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Association of Weight of Premature Infant and Aromatherapy: A Systematic Review

Ranna Tafrishi[1], Sara Ghahremani[2], Somayeh Moeindarbary[3], Mohaddese Badpeyma[4], Omolbanin Heydari[5], Farzane Ashrafinia[6], Roozbeh Nasibeh[7], *Masoud Mortezaei[8], Mohammad Ahmadian[9]

[1]Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [2]Assistant Professor of Pediatrics, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [3]Assistant Professor, Department of Obstetrics and Gynecology, Neonatal and Maternal Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. [4]Department of Nutrition, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [5]Department of Nursing and Midwifery, Razi School of Nursing and Midwifery, Kerman University of Medical Sciences, Kerman, Iran. [6]Students Research Committee, Razi School of Nursing and Midwifery, Kerman University of Medical Sciences, Kerman, Iran. [7]Mother and Child Welfare Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. [8]Fellowship of Pediatric Intensive Care, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract

Background: Few studies assessed the association of weight of premature infant and aromatherapy as a secondary outcome. Aim of study was to evaluate all clinical trials on the association of weight of premature infant and aromatherapy.

Materials and Methods: All clinical trials evaluating the association of weight of premature infant and aromatherapy with the alleviation of pain were searched on the electronic databases of Scopus, EMBASE, Cochrane, Web of Science and Medline (via PubMed) with no language or time restrictions till December 26, 2019. Jadad scale as a valid and reliable tool was applied to assess the quality of included studies.

***Results*:** Finally, five studies with a total of 367 participants were enrolled in this systematic review. In the first study over that time interval, the mean daily weight gains did not differ significantly between the infants in the milk versus water-exposure conditions. In the second study the evaluation of the mean weight of subjects at discharge and the mean weight gained between hospitalization and discharge showed that there were no significant differences between the study and control groups. In third study, the infants' weight did not differ significantly among three groups: vanilla, placebo and rose. In the fourth study, the mean weight of preterm infants at discharge and between hospitalization and discharge showed no significant difference between two groups' impregnated pad with breast milk and control. In the fifth study, combining milk odor and nonnutritive sucking (NNS) than single NNS were effect in achieving oral feeding and earlier discharge from the hospital.

***Conclusion*:** Aromatherapy with a single oil or a combination of two or more aroma oils, were not effective on weight among high-risk and vulnerable infant, such as preterm infant and very low birth weight, there is a need for more accurate and robust future studies.

Key Words: Aromatherapy, Infant, Premature, Systematic review.

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Corresponding Author:

Masoud Mortezaei, M.D, Fellowship of Pediatric Intensive Care, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Email: mortezaeem2@mums.ac.ir

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1- INTRODUCTION

A Preterm infant is said to be a baby born before 37 weeks of gestation despite the birth weight. Preterm birth is associated with a high percentage of deaths. Short-term and long-term complications, including neurodevelopmental disorders in infants (1) have been reported. Recently, studies have shown that preterm birth is one of the major causes of neurodevelopmental injuries. These injuries are inversely related to gestational age and birth weight (2). The prevalence of preterm birth varies from 6 to 15% of deliveries, and depends on the demographic and geographical characteristics of the population under study (3). Since the preterm infant is born for every ten children in the world each year, to this end, World Prematurity Day on November 17 strives to raise awareness about the issues associated with preterm birth (4). The preterm birth is the most common cause of neonatal death and the second leading cause of death in children younger than five years (5).

