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Pediatrics and Neonatology (2013) 54, 322–325

Available online at www.sciencedirect.com

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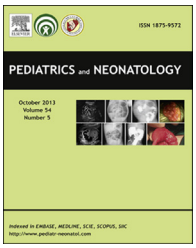

ORIGINAL ARTICLE

The Calming Effect of Maternal Breast Milk Odor on Premature Infants

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Received Jul 5, 2012; received in revised form Nov 23, 2012; accepted Apr 19, 2013

Key Words
breast milk odor;
pain;
PIPP score;
preterm newborn

Background: To compare the effectiveness of maternal breast milk odor and formula milk odor in soothing premature infants undergoing heel lancing.
Materials and methods: Fifty preterm infants born between 32 weeks and 37 weeks gestation were randomly assigned into two groups. During heel lancing, we used formula milk odor for the first group and breast milk odor for the second group. A filter paper (containing either formula or breast milk) was placed near the infant's nose from 3 minutes prior to and up to 9 minutes after the heel blood sampling. The pain score was measured using premature infant pain profile (PIPP) score. We also evaluated crying duration and salivary cortisol prior to and after heel lancing.
Results: After the heel lancing, the PIPP score was found to be significantly lower in the breast milk group than the formula milk group (5.4 compared to 9 with $p < 0.001$). Also, the level of salivary cortisol had significantly increased in the formula milk group, but not in the breast milk group (25.3 nmol/L compared to 17.7 nmol/L ($p < 0.001$).
Conclusion: Breast milk odor has an analgesic effect in preterm newborns and can be used as a safe method for pain relief.
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1. Introduction

Premature infants are exposed to multiple painful invasive procedures in the neonatal intensive care unit (NICU).[1] Frequent painful interventions will lead to increased susceptibility to tissue damage and reduce the pain threshold.[1,2] In addition, it causes substantial psychological and behavioral changes in response to the pain. These changes include the facial movements, cardio-vascular responses, and cortisol secretion.[1] It has also been shown that pain thresholds in premature infants are significantly lower and that acute painful stimuli lead to the development of

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http://dx.doi.org/10.1016/j.pedneo.2013.04.004

prolonged periods of hyperalgesia.[3] Grunau and coworkers have reported a blunting of hypothalamic pituitary-adrenal response in infants who have undergone repeated painful procedures.[4] Neurological studies have shown that pain and stress potentially affect the developing cytoarchitecture of the brain.[5] Therefore, painful stimuli could affect behavioral responses in future. Methods of preventing or reducing pain in infants include pharmaceutical and non-pharmaceutical measures. Nonpharmacologic measures include the use of oral sucrose or glucose, breast feeding, nonnutritive sucking, skin-to-skin contact with the mother, swaddling, facilitated tucking (holding the arms and legs in a bent position), and sensory saturation, including the sense of touch (massaging), sound, smell, and vision.[6] These measures are more effective when used together.[6] By contrast, several studies have shown that infants are able to detect odors from the birth time.[7–9] Smells that are familiar to the baby, such as the smell of the mother, have soothing effects on infants.[7] The human infant is able to detect the smell of his or her mother's breast without the experience of consuming it during the first days of life.[8,9] Infants who consume their mothers' milk (from 4 days to 15 days after the birth) prefer the smell of their mothers' breast milk to that of other nursing mothers.[10,11] Infants from 1 day to 10 days are capable of smelling the neck, axilla, and other parts of their mother's body to distinguish and differentiate from others.[12] Studies have also shown that body odor and the mother's breast milk odor could decrease pain and distress in newborn infants.[12,13] Owing to the complications of pain in neonates and many painful procedures performed on them (especially on premature infants), it is important to find reliable and useful ways to control pain. The aim of this study is to evaluate the analgesic effect of breast milk odor in reducing the pain in preterm infants during heel prick blood sampling.

