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Effect of Spike Lavender Lakhlakhe on Pain Intensity Due to Phlebotomy Procedure in Premature Infants Hospitalized in Neonatal Intensive Care Unit: A Randomized Clinical Trial

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ABSTRACT

***Background*:** A Premature infants undergo multiple painful procedures during treatment; thus, it must be tried to limit complications caused by diagnostic and treatment procedures using simple and practical methods. This study was performed to evaluate the effect of spike lavender lakhlakhe on pain intensity due to phlebotomy in hospitalized premature infants.

***Methods*:** This single-arm, randomized clinical trial was performed on 30 infants chosen through convenience sampling method. Each newborn was considered as its own control. For the test group, one drop of pure (100%) spike lavender lakhlakhe was taken by a standard dropper and diluted with 4 ml of warm distilled water by the research assistant. This mixture was stirred at 2-3 cm distance of the newborns' nose from 60 minutes before until 2 minutes after phlebotomy, such that it could be smelled by the newborns. In both groups, heart rate and blood oxygen saturation were measured by a standard portable device, and the corresponding data was recorded in data collection sheets. Moreover, the infants' facial expression changes were recorded by a camera and the intensity of pain was measured by Premature Infant Pain Profile before and after the procedure. Finally, the data was analyzed by paired comparison analysis test in SPSS, version 17.

***Results*:** Comparison of mean pain intensity caused by phlebotomy in the control and test groups showed a significant difference (7.667±0.311 vs. 4.882±0.311; P<0.001).

Conclusion: Spike lavender lakhlakheh can be used as an easy, available, and safe method to decrease infants' pain during phlebotomy procedure.

Keywords: Lakhlakhe (extract) of spike lavender, Pain intensity, Premature infants, Vein blood collection, Vein blood sampling

Introduction

Birth before 37 weeks of gestation is considered premature birth (1), which is globally the main cause of neonatal mortality and pathogenicity (2). These infants often need to be hospitalized at neonatal intensive care units to survive. During NICU stay, these infants undergo numerous care efforts and invasive procedures, which are painful and stressful and can interfere with the infant's nervous system evolution and growth (3).

Premature infants are more sensitive to pain compared to normal ones. These neonates are twice as much sensitive to pain as adults due to immature development of descending balancing

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system, pain transmission via unmyelinated C fibers, and less transmission via spinal cord (4). Infants show severe physiological, behavioral, hormonal, and metabolic responses to stimulations. These responses can have harmful short- or long-term effects.

There is ample evidence showing that premature and continuous exposure to pain before nervous system development can lead to permanent behavioral changes (5). Infants on average undergo 16 painful and stressful procedures every day at neonatal intensive care units (NICUs). These procedures include tracheal intubation, chest tube placement, nasogastric intubation, blood sampling, vein finding, tracheal extubation, surgery, and suction. These procedures may be performed for an infant 2 to 14 times per day (6, 7). Blood vein sampling is a painful but necessary diagnostic procedure performed on every infant 1 to 21 times a day and accounts for 8-13% of all invasive procedures. This procedure is necessary for diseases diagnosis and controlling and maintaining body homeostasis. However, it is one of the major causes of stress and pain and can lead to bleeding, hematoma, infection, and pain (8).

A wide range of pharmaceutical and non-pharmaceutical methods was introduced to manage pain in infants. Non-pharmaceutical interventions comprise of environmental and behavioral interventions that are performed with or without drug treatment. Drug side effects, such as respiratory distress, physical dependence, addiction in cases of narcotics use, rash, skin irritation, and erythema, are always a major concern (9). Accordingly, new developments were made in the realm of herbal medicine to diminish pain in neonates. One of these herbal methods that has recently well-developed is the use of herbal aroma that is known as “lakhlakhe” in traditional medicine.

In herbal medicine, lakhlakhe is defined as the mixture of an herb well stirred with liquids in a container in order to be smelled (10). Fragrant materials can affect through both psychological and physiological responses. It is believed that aromas can activate olfactory nerve cells leading to the stimulation of a part of the limbic system called hippocampus. The role of hippocampus is specifically related to memory and short-term memory’s conversion into long-term memory.

