



Promising effects of purslane cream on the breast fissure in lactating women: A clinical trial



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ABSTRACT

Objectives: The traditional uses of *Portulaca oleracea* L. (purslane) with anti-inflammatory and anti-cancer activity as well as anti-oxidants properties were expressed previously. This is a double-blind randomized clinical trial to evaluate the protective effects of purslane cream on the nipple fissure.

Methods: After expressing the goals and methods of the study and obtaining written consent from 86 lactating women with nipple fissure, they were randomly divided into two groups: 43 in purslane cream group and 43 in lanolin ointment group. The score of nipple fissure before the intervention and on the third and eighth day after the study was measured using the Stour scale.

Results: The mean score of left and right breast fissures in the group of treatment with lanolin group similar to the group of treatment with purslane cream showed a significant decrease at the third day and eighth day ($P=0.001$). Mann-Whitney test comparing mean score of the fissure between two groups showed that two groups were homogeneous before the intervention, but there was a significant difference between two groups on the third and eighth days ($p < 0.001$). The recovery process occurred faster in the group of treatment with purslane cream.

Conclusion: We showed that the use of purslane cream without any complications could accelerate the repairing of nipple fissure. Based on this clinical trial, purslane cream (2% w/w) can be used as an accelerator for improving the nipple fissure in lactating women.

1. Introduction

Undoubtedly, breast milk is known as the best sources for baby's food during the first six months of the birth, that has a crucial role in promoting the mental health, physical growth, children's favorable development and emotional relationships in the society.^{1,2} The world health organization (WHO) and united nations international children's emergency fund (UNICEF) have recommended the exclusive breastfeeding during the first 4–6 months of infancy and continuing until the age of 2 years along with complementary nutrition.³ According to the recent estimation by WHO, 98% of women around the world are physically capable of breastfeeding,⁴ while 35% of children are only breastfed between the birth and the fifth month.⁵ Nipple fissure is one

of the main causes of early lactation stopping. The highest incidence of nipple fissure is observed between the 3rd and 7th days after childbirth, therefore treatment during this period can help to maintain exclusive breastfeeding.^{6,7} According to the available reports, 80–90% of lactating women experience nipple wounds and damage.^{8,9}

Nipple fissure repairing is a difficult process due to repeated irritation by baby sucking and exposing to the baby's oral flora. In the absence of effective treatment, it may lead to problems such as pain and bleeding.^{10,11} The most common cause of breast fissure is improper positioning of the baby at the breast.^{12,13} Nipple infection with *Staphylococcus aureus* and *Candida albicans*, strong or weak sucking of the baby, short frenulum, the tiny tongue of an infant, nipple washing with soap, no exposure to sunlight, vitamin deficiency, use of pacifier are

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from other probable factors causing the nipple trauma and pain.^{14–16}

Effectiveness and rapid treatment of this problem are paid more attention and considered an important factor in the success of breastfeeding and the prevention of complications such as mastitis and breast abscess.¹⁷ There are several studies introducing the new treatment with various effects on nipple fissure such as hot water compressors, using the different medicinal plants, lanolin, antiseptic sprays, anti-inflammatory agents glucocorticosteroids, hydrogel, glycerin, phototherapy, and silver cap, as well as in many cultures, breast milk is used to treat breast fissure that none of them have therapeutic superiority pain.^{2,18–20} Lanolin is the most common treatment for nipple fissure that by creating a dermatological humid environment, prevents wound and by accelerating the epithelial re-growth leads to improvement of the nipple fissure.²¹ The controversial effects of lanolin effect on nipple fissure treatment are reported. Abou-Dakn et al. showed that the use of lanolin in the treatment of nipple fissure was more effective than breast milk.²² On the other hand, in Jackson's study, it was shown that the use of lanolin in comparison with breast milk did not affect the pain and repair of the nipple fissure.¹⁷ However, there is no effective treatment for this problem.

Nowadays, the use of herbal drugs has a high prevalence among people for treating the of many diseases due to its low cost and easy access.²³ The use of medicinal herbs for the treatment of wounds has a long history and research on herbal factors affecting wound healing is one of the areas of medical and developmental biology progress.²⁴ One of these herbal medicines is *Portulaca oleraceae* (purslane) belonging to the *Portulacaceae* that as a traditional drug has many medical usages in various countries and cultures.^{25–27} Its therapeutic effects include reducing the pain and swelling, antiseptic, and antifungal effects, and repairing the oral wounds and burning ulcers.^{25–27} Additionally, it was noticed that the active constituents of purslane extract such as coumarins, flavonoids, and saponins have antiseptic, bactericidal and antifungal effects.²⁸ Purslane extract increases blood flow and oxygenation to the site of the wounds through angiogenesis and increases the collagen level leading to the wound healing acceleration.^{29,30} Also, by inhibiting the production of prostaglandin and thromboxane from arachidonic acid, it has an anti-inflammatory effect and improves wound healing.