2. Materials and Methods

A total of 50 preterm infants (aged 1-30 days) were recruited for the study. The samples were selected from premature infants (gestational age of 32-37 weeks) who were hospitalized in the NICU of Al-Zahra and Shahid Beheshti University Hospitals, Isfahan, Iran from April 2011 to November 2011, who required heel blood sampling for testing blood glucose levels in accordance with the physician's direction. The Ethics Committee of Isfahan University of Medical Sciences confirmed the study and parents' written consent was obtained from all the participants. The exclusion criteria were sedative or analgesic consumption during the past 48 hours, evidence of neurological problems, severe congenital malformations, need for mechanical ventilation or continuous positive airway pressure, 5-minute Apgar score less than 6, seizures, necrotizing enterocolitis, sepsis, and the need for supplemental oxygen at the time of the study. The gestational age of the infants was determined based on the new Ballard score. The random selection of the patients as formula milk and breast milk groups was based on a selected box number from one to 50. Even numbers were allocated to the formula milk group and odd numbers to the breast milk group. At first, the baby was placed under a radiant warmer in a quiet room. Each newborn had continuous monitoring of heart rate and oxygen saturation throughout the study. Two milliliters of mother's milk in the morning was expressed manually (to minimize the effect of diet on the mother's milk odor). It was poured on a filter paper, which was placed near the nose of the infant from 3 minutes prior to and up to 9 minutes after heel prick blood sampling. A single independent investigator who was not involved in the post heel lancing observations and analysis prepared the filter paper. The smell of Nan synthetic milk (nestle-Switzerland Co) was used in the control group. We assessed the pain response using premature infant pain profile (PIPP) as a standard criterion for assessing the pain in premature infants and the length of crying time. PIPP is a pain measure with good validity and excellent inter- and intraobserver reliability for the assessment of procedural pain in premature infants.[14] It is a 7-indicator scoring system, including one indicator for gestational age, one for behavioral state (active or relaxed, asleep or awake), three indicators for occurrence of facial actions (eyes open or closed, presence or absence of facial movement), one for heart rate, and one for oxygen saturation.

The salivary cortisol was collected 1 minute prior to the baby familiarizing the smell of milk and 20 minutes after the heel lancing with a 2-mL syringe. They were washed in the laboratory with Washer Elisa instrument (SeaChange International, *Inc.*, Italy) and then they were measured by Diametra kits from Italy by the American Awareness instrument (Stat Fax model).

Counting the first type of error with the index equal to 0.05, with study power equal to 80% and to show at least a 0.8-s difference in PIPP scores between the two groups, there was a minimum sample size of 25 patients in each group. Obtained data were analyzed by independent t test, t-paired test, and Pearson correlation coefficient in the SPSS software (version 18; SPSS Inc, Chicago, IL, USA).

3. Results

Demographic characteristics of infants are shown in Table 1. It can be seen that there are no significant differences in demographic characteristics between the two groups (Table 1). Independent *t* test showed that the mean PIPP score and crying time in breastfeeding group after the blood sampling from the heel were significantly lower than for the formula milk group ($p < 0.005$; Table 2). The mean salivary cortisol prior to the heel prick blood sampling was not significantly different between groups ($p = 0.53$). However, after blood sampling from the heel, the mean salivary cortisol in formula milk group was significantly higher than in the breastfeeding group ($p < 0.001$; Table 2). Pearson correlation test showed that there was a significant relationship in the formula milk group between the infant birth weight and duration of crying, PIPP score and salivary cortisol after heel prick blood sampling (with increasing birth weight, the crying time, PIPP score, and salivary cortisol after blood sampling were increased). There was no significant relationship between the birth weight and salivary cortisol prior to the heel lancing. In the breast milk group, with increasing birth weight, the infant crying duration, PIPP score, and salivary cortisol prior to and after

Table 1 Frequency distribution in terms of gender and the mean ± standard deviation of birth weight, gestational age, and postnatal age in the breast milk odor group and formula milk odor group.

Group	Gender		Gestational age (wk)	Birth weight (g)	Age (d)
	Boy	Girl			
Breast milk	10 (40)	15 (60)	34.11 ± 1.5	2098.80 ± 527.44	4.48 ± 3.5
Formula milk	12 (48)	13 (52)	34.53 ± 1.3	2287.20 ± 105.48	3.24 ± 1.26
p	0.09		0.293	0.178	0.1

Data are presented as *n* (%) or mean ± SD.

the sampling were increased, but this relationship was not significant (Table 3).

4. Discussion

In this study, we tried to find an alternative method for pain control in premature infants. We found that breast milk odor had better ability to control the pain in comparison with formula milk odor in preterm infants. Babies who were exposed to the smell of milk of their mothers during painful procedures had lesser increases in salivary cortisol levels than the group that was exposed to formula milk odor. Therefore, breast milk odor had a better analgesic effect in premature infants.