Nerve cells can release various neurotransmitters depending on the type of smell. These neurotransmitters include enkefalin, endorphin, noradrenalin, and serotonin (11). One famous fragrant herb in this category is "spike lavender" that has been used in traditional medicine for various reasons since many years ago. The name of this herb means "keeper of souls" in Greek and belongs to the order of mint plants. The plant is grassy, fragrant, and evergreen and contains flavoring oil, spike essence, lynalyl, gylanyl, geranial, pinan, sineoil, and tanan. It has antibacterial, antifungal, anti bloat, muscle relaxant, anti-stress, and analgesic properties (10, 12, 13). Lynalol and lynalyl acetate in this plant can stimulate the parasympathetic system, and lynalyl acetate has narcotic effects; they can act as sedatives.

Although the exact neural mechanism of action of spike lavender is inconspicuous, it might have some effects similar to benzodiazepines and can increase the effect of gamma-aminobutyric acid (12). Nowadays, complementary interventions, provided as part of nursing care, can enhance the quality of care given to premature infants. Herbal medicines are simple, accessible, and cost-effective; they do not require exact time of use and sophisticated equipment.

Given the scarcity of references and studies on the sedative and analgesic effects of spike lavender on infants and strong recommendation of its application in traditional medicine, we sought to study its effects on pain caused by blood sampling in premature infants.

Methods

In this single-arm, randomized clinical trial, infants admitted to NICU were chosen through convenience sampling method. Each infant was studied once as the control and once as the test group, such that each infant underwent blood sampling through the ordinary method during the first 24 hours of admission, and in the next 24 hours, phlebotomy was performed again with the use of lakhlakhe of spike lavender.

The inclusion criteria were gestational age of 27 to 36 weeks, lack of receiving short- or long-term sedatives and analgesics by the mother and infant, stability of physiological conditions, daily need for blood sampling, disinfection of phlebotomy area on infant’s body, parent satisfaction, lack of feeding 30 minutes before blood sampling (e.g., milk and sweet liquids), and no history of allergy in the mother.

The exclusion criteria comprised of parent disinclination to participate and physiological instability of the infant. The data collection tools included a data collection sheet, pulse oximeter, recording camera, and Premature Infant Pain Profile (PIPP) sheets (Table 1).

Table 1. Premature Infant Pain Profile (PIPP)

Indicator	Finding	0	1	2	3	Total
	Gestational age	>=36 weeks	32 weeks to 35 weeks 6 days	28 weeks to 31 weeks 6 days	<28 weeks	
Observe the infant for 30	Behavioral state	Active/awake eyes open facial movements	Quiet/awake eyes open no facial movements	Active/sleep eyes closed facial movements	Quiet/sleep eyes closed no facial movements	
Observe heart rate and oxygen saturation for 30	Heart rate maximum	0-4 beats per minute increase	5-14 beats per minute increase	5-14 beats per minute increase	15-24 beats per minute increase	
	Oxygen saturation	0 to 2.4% decrease	2.5 to 4.9% decrease	5.0 to 7.4% decrease	7.5% decrease or more	
Observe Facial expression of infant for 30 seconds	Brow bulge	None (<= 9% of time)	Minimum (10-39% of time)	Minimum (10-39% of time)	Maximum (>= 70% of time)	
	Eye squeeze	none (<= 9% of time)	Minimum (10-39% of time)	Minimum (10-39% of time)	Maximum (>= 70% of time	
	Nasolabial furrow	None (<= 9% of time)	Minimum (10-39% of time)	Minimum (10-39% of time)	Maximum (>= 70% of time	

The higher the score the greater the pain behavior (14)
- Minimum score: 0
- Maximum score: 21

Prior to the study, the researcher introduced herself to the supervisor, and the infants who met the inclusion criteria were identified. Moreover, informed consent was obtained from the parents. Pure spike lavender extract (efensialis) was acquired from the laboratory of Shiraz University of Medical Sciences. One drop of the extract was taken by a standard dropper and mixed with 4 ml of warm distilled water and then was stirred at 2-3 cm distance of the infants' nose, such that it could be smelled by the infant. The intervention was performed from 60 minutes before till 2 minutes after blood sampling. In each group, heart rate and blood oxygen saturation at 1 minute before, during, and 2 minutes after phlebotomy, were measured by a standard portable device (CT, 06492 Novametrix Wallingford).