On the basis of the protective effects of purslane extract, and considering the high prevalence of nipple fissure and the lack of definitive treatment, the researcher attempted to perform this study by evaluating the possible protective effects of purslane on the nipple fissure and comparing this effect to lanolin.

2. Material and methods

2.1. Preparation of plant extract and characterization

PO was collected from Sabzevar, Khorasan Razavi, Iran in the month of July 2016 (herbarium No. 12-1615-240). The plant was identified by Mr. Jouharchi, and a voucher of a sample was served as references in the herbarium of the school of pharmacy at Mashhad University of Medical Sciences (Deposition/Herbarium No: 12-1615-240). The leaves were dried in shadow and powdered and extraction was performed by the maceration method.³¹ 100 g of leaves powder was soaked with 1 lit 70% ethanol for 48 h at controlled room temperature. The extract was concentrated via rotary evaporator and then freeze-dried. The yield of dried extract was 17.5%. Using Folin–Ciocalteu (FC) reagent, the TPC was determined according to the previous studies with minor modification.^{32–35} In Brief, one hundred microliters of the extract (20 µg/mL) were combined with the same volume of water in a test tube. Then, about 200 µL of FC reagent was added to the tube with following 2600 µL of 5% (w/v) sodium carbonate solution. The mixture was incubated at 40 °C for 20 min along with fine shaking. The tubes were then quickly cooled and the developed color was read at 760 nm using a MultiSpec UV–Vis spectrophotometer (Shimadzu,

Tokyo, Japan). Estimation of phenolic compounds was carried out regarding the polyphenol reference calibration curve of the ethanolic solution of Gallic acid (GA) in a range of 0.5 to 10 mg/L.^{33–37} The amount of TPC was measured regarding mg of GA equivalent (GAE) per gram of dry extract. An identical process was performed for blank using of 100 µl of distilled water instead of the extract.

2.2. Ethical statement and clinical trials registration

This double-blind randomized clinical trial was performed on 86 women eligible for the study referred to the neonatal hypothyroidism unit of health centers in Mashhad in 2016. After approving the research project by the Ethics Committee with code 950,010 and obtaining written permission from Mashhad University of Medical Sciences, Mashhad, Iran, the clinical trial was registered on the Iranian Registry of Clinical Trials by ID of IRCT2015042421915N1, on 28 January 2017.

2.3. Purslane cream preparation, packaging and blinding

Purslane cream 2% (w/w) was prepared from the purslane extract and cold cream (USP). In the present study, lanolin and cold cream were purchased from Farabi® Company, Iran. Drugs were packed by the pharmacist who un-known regarding the process of the study, in the same tubes of 30 g and was coded (A and B).

2.4. Study design

In the present study, multi-stage sampling was performed. In the first stage, sampling was done in a class. The classes are the five regions of health centers (1–5) of Mashhad, Iran. They were randomly selected from two classes (center number 3 and 5). The second phase of sampling was randomly carried out according to the ratio of the patients referred to the thyroid clinic of centers 3 and 5. In the third stage, among the lactating women referring to these 4 thyroid clinic centers, firstly, the units of study were selected by inclusion criteria and then placed in two groups of lanolin and purslane creams on the basis of random numbers. Noteworthy, mothers along with their children should be routinely visited by their health centers on the third to fifth day after childbirth to screen and prevent the hypothyroidism and related disorders. In this regard, these centers were selected to provide more access to lactating women during this period. Following the selection, required explanations regarding the research design, the method of research, how to use drugs and the probability of drug allergy were given to them. If they wished to participate in the research, written consent was obtained in order to observe the ethical issues, they were assured about the confidentiality of their information and they can leave the study at any time desired. Using the number cruncher statistical system (NCSS) software, the samples were randomly assigned to one of the two groups of lanolin and purslane cream.

2.4.1. Inclusion criteria

The inclusion criteria were Iranian nationality, the resident of Mashhad, single and term pregnancy, the possibility for a phone call, being literate, exclusive breastfeeding, obtaining the score of at least 2 from the Store scale.

