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Original article

Semi-seated holding position to reduce stress responses in spontaneously crying newborns in the neonatal intensive care unit: A randomised experimental study

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Abstract. *Background and aim:* Crying in newborns in the neonatal intensive care unit (NICU) is often a sign of stress caused by various stressors. Early-life stress can disrupt brain development, leading to lifelong neurodevelopmental disorders. Effective methods to reduce stress responses in newborns are therefore critical. This study aimed to investigate and compare the effects of a semi-seated holding position (SSHP) and facilitated tucking in a side-lying position (FTP) on hormonal and physiological stress responses in spontaneously crying newborns hospitalized in the NICU. *Methods:* An open-label, randomized experimental study was conducted between July and November 2023 at the NICU of Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia. Newborns were randomized into two groups: SSHP (45° semi-seated holding) or FTP (facilitated tucking in a side-lying position). Salivary cortisol and oxytocin levels were measured as primary outcomes, while physiological responses (heart rate, respiratory rate, body temperature, and O2 saturation) were secondary outcomes. Measurements were taken before and after positioning. *Results:* A total of 45 newborns completed the study. Cortisol levels decreased in the SSHP group and increased in the FTP group; however, the changes were not statistically significant. Oxytocin levels significantly decreased in the SSHP group but not in the FTP group. Heart and respiratory rates decreased significantly in both groups following positioning, with no significant differences between groups. *Conclusions:* The SSHP is as effective as FTP in reducing stress responses among crying neonates in the NICU. This simple, equipment-free positioning method offers a practical alternative for promptly soothing infants. (www.actabiomedica.it)

Key words: newborn, positioning, stress, crying, NICU

Introduction

Crying can be a sign of stress in neonates, whether caused by pain, discomfort, hunger, thirst, or loneliness (1,2). In addition, environmental factors, including lightning, noise, and unpleasant odors, can also induce stress in newborns, as can medical and nursing procedures in the neonatal intensive care unit (NICU). Stress has been linked to many negative immediate and long-term consequences, including increased heart rate and blood pressure, reduced oxygen levels (3), increased cerebral blood pressure, initiation

of the stress response, depleted energy and oxygen reserves, disrupted mother-infant interaction caused by delayed interaction with preterm (4), brain damage, cardiac dysfunction and to interactional deficits with caregivers (5). In addition, separation from the mother has potential long-term effects on brain development and function, especially in premature infants (6). The separation between mother and infant can be attributed to parental stress, which is linked to emotional and behavioral problems in their children (4,7). Early mother-infant interactions during hospitalization have improved due to daily care interventions that promote attachment, reduce infant stress, and enhance infant development (4). However, the neonates are more vulnerable to stress, particularly oxidative stress, due to their immature antioxidant systems during the transition n from the intrauterine to the extrauterine environment (8). In the NICU, neonates undergoing intensive care often face repeated invasive procedures, leading to significant pain and distress that must be addressed (9). Neonatal behavioral responses include limb movements, changes in muscle tone, crying, and distinctive facial expressions. It is crucial to acknowledge that crying is frequently deemed the least reliable indicator of pain in newborns (10,11). The experience of stress during NICU hospitalization impacts the neonatal neuroendocrine system through dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which is involved in the stress response (12). If left unattended, crying infants may experience panic and anxiety, resulting in the release of cortisol, which can negatively impact brain development. Conversely, reduced stress reactivity can improve learning and memory in infants (3). Meanwhile, oxytocin, commonly called the "love hormone," regulates stress, anxiety, and autonomic functions, including heart rate. The reduction of stre ss and anxiety in humans and animals through oxytocin activity is called oxytocinergic activity (13). Interventions to prevent and reduce crying in infants have been widely utilized, including swaddled holding, pacifiers, sugar water, non-sucrose sweet-tasting solutions, heartbeat sounds, lullabies or mothers voice for distraction, rhythmic movements, reduction of external stimuli, and proper positioning (14–16). However, the effectiveness of these strategies tends to decline with frequent usage, emphasizing the importance of exploring alternative methods to soothe infants, especially in the NICU (17). It is important to note that crying can be harmful to infants and should not be viewed as a necessary evil. A study found that during a crying episode, physiological and hemodynamic indicators, such as heart rate (HR), respiratory rate (RR), and levels of systemic and regional cerebral oxygen saturation, underwent significant changes, regardless of the infant's gestational age (18). Responding promptly, consistently, and comprehensively to infant cries is essential, as it is not recommended to let infants cry for extended periods (3,17). Positioning serves as a subtle intervention strategy promoting infant neurobehavioral and neuromotor stability (19). Proper positioning of infants is crucial for their overall well-being and development, particularly in reducing unnecessary energy expenditure, decreasing stress, and enhancing self-regulation and physiological stability (19). Among various care positions for neonates, facilitated tucking on the side-lying position is frequently employed to minimize stress (16,20). Additionally, the semi-seated position at a 45-degree angle has been utilized in children and adults for supportive therapy or enhanced comfort in certain conditions (21). Currently, there is a lack of published research on the effectiveness of facilitated tucking in alleviating stress responses and its impact on stress hormone levels in newborns hospitalized in the NICU. This study aimed to investigate and compare cortisol and oxytocin levels, as well as physiological stress responses, between newborns who spontaneously cried in the semi-seated holding position (SSHP) and those in facilitated tucking in a side-lying position (FTP), the latter being a standard NICU protocol. Notably, this is the first study to evaluate the effects of SSHP on stress responses in spontaneously crying neonates hospitalized in the NICU.