The probe of the device was attached to the infants' left leg. All the gathered data was recorded in data collection sheets. Also, the infants' facial expression changes were recorded by a video recorder (canon Lxus132) and the pain severity score resulted was measured by PIPP scale, before, during, and after blood sampling. Afterwards, images of facial expression changes were interpreted by an expert via PIPP scale and the corresponding scores were recorded. The expert was blinded to the study objectives. Blood sampling process was performed at 7 a.m. by a single, well-trained, and expert nurse (the researcher) on a radiation warmer.

The infant's body temperature ranged between 36.5°C and 37.2°C during the blood sampling procedure by temperature-regulating action of the radiant heater. The nurse determined the appropriate vein after washing hands and wearing gloves. The site was massaged and warmed up and a tourniquet was installed at 2-3 cm proximal to the vein in order to fill and signify it. The needle site was disinfected by 70% ethylic alcohol. Then phlebotomy was performed by a 23-gauge (Iran Medical Co., Iran) by entering it to the vein at 25 to 45 degrees.

The collected data was analyzed by paired comparison analysis test in SPSS, version 17. To perform this study, we obtained approval of the hospital authorities, the parents were informed of the study objectives and the voluntary nature of participation in the study, and the parents were also assured of the confidentiality of the data. In the end, the obtained results were offered to the managers of the hospital.

Results

A total of 30 infants were enrolled (11 [36.7%] boys and 19 [63.3%] girls). Birth weight ranged between 810 and 2900 g and its mean was 1594.16±495.10 g. Mean gestational age was 32.566±2.486 weeks (age range: 27 to 36 weeks). Furthermore, the Apgar score ranged between 7 and 9 (mean: 9.133±0.809). Moreover, 24 (80%) of the mothers were within the age range of 20 to 30 years and 6 (20%) were between 30 and 40

Table 2. Comparison of mean pain intensity scores between the two methods

Method of blood sampling	Ordinary method mean±SD	Lakhlakhe method Mean±SD	P-value
Pain intensity score	7.667±311.	882.4±311.	<0.001

Table 3. Comparison of mean heart rate between the two methods

Method of blood sampling	Ordinary method Mean±SD	Lakhlakhe method Mean±SD	P-value
Before and during sampling	9.133±6.652	1.233±4.074	<0.001
Two minutes after sampling	7.133±7.709	-3.433±7.454	<0.0108

Table 4. Comparison of mean oxygen saturation between the two methods

Method of blood sampling	Ordinary method Mean±SD	Lakhlakhe method Mean±SD	P-value
Before and during sampling	-4.500±2.797	-0.500±2.850	<0.001
Two minutes after sampling	-4.066±3.759	1.566±3.169	<0.0001

years old.

Because each infant was considered once as control and once as test, variables such as sex, gestational age, age, and weight were all homogenous. Pain intensity (severity) was measured via facial expression changes score and physiological parameters in the three stages of before, during, and after sampling. According to our findings, mean blood sampling pain intensity scores in the ordinary and spike lavender lakhlakhe groups were 7.677±0.311 and 4.882±0.311, respectively, showing a significant difference between the two groups (P<0.001) and a marked pain reduction in the test group.

Table 2 shows that means of heart rate fluctuation at the three stages of before, during, and after sampling were respectively 9.133±6.652 and 7.133±7.709 bpm in the ordinary method versus 1.233±4.074 and 7.454±3.433 bpm in the lakhlakhe method; their comparison demonstrated a marked reduction in heart rate in the test group infants (P<0.001; Table 3). Average blood oxygen saturation at 3 stages were 4.500±2.797 and 4.066±3.759 in ordinary method against 1.566±3.169 and 0.500±2.850 in lakhlakhe method and their comparison shows marked increase in blood oxygen saturation in test group infants (P<0.001; Table 4).

$$N= \frac{2(1-\rho)(Z_{1-\alpha/2}+Z_{1-\beta})^2\sigma_1^2}{(\mu_2-\mu_1)^2} \qquad \alpha=/05$$

Power=90%

Discussion

Pain is an experience that has sensing and emotional dimensions (15). Pain is described as an undesirable feeling that can bring about potential and actual harm to the tissues (16). Until 1980, it was believed that infants do not feel pain, but studies showed that physiological components of pain feeling system are developed in early embryonic stages and that pain threshold of nerve endings in infants is the same as adults (17). Therefore, serious dangers and complications of pain in infants such as elevated blood ketone bodies, lactate, pyrovate, and non-steroidal acids must be further considered (18).

