

Effect of Massage on Salivary Cortisol Level in Preterm Neonates

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ABSTRACT

Background: Stress in preterm neonates is associated with morbidity and mortality. Preterm newborns who are in need of special care are at risk of experiencing stress because of separation from the mother, ambient noises, lighting intensity, and medical procedures. Massage is believed to reduce stress through touch stimulation, and the cortisol is one of the indicators of the stress response. This study aimed to identify the effects of touch stimulation in the form of massage on salivary cortisol in preterm neonates.

Methods: This study was conducted based on a quasi-experimental design. The neonates were divided into intervention and control groups who received massage and standard therapy (n=19) and only the standard therapy (n=20), respectively. The massage was given to the infants three times daily for 15 min. Salivary cortisol was measured after 10 days of intervention.

Results: According to the results, the mean salivary cortisol concentration of the control group was higher (0.53±0.73 µg/dL) than that in the intervention group (0.05±0.32 µg/dL). Moreover, there was a significant difference between the groups regarding the salivary cortisol level at pre- and post-test (P=0.001). Based on the pre-test and post-test results, there was a significant decrease in salivary cortisol levels in the intervention group, compared to the control group (P=0.03 versus P=0.53). It should be noted that there were no observable side effects during the intervention.

Conclusion: Based on a decrease in salivary cortisol levels, this study suggests that touch stimulation given as a massage may reduce the level of stress in preterm neonates.

Keywords: Complementary medicine, Cortisol, Massage, Preterm neonate, Stress

Introduction

A neonate born before 37 weeks of gestation is defined as preterm (1). Studies have shown that there are an estimated 15 million babies born prematurely every year (5%-18% of all live births). Premature births were the main cause of one million deaths in children under 5 years of age in 2015 (2, 3). Preterm infants are not physiologically prepared to live in the environment outside the mother's womb. Furthermore, medical procedures in the neonatal intensive care units (NICUs) may induce a stress response that results in slow healing (2, 4, 5). A study showed that infants who were treated in the NICU are at the risk of experiencing stress after birth due to the separation from the

mother, noise, intensity of lighting, and medical procedures (6). This may further cause problems in which chronic stress in the preterm baby might inhibit brain development (6-8).

Stress stimulates the production of adrenocorticotrophic hormone in the pituitary gland. In response, there is an increase in glucocorticoid hormone secretion by the adrenal cortex. One of these glucocorticoid hormones is cortisol, which can serve as a stress indicator (9). A study showed that salivary cortisol levels in premature infants increased along with the amount of pain exposure in the neonatal period (7).

According to Medical Subject Heading, massage is a systematic and methodical manipulation of

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body tissues, best performed with the hands, for the purpose of affecting the nervous and muscular systems and the general circulation. Scientifically, massage has been proven to reduce both cortisol and norepinephrine levels and increase vagal tone further causing relaxation (1, 10, 11).

Regarding the neonatal care, studies have shown that massage is able to help increase weight gain, stimulate motor development, improve sleep patterns, increase the immune response, and reduce care time in the NICU (12-14).

A study showed that preterm infants receiving Gentle Human Touch (GHT) or field massage had lower amounts of urine cortisol, compared to those not treated with massage (15).

As a stress hormone, cortisol is not only found in the bloodstream but also in urine and saliva (15, 16). Salivary cortisol assessment is a reliable method to assess stress levels non-invasively. It also correlates with blood free cortisol levels and reflects the activity of the hypothalamic-pituitary-adrenal axis (16-21). Although the baby massage is widely known in Indonesia, the measured effect of massage on premature neonates' level of stress as reflected by salivary cortisol levels is still unknown. Therefore, this study was conducted to investigate the effect of massage on salivary cortisol levels in premature infants.

Methods

Study Design

This quasi-experimental clinical trial was conducted in the neonatal care unit of Dr. Soetomo Hospital, Surabaya, Indonesia, from June to August 2018. The study protocol was approved by the Research and Development Deputy of Dr. Soetomo Hospital. Moreover, the ethical clearance was issued by the Ethical Committee of Dr. Soetomo Hospital (No. 50/Panke.KKE/II/2018). This study is registered to the Thai Clinical Trial Registry with ID No. 20190110001.

Study Participants

The participants were selected using a consecutive sampling method. The inclusion criteria were: 1) preterm infants under 28 days of age, 2) stable clinical status, 3) no dependence on artificial ventilation, and 4) the absence of congenital anomalies. On the other hand, the infants who were discharged from the hospital within ten days, or those who received heavily invasive procedures and were critically ill and noncompliant with the study protocol were excluded from the study. Furthermore, written informed consent was obtained from the parents

or guardians of the participants. The neonates were then divided into two groups of intervention and control. The intervention group received both routine preterm neonate care and massage; however, the control group received only routine preterm newborn care, including kangaroo mother care.

