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Comparison of the Effect of Aloe Vera Extract, Breast Milk, Calendit-E, Curcumin, Lanolin, Olive Oil, and Purslane on Healing of Breast Fissure in Lactating Mothers: A Systematic Reviwe

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Abstract

Background: Sore nipples are a common problem in breast-feeding women which can cause early cessation of breast-feeding. We aimed to evaluate the effect of Aloe Vera extract, breast milk, Calendit-E, Curcumin, Lanolin, Olive oil, and Purslane on healing of breast fissure in lactating mothers.

Materials and Methods: All clinical trials evaluating the effect of Aloe Vera extract, breast milk, Calendit-E, Curcumin, Lanolin, Olive oil, and Purslane on healing of breast fissure in lactating mothers were searched on the online databases of Scopus, EMBASE, Cochrane, Web of Science and Medline with no language or time restrictions using the combination related keywords of Mesh. Study selection was done by two reviews.

Results: Six studies were included here with a total sample size of 546 subjects. The results showed that aloe vera gel and Purslane cream are more effective than lanolin ointment for healing sore nipples. Calendit-E cream, and aloe vera gel were more effective than breast-fed milk for treating sore nipples. However, no significant difference was observed between the mother's breast milk group and olive oil. Concerning the limited side effects, as well as greater impact and antimicrobial activity of curcumin in the short term, it was suggested to use curcumin for treating sore nipples.

Conclusion: Aloe vera gel and purslane cream, Calendit-E cream, and curcumin can have beneficial effects on improving sore nipples. Usage of these therapeutic methods is suggested to improve sore nipples given their low cost and limited side effects.

Key Words: Breast Fissure, Mothers, Olive Oil, Aloe Vera Extract, Curcumin, Purslane.

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1- INTRODUCTION

Exclusive feeding with breast-feeding is considered as the best nutrition for a child up to six months of age. This has been one of the most important recommendations of the World Health Organization and UNICEF over the past few years (1). If globally every child is fed with breastmilk exclusively within the first six months of life, the lives of around 1.3 million people will be saved annually (2). Meanwhile, sore nipples are one of the common complaints among breast-feeding women and the second cause of early cessation of breast-feeding after failure to supply adequate milk. It is one of the main reasons of tendency of mothers to use artificial feeding (3). Cessation of breast-feeding deprives the infant of the major nutrients, growth factors, and important immunological components in the breastmilk. Further, cessation of breast-feeding increases post-delivery hemorrhage as well as the risk of ovarian and breast cancer for the mother (4).

Prevalence of sore nipples has been reported to be 34-96% (5), which can last up to six weeks for some women; its major incidence occurs between the third and seventh weeks post-delivery (6). Several predictive factors have been mentioned for sore nipples including poor attachment to the breast, improper position of the child during breast-feeding, wrong suckling because of functional or organic reasons, inappropriateness of the nipple for breast-feeding, unsuitable hygiene of the nipples, atopic skin, or tight underwear (7). The healing of sore nipples is challenging because of frequent stimulation through the infant suckling and exposure to the oral flora of the infant. In case of failure of treatment, it may lead to problems such as pain and bleeding (8). It can also function as a site for entrance of bacteria, thereby causing edema and mastitis (9). Therefore, treatment of sore nipples immediately and effectively is an important factor in enhancing the mother's confidence in breast-feeding and its persistence (10). In recent years, various treatments have been proposed with different effects for sore nipples. They include warm water compress and teabag, curcumin, lanolin, antiseptic sprays, corticosteroids, hydrogel, glycerin, Epicar ointment (honey therapy), phototherapy, silver caps, menthol extract, aloe vera, and, in many cultures, the breastmilk itself (11, 12). Today, considering the failure of therapeutic methods, researchers are working on using alternative medicine, where herbal medicine is approved by around 80% of people as a branch of alternative medicine (13). Olive oil and aloe vera are among analgesic and anti-inflammatory herbal drugs (13). In traditional medicine, usage of olive oil promotes wound healing (14).

In some studies, the effectiveness of olive oil on preventing sore nipples has been confirmed (15). Aloe vera enjoys healing, anti-inflammatory, analgesic, antiviral, antibacterial, antifungal, and moisturizing effects (16). In some studies, its analgesic and anti-inflammatory effects against sore nipples (17, 18) have been confirmed. The milk obtained from the mother's breasts has also been recommended for treating sore nipples. It is because the mother's milk has both softening and antiseptic properties and can be effective for treatment of sore nipples (19).

