe retinopathy of prematurity. **J Pediatr 2010**; 157(1): 69–73.
7. Martin RJ, Wang K, Koroglu O, Di Fiore J, Kc P. Intermittent hypoxic episodes in preterm infants: do they matter? **Neonatol 2011**; 100(3): 303–310.
8. Janvier A, Khairy M, Kokkotis A, Cormier C, Messmer D, Barrington KJ. Apnea is associated with neurodevelopmental impairment in very low birth weight infants. **J Perinatol 2004**; 24(12): 763–768.
9. Pillekamp F, Hermann C, Keller T, von Gontard A, Kribs A, Roth B. Factors influencing apnea and bradycardia of prematurity-implications for neurodevelopment. **Neonatol 2007**; 91(3): 155–161.
10. Lodha A, Seshia M, McMillan DD, Barrington K, Yang J, Lee SK. Association of early caffeine administration and neonatal outcomes in very preterm neonates. **JAMA Pediatr 2015**; 169(1): 33–38.
11. Sale SM. Neonatal apnea. Best practice and research clinical. **Anaesthesiol 2010**; 24(3): 323–336.
12. Zhao J, Gonzalez F, Mu D. Apnea of prematurity: from cause to treatment. **Eur J Pediatr 2011**; 170(9): 1097–1105.
13. Faille EO, Setya A, Eisenfeld L. A computerized system to diagnose and treat neonatal apnea using vibrotactile stimulation. **Conn Med 2013**; 77(9): 517–522.
14. Smith VC, Kelty-Stephen D, Qureshi Ahmad M, Mao W, Cakert K, Osborne J. Stochastic resonance effects on apnea, bradycardia, and oxygenation: a randomized controlled trial. **J Pediatr 2015**; 136(6): 1561–1568.
15. Gaugler C, Marlier L, Messer J. Sensory stimulations for the treatment of idiopathic apneas of prematurity. **Arch Pediatr 2007**; 14(5): 485–489.
16. Kesavan K, Frank P, Cordero DM, Benharash P, Harper RM. Neuromodulation of limb proprioceptive afferents decreases apnea of prematurity and accompanying intermittent hypoxia and bradycardia. **PLos One 2016**; 11(6): 1–16.
17. Potts JT, Rybak IA, Paton JF. Respiratory rhythm entrainment by somatic afferent stimulation. **J Neurosci: Off J Soc Neurosci 2005**; 25(8): 1965–1978.
18. Iwamoto E, Taito S, Kawae T, Sekikawa K, Takahashi M. The neural influence on the occurrence of locomotor-respiratory coordination. **Respir Physiol Neurobiol 2010**; 173(1): 23–28.
19. Kulkarni A, Kaushik S, Gupta P. Massage and touch therapy in neonates: the current evidence. **Indian Pediatr Mag 2010**; 47: 771–776.
20. Gozal D, Simakajornboon N. Passive motion of the extremities modifies alveolar ventilation during sleep in patients with congenital central hypoventilation syndrome. **Am J Respir Crit Care Med 2000**; 162(5): 1747–1751.
21. Janvier A, Khairy M, Kokkotis A, Cormier C, Messmer D. Apnea is associated with neurodevelopmental impairment in very low birth weight infants. **J Perinatol 2004**; 24(12): 763–768.
22. Cohen G, Lagercrantz H, Katz-Salamon M. Abnormal circulatory stress responses of preterm graduates. **Pediatr Res 2007**; 61(3): 329–334.

23. Hibbs AM, Johnson NL, Rosen CL, Kirchner HL, Martin R. Prenatal and neonatal risk factors for sleep disordered breathing in school-aged children born preterm. **J Pediatr 2008**; 153(2): 176–182.
24. Martin RJ, Di Fiore JM, Walsh MC. Hypoxic episodes in bronchopulmonary dysplasia. **Clin Perinatol 2015**; 42(4): 825–838.
25. Cramer SJ, Dekker J, Dankelman J, Pauws SC, Hooper SB, te Pas AB. Effect of tactile stimulation on termination and prevention of apnea of prematurity. A systematic review. **Front Pediatr 2018**; 6(45): 7–10.
26. Dong L, Li Y, Zhang Y, Qiao S. A pilot study of limb stimulation for the treatment of neonatal apnea. **Med 2018**; 97(49): 12827.