Preterm infants are subject to persistent problems in all areas of growth and development. Preterm birth can be associated with short-term and long-term complications such as bronchopulmonary dysplasia, necrotizing enterocolitis, premature retinopathy, cognitive disorders, and an increased risk of diseases such as hypertension and diabetes in adulthood (6). Survived very-low-birth-weight (VLBW) infants suffer from short-term and long-term physical and psychological disabilities and problems two to three times more than those of other infants. The lower the birth weight, the greater the likelihood of neurological complications and mental retardation, so that 50% of infants weighing between 500 and 750 g are at risk of developing severe neurodevelopmental disabilities, such as blindness, hearing loss, mental retardation and cerebral palsy (7). Clinical and scientific advances in neonates continuously improve the survival of preterm infants, especially at low birth weight. One of the main goals is adequate and early feeding of preterm infants (8). The American Academy of Pediatrics (AAP) has also found breast milk to be the ideal nutritive milk for preterm infants. Breastfeeding improves nutritional, immunological, and developmental outcomes (8, 9). Human milk has been recommended as the optimal and exclusive source of early infant nutrition as a result of potent immune factors and a unique composition of nutrients that evolve in tandem with the growth and developmental needs of the infant; especially preterm infant, for infants who are born preterm, exposure to the immune factors of human milk is of paramount importance as these infants are born with an immature immune system. For these infants, human milk not only provides protection from disease pathogenesis in the short term, but it also helps to ensure the development of a healthy immune response in the long term (10).

Milk production in mothers of preterm infants can be affected by a variety of factors, including stress, health problems, delayed breastfeeding, and being away from infants (8). The aromatherapy refers to the skill and application of essential oils to enhance physical and mental health and overall well-being and improve quality of life. Aromatherapy is one of the rapidly expanding complementary therapies. Studies on adults have shown that different odors evoke different autonomic responses, and show different reactions to pleasant and unpleasant odors (11). Olfactory stimulation may cause various emotional and physiological changes and may have a significant impact on the growth and development of preterm infants. Nasal inhalation causes odor particles to pass through the nostrils to reach the olfactory receptors and signal to

the brain. This signal reaches the limbic system by the nerves through the hypothalamus and amygdala, which controls not only the sense of smell, but also the emotions and memories. Through this process, all mammals, including the fetus, remember the smell of breast milk and amniotic fluid as the smell of mother and love (12). The importance of olfaction for infants, especially the smell of mother, is well known. Active effective olfactory receptor neurons are found in preterm infants in the early weeks of gestation (24-27 weeks). Therefore, it is assumed that the olfactory stimulation works in preterm infants (13). Since the infants have a strong and evolved sense of smell at birth, olfactory stimuli also influence the physiological responses of infants. Pleasant odor causes increased breathing and oxygen saturation in infants and preterm infants. It significantly reduces apnea in preterm infants, while bad smell may cause infants and preterm infants to become disinterested in breast milk and may increase pulse rate. There is a lack of research on how olfactory stimuli affect the health and the development of preterm infants (12).

The use of complementary therapies as a low-risk, cost-effective, easy-to-use treatment with limited side effects is expanding in healthcare settings (14-16). Aromatherapy is one of the methods of complementary and alternative medicine (17). Various studies have shown that aromatherapy can be useful in relieving pain and fatigue, as well as in wound healing. The exact mechanism of action is unclear, but the aroma of the scent appears to activate the nerve cell, leading to stimulation of the limbic system. Different neurotransmitters are released depending on the types of odors, including enkephalin, noradrenaline, and serotonin. Therefore, perfumes can affect the sense of smell (18). Complementary and alternative therapies are expanding in the nursing care of many health care centers as a low-risk, cost-effective, natural treatment with limited complications. Aromatherapy is one of the complementary therapies as a holistic treatment that reduces the difficulties and stresses of the nursing profession (19). Engen et al. (1963), have reported a change in breathing after exposure to the aroma and olfactory stimulation. The results of their study had two parts, which showed that the infants responded differently to various fragrances (acetic acid, anise essential oil , and phenyl ethyl alcohol); therefore, increased responses (breathing) were observed with increasing frequency of stimulation (20). In another study Nishitani et al. showed that breast milk odor increased brain tissue oxygenation (21). Also, Karbandi et al. evaluated the effect of breast milk odor on oxygen saturation percentage and respiratory rate of preterm infants (11). Few studies assessed the association of weight of premature infant and aromatherapy as a secondary outcome. Aim of this study was to evaluate all clinical trials that related theweight of premature infant and aromatherapy.