Dripping some drops of mother's milk on the nipple has been confirmed by the Ministry of Health and Medical Education as one of the solutions for treatment of sore nipples (20). Lanolin is the common treatment for sore nipples (21). However, different papers have mentioned contradictory effects for lanolin on sore nipples (22, 23). Burning, itching, and infection of sore nipples are among the complications of lanolin, as mentioned in some studies (24, 25). Herbs have a long history for wound treatment (26). One of these herbs is porulaca (27). The anti-

inflammatory, analgesic, and restorative properties of this herb are attributed to flavonoid, tannin, saponin, and terpenoids present in it (28). Turmeric is one of the oldest herbs belonging to the ginger family with the scientific term of Curcuma longa, whose active ingredient is curcumin. This plant has been traditionally used in Asia for treatment of skin diseases and wound healing (29). One of the properties of curcumin making it suitable for therapeutic purposes is its low toxicity (30). Calendit-E cream is composed of a mix of Hydroalcohol extract of two plants: Calendula Officinalis known as pot marigold along with Echinacea Angustifolia, or narrow-leaved purple coneflower. These two compounds synergistically resolve skin inflammation and are very effective for wound healing.

These two herbs have no proven toxic effect and neither are allergic. Their consumption during pregnancy and breast-feeding has no established contraindication. Considering the established impact of the extract of Echinacea herb present in this cream causing increased rate of wound healing, promoting treatment of wounds, anti-inflammatory properties, antibacterial properties, this plant has no harmful effect for the body (31-34).

Considering the high prevalence of sore nipples and since the pain in sore nipples is one of the important factors for cessation of breast-feeding by mothers, and regarding absence of any agreed treatment for this disease, the present study has been performed with the aim of reviewing the research conducted in this regard; so we aimed to evaluate the effect of some non-pharmacological methods (Aloe Vera Extract, Breast Milk, Calendit-E, Curcumin, Lanolin, Olive Oil, and Purslane) on healing of breast fissure in lactating mothers.

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. Eligibility criteria

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

Participant: Lactating Mothers.

Interventions*:* Any type of treatment of breast fissure with Aloe vera OR Breast Milk OR Calendit-E Cream OR Calendula officinalis OR Curcumin OR Lanolin OR Purslane OR Portulaca OR Olive oil as the primary treatment.

Comparators*:* Treatment vs. control group, treatment vs. different type of treatment, before vs. after treatment.

Outcome: Reduction of breast fissure in lactating mothers.

2-3. Included studies

Randomized controlled trials (RCT), clinical studies both randomized and nonrandomized either retrospective or prospective. Due to the limited number of published RCT in the literature other types of clinical studies were included. Pilot, preliminary and case report studies were not included due to limited sample size and higher risk of bias. Studies published in Persian and English till November 2019.

2-4. Search strategy

All clinical trials evaluating the effect of Olive Oil, Aloe Vera Extract, Pot marigold, Curcumin, and Purslane on breast fissure were searched on the electronic databases of Scopus, EMBASE, Cochrane, Web of Science and Medline (via PubMed) with no language or time restrictions (till August 2019) using the combination keywords of: (Sore OR

Nipples OR, Nipple OR Treatment OR Therapeutics OR Therapy OR Trauma OR Wound OR Fissure) AND (Breastfeeding) AND (Aloe vera OR OR Milk OR Milk, Human OR Breast Milk OR Calendit-E Cream OR Calendula officinalis OR Curcumin OR Lanolin OR Purslane OR Portulaca OR Olive oil) and their Persian synonyms and all their possible combinations, were searched in the national databases (Magiran, SID, and Iran.Doc). PRISMA flow diagram was used to show the process of study selection (**Figure.1**). Two independent researchers performed the search process and a supervisor judged any disagreement in this regard.