Methods

Subjects and design

This open-label, randomized experimental study was conducted between July and November 2023 at the NICU of Dr. Wahidin Sudirohusodo Hospital, a

tertiary national referral hospital in Makassar, South Sulawesi, Eastern Indonesia that had the largest NICU facility in the region.

This study has received approval from the Ethics Committee for Biomedical Research in Humans, Faculty of Medicine Hasanuddin University Review Board under with approval number UH23030202. Written inform consents has been obtained from the patient's guardians/parents. Subjects were selected from infants hospitalized in the NICU who met the inclusion criteria: the gestational age > 30 weeks, stable condition, and not on CPAP or ventilator. The exclusion criteria were the infant with a major congenital defect, intracranial hemorrhage, and shock. The sample size was estimated based on previous studies by White-Traut et al. (22). Openepi.com was used to calculate the sample size. To assess the level of salivary cortisol level with a 95% confidence interval and 80% power, with the mean of a control group (3.0 mmol/L) and intervention group (3.82 mmol/L), the deviation standard of a control group (1.3 mmol/L) and intervention group (0.9 mmol/L) and 10% drop out estimation, at least 22 samples each group should be enrolled in this study. The power analysis of this sample size by using G*Power 3.1 was 0.812 (effect size 0.9; Power 0.8). All eligible participants in one time were simultaneously entered into the database and given participant IDs sequentially. The researcher then conducted a randomization process using a website tool, www.gigacalculator.com, by entering the total number of samples available. The system generated a random selection for the intervention of the SSHP. Participants not selected during the randomization process were allocated to the facilitated tucking-in side-lying group.