2- MATERIALS AND METHODS

2-1. Study design

Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) checklist was used as a template for this review (http://www.prisma-statement.org/).

2-2. Search strategy

All clinical trials evaluating the association of weight of premature infant and aromatherapy with the alleviation of pain were searched on the electronic databases of Scopus, EMBASE, Cochrane, Web of Science and Medline (via PubMed) with no language or time restrictions using the combination keywords of (Aroma OR Aromatherapy OR Olfactory OR Odorants) AND (Weight OR Body Weight

OR Fetal Weight OR Weight Gain OR Weight Loss OR Weights and Measures) AND (Preterm Infant OR Premature Birth). The flow chart of selection process is shown in **Figure.1**. Two independent researchers performed the search process and a supervisor judged any disagreement in this regard.

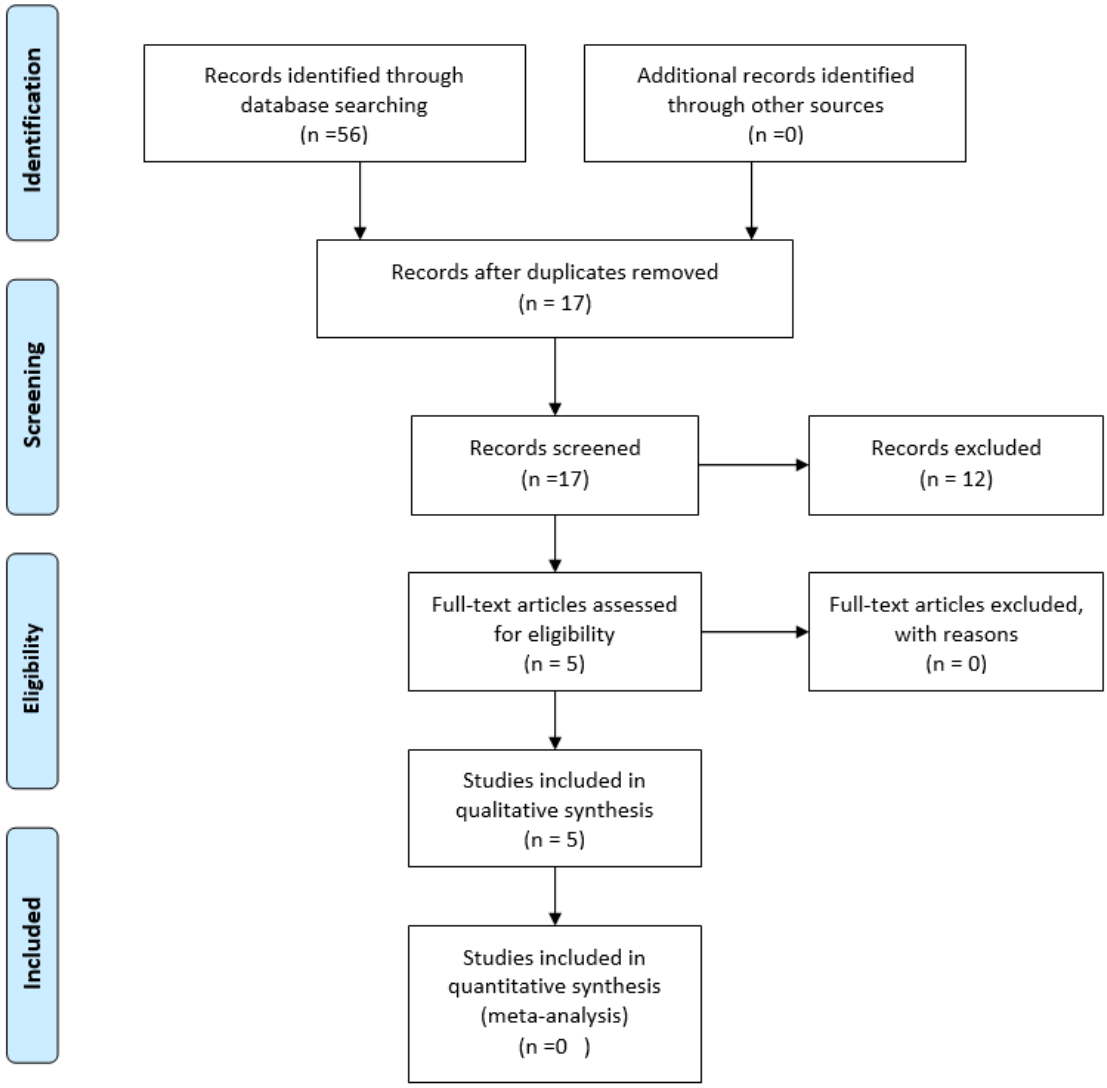

Fig.1: PRISMA flowchart.

2-3. Eligibility criteria

Participants, interventions, comparators, and outcomes (PICO) was used to formulate the review objective and inclusion criteria (22).

Participant: Preterm infants were defined as infants with birthweight ≤2,000 or gestation < 32 weeks.

Interventions*:* Studies comparing a type of aromatic herbal oil or combination of two types or more aromatic oil were considered as intervention group.

Comparators*:* Herbal medicine, milk, placebo and no treatment were considered as control group, treatment vs. control group, treatment vs. different type of treatment, before vs. after treatment.

Outcome: The outcome was effect of aromatherapy on premature infant's weight.

2-4. Include studies

Both randomized and non-randomized controlled trials with prospective or retrospective design and studies published in English till December 26, 2019 were included in the search process. However, all case reports, conference articles, letter to the editor, editor's notes, animal studies, preliminary and pilot studies were excluded because of higher risk of bias and small sample size.

2-5. Selection process