Our results revealed higher level of pain in the control group compared with the intervention group and showed that simple methods can be performed to soothe pain during painful procedures. One of the most important moral duties in medical ethics is protecting patients from any kind of harm, in this regard, pain reduction in infants is of great importance. Based on our results, comparison of mean pain intensity scores between the ordinary and lakhlakhe of spike lavender methods (7.667±0.311 vs. 4.882±0.311) showed a significant difference.

Nishitani et al. (2009) demonstrated the effect of breast milk as an olfactory stimulant on reducing infant crying time during capillary blood collection from the heel, while such a change was not observed by other milks. They showed that an unfamiliar olfactory stimulant cannot reduce pain in infants as a “mind distracter”. Therefore, an olfactory stimulant can be effective in pain reduction only when it is an “experienced mind distracter” (19).

Moreover, in the study by Varandi et al. (2009), stimulation with amniotic fluid smell could significantly shorten infants’ crying time after birth. They believed that amniotic fluid smell can remind the calm and comfortable environment of

the uterus for the infant, and therefore, can pacify it. In all of these studies, an integral variable that was studied is background. Background is regarded as a sensing and random stimulant that exists during memory consolidation, and its re-existence can help remember that memory and all target information; thus, it can affect the behavior and function of an individual. Studies showed that olfactory stimulants can be effective background keys to remember memories (20). Study of Sadat Husseiny et al. (2010) was undertaken to study the effect of familiar olfactory stimulants on pain responses due to blood sampling. They showed that familiar olfactory stimulants can reduce infant crying time during arterial blood sampling (21). Additionally, we found that olfactory stimulation can affect changes of physiological indices, including heart rate decrease and increase of blood oxygen saturation percentage, during vein blood sampling.

Comparison of mean heart rate changes at one minute before, during, and two minutes after sampling between ordinary method (9.133±6.652 and 7.133±7.709) and lakhlakhe method (1.233±4.074 and -3.433±7.454) showed that spike lavender lakhlakhe can significantly lower heart rate and pain.

Chang et al. (2007) studied the effect of swaddling on physiological indices in premature infants during suction and found that heart rate of a swaddled infant is more stable than non-swaddled ones; they also proposed that this can help infants retain more energy (22). Gary et al. (2000) showed that pain of heel blood sampling in infants can naturally elevate heart rate and skin-to-skin touch can decrease crying time, facial expression changes, and heart rate in infants (23).

Castial et al. (2008) proposed that direct mother and infant skin to skin touch during heel blood sampling can reduce facial expression changes, heart rate, and crying time in test group (24). In this study, comparison of mean blood oxygen saturation at one minute before, during, and two minutes after sampling in the ordinary method (-4.066±3.759 and -4.500 ±2.797) with lakhlakhe method (1.566±3.169± and -0.500±2.850) demonstrated raised blood oxygen saturation in test group.

In a study entitled as "olfactory cortex activation caused by olfactory stimulation in infants", near-infrared spectroscopy was conducted by Badtocei et al. (2000) in the USA. The results showed that oxygen binding capacity of hemoglobin (HbO_2) significantly increases in infants exposed to vanilla smell (25). Standly and Cosidy in their study entitled as "effect of music on premature infant's physiological responses" found that music exerts a positive effect on blood oxygen saturation, heart rate, and respiratory rate (26).

Conclusion

Medical and health personnel are the protectors of premature infants and are responsible for prevention of pain and its harmful effects on preterm infants. They must find methods to reduce pain complications to provide them quality care. Therefore, offering education and appropriate methods to promote the culture of pain prevention is essential. Regarding the positive effect of spike lavender lakhlakhe on reducing pain, its regular use is recommended during blood sampling procedure.

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Conflicts of interests

None.

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