27. Scapelli E, Condorelli S, Cosmi E. Cutaneous stimulation and generation of breathing in the fetus. **Pediatr Res 1977**; 11(1 Pt 1): 24–28.
28. Ronca AE, Alberts JR. Cutaneous induction of breathing in perinatal rats. **Psychobiol 1995**; 23(4): 261–269.
29. Dekker J, Martherus T, Cramer SJE, van Zanten HA, Hooper SB, te Pas AB. Tactile stimulation to stimulate spontaneous breathing during stabilization of preterm infants at birth: a retrospective analysis. **Front Pediatr 2017**; 5(1–6): 61–67.
30. Bhatia J. Current options in the management of apnea of prematurity. **Clin Pediatr (Phila) 2000**; 39(6): 327–336.
31. Lee AC, Cousens S, Wall SN, Niermeyer S, Darmstadt GL, Carlo WA. Neonatal resuscitation and immediate newborn assessment and stimulation for the prevention of neonatal deaths: a systematic review, meta-analysis and Delphi estimation of mortality effect. **BMC Public Health 2011**; 11(Suppl 3): 12–30.
32. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM. Part 13: neonatal resuscitation: American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. **Circ J 2015**; 132(18 Suppl 2): 543–560.
33. Wyllie J, Perlman JM, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R. Part 7: neonatal resuscitation: 2015 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. **Resuscitation 2015**; 95: e169–201.
34. Marayong P, Mostoufi MS. Foot vibrotactile device for central apnea interruption in premature infants. **Stud Health Technol Inf 2009**; 142(17): 180–182.
35. Feijo L, Hernandez-Reif M, Field T, Burns W, Valley-Gray S, Simco E. Mothers' depressed mood and anxiety levels are reduced after massaging their preterm infants. **Infant Behav Dev 2006**; 29(3): 476–480.
36. Jain S, Kumar P, McMillan DD. Prior leg massage decreases pain responses to heel stick in preterm babies. **J Paediatr Child Health 2006**; 42(9): 505–508.
37. Hernandez-Reif M, Diego M, Field T. Preterm infants show reduced stress behaviors and activity after 5 days of massage therapy. **Infant Behav Dev 2007**; 30(4): 557–561.
38. Mendes EW, Procianoy RS. Massage therapy reduces hospital stay and occurrence of late-onset sepsis in very preterm neonates. **J Perinatol 2008**; 28(12): 815–820.
39. Diego MA, Field T, Hernandez-Reif M. Procedural pain heart rate responses in massaged preterm infants. **Infant Behav Dev 2009**; 32(2): 226–229.
40. Ho YB, Lee RS, Chow CB, Pang MY. Impact of massage therapy on motor outcomes in very low-birthweight infants: randomized controlled pilot study. **Pediatr Int 2010**; 52(3): 378–385.
41. Procianoy RS, Mendes EW, Silveira RC. Massage therapy improves neurodevelopment outcome at two years corrected age for very low birth weight infants. **Early Hum Dev 2010**; 86(1): 7–11.
42. Guzzetta A, D'Acunto MG, Carotenuto M, Berardi N, Bancale A, Biagioni E. The effects of preterm infant massage on brain electrical activity. **Dev Med Child Neurol 2011**; 53(4): 46–51.
43. Ang JY, Lua JL, Mathur A, Thomas R, Asmar BI, Savasan S. A randomized placebo-controlled trial of massage therapy on the immune system of preterm infants. **J Pediatr 2012**; 130(6): 1549–1558.
44. Moyer-Mileur LJ, Haley S, Slater H, Beachy J, Smith SL. Massage improves growth quality by decreasing body fat deposition in male preterm infants. **J Pediatr 2013**; 162(3): 490–495.
45. Smith SL, Lux R, Haley S, Slater H, Beachy J, Moyer-Mileur LJ. The effect of massage on heart rate variability in preterm infants. **J Perinatol 2013**; 33(1): 59–64.
46. Basiri-Moghadam M, Basiri-Moghadam K, Kianmehr M, Jani S. The effect of massage on neonatal jaundice in stable preterm newborn infants: a randomized controlled trial. **J Pak Med Assoc 2015**; 65(6): 602–606.