Procedure intervention

Parents were approached for pre-consent after eligibility screening was completed. The parents were informed of the study's objectives, methodology, confidentiality, and their ability to withdraw at any moment. Following consent, infants were monitored until all inclusion criteria were met. Upon the infant's observed crying, the researcher collects saliva (1-3 minutes while the baby is crying) and asses the infant's vital signs (heart rate, respiratory rate, saturation, and body temperature). Immediately after saliva collection, proceed to the infant's position based on the randomized result (SSHP or FTP). Following our protocol in the NICU, all babies sleep side-lying with nesting. The SSHP group is achieved by holding and positioning the infant's body into a semi-sitting posture ($45\text{-}90^0$). Next, the dominant hand supports the head, neck, and shoulder, crosses the infant's left and right hands in front of the chest, and then holds them using the non-dominant hand. Keep the infant's legs relaxed and suspend this action until 5 minutes after the infant stops crying; the post-intervention saliva collection was performed. Vital signs, including heart rate, respiration rate, and oxygen saturation were evaluated using a monitor attached to the infant, while the body temperature was measured using a digital thermometer placed in the axilla. Infants were observed crying again within 10 minutes of being repositioned to the starting position. The group-facilitated tucking position (FTP) is achieved by putting the infant into a side-lying position (left or right), following one palm cradles the infant's head, the other hand supports the infant's hip and buttock, the infant's legs are flexed, making contact with the nest and the infant's hands are positioned on either side of the face. Suspend this action until 5 minutes after the infant stops crying, and the post-intervention saliva collection was performed; the heart rate, respiration rate, oxygen saturation, and body temperature were evaluated, and the infant. Infants were observed to cry again within 10 minutes after being repositioned to the starting position. The researcher evaluated the infant's vital signs (heart rate, respiratory rate, saturation, and body temperature).

Specimen

The infant's saliva was collected to determine cortisol and oxytocin by an enzyme immunoassay in human saliva. Two saliva samples were taken at distinct times (before and after positioning). A gentle oral cavity examination was performed to minimize the risk of contamination with milk that could have interfered with the assay. A sterile cotton swab was placed on the bottom portion of the tongue for about 30 seconds to collect saliva samples.

The cortisol level was analyzed using DBC-Diagnostics Biochem Canada Inc. Saliva Cortisol Kit (Ref. CAN-C-240). The collected saliva was placed into a clean glass tube. Before saliva samples were tested using the enzyme-linked immunosorbent assay technique, they were kept at -10 to -80 degrees Celsius. The specimen is to be thawed and centrifuged before analysis. The sensitivity of the cortisol saliva ELISA kit is 0.033 ng/ml. The oxytocin level was analyzed using the Human OOT (oxytocin) ELISA Kit (HUFI04737). The collected saliva was placed into a clean glass tube. Before saliva samples were tested using the immunoassay, they were kept at -10 to -80 degrees Celsius. The specimen was centrifuged for 20 mins at 2000-3000 rpm. The sensitivity of the cortisol saliva ELISA kit is <9.375pg/ml. The saliva samples were examined in the Research Laboratory Unit of the Faculty of Medicine and Hasanuddin University Hospital.

Statistical analysis

All data were analysed using SPSS Version 26. The homogeneity of infant characteristics between the two groups was evaluated using chi-square for categorical data, whereas the numeric data was assessed using the Mann U Whitney test. Differences were considered significant if the p-value was < 0.05. The vital signs and stress hormone levels before and after positioning were evaluated using Wilcoxon. The differences in the score of critical signs and stress hormone levels between the two groups were assessed using the Mann U Whitney test and Independent T-test.

Results

Out of 63 infants assessed for eligibility, 18 patients were excluded based on the inclusion and exclusion criteria. A total of 45 infants in clinically stable condition who cried spontaneously without any medical or nursing procedure completed the study and randomly assigned into two groups. There were 23 in the SSHP group and 22 in the FTP group (Figure 1). Table 1 illustrates the demographic and clinical features of the infants. Both groups exhibited comparable demographic characteristics in terms of infant sex ($p > 0.05$), type of birth ($p > 0.05$), birth weight ($p > 0.05$), gestational age ($p > 0.05$), and current weight ($p > 0.05$). Additionally, there were no discernible differences in clinical characteristics, including the duration of hospital stay and the length of crying before assuming a position, between the two groups. Table 2 compares the average stress hormone levels (salivary cortisol and oxytocin) and vital signs (Heart rate, respiration rate, body temperature, and saturation) in both groups before and after the infant underwent crying and positioning. According to the findings, a statistically significant disparity in oxytocin levels was observed before and after in the SSHP group ($p < .05$). Conversely, no notable difference was found in the FTP group. On the other hand, there was no statistically significant change in cortisol levels before and after in both groups ($p > .05$). Interestingly, the cortisol level decreased after assuming the SSHP. In contrast, in the FTP, there was an increase. The average vital signs are also depicted in Table 2. Both positions exhibited a significant decrease in heart rate and respiration rate ($p < .05$). Conversely, there was no significant difference in body temperature and saturation in either group, and these variables were still within average values.