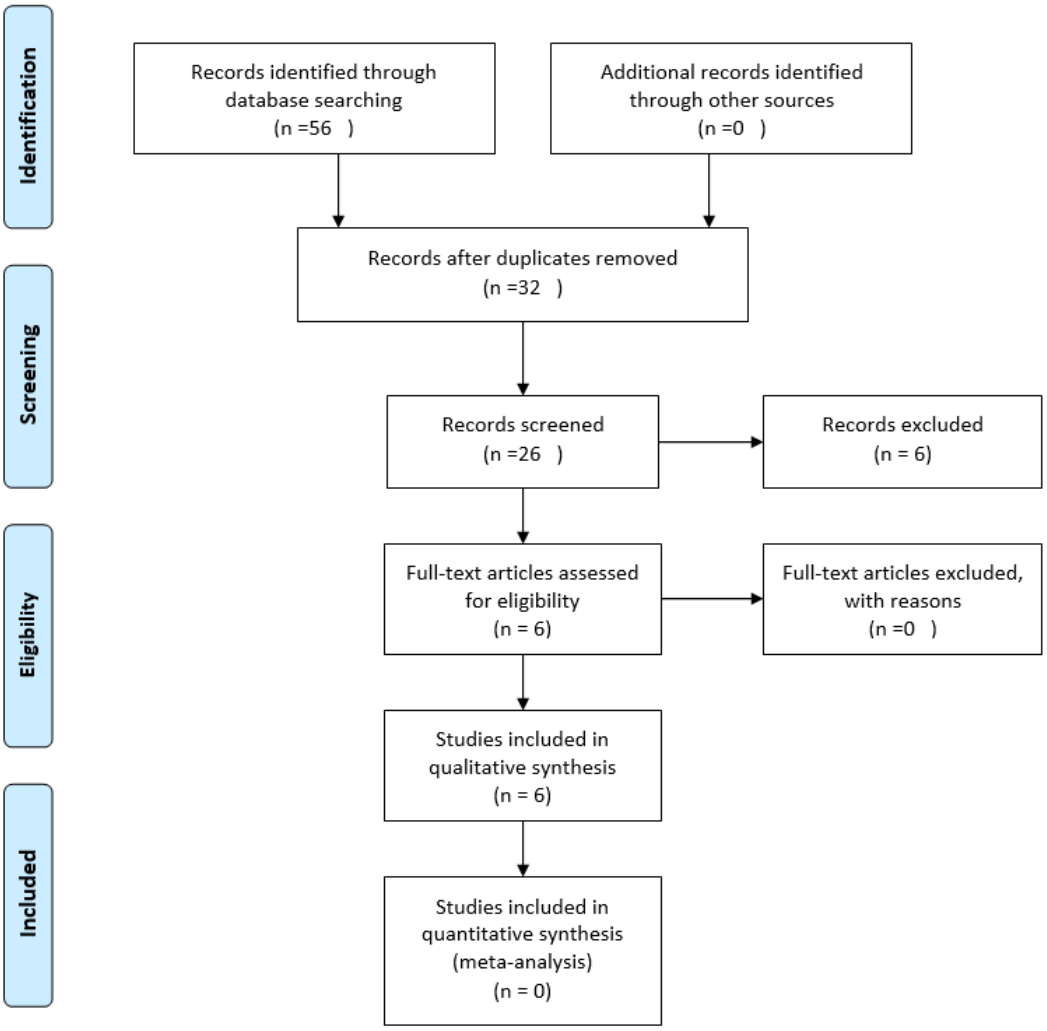

Fig1: PRISMA flowchart.

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 first author, year of

publication, study design, sample size, intervention period, intervention results, drop out, and assessment tool. 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 forcing us to report the results qualitatively.

2-7. Quality assessment

Jadad scale (35) 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 0 and 5. This step was also accomplished by the two independent reviewers and any discrepancy was judged by the third party (**Table.2**).

Table-1: General characteristics of studies included in systematic review.

Author, Year, Reference	Study design	Sample size	Intervention period	Intervention	Control	Drop out	Assessment tool	Results	Adverse effects
Shinizadeh et.al, 2015,(37)	RCT	84	two times a day for seven days	Curcumin	Breast milk	-	Storr scale	Curcumin was recommended for treatment of nipples fissure.	-
Saeidi et al., 2015, (39)	RCT	100	three times a day for seven days	Aloe Vera gel	Lanolin	-	Storr scale	Aloe Vera is more effective than lanolin on nipple soreness healing.	-
Kazemirad et.al, 2013, (36)	RCT	82	three times a day for seven days	Calendit -E	Breast milk	-	Storr scale	Calendit -E is more effective than breast milk on nipple soreness healing.	-
Tafazoli et.al, 2010, (9)	RCT	100	three times a day after breastfeeding	Olive oil	Lanolin	-	Storr scale	Aloe Vera is more effective than lanolin on nipple soreness healing.	-
Niazi et.al., 2018,(38)	RCT	86	three times a day for seven days	Purslane	Lanolin	6%	Storr scale	Purslane cream was more effective in the treatment of nipple pain.	-
Eshghizade et.al., 2016,(40)	RCT	90	after breastfeeding for seven days	Olive oil and Aloe Vera	Breast milk	-	Storr and visual analog scale	Aloe Vera is more effective than Olive oil and breast milk.	-

RCT: randomized controlled trial.

Table-2: Quality Assessment using Jadad scale (35).