Massage Therapy

Prior to the massage therapy, the newborns in the intervention group fasted for 1.5 h. The massage was performed by investigators who had participated in training sessions for premature infant massage. In this massage therapy, two types of touch stimulation were delivered, namely tactile and kinesthetic stimulations. Tactile stimulation is defined as a therapy which provokes the sensation of touch and texture. On the other hand, tactile stimulation is carried out in a supine and prone position with stroking movements using the fingers. Kinesthetic stimulation is defined as passive motions of the limbs (11).

Each session of massage therapy included five min of tactile stimulation followed by five min of kinesthetic stimulation ending with five more min of tactile stimulation. Tactile stimulation was given to the head, shoulders, back, hands, and feet (10 sec per part) for a total of five min. Moreover, this stimulation was initially given in the supine position and then repeated in the prone position. The massage was performed three times daily for ten days.

Salivary Cortisol Sample Collection and Measurement

In all groups, a sample of saliva was taken on the first and tenth days. Samples were taken using SalivaBio Infant's Swabs (Salimetrics LLC, United States). The collected samples were immediately transferred to the Dr. Soetomo Hospital laboratory, Surabaya, Indonesia. The cortisol levels ($\mu\text{g/dL}$) were measured by immunoassay using the Salimetrics Cortisol Assay Kit (Catalog No. 1-3302; Salimetrics LLC, United States).

Data Analysis

The data were analyzed in SPSS software (version 21.0) through descriptive statistics (i.e., mean, standard deviation, frequency, and percentage). The normality of the data distribution was also performed using the Kolmogorov-Smirnov test. In addition, the Mann-Whitney U test was used for statistical comparison of cortisol levels before and after the intervention for both groups.

In the same line, cortisol levels before and after the intervention were compared within each group using the Wilcoxon test. A P-value less than 0.05 was considered statistically significant.

Results

In total, 39 preterm newborns were included in this study. There were 20 and 19 neonates in the control and intervention groups, respectively. All subjects completed the study during the intervention. Table 1 summarizes the demographic characteristics of the subjects in both groups. The results of the Chi-square and t-tests showed no statistical differences between the groups in terms of these characteristics.

Table 2 compares the mean stress hormone levels in both groups on the first and tenth days

of the study. According to the results, cortisol levels were significantly decreased in the massage group on the tenth day (0.58 ± 0.58 $\mu\text{g/dL}$), compared to that on the first day (1.12 ± 1.02 $\mu\text{g/dL}$). In the control group, salivary cortisol levels on the tenth day were statistically the same as those on the first day. The difference between the pre-test and post-test salivary cortisol levels (ΔCL) was measured to compare the changes in salivary cortisol levels between groups. According to the results of the Mann-Whitney U test, a significant difference was observed between the groups regarding the ΔCL value ($P=0.001$). Moreover, the mean rank showing favorable salivary cortisol reduction in the massage group, compared to the control group (14.65 vs. 25.65).

Table 1. Demographic characteristics of the neonates

Characteristic	Massage (n=19)	Control (n=20)	P
Neonates			
Gestational age	30.47 \pm 2.61	31.05 \pm 2.58	0.493 ^a
Gender			
Female	10 (52.63%)	12 (60.00%)	0.643 ^b
Male	9 (47.37%)	8 (40.00%)	
Birth weight (g)	1314.47 \pm 388.87	1520.00 \pm 388.75	0.086 ^a
Birth length (cm)	39.26 \pm 5.34	40.10 \pm 4.96	0.615 ^a
Mothers			
Family income			
< IDR 650,000	6 (31.58%)	7 (35.00%)	0.380 ^b
IDR 650,000–1,300,000	4 (21.05%)	3 (15.00%)	
> IDR 1,300,000	9 (47.37%)	10 (50.00%)	
Education			
Elementary school	4 (21.05%)	4 (20.00%)	0.380 ^b
Junior high school	3 (15.79%)	5 (25.00%)	
Senior high school	6 (31.58%)	9 (45.00%)	
Bachelor degree	6 (31.58%)	2 (10.00%)	
Number of children			
≤ 2	12 (63.16%)	16 (80.00%)	0.243 ^b
3–5	7 (36.84%)	4 (20.00%)	

^a t-test

^b Chi-square test, P-value less than 0.05 was statistically significant

Table 2. Salivary cortisol level

Measured condition	Salivary cortisol level ($\mu\text{g/dL}$)		P ^b
	Control group	Massage group	
Pre-test	0.85 (0.87)	1.12 (1.02)	0.001*
Post-test	0.90 (0.85)	0.58 (0.58)	
ΔCL	-0.05 \pm 0.32	0.53 \pm 0.73	
P ^a	0.53	0.03*	

SD: standard deviation; ΔCL : difference in salivary cortisol levels between pre-test and post-test; P^a: p-value of comparison between pre-test and post-test salivary cortisol levels in the same group based on the Wilcoxon test result; P^b: comparison of salivary cortisol difference based on the Mann-Whitney U test; *: statistically significant.