Schaal and colleagues demonstrated that prenatal exposure to anise odor could affect behavioral responses of newborn infants. They also showed that the infants are able to identify familiar odors from the birth, and various odors cause pleasant or unpleasant effects on newborn infants.[15] In our study, it was also found that infants are able to detect odors and that the odor can affect infant behavior. Nishitani and colleagues, in a study that was conducted on 48 term infants, showed that infants who were exposed to the smell of breast milk during the heel prick blood sampling felt less pain than the babies exposed to formula milk smell or milk of other mammals. Salivary cortisol was also used in their study as an index of biochemical responses to pain in infants. It was found that salivary cortisol in the control group was significantly higher than those who were exposed to the smell of breast milk.[16] In our study, PIPP scores, and increased levels of salivary cortisol after a heel prick blood sampling were significantly lower in the breast milk group than the formula milk group. These findings were consistent with the findings of Nishitani and colleagues. Similar results were obtained by Rattaz and colleagues. In their study, the duration of crying, facial changes resulting from the pain, and head movements in newborns who were exposed to the smell of their mothers' milk were significantly lower than the control group. In addition, the infants who were exposed to the smell of their mothers' milk had less irritability than the control group.[17] We confirmed these results in premature infants. Goubet and coworkers assessed the effect of exposure to familiar and unfamiliar odors during the heel stick. In this study, a group of infants was exposed to vanilla odor through their mother or their bed and were familiar with it. Another group of babies was not exposed to any odor. Infants exposed to familiar odors had less distress and showed more oral movements. Goubet et al concluded that exposure to familiar odors could be effective in reducing the infant crying and facial changes during painful procedures.[18] Among the very few studies on preterm infants, one was conducted by Bingham and colleagues on seven infants who were fed through tubes. It was shown that in 6 of 7 newborn infants who were exposed to their mother's milk odor, the number of non-nutritive sucking was increased, and the smell of breast milk strengthened their sucking.[19] This study showed the effect of smelling breast milk on infant sucking, but it did not show any analgesic effect. Our study, however, showed an analgesic effect of odor of breast milk in preterm infants. The sedative effect of familiar odors (such as the smell of the mother's clothes) was also proved in a study that was conducted by Sullivan and colleagues. In this study, the infants were divided into four groups and their behavior was examined when they were exposed to a familiar odor during times of crying and waking up. The first group was exposed to their mother's clothes smell. The second group was exposed to other mothers' clothes smell. The third group was given a clean cloth, and the fourth group was not exposed to any odor. It was demonstrated that crying stopped sooner in infants who were familiarized with the smell of their mothers' clothes or the dresses of other mothers. The infants who were awake showed more movements, especially when exposed to their mother's clothes.[13] The above mentioned study and other studies in this field showed that apart from the breast milk odor, other odors associated with the mother could be effective on pain responses in newborn infants.

In our study, only the sedative effect of breast milk has been studied and compared with the smell of formula milk

Table 2 Premature infant pain profile (PIPP) score, crying time, and salivary cortisol prior to and after blood sampling from the heel in the breast milk odor group and formula milk odor group.

Variable	Breast milk group	Formula milk group	*p*
PIPP score	5.4 ± 1.9	9 ± 3.1	<0.001
Crying time (s)	5.1 ± 2.4	7.6 ± 3.8	0.02
Salivary cortisol prior to blood sampling (nmol/L)	16.0 ± 7.0	14.9 ± 5.5	0.3
Salivary cortisol after blood sampling (nmol/L)	17.7 ± 5.8	25.3 ± 9.1	<0.001

Data are presented as mean ± standard deviation.

Table 3 Mean ± standard deviation of the variables of premature infant pain profile (PIPP) score, crying time, and salivary cortisol prior to and after blood sampling from the heel based on birth weight in the breast milk and formula milk odor groups.

Variable		Less than 2000 g	2000–2500 g	More than 2500 g	*p*	Pearson correlation
PIPP score	Breast milk	4.60 ± 2.07	5.33 ± 1.32	5.91 ± 2.34	0.10	−0.265
	Formula milk	7.13 ± 3.52	8.88 ± 1.95	10.11 ± 3.75	0.016	0.431
Crying time (s)	Breast milk	3.18 ± 4.07	3.78 ± 3.42	4.60 ± 1.14	0.187	0.186
	Formula milk	4.38 ± 2.87	6.50 ± 3.74	8.00 ± 5.43	0.023	0.40
Salivary cortisol prior to blood sampling (nmol/L)	Breast milk	14.11 ± 6.50	16.36 ± 7.35	19.18 ± 8.04	0.281	0.122
	Formula milk	14.63 ± 7.98	11.13 ± 2.80	13.22 ± 5.49	0.449	−0.027
Salivary cortisol after blood sampling (nmol/L)	Breast milk	13.44 ± 6.80	18.36 ± 5.93	20.20 ± 7.66	0.384	0.062
	Formula milk	23.63 ± 9.51	25.75 ± 13.35	29.67 ± 12.48	0.042	0.316

odor. However, in addition to using the behavioral indexes to evaluate the pain, we used the biochemical index (salivary cortisol levels) for the assessment of pain responses in newborns. Another important aspect of this study is that it was performed on premature infants, while other studies only evaluated the analgesic effects of breast milk odor or other familiar odors on term infants. In addition, the measurement of salivary cortisol levels could confirm the positive results of this important finding. The present study was conducted with a small sample number. Therefore, conducting other studies with larger sample size may lead to more valuable findings.

In conclusion, by using different behavioral and biochemical indexes, we have shown that the smell of breast milk rather than formula milk could decrease the behavioral responses to pain in premature infants. The smell interventions could be used as an alternative way to reduce pain in premature infants.

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