Authors, Year, Reference	Randomization			Blinding			Report of dropping out
	Mention randomization	Appropriate method	Inappropriate Method	Mention blinding	Appropriate method	Inappropriate method	
Tafazoli et.al, 2010, (9)	☹	☹	☹	☹	☹	☹	☹
Kazemirad et.al, 2013, (36)	☺	☺	☹	😐	☹	☹	☹
Sheinizadeh-Emadi et al., 2015, (37)	☺	☺	☹	☹	☹	☹	☹
Niazi et al., 2018, (38)	☺	☺	☹	☺	☺	☹	☺
Saeidi et al., 2015, (39)	☹	☹	☹	☹	☹	☹	☹
Eshghizade et.al., 2016,(40)	☺	☺	☹	☺	☺	☹	☹

☺: Yes; ☹: No; 😐: Unclear.

3- RESULTS

Six clinical trial studies with a total sample size of 546 subjects were included here. Kazemirad et al. (2012) performed a single blind randomized clinical trial study. The research subjects consisted of 82 breast-feeding women with sore nipples. The samples were randomly categorized into two groups: Calendit-E cream and expressed breastmilk, who underwent treatment for one week. Both of the groups received training about the proper way of breast-feeding as well as the method of applying the cream or breast milk. The results showed that reduction in the severity of sore nipples on the third day did not differ significantly between the two groups. However, on the seventh day in Calendit-E cream, this reduction was greater and significant. Thus, Calendit-E cream was more effective than breastmilk for treatment of sore nipples (36).

Sheinizadeh-Emadi et al. (2015) in a randomized clinical trial study examined 88 breast-feeding mothers with sore nipples by dividing them randomly into two equal groups: treatment with curcumin group and leaving milk drop on the mother’s breast group. On the third day, the mean score of sore nipples was significantly lower in the curcumin group compared to the group in which the mothers' breast milk drop was remained. Further, the mean difference of the sore scores was significant before and treatment with the third day as well as with the seventh day post-treatment in both groups (37). Hence, curcumin and mother's milk are both effective for the treatment of sore nipples. However, considering the limited side effects as well as greater antimicrobial activity and impact of curcumin in the short run, it was suggested to use curcumin for treatment of sore nipples. Tafazoli et al. (2010) conducted a single blind two-group clinical trial study entitled "comparing the impact of Aloe vera gel and Lanolin ointment on the treatment of sore nipples", where 50 mothers with sore nipples were randomly assigned into two groups: treatment with Lanolin ointment and aloe vera gel. Further, both groups received treatment on proper techniques of breast-feeding and method of drug usage. There was a significant difference between the two groups in terms of the mean score of sore nipples on the third and seventh days, where aloe vera gel was more effective than Lanolin ointment for treating sore nipples (9). Niazi et al. (2018) performed a double-blind randomized clinical trial study on 86 breast-feeding women with sore nipples and Mashhad. The subjects were randomly assigned into two groups: purslane cream and lanolin (n=43 in each group). Subjects of both groups were trained on the proper way of breast-feeding and method of applying the drug. They were asked to continue the treatment for one week, three times a day.

Based on the results of Mann-Whitney test, the two groups before the intervention were homogeneous in terms of the mean score of sore nipples. However, there was a statistically significant difference between the two groups on the third and eighth days; improvement was faster in the purslane cream than in the lanolin group (38). Saeidi et al. (2009) in Mashhad did a clinical trial study on breast-feeding mothers and performed the sampling as nonrandomized and purposeful. The samples were randomly assigned into two groups: aloe vera and lanolin (n=50 in each group). There was a significant difference between the two groups between the third and seventh days; the score of the nipple pain on the third and seventh days diminished considerably. They concluded that aloe vera is more effective than lanolin for mitigating the pain of sore nipples (39). Eshgizade et al. (2016) conducted a clinical trial study in which 90 breast-feeding mothers with sore nipples were randomly assigned into three 30-subject groups. Group I mothers

received 0.5 ml of olive oil, Group II received 0.5 ml of aloe vera extract plus 3-4 drops of their own milk three times a day (they rubbed it on their nipples and areola after every breast-feeding). Group III rubbed 3-4 drops of their own milk on the nipple and areola after every breast-feeding. At the end of the intervention, there was a significant difference between the three groups in terms of severity of pain and sore nipples; the group receiving aloe vera extract experienced less pain and sore nipples compared to the other groups. No significant difference was found between the mother's breast milk and olive oil groups (40).