Discussion

This study aimed to investigate the effects of massage on the saliva cortisol levels in preterm neonates. There are many stressors for preterm

newborns in the NICU, and it is important to provide interventions that reduce the impact of stress (23). The stress level itself can be measured

quantitatively by the cortisol level since increased cortisol level is known to correlate positively with the amount of stress experienced (9). The results of this study indicated that the massage group showed reduced salivary cortisol levels, compared to the control group.

The sensory stimulation is important for infant development. Evidence has shown that a lack of sensory stimulation in preterm newborns can cause growth and developmental problems, whereas the introduction of sensory stimulation helps to avoid these complications (24, 25). Massage provides this kind of stimulation through a systematic application of tactile and kinesthetic stimuli. Tactile sensory stimulation can be achieved through touch and texture sensation. Meanwhile, kinesthetic stimuli can be provided as a gentle passive movement of the joints (22). Massage provides the stimuli that reduce vagal nerve tone, which further stimulates oxytocin secretion causing relaxation that aids in brain development (10, 11).

Furthermore, other studies showed that infant massage helped infant growth by increasing weight gain (10, 12). Additional studies revealed that massage could reduce cortisol level which was an indication of reduced stress (26-28). A study conducted on 11 preterm newborns with a mean birth weight of 980 g and mean gestational age of 29 weeks. The results obtained from this study showed that massage from the chest through the feet for 20 min might reduce plasma cortisol levels (29).

It was found that preterm babies who were subjected to massage by the Yakson and GHT methods had significantly lower urinary cortisol levels, compared to those who received conventional therapy (30). The results of this study are in line with those of another study in which preterm babies who were treated with the GHT or Field methods had lower urinary cortisol levels, compared to preterm neonates who did not receive massage (15).

Finally, according to the findings of this study, it is suggested that massage therapy be considered as a complementary therapeutic approach for preterm neonates. Moreover, the standardization and implementation of this procedure in the clinical setting will require the attention of health policymakers and health care providers.

Conclusion

The results of the present study showed that massage therapy reduced the salivary cortisol

levels of preterm newborns. Furthermore, the findings in this study are in line with those of previous studies in which they confirmed the importance and safety of massage for preterm newborns. These procedures can reduce stress hormone levels in preterm neonates.

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Conflicts of interest

The authors declare no conflicts of interest related to financial support or relationships during the proposal and manuscript writing, as well as data collection and analysis, in this study.

References

- Gomella T, Cunningham MD, Eyal FG. Intrauterine growth retardation. In: Gomella T, Cunningham MD, Eyal FG, editors. Neonatology. New York: McGraw-Hill Medical Education, LLC; 2013. P. 732-42.
- Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet*. 2016; 388(10063): 3027-35.
- Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet*. 2012; 379(9832):2162-72.
- Montirosso R, Tronick E, Borgatti R. Promoting neuroprotective care in neonatal intensive care units and preterm infant development: insights from the neonatal adequate care for quality of life study. *Child Dev Perspect*. 2017; 11(1):9-15.
- Cignacco E, Hamers JP, Stoffel L, van Lingen RA, Gessler P, McDougall J, et al. The efficacy of non-pharmacological interventions in the management of procedural pain in preterm and term neonates. A systematic literature review. *Eur J Pain*. 2007; 11(2):139-52.
- Kugelman A, Colin AA. Late preterm infants: near term but still in a critical developmental time period. *Pediatrics*. 2013; 132(4):741-51.
- Holsti L, Weinberg J, Whitfield MF, Grunau RE. Relationships between adrenocorticotrophic hormone and cortisol are altered during clustered nursing care in preterm infants born at extremely low gestational age. *Early Hum Dev*. 2007; 83(5):341-8.
- Chen Y, Baram TZ. Toward understanding how early-life stress reprograms cognitive and emotional brain networks. *Neuropsychopharmacology*. 2016;