2.4.2. Exclusion criteria

The exclusion criteria included maternal nipple abnormalities (inverted or flattening nipple, very large and bright, or any clear deformation nipple), known psychological and cardiovascular diseases in mother. Moreover, other exclusion criteria were abscess an infection of breast in the mother, use of pacifier, milk glass and plastic breast nipple, infant's disease, infant's infection to oral mucosa during the study, mother's infection to infectious diseases, sensitivity to purslane cream and lanolin during use, lack of visits at determined days for any reason, the mother's use of other treatments such as using milk, or

antibiotics during the study period, not using the treatment for one day or less than three times a day, and mother's use of cold or hot compresses.

2.4.3. Assessment of the nipple fissures

The tools used in this research included: interview and examination form to select the research unit, Individual and Midwifery Inventory Questionnaire, health status assessment form, and the Store scale. The validity of interview and examination forms, Individual and Midwifery Inventory Questionnaire, health status assessment form were determined through content validity using the views of 7 professors and faculty members. The equivalence method was used to determine the reliability of these forms and the reliability of these tools was confirmed with $r = 0.90$, $r = 0.95$, $r = 0.98$, respectively.

A 5-degree Store scale was used to measure nipple fissure. The painless nipple with a natural color was scored as 0, a little red nipple with pain only at the start of breastfeeding, score 1, red nipple with pain during lactation and in the interval between lactations, score 2, when the nipple started to crack and there was pain at the start of lactation and in the interval between lactations, score 3, and if the nipple had a fissure (with or without bleeding) with pain at the start of lactation and during lactation and in the interval between lactations, score 4. This scale is a valid tool which is validated by Ebrahimi.³⁸ The reliability of the Store scale in our study was confirmed by an equivalence reliability method with a correlation coefficient of 0.81.

On the day of referring, after completing the consent form in both groups, the correct lactation technique (including the correct state of the mother during lactation, how to place the breast in the mouth of the baby, how to embrace the baby, etc.) were taught to the mother individually along with educational pamphlet by the researcher. In order to determine the sensitivity to the drug, the mother was asked to apply it to the skin eight hours before taking the drug, and if she was not allergic, use it on the nipple as amount of a finger, three times a day immediately after breastfeeding, to cover the entire thin layer of the fissure and continue treatment up to seven days. Before the intervention, the third day after the start of treatment and the day after the end of the treatment, the researcher completed the Store scale.

During this period, the researcher followed the mothers by phone and asked whether the complication was created or not and the process of recovery was asked. In the case of any problem and no improvement, the mother was referred to the clinic's physician. During the study, 6 cases were excluded from the study due to having one of the exclusion criteria. In the lanolin group, 2 cases were excluded due to breast fissure infection, 1 due to lack of regular use of lanolin, and in purslane group, 3 patients due to lack of timely use of cream (Fig. 1).

2.5. Statistical analysis and sample size

The sample size was determined based on the preliminary study (to obtain the mean and standard deviation of the population under study) and then using the formula for a comparison of the averages. A preliminary study was conducted on 26 subjects (13 in each group) that randomly divided into two groups. The improvement index of nipple fissure was used to determine the sample size. The highest sample size was related to the comparison of the improvement in the eighth day between two groups. Thus, on the eighth day, 80% improvement was observed in the purslane group and 50% in the lanolin group. Therefore, with a confidence of 95% and a power of 90%, the sample size was at least 36 in each group (Eq. 1). For more accuracy and possible sample losing, with a possible 15% drop, 86 people were included in the study.

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2(\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2} \quad (1)$$

$$n = \frac{(1.96 + 0.84)^2((0.5 \times 0.5) + 0.8 \times 0.2)}{(0.8 - 0.5)^2} = 36$$

Data were analyzed by SPSS software (version 22), data *t*-test, variance analysis with repeated measures, Mann-Whitney, Chi-square. Data were shown as mean \pm standard deviation (SD) and number and percentage. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of quantitative variables. For comparing the qualitative variables, Chi-square and Fisher's tests were used in both intervention and control groups. For comparison of quantitative variables with normal distribution between two groups, unpaired *t*-test was used, and for abnormal distribution, the Mann-Whitney test was applied. In order to compare the abnormal quantitative variables before the intervention, after 3 and 8 days in each group, a nonparametric test was used in repeated data (Friedman test). Finally, analysis of covariance was used in repeated data to control the intervention variable. The significance level in the tests was 0.05

3. Results

3.1. The extract standardization and total phenolic contents of purslane extract

The yield of extract was 17.5% w/w in the proportion of raw dried purslane. TPC was also determined 9.1 ± 0.45 as mg GAE/ g dried extract.