Table 3 compares changes in vital signs and stress hormone levels between the pre and post-intervention. No significant difference was observed between the groups regarding these changes ($p > .05$). Table 4 shows the infant crying responses after 10 minutes SSHP and FTP. No significant difference was observed between the groups regarding the position ($p > 0.05$).

Discussion

Crying is the infant's only means of communication. In the NICU, crying indicates distress due to pain from a procedure or discomfort from external stimuli (such as bright lights, noise, and unpleasant odors), hunger, or separation from the mother. Biological processes such as immune function, the autonomic nervous system, the hypothalamic-pituitary-adrenal axis, and gene expression can be modified by exposure to stress during critical periods of brain development,

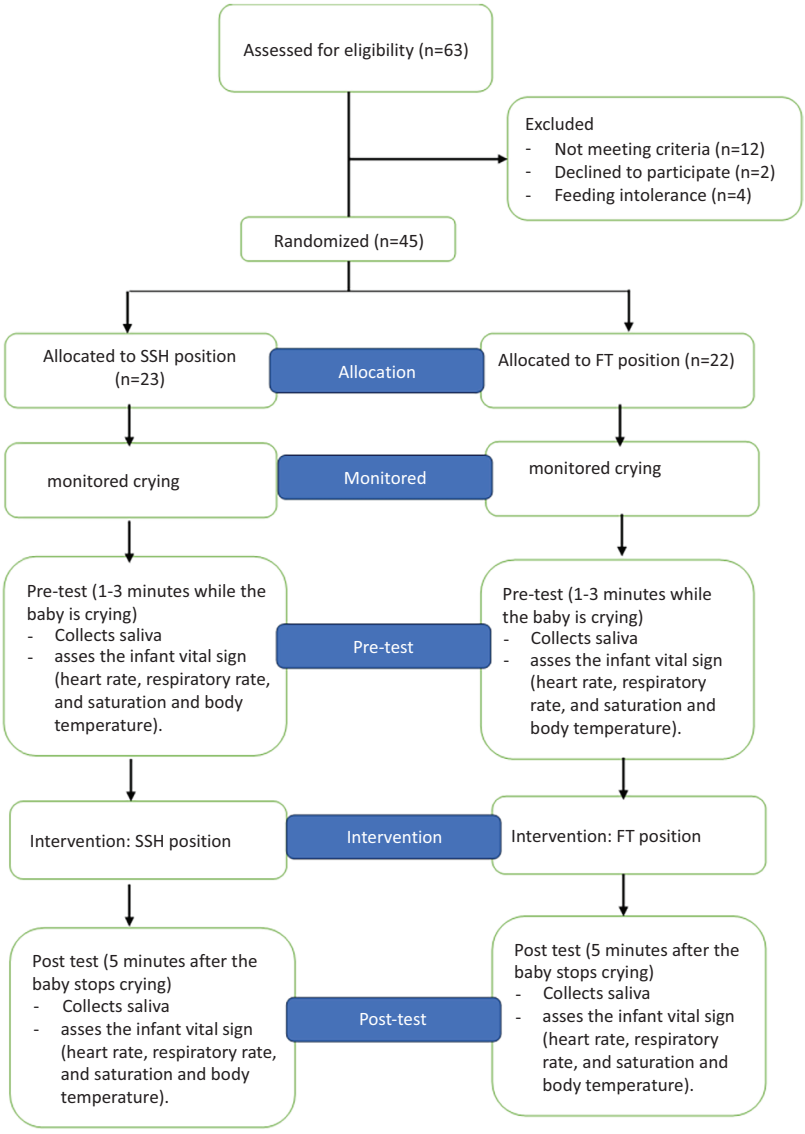

Figure 1. Study Flowchart.