The relevant studies were chosen independently by two reviewers, who initially reviewed the abstracts of searched articles and then downloaded their full text to review carefully. Finally, the articles that met the inclusion criteria were enrolled in the systematic review, and their used relevant references were also reviewed to find further studies. Any disagreement was judged by the third party.

2-6. Data extraction

Table.1 shows a checklist containing the required data for our systematic review, including name of authors, year of publication, type of intervention, type of control, sample size, age of participants, type of design, country of study, and main outcomes (*Please see the table at the end of paper*). Two independent reviewers were responsible for the data collection and analysis. The third party judged any discrepancies. We were unable to implement the meta-analysis because of high heterogeneity between the outcomes and the small number of included studies, thereby obliging us to report the results qualitatively.

2-7. Synthesis of results

Due to the difference in the included studies, study designs, lack of control groups in some studies, sample size, type of intervention used, duration of treatment, and duration of follow- up meta-analysis was not be conducted.

2-8. Quality assessment

Jadad scale (23) as a valid and reliable tool was applied to assess the quality of included studies, indicating randomization, blindness, and dropout or withdrawal. The scores of this tool range between between zero (very poor), and five (rigorous). This step was also accomplished by the two independent reviewers and any discrepancy was judged by the third party (**Table.2**).

Table-2: Quality Assessment using Jadad scale (23).

Authors, Reference	Randomization			Blinding			Withdrawals and dropouts
	Mention randomization	Appropriate method	Inappropriate Method	Mention blinding	Appropriate method	Inappropriate method	
Raimbault et al., 2007, France	☹	☹	☹	☹	☹	☹	☹
Yildiz et al., 2011, Turkey	☺	☺	☹	☹	☹	☹	☹
Schriever et al., 2018, Germany	😐	☹	☹	😐	☹	☹	☺
Iranmanesh et al., 2015, Iran	☺	☺	☹	☺	☺	☹	☹
Khodagholi et al. 2018, Iran	☺	☺	☹	😐	☹	☹	☹

☺: Yes; ☹: No; 😐: Unclear.