3.2. Demographic and homogeneity of the subjects

Out of 86 subjects, 80 cases completed the study. The findings of this study showed that two groups were homogeneous and baseline characteristics of the patients are summarized in Table 1. There were no significant differences in maternal age, maternal BMI, neonatal birth weight, neonatal age, duration of pregnancy, as well as qualitative variables such as mode of the delivery, dominant breast in lactation, employment status.

3.3. The effects of purslane cream and lanolin on the mean score of the breast fissure

3.3.1. Right breast

The mean score of right breast fissure in the purslane cream showed a significant decrease at the third and eighth day of the study compared to the pre-intervention day ($p = 0.001$ for all cases, Table 2).

By analyzing the variance in repeated measures and controlling the values before intervention as interfering results, the results on the third days after intervention showed that the nipple fissure score was significantly decreased 1.43 unit in the purslane cream compared to the lanolin ($p < 0.001$, Tables 2 and 3), which at 8th days of intervention, the significant difference was 0.76 unit between purslane cream and lanolin groups ($p < 0.001$, Tables 2 and 3).

3.3.2. Left breast

Our findings showed that the mean score of the fissure in this group showed a significant decrease at the third and eighth days of the study compared to the pre-intervention ($p = 0.001$ for all cases, Table 4).

The results of analysis of variance in repeated measures on left breast fissure showed a significant decrease of 1.55 units in the third day in the group of purslane versus lanolin ($p < 0.001$, Tables 4 and 5), whereas at 8th days of intervention, the significant difference was 0.76 unit between purslane cream and lanolin groups ($p < 0.001$, Tables 4 and 5).

The mean score of left and right breast fissures in the group of treatment with lanolin group similar to the group of treatment with purslane cream showed a significant decrease at the third day and eighth day ($P = 0.001$, Tables 2–5). Mann-Whitney test comparing