impacting brain structure and function (3). Alongside the structural and functional brain changes, early stress experiences have a noteworthy impact on neurodevelopmental outcomes, encompassing learning, cognition, and behavioral issues (23–25) in later school-age, involving their capability to maintain attention and learn (24,26). Human babies are born with a need for social bonding. As a result, they have a biological tendency to seek the help of others when they are in distress (6). Signaling caregivers is widely regarded as an evolutionary survival strategy (27). The ability of the caregiver to comprehend the meaning of the baby's cries is essential in establishing a robust and secure relationship (28). Infants who are hospitalized in the NICU often cry for no apparent reason, and these stressors must be addressed promptly to prevent harmful effects on the infant's health and development. Numerous studies have demonstrated the effectiveness of non-pharmacologic interventions in reducing stress and procedural pain, such as administering oral sucrose, utilizing non-nutritive sucking (29), providing breast milk (15,30) implementing skin-to-skin contact

Table 1. Demographic and clinical characteristics of the subjects

Variable	f(%)	Mean (SSD)	Min -Max	SSHP (n=23)		FTP (n=22)		P value
				f(%)	Mean (SSD)	f(%)	Mean (SSD)	
A. Demographic characteristic								
Infant sex								
Male	25 (55.5)			15 (33.3)		10 (22.2)		0.301*
Female	20 (44.5)			8 (17.8)		12 (26.7)		
Type of birth				4 (8.9)		3 (6.7)		1.00*
Normal	7 (15.6)			19 (42.2)		19 (42.2)		
Cesarean	38 (84.4)							
Birth weight (gram)								
Normal	14 (31.2)	2289.22	935 - 3800	7 (15.6)		7 (15.6)		1.00*
Low birth weight	31 (68.9)	(613.491)		16 (35.6)		15 (33.3)		
Gestational age (week)								
Term	17 (37.8)	35.78	30 - 40	8 (17.8)		9 (20.0)		0.908*
Preterm	28 (62.2)	(2.619)		15 (33.3)		13 (28.9)		
Current weight (gram)								
Normal	14 (31.2)	2307.31	1360 -3755	7 (15.6)		7 (15.6)		1.00*
Low	31 (68.9)	(543.93)		16 (35.6)		15 (33.3)		
B. Clinical Characteristic								
Day of hospital stay (days)		11.96 (10.34)	1 - 60		10.43 (6.84)		13.55 (13.02)	0.741**
Length of crying before positioning (second)		133.20 (83.09)	15 - 420		121.70 (75.39)		145.23 (90.64)	0.357**

Evaluated using *Chi-square; **Mann U Whitney test Significance level: P < 0.05. *Abbreviations:* SSHP: Semi-seated holding position, FTP: facilitated tucking in a side-lying position, SSD: Standard deviation.

(31), using swaddling, and adjusting the positioning, including prone, supine, and side-lying positions, with or without facilitated tucking (16, 20, 24, 32). An important neuroprotective strategy, particularly for neonates admitted to the NICU, is infant positioning (33). Proper positioning of infants is essential for their well-being and development. It supports healthy growth, prevents tight muscles and uneven body shapes, and reduces unnecessary stress. Good positioning creates a sense of safety and clear boundaries, enhancing the infant's ability to self-regulate and encouraging self-soothing behaviors. It also promotes a healthy head shape and allows for meaningful sensory exploration of their bodies and surroundings (19). FTP on side-lying is a positioning method widely studied for comforting infants hospitalized in the NICU. This strategy involves containing the infant firmly using the head and lower limbs hands-on to maintain a "folded-in" or tucked position. FTP has been deemed an effective intervention for preterm pain management in several reviews. A recent review by Neto et al. showed that facilitated tucking is associated with a significant reduction in pain compared to routine care but not compared to opioid or oral glucose administration (16,20,24,32). There are mixed results regarding the efficacy of FTP due to variations in painful procedures and pain measurement timing across studies. Nonetheless, the intervention remains a popular research topic and is frequently found to be effective. Through their research, Taplak and Bayat (34) showed that FTP was more effective than routine care in reducing behavioral pain scores before and after endotracheal suctioning, although not during the procedure (32). Meanwhile, Cirik and Effy discovered that facilitated tucking