4- DISCUSSION

In recent years, various treatments with different impacts have been propounded for sore nipples. They include warm water compress and teabag, curcumin, lanolin, antiseptic sprays, corticosteroids, hydrogel, glycerin, Epicar ointment (honey therapy), phototherapy, silver caps, menthol extract, and in many cultures breastmilk (11, 12). Meanwhile, the special attention paid to progressive use of aloe vera, purslane, and olive oil in all these studies highlights the importance of these three treatment. The results of this review study showed that aloe vera gel and purslane cream are more effective than lanolin ointment for treating sore nipples. Calendit-E cream, menthol, and aloe vera are more effective than the breast milk itself for treatment of sore nipples. However, no significant difference was observed between the mother's breast milk and olive oil. In a study performed by Tafazoli et al. for comparing the impact of aloe vera gel and lanolin ointment on treating sore nipples, 50 mothers with sore nipples were randomly assigned into two groups: treatment with lanolin ointment and aloe vera gel. There was a significant difference between the two groups in terms of the mean score of sore nipples on the third and seventh days, where aloe vera gel was more effective than Lanolin ointment for treating sore nipples (9). In addition, in the studies by Eshgizade et al. (40), and Alamolhoda et al. (17), the effect of aloe vera on sore nipples has been examined. Aloe vera is an herb traditionally used since 1500 B.C. in many countries including Greece, China, and Mexico. For centuries, it has been used as a traditional drug for different diseases and skin lesions (12). Further, aloe vera has anti-inflammatory, antiseptic, antibacterial, antiviral, and antifungal effects. It is also nutritious for tissues and causes enhanced immunity and prevention of itching and skin irritation. On the other hand, an established effect has been presented for the collagen and aldehydrate content and thus rapid wound healing. The effect of aloe vera on wound healing has been found in different papers for various diseases including ulcerative colitis, acne, dermatitis, psoriasis, oral ulcers, diabetic ulcers, herpes, and even bedsores (9). By inhibiting interleukin-6 and interleukin-8, aloe vera is effective in reducing adhesion of leukocytes, increasing the level of interleukin-10, and reducing the level of tumor necrotizing factor-alpha for inhibiting inflammatory reactions.

In animal models, aloe vera has been used for treatment of diabetes, wound healing, tumors, and inflammatory bowel diseases both orally and parenterally (41). Lanolin, by creating moisture, prevents new ulcers, which promotes wound healing by increasing the epithelial regrowth. Ester is the active ingredient of lanolin. Esters possess wound healing properties in a moist environment. Further, they are anti-inflammatory, antibacterial, and protective for damaged breast skin (42). Purslane is an herb with anti-inflammatory, analgesic, and restorative properties because of containing flavonoid, tannin, saponin, and terpenoids (28), for which no proximity has been reported (43). Niazi et al. (2016) performed a double-blind randomized

clinical trial study on 86 breast-feeding women with sore nipples in Mashhad. The subjects were randomly assigned into two groups: purslane cream and lanolin (n=43 in each group). The proper way of breast-feeding and method of applying the drug were trained to the subjects of both groups. They were asked to continue the treatment for one week, three times a day. Based on the results, the two groups before the intervention were homogeneous in terms of the mean score of sore nipples. However, there was a statistically significant difference between the two groups on the third and eighth days; improvement was faster in the purslane cream than in the lanolin group (38).

Olive oil compounds including oleuropein with antioxidant and anti-inflammatory properties, polyphenol with free radical and cell repair properties, and Oleocanthal with prostaglandin synthesis inhibiting properties are analgesic and anti-inflammatory. The anti-inflammatory effects of aloe vera are attributed to presence of salicylic acid (effective in inhibiting formation of bradykinin and histamine), and oxidation of arachidonic acid (effective in the synthesis of prostaglandin). In a randomized clinical trial, it was found that olive oil, aloe vera extract, and breastmilk resulted in diminished severity of pain of sore nipples and long breast-feeding mothers, but aloe vera extract was more effective than olive oil and breastmilk (40). The results of a study to determine the impact of Hydroalcohol extract of curcumin showed that curcumin and breastmilk are both effective for the treatment of sore nipples. However, considering limited side effects as well as greater antimicrobial activity and impact of curcumin in the short-term, it was suggested to use this drug for treating sore nipples (37). Turmeric is one of the oldest herbs belonging to the ginger family with the scientific term of Curcuma longa, whose active ingredient is curcumin. Curcumin covering 6-70% of the raw turmeric extract has different properties. They include anti-inflammatory and analgesic, antibacterial, antifungal, antioxidant, and healing properties (44). Topical use of curcumin even at low doses has beneficial effects on redness, inflammation, and pain of the skin soft tissue. Alcoholic extract of turmeric as well as ointments made of curcumin significantly improve skin lesions, and no special complication has been reported for its topical usage (45). Further, breastmilk contains fat-soluble vitamins especially vitamins A and E, causing lubrication of the skin and wound healing. There is usually no need to cleanse the nipple after rubbing milk on it and before the next breast-feeding, as it does not cause allergy (46). Leaving one or two drops of breastmilk on damaged nipples is one of the oldest therapeutic methods.