3- RESULTS

Finally, three studies with a total of 367 participants were enrolled in this systematic review. In Raimbault et al., over that time interval, the mean daily weight gains did not differ significantly between the infants in the milk versus water-exposure conditions (mean daily weight gain for the milk condition=33.3 g, mean for the water controls = 27.6 g) (13). In Yildiz et al.'s study, the evaluation of the mean weight of subjects at discharge and the mean weight gained between hospitalization and discharge showed that there were no significant differences between the study and control groups (24). In Schriever et al.'s study, these infants's weight did not differ significantly among three groups of Vanilla, placebo and rose (25). Iranmanesh et al.'s study showed that the mean weight of preterm infants at discharge and between hospitalization and discharge showed no significant difference between two groups impregnated pad with breast milk and control (26). In Khodagholi et al.'s study, combining milk odor and nonnutritive sucking (NNS) than single NNS were effect in achieving oral feeding and earlier discharge from the hospital (27).

4- DISCUSSION

We aimed to evaluate the association of weight of premature infant and aromatherapy. Breastfeeding is a top priority for preterm infants, according to a recent statement from the World Children's Academy. Its great benefits are still of particular importance despite its inadequacy for preterm infants and the need to enhance milk quality (28). Based on previous research, breast milk odor and taste affect preterm infant feeding behaviors as a potent initiator stimulus, as it affects the physiological process of digestion and nutrient metabolism. Beker et al. (29) in 2017 found that a regular and continuous experience of aroma and taste of breast milk as aromatherapy in preterm infants fed a tube was effective in shortening the duration of infant discharge to 36 weeks. In addition, other side effects of neonatal enteral and parenteral nutrition in the intensive care unit have been addressed with exposure to breast milk odor, including improved outcomes of the nervous system development. However, exposure to breast milk smell had no effect on weight gain in preterm infants compared to controls (2). Raimbault et al. in 2007 evaluated the impact of breast milk smell exposure under the condition that the infant was in the mother's arms and face close to the mother's nipple but without physical contact before and during infants' feeding for 35 weeks, and observed a longer sucking reflex. This exposure was compared simultaneously with preterm infants compared with water-immersed applicators. The infants exposed to the breast milk smell consumed more milk volume and had shorter discharge time (13). Yildiz et al. in 2011 in Turkey found that the aromatherapy with breast milk was an effective way to shorten the transition from gavage to total oral feeding. In fact, the breast milk smell acts as a feeding stimulant that can stimulate the tendency to consume the milk from a synthetic source, and speed up the process of digestion in preterm infants, thereby replacing gavage with oral feeding earlier and subsequently shortening the duration of hospitalization. However, no significant difference was observed in the weight gain of preterm infants compared to the control group (24). Iranmanesh et al. (26) in 2015 supported the results of a previous study by re-examining the effect of breast milk smell on shortening the time of gavage feeding, establishing oral feeding and length of stay in the neonatal intensive care unit as an interventional study. In Khodagholi et al.'s study, the 12-day reduction in the duration of hospitalization of preterm infants stimulated before and during gavage with the maternal breast

milk pad near the nostril and the possibility of oral feeding were evidence of the effectiveness of the intervention (27). Khodagholi et al. in 2018 evaluated the effect of the aromatherapy with breast milk along with nutritional supplements in 28-32 week-old infants and the group receiving only nutritional supplements without stimulation of the olfactory system on the weight gain of infant and shortening the duration of hospitalization. There was no significant difference in the mean weight between the two groups at discharge (27). Schriever et al. in 2018 investigated 27-week-old preterm infants, without any invasive ventilation, divided into three groups: rose aromatherapy, vanilla aromatherapy and placebo. The Sniffin' Sticks odor identification test kit was exposed within two centimeters of the infant's nostril for approximately ten seconds before feeding by bottle or nasogastric tube but breastfeeding and any mother-infant relationship were absent in this study. Neonatal weight was measured in the first week, second week and time of discharge. The results of this study reported that vanilla aromatherapy was more effective in shortening discharge time and improving feeding behaviors than the other two groups (25).