Table 2. Comparison of vital signs and stress hormone levels before and after positioning

Variable	SSHP		FTP	
	Mean (SSD)	P value	Mean (SSD)	P value
A. Vital signs				
Heart rate (bpm) Before After	 164.91 (13.00) 144.43 (12.41)	 0.000	 161.27 (13.57) 145.86 (14.30)	 0.000
Respiration rate (bpm) Before After	 57.43 (9.36) 48.09 (5.92)	 0.000	 54.68 (9.86) 47.45 (7.73)	 0.001
Body temperature (^{0}C) Before After	 36.89 (0.27) 36.86 (0.23)	 0.184	 36.93 (0.27 36.89 (0.22)	 0.190
SPO2 (%) Before After	 97.70 (1.94) 98.09 (1.31)	 0.156	 97.18 (2.61) 97.41 (2.56)	 0.493
B. Stress hormone levels				
Cortisol level (ng/ml) Before After	 0.589 (0.632) 0.338 (0.424)	 0.136	 1.255 (3.04) 1.899 (3.99)	 0.236
Oxytocin level (ng/ml) Before After	 776.611 (652.780) 436.219 (360.859)	 0.013	 848.27 (583.71) 540.01 (433.85)	 0.082

Evaluated using *Wilcoxon; Significance level: P < 0.05. *Abbreviations:* SSHP: Semi-seated holding position, FTP: facilitated tucking in a side-lying position, SSD: Standard deviation.

Table 3. Comparison of the change in stress responses

Variable	SSHP Mean (SSD)	FTP Mean (SSD	P value
Difference of Heart rate (bpm)	-20.478 (13.003)	-15.409 (12.469)	0.917*
Difference in Respiration rate (bpm)	-9.3478 (8.579)	-7.227 (7.584)	0.932*
Difference of Body temperature (^{0}C)	-0.0304 (.1146)	0.0048 (0.1413)	0.361**
Difference of SPO2	0.3478 (1.369)	0.2273 (1.1519)	0.882**
Difference of Cortisol level (ng/ml)	-0.0611 (.930)	0.3885 (2.121)	0.061**
Difference of Oxytocin level (ng/ml)	-197.042 (604.69)	-471.334 (767.98)	0.785*
Crying after position			1.000***

Evaluated using *Mann-Whitney U test; **Independent T-Test, ***chi square. Significance level: P < 0.05. *Abbreviations:* SSHP: Semi-seated holding position, FTP: facilitated tucking in a side-lying position, SSD: Standard deviation.

did not produce a significant reduction in pain during orogastric tube insertion in preterm infants (34). All the mentioned studies evaluated the effectiveness of nonpharmacological pain management when undergoing painful procedures. This study is the first to examine the effect of positioning on spontaneously crying infants who are not undergoing painful procedures. It is also the first to evaluate whether SSHP is as effective as FTP in reducing stress responses. The study findings suggest SSHP and FTP have comparable effects in decreasing physiological stress indicators, such as heart and respiration rates. Although not

Table 4. Comparison of the crying responses after positioning

Position	Crying after position		P value
	Yes (f,%)	No (f,%)	
SSHP (n=23)	3 (13)	20 (87.0)	1.000
FTP (n=22)	3 (13.6)	19 (86.4)	