On the other hand, some studies have shown that complete improvement of sore nipples symptoms such as pain and soreness can be achieved 3 to 4 weeks after initiating the treatment by leaving the breast milk drops, which is considered a long course for improving the soreness. Accordingly, one third of mothers who particularly experience these symptoms at six weeks post-delivery become psychologically and clinically disturbed, and change their infant feeding method alternatively and use sugar water or powdered milk (47). Considering the effects of curcumin in accelerating nipples wound healing, it has been suggested to use this drug as a sore nipple healing promoting and accelerating agent alongside training the proper method of breast-feeding as well as application of the breastmilk drop in breast-feeding women (37). Comparing the effect of Calendit-E cream and the mothers' breast milk on treating sore nipples, a research found that Calendit-E cream is more effective than breastmilk for treating sore nipples.

Calendit-E cream is composed of a mix of Hydroalcohol extract of two plants: Calendula Officinalis known as pot marigold along with Echinacea Angustifolia, or narrow-leaved purple coneflower. These two compounds synergistically resolve skin inflammation and are very effective for wound healing (36). These two herbs have no proven toxic effect and are not allergic. Their consumption during pregnancy and breast-feeding has no established contraindication (29, 30).

4-1. Limitations of the study

The methodologic quality of some of the studies examined in this systematic review was low. The defects included lack of or unsuitable report on randomized allocation sequence, lack of or inappropriate report on blinding, lack of intention to treat analysis. Accordingly, it is proposed that future studies be designed and report their findings based on consort. Another limitation was limited number of studies and their low sample size, highlighting the need forfurther studies with larger sample sizes in this regard.

5- CONCLUSION

Aloe vera gel and purslane cream are more effective than lanolin ointment for treating sore nipples. Calendit-E cream also has beneficial effects on improving sore nipples. Considering limited side effects, as well as greater antimicrobial activity and impact of curcumin in the short-term, it was suggested to use curcumin for treating sore nipples. Considering the interest of patients in alternative medicine and the inexpensiveness of these therapeutic methods, use of their beneficial effects is suggested for improving sore nipples. The findings of this study should be interpreted with caution because of great heterogeneity across studies as well as limited number of studies and small sample size.

6- CONFLICT OF INTEREST: None.

7- REFERENCES

1. Aghajani F, Radmehr M. Infant Temperament in Exclusive Breastfeeding and Dominant Formula Feeding. Journal of Nursing Education. 2019;8(4):19-26.

2. Hosseini F, Rasekhi A, Lamyian M. Factors associated with exclusive breastfeeding among primiparous women. Journal of Nursing Education (JNE). 2019;8(2):52-7.

3. As'adi N, Kariman N, Mojab F, Pourhoseingholi MA. The effect of Saqez (Pistacia atlantica) ointment on the treatment of nipple fissure and nipple pain in breastfeeding women. Electronic physician. 2017;9(8):4952.

4. Campos TM, dos Santos Traverzim MA, Sobral APT, Bussadori SK, Fernandes KSP, Motta LJ, et al. Effect of LED therapy for the treatment nipple fissures: Study protocol for a randomized controlled trial. Medicine. 2018;97(41).

5. Shahrahmani N, Akbari SAA, Mojab F, Mirzai M, Shahrahmani H. The Effect of Zizyphus Jujube Fruit Lotion on Breast Fissure in Breastfeeding Women. Iranian journal of pharmaceutical research: IJPR. 2018;17(Suppl):101.

6. Cunningham F. Williams obstetrics. New York: McGraw Hill Professional; 2014. P.674.

7. Marrazzu A, Sanna MG, Dessole F, Capobianco G, Piga MD, Dessole S. Evaluation of the effectiveness of a silver-impregnated medical cap for topical treatment of nipple fissure of breastfeeding mothers. Breastfeeding Medicine. 2015;10(5):232-8.

8. Niazi A, Yousefzadeh S, Rakhshandeh H, Esmaily H, Askari VR. Promising effects of purslane cream on the breast fissure in lactating women: A clinical trial. Complementary therapies in medicine. 2019;43:300-5.