Neonates are able to perceive olfactory stimuli during the 28th week of intrauterine life, so that maternal nutritional patterns and different maternal peripheral aromas influence postnatal life and infant feeding patterns. For example, offspring of mothers who consumed anise during the final weeks of pregnancy showed a greater tendency to anise odor after birth than non-exposed infants. Understanding the odor of amniotic fluid before birth indicates the sensitivity of the olfactory system. This sensitivity to the differentiation of odors in the environment can affect infants' behavior patterns (30). The infants are able to differentiate important odors, such as the breast milk smell from rose odor. Studies have shown that breast milk is effective in the development of the sucking, swallowing, and breathing reflexes of infants, and is even effective in weaning preterm infants from a synthetic power source (24). Studies to date have shown that the aromatherapy has been effective physically and mentally in relieving neonatal pain in painful procedures such as venipuncture, reducing neonatal apnea, and improving feeding behaviors such as sucking. Some odors, such as breast milk smell, are particularly appealing to infants; these can be doubly effective if these odors, such as the vanilla odor, are accompanied by breast milk smell (29). Benefiting from the impact of the odors and sensitivity of the neonatal olfactory system at birth, and especially on high-risk and vulnerable groups, such as preterm infant and very low birth weight, could be the basis for more accurate and robust future studies.

4-1. Study Limitations

Small sample size and low number of studies are considered as limtataions of the systematic review.

5- CONCLUSIONS

Aromatherapy alone or a combinition of two or more aroma oils were not effective on weight in high-risk and vulnerable infant, such as preterm infant and very low birth weight, there is a need for more accurate and robust future studies.

6- CONFLICT OF INTEREST: None.

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Table-1: General demographic and clinical characteristics of the studies included in the systematic review.

Author, Year, Country, Reference	Study Design	Aromatherapy type	Outcomes	Subject	Intervention	Control	Drop out	Assessment tool	Results	Adverse effects
Raimbault et al., 2007, France, (13)	RCT	Milk-odor	Breastfeeding behavior Released from NICU	7/6	A cotton-tipped applicator moistened with the stimulus liquid was held 1 cm from the baby's nostrils	Water	-	Hand-held VCR	The odor of mother's milk had a positive effect on sucking behavior and milk ingestion of preterm babies.	-
Iranmanesh et al., 2015, Iran, (26)	RCT	Breast milk smell	Transition time from gavage to oral feeding and hospital stay	46/46	A 1-mL volume of breast milk was poured on the cotton and placed near the infant's nasal septum (1.5-2 cm)	No intervention	-	Self-records	Preterm infants exposed to breast milk odor during gavage feeding made a transition to oral feeding sooner	-
Schriever et al., 2018, Germany, (25)	Prospective randomized controlled	Vanilla and Rose odor	Duration between study entry and complete oral food intake defined as solely oral feeding for at least 24 hours	150	Odors were presented to the infants before each feeding. The "Sniffin' Sticks" were used for odor	Odorless probe	10%	Self-records	Odor stimulation with vanilla has an impact on oral feeding in premature infants	-
Yildiz et al., 2011, Turkey, (24)	Prospective experimental study	Milk-odor	Transition time from gavage to oral feeding and hospital stay	40/40	The stimulus of breast milk started with feeding by placement of a sterile pad soaked in breast milk 2 cm from the infant nose.	No intervention	-	Self-records	Stimulation with breast milk odor is an effective method for decreasing transition of preterm infants from gavage	-
Khodagholi et al., 2018, Iran, (27)	RCT	Milk-odor	Time of achieving oral feeding, hospital discharge, the duration of hospital stay, daily weight gain and weight at discharge	32	The olfactory stimulations were performed with cotton pads impregnated with breast milk from the infant's mother and held around 2-3 cm from the infant's nose.	Nonnutritive sucking	-	Self-records	Combining milk odor and nonnutritive sucking as two important methods in achieving oral feeding	-

RCT: randomized controlled trial; NICU: neonatal intensive care unit.