Abbreviations: SSHP: Semi-seated holding position, FTP: facilitated tucking in a side-lying position.

statistically significant, there is a noticeable trend of increased oxygen saturation. This trend could be attributed to the deliberate and gradual process of gently positioning the infant in a partially upright position by crossing the arms over the baby's chest, replicating the sensation of being in the womb or swaddled. Proper body placement is crucial for infants, particularly premature newborns who cannot handle the effects of gravity, maintain appropriate alignment of their body at the center, or sustain their natural flexed position. These factors are essential for promoting optimal neurodevelopment. Insufficient positions are an additional cause of stress for this population, impacting behavior and potentially autonomic regulation. The potential influence of a baby's posture on a newborn's stress levels in the NICU should be considered. Proper positioning is crucial in promoting self-regulation and stability in infants, particularly premature neonates (35). The measurement of salivary cortisol concentration is a precise method for indicating neonatal stress and has been validated as a non-invasive measure of stress reactivity in infants (2). A review of 16 articles analysing cortisol, a hormone that assesses stress, revealed that pain-related procedures such as retinopathy examination and heel puncture increased salivary cortisol levels. Conversely, measures such as music, prone position, and using the same crib between twins reduced salivary cortisol levels (36). In this study, the SSHP group exhibited a reduction in cortisol levels, although the decline was not statistically significant. This result may be because the intervention is performed within a short timeframe of a few seconds when the baby initiates crying (ranging from 15 to 420 seconds). Ludington's findings in 2002 indicate that prolonged crying is strongly associated with elevated cortisol levels (5). However, it often occurs approximately 20 minutes after the baby undergoes a pain-inducing procedure. In this study, we couldn't let babies cry longer because it was unethical. Oxytocin, a hormone involved in social bonding and stress regulation, can also affect the crying behavior of newborns in the NICU. One study found that oxytocin levels increased in response to skin-to-skin contact, associated with decreased crying behavior (13,37). A variety of stressors could induce oxytocin secretion in both blood and brain. Brain oxytocin plays a role in controlling neuroendocrine stress responses by inhibiting the secretion of adrenocorticotropic hormone (ACTH) and thus decreasing the production and release of cortisol (38). The cortisol decline in this study may not have been due to the inhibitory effect of oxytocin secretion because oxytocin levels decreased significantly. The average length of stay of the subjects in this study was more than ten days, thereby, it is possible that this causes mutual dysregulation of the cortisol and oxytocin systems. According to Li et al. (38), oxytocin and cortisol systems can be mutually dysregulated as a consequence of traumatic stress, for example, due to separation from the mother or exposure to stressors at an early age, such as in infants admitted to the NICU. Moreover, the decreased stress response may also be due to neural mechanisms not studied in this study (39). Only three infants out of 23 in the SSHP group cried back within 10 minutes of the intervention. Holding, lifting, and placing the baby in a half-sitting position may be a touch that promotes a feeling of security, and the physical contact that occurs helps regulate emotions in babies who are crying due to stress. Infants who get secure attachments tend to perceive caregivers as safe, available, and responsive. Therefore, they interpret their stressors as manageable (40).

Conclusion

The SSHP is as effective as FTP in minimizing stress responses among crying neonates hospitalized in the NICU. This position provides a simple, equipment-free alternative for promptly soothing infants.

Ethic Approval: This study has received approval from the Ethics Committee for Biomedical Research in Humans, Faculty of Medicine Hasanuddin University Review Board under approval number UH23030202 which was released on June 17, 2023.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: ADBF, EA: Concept or design; MW, AK, AA: Acquisition of data; ADBF, SH, MH: Analysis or interpretation of data; BS, AK, AYC: Drafting of the article; All Authors: Critical revision for important intellectual content, full access to the data, contribution to the study, approval of the final version for publication, responsibility for its accuracy and integrity.

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