9. Tafazoli M, Saeedi R, Gholami Robatsangi M, Mazloom R. Aloevera gel Vs. lanolin ointment in the treatment of nipple sore: a randomized clinical trial. Tehran University Medical Journal.2010;67(10):699-704.

10. Niazi A, Yousefzadeh S, Rakhshandeh H, Esmaeily H. The Effect of nipple soreness treatment with Purslane Cream and Lanolin on Frequency and duration of Breastfeeding in nursing mothers: A Randomized Clinical Trial. Journal of Midwifery and Reproductive Health. 2019;7(1):1527-35.

11. Asaadi N, Kariman N, Shahrahmani H, Ghalandari S, Khodakarami N. A systematic review of clinical trials in the treatment of sore nipple and nipple pain in breastfeeding women. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2016;19(6):22-33.

12. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The effect of aloe vera clinical trials on prevention and healing of skin wound: A systematic review. Iranian journal of medical sciences. 2019;44(1):1.

13. Iranian Ministry of health and medical education. Deputy ministry for food and drug. Iranian herbal pharmacopoeia. Tehran: Iranian Ministry of Health and Medical Education Pub; 200.

14. Behmanesh F, Aghamohammadi A, Zeinalzadeh M, Khafri S. Effects of olive oil sitz bath on improvement of perineal injury after delivery. koomesh. 2013; 14 (3): 309-15.

15. Gungor AN, Oguz S, Vurur G, Gencer M, Uysal A, Hacivelioglu S, et al. Comparison of olive oil and lanolin in the prevention of sore nipples in nursing mothers. Breastfeed Med. 2013;8(3):334-5.

16. Nejatzadeh-Barandozi F. Cytogenetical Survey of Aloe vera populations in Iran. NCMBJ. 2014; 4 (13): 37-42.

17. Alamolhoda SH, AmirAliAkbari S, Baghban AA, Esmaili S. Effects of Aloe vera gel on breast fissures in breastfeeding women. Pajoohandeh Journal. 2014;19(1):13-7.

18. Tafazoli M, Saeedi R, Gholami Robatsangi M, Mazloom R. Aloevera gel Vs. lanolin ointment in the treatment of nipple sore: a randomized clinical trial. Tehran University Medical Journal. 2010;67(10): 699-704.

19. Gharekhani P, Sadatian SA. Cardinal manifestations and management of diseases obstetrics (CMMD series 11). 5th ed. Tehran: Noordanesh Pub; 2009.pp.333-9.

20. Valafar Sh. The integration of maternal health care (Services outside the hospital) special midwife-general physician.5th ed. Tehran: Sayah Roshan; 2008.

21. Cable B, Stewart M, Davis J. Nipple wound care: a new approach to an old problem. J Hum Lact 1997; 13(4):313-8.

22. Jackson KT, Dennis CL. Lanolin for the treatment of nipple pain in breastfeeding women: a randomized controlled trial. Matern Child Nutr 2016;13: 3-14.

23. Abou-Dakn M, Fluhr JW, Gensch M, Wöckel A. Positive effect of HPA lanolin versus expressed breastmilk on painful and damaged nipples during lactation. Skin Pharmacol Physiol 2011; 24(1):27-35.

24. Dennis CL, Schottle N, Hodnett E, McQueen K. An all-purpose nipple ointment versus lanolin in treating painful damaged nipples in breastfeeding women: a randomized controlled trial. Breastfeed Med 2012; 7(6):473-9.

25. Dodd V, Chalmers C. Comparing the use of hydrogel dressings to lanolin ointment with lactating mothers. J Obstet Gynecol Neonatal Nurs 2003; 32(4):486-94.

26. Kumar B, Vijayakumar M, Govindarajan R, Pushpangadan P. Ethnopharmacological approaches to wound healing exploring medicinal plants of India. J Ethnopharmacol 2007; 114(2):103-13.

27. Niazi A, Yousefzadeh S, Rakhshandeh H, Esmaeili H, Habibollah. Comparison of purslane cream and lanolin on nipple pain among breastfeeding women: a randomized clinical trial. Iran J Obstet Gynecol Infertil 2018; 20(12):77-85.

28. Wanyin W, Liwei D, Lin J, Hailiang X, Changquan L, Min L. Ethanol extract of Portulaca oleracea L. protects against hypoxia-induced neuro damage through modulating endogenous erythropoietin expression. J Nutr Biochem 2012; 23(4):385-91.