- 41(1):197-206.
9. Cabral DM, Antonini SR, Custódio RJ, Martinelli CE Jr, da Silva CA. Measurement of salivary cortisol as a marker of stress in newborns in a neonatal intensive care unit. *Horm Res Paediatr*. 2013; 79(6):373-8.
 10. Diego MA, Field T, Hernandez-Reif M. Preterm infant weight gain is increased by massage therapy and exercise via different underlying mechanisms. *Early Hum Dev*. 2014; 90(3):137-40.
 11. Uvnäs-Moberg K, Handlin L, Petersson M. Self-soothing behaviors with particular reference to oxytocin release induced by non-noxious sensory stimulation. *Front Psychol*. 2014; 5:1529.
 12. Pepino VC, Mezzacappa MA. Application of tactile/kinesthetic stimulation in preterm infants: a systematic review. *J Pediatr (Rio J)*. 2015; 91(3):213-33.
 13. Pados BF, McGlothen-Bell K. Benefits of infant massage for infants and parents in the NICU. *Nurs Womens Health*. 2019; 23(3):265-71.
 14. Wang L, He JL, Zhang XH. The efficacy of massage on preterm infants: a meta-analysis. *Am J Perinatol*. 2013; 30(9):731-8.
 15. Asadollahi M, Jabraeili M, Mahallei M, Asgari Jafarabadi M, Ebrahimi S. Effects of gentle human touch and field massage on urine cortisol level in premature infants: a randomized, controlled clinical trial. *J Caring Sci*. 2016; 5(3):187-94.
 16. Forclaz MV, Moratto E, Pennisi A, Falco S, Olsen G, Rodríguez P, et al. Salivary and serum cortisol levels in newborn infants. *Arch Argent Pediatr*. 2017; 115(3):262-6.
 17. Okamura H, Kinoshita M, Saito H, Kanda H, Iwata S, Maeno Y, et al. Noninvasive surrogate markers for plasma cortisol in newborn infants: utility of urine and saliva samples and caution for venipuncture blood samples. *J Clin Endocrinol Metab*. 2014; 99(10):E2020-4.
 18. Provenzi L, Giusti L, Fumagalli M, Tasca H, Ciceri F, Menozzi G, et al. Pain-related stress in the neonatal intensive care unit and salivary cortisol reactivity to socio-emotional stress in 3-month-old very preterm infants. *Psychoneuroendocrinology*. 2016; 72:161-5.
 19. Calixto C, Martinez FE, Jorge SM, Moreira AC, Martinelli CE Jr. Correlation between plasma and salivary cortisol levels in preterm infants. *J Pediatr*. 2002; 140(1):116-8.
 20. Montero-López E, Santos-Ruiz A, González R, Navarrete-Navarrete N, Ortego-Centeno N, Martínez-Augustín O, et al. Analyses of hair and salivary cortisol for evaluating hypothalamic-pituitary-adrenal axis activation in patients with autoimmune disease. *Stress*. 2017; 20(6):541-8.
 21. Gunnar MR. Reactivity of the hypothalamic-pituitary-adrenocortical system to stressors in normal infants and children. *Pediatrics*. 1992; 90(3 Pt 2):491-7.
 22. Aliabadi F, Askary RK. Effects of tactile-kinesthetic stimulation on low birth weight neonates. *Iran J Pediatr*. 2013; 23(3):289-94.
 23. Irwanto. Strategies of intervention for preterm infants to optimize growth and development. 2nd Symposium & Workshop Update Neonatal. Departemen Ilmu Kesehatan Anak Fakultas Kedokteran Universitas Airlangga/RSUD Dr Soetomo Surabaya, Indonesia; 2017. P. 25-46.
 24. Schanberg SM, Field TM. Sensory deprivation stress and supplemental stimulation in the rat pup and preterm human neonate. *Child Dev*. 1987; 58(6):1431-7.
 25. Lecuona E, Van Jaarsveld A, Raubenheimer J, Van Heerden R. Sensory integration intervention and the development of the premature infant: a controlled trial. *South Afr Med J*. 2017; 107(11):976-82.
 26. Feldman R, Singer M, Zagoory O. Touch attenuates infants' physiological reactivity to stress. *Dev Sci*. 2010; 13(2):271-8.
 27. Neu M, Pan Z, Workman R, Marcheggiani-Howard C, Furuta G, Laudenslager ML. Benefits of massage therapy for infants with symptoms of gastroesophageal reflux disease. *Biol Res Nurs*. 2014; 16(4):387-97.
 28. Guzzetta A, Baldini S, Bancale A, Baroncelli L, Ciucci F, Ghirri P, et al. Massage accelerates brain development and the maturation of visual function. *J Neurosci*. 2009; 29(18):6042-51.
 29. Acolet D, Modi N, Giannakouloupoulos X, Bond C, Weg W, Clow A, et al. Changes in plasma cortisol and catecholamine concentrations in response to massage in preterm infants. *Arch Dis Child*. 1993; 68(1 Spec No):29-31.
 30. 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.