47. Mortimer BJP, Zets GA, Cholewiak RW. Vibrotactile transduction and transducers. **J Acoust Soc Am 2007**; 121(5): 2970.
48. Binks AP, Bloch-Salisbury E, Banzett RB, Schwartzstein RM. Oscillation of the lung by chest-wall vibration. **Respir Physiol 2001**; 126(3): 245–249.
49. Schelegle ES, Green JF. An overview of the anatomy and physiology of slowly adapting pulmonary stretch receptors. **Respir Physiol 2001**; 125(1–2): 17–31.
50. Pichardo R, Adam JS, Rosow E, Bronzino J, Eisenfeld L. Vibrotactile stimulation system to treat apnea of prematurity. **Biomed Instrum Technol 2003**; 37(1): 34–40.
51. Bloch-Salisbury E, Indic PP, Bednarek F, Paydarfar D. Stabilizing immature breathing patterns of preterm infants using stochastic mechanosensory stimulation. **J Appl Physiol 2009**; 107(4): 1017–1027.
52. Camargo VC, Honorato da Silva S, Freitas de Amorim M, Nohama P. Instrumentation for the detection and interruption of apnea episodes for premature newborn. **Conf Proc Ann Int Conf IEEE Eng Med Biol Soc 2014**; 2014: 2127–2130.
53. Livingston K, Beider S, Kant AJ, Gallardo CC, Joseph MH, Gold JI. Touch and massage for medically fragile infants. **J Evid Based Complement Altern Med 2009**; 6(4): 473–482.
54. Wyllie J, Perlman JM, Kattwinkel J, Atkins DL, Chameides L, Goldsmith JP. Neonatal Resuscitation Chapter Collaborators. Part 11: neonatal resuscitation: 2010 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. **Resuscitation 2010**; 81(1): 260–287.
55. Di Fiore JM, Poets CF, Gauda E, Martin RJ, MacFarlane P. Cardiorespiratory events in preterm infants: etiology and monitoring technologies. **J Perinatol 2016**; 36: 165–171.
56. Schmolzer GM, Kumar M, Pichler G, Aziz K, O'Reilly M. Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis. **BMJ 2013**; 347: 5980.
57. Osborn DA, Henderson-Smart DJ. Kinesthetic stimulation for treating apnea in preterm infants. **Cochrane Database Syst Rev 2000**; 2: CD000499.
58. Martin S, Thome UH, Grunwald M, Mueller SM. Light or deep pressure: medical staff members differ extensively in their tactile stimulation during preterm apnea. **Front Pediatr 2020**; 8: 102.
59. Blackburn S. Environmental impact of the NICU on developmental outcomes. **JPN 1998**; 13: 279–289.
60. Holditch-Davis D, Bartlett TR, Belyea M. Developmental problems and interactions between mothers and prematurely born children. **J Pediatr Nurs 2000**; 15: 157–167.

61. Lester BM, Tronick EZ, LaGasse L, Seifer R, Bauer CR. The maternal lifestyle study: effects of substance exposure during pregnancy on neurodevelopmental outcome in 1-month-old infants. **Pediatr 2002**; 110: 1182–1192.
62. McNamara F, Wulbrand H, Thach BT. Characteristics of the infant arousal response. **J Appl Physiol 1998**; 85(6): 2314–2321.
63. Trippenbach T, Flanders D. Interaction between somatic and vagal afferent inputs in control of ventilation in 2-week-old rabbits. **Respir Physiol 1999**; 116(1): 25–33.
64. Garcia AP, White-Traut R. Preterm infants' responses to taste/smell and tactile stimulation during an apneic episode. **J Pediatr Nurs 1993**; 8(4): 245–252.
65. Sale SM. Neonatal apnea. **Best Pract Res Clin Anaesthesiol 2010**; 24(3): 323–336.
66. Vergales BD, Paget-brown AO, Lee H, Guin LE, Smoot TJ. Accurate automated apnea analysis in preterm infants. **Am J Perinatol 2014**; 31(2): 157–162.

How to cite this article: Abdel Mageed ASA, Olama KA, Abdel Rahman SA, El-Gazzar HE. The effect of sensory stimulation on apnea of prematurity. J Taibah Univ Med Sc 2022;17(2):311–319.