29. Fallah Huseini H, Zahmatkash M, Haghighi MA. Review on pharmacological effects of Curcuma longa (Turmeric). Journal of Medicinal Plants. 2010; 9(33): 3-15.

30. Hemati S, Saeedi A. Clinical evaluation of oral curcumin in prevention of acute dermatitis

in breast cancer radiotherapy. J of Isfahan Medical School.2011;29(152):1216-23.

31. Jeschke E, Ostermann T, Lüke C, Tabali M, Kröz M, Bockelbrink A, et al. Remedies containing Asteraceae extracts: A prospective observational study of prescribing patterns and adverse drug reactions in German primary care. Drug Safety: An International Journal of medical Toxicology and Drug Experience. 2009; 32 (8) 691-706.

32. Gruenwald J et al (2004). PDR for Herbal Medicines. 3rd edition. New Jersey. Thomson PDR Montvale. 267-74. Available at: https://naturalingredient.org/wp/wp-content/uploads/Pdfor_Herbal_Medicines.pdf.

33. Muley BP Khadabadi SS Banarase NB. Phytochemical constituents and pharmacological activities of Calendula Officinalis Linn (Asteraceae): A review. Tropical Journal of Pharmaceutical Research.2009; 8 (5) 455-65.

34. Zargari A. Medicinal Plants. 6th edition. Volume 3. Tehran Iran. Tehran University Publishing. 1997; pp: 1 - 5 & 185 - 193. (Persian)

35. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996; 17(1):1-12.

36. Kazemirad M, Khodakarami N, Kazemi M, Salamzadeh J, Nasiri N, Moattar F. Comparison Between Calendit-E Cream and Expressed Breast Milk in Nipple Pain Treatment in Breastfeeding Women. Modern Care Journal 2012; 9(3):199-207.

37. Sheinizadeh-Emadi S, Ehsani P, Dahanzadeh S, Haghighizadeh M. Comparison evaluation of Curcumin (Curcuma longa extract)with the application of expressed breast milk in the treatment of nipple cracks in lactating primiparous women: A randomized clinical trial. Journal of Clinical Nursing and Midwifery. 2015; 4 (2):11-9.

38. Niazi A, Yousefzadeh S, Rakhshandeh H, Esmaily H. Comparison of the effects of Purslane cream and Lanolin for treatment of Breast Fissure on Lactation Self-efficacy: A Randomized Clinical Trial. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2018;21(8):75-83.

39. Saeidi R, Tafazoli M, Gholami M, Mazloom R. New treatment for nipple soreness in breastfeeding mothers: A clinical trial study. Iranian Journal of Neonatology IJN, 2015; 6(2): 48-51. doi: 10.22038/ijn.2015.4495.

40. Eshgizade M, Basiri Moghaddam M, Mohammadzadeh Moghaddam H, Mahmoudian A, Mina M. Comparison of the Effect of Olive Oil, Aloe Vera Extract and Breast Milk on Healing of Breast Fissure in Lactating Mothers: A Randomized Clinical Trial. Qom University of Medical Sciences Journal. 2016; 10(3):19-27.

41. Sabzaligol M, Safari N, Baghcjeghi N, Latifi M, Bekhradi R, Taghizadeh M, et al. The effect of Aloevera gel on prineal pain & wound healing after episiotomy. Complementary Medicine Journal of faculty of Nursing & Midwifery. 2014;4(2):766-75.

42. Shanazi M, Khalili AF, Kamalifard M, Jafarabadi MA, Masoudin K, Esmaeli F. Comparison of the effects of lanolin, peppermint, and dexpanthenol creams on treatment of traumatic nipples in breastfeeding mothers. Journal of caring sciences. 2015;4(4):297.

43. Yen G, Chen H, Peng H. Evaluation of the cytotoxicity, mutagenicity and antimutagenicity of emerging edible plants. Food and Chemical toxicology. 2001;39(11):1045-53.

44. Huseini HF, Zahmatkash M, Haghighi M. A review on pharmacological effects of Curcuma longa L.(turmeric). Journal of Medicinal Plants. 2010;9(33):1-182.

45. Mehrabani D, Farjam M, Geramizadeh B, Tanideh N, Amini M, Panjehshahin MR. The healing effect of curcumin on burn wounds in rat. World journal of plastic surgery. 2015;4(1):29.

46. Smith JW, Tully MR. Midwifery management of breastfeeding: using the evidence. Journal of midwifery & women's health. 2001;46(6):423-38.

47. Essa RM, Ebrahim EM. Effect of breast milk versus therapeutic honey (Apicare) on cracked nipples' healing. Life Sci J. 2013;10(1):2137-47.