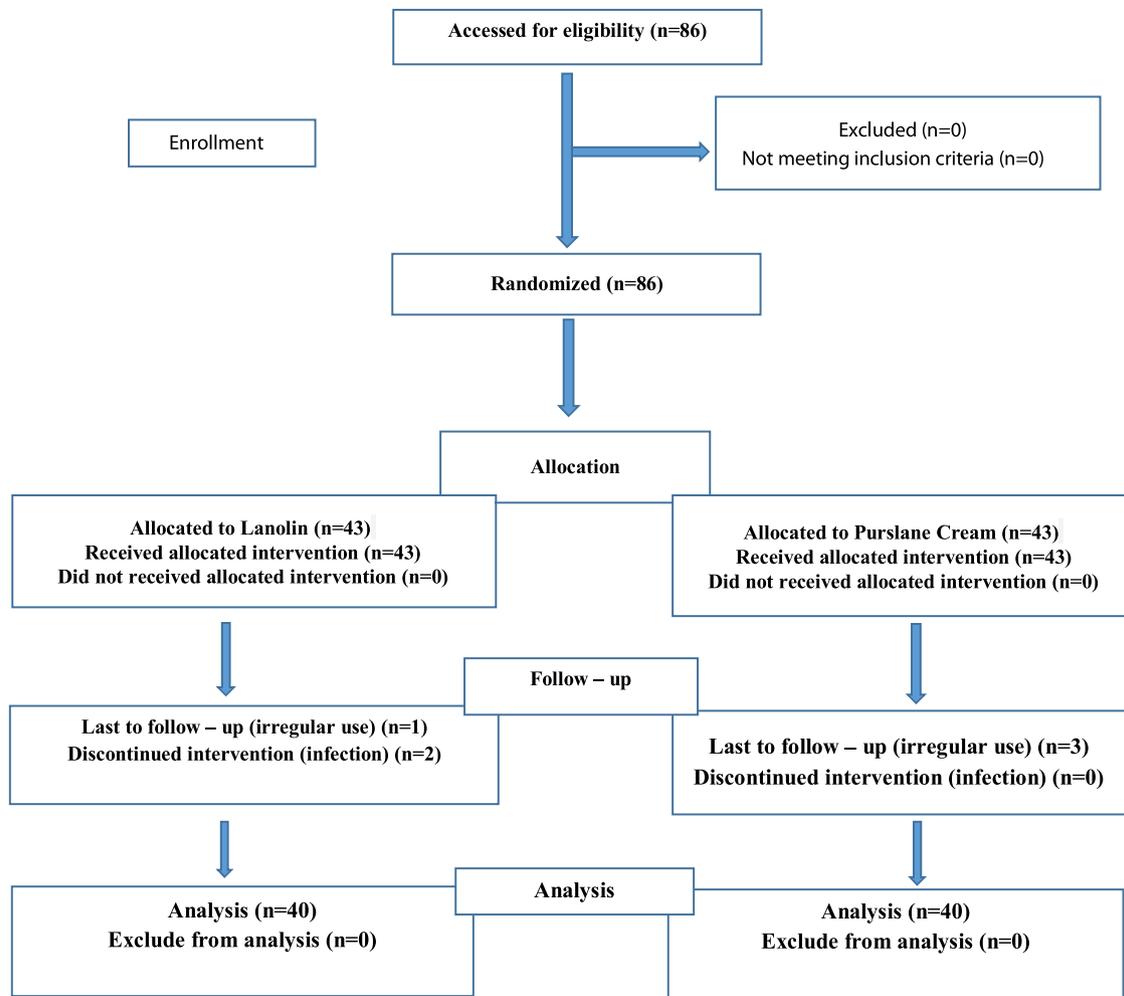


Fig. 1. Flow diagram of participants.

Table 1
Baseline characteristics of the studied groups.

variables	groups		P value
	lanolin	Purslane cream	
	Mean ± SD	Mean ± SD	
Maternal age	29.2 ± 6.8	27.5 ± 6.0	*P=1.173, t=0.244
maternal BMI	25.8 ± 4.6	24.6 ± 3.7	*P=0.200, t=1.291
neonatal birth weight(g)	3297.0 ± 431.2	3245.3 ± 369.6	*P=0.566, t=0.576
neonatal age(day)	4.4 ± 0.8	4.2 ± 0.8	Z=0.919 **P=0.358
duration of pregnancy(week)	39.5 ± 1.0	39.2 ± 1.0	Z=0.097 **P=0.231
qualitative variables			
mode of delivery	vaginal 28(70%) Cesarean 11(27.5%)	29(72.5%) 12(30%)	***P=0.549
employment status	housewife 28(70%) Employed 12(27.5%)	31(77.5%) 9(22.5%)	***P=0.446
dominant breast in lactation	left 5(12.5%) right 3(7.5%) both 32(80%)	7(17.5%) 4(10%) 29(72.5%)	×P=0.739

P-values calculated using * t–test, ** Mann-Whitney, *** Chi-square, and ×Fisher's tests.

mean score of the nipple fissure between two groups showed that two groups were homogeneous before the intervention, but there was a significant difference between two groups on the third and eighth days ($p < 0.001$, Tables 2–5).

4. Discussion

The present study was conducted to determine and compare the effects of purslane cream and lanolin on the healing of nipple fissure in lactating women. As the results showed, the mean score of fissure showed a significant decrease in the third day and eighth day compared with before the intervention in both groups of purslane cream and lanolin. There are several important studies notion that the highest incidence of nipple fissure is between the 3rd and 7th days after childbirth, therefore treatment during this period can help to maintain exclusive breastfeeding.^{5,7} In this regard, days 3 and 7 after delivery were selected for evaluation and the subjects evaluated on the third day and one day after treatment (day 8).

A significant reduction in the Stour mean score on the third day and eighth day after treatment with purslane cream compared with lanolin indicates more improvement in a shorter time after initiation of treatment with purslane cream. Inflammation is the defensive response of the body against tissue damage. Pain, warmth, redness, and swelling are local symptoms of inflammation.^{37,39–43} Phenolic compounds such as saponin and flavonoids are of the most active ingredients in purslane that due to its anti-inflammatory and antibacterial properties reduces the redness and edema of the wound. There are several studies indicating that Purslane has healing effects. Oktaffrastya et al. (2016)

Table 2

Comparison of research units according to the status of the right nipple fissure in the studied groups before the intervention, on the third and the eighth days after intervention.

Time	groups		Mann-Whitney Test Result
	Purslane cream Mean ± SD	lanolin Mean ± SD	
baseline	2.92 ± 2.8	2.95 ± 0.8	Z = 0.143, P = 0.889
Third day	0.20 ± 0.4	1.65 ± 1.1	P < 0.001, Z = 5.61
Eighth day	0.00 ± 0.0	0.77 ± 0.9	P < 0.001, Z = 4.91
Changes between of the third day and baseline	2.72 ± 0.64	1.30 ± 0.9	P < 0.001
Changes between of the eight-day and baseline	2.92 ± 0.8	2.17 ± 0.9	P = 0.001
P ¹	χ ² = 76, P = 0.001	χ ² = 67.7, P = 0.001	

P¹ denotes nonparametric repeated measurement (Friedman test).

Table 3

Comparison of changes of the right nipple fissure in the studied groups.

Time		β	SE	repeated measures Test Result
Third day	Purslane cream	-1.43	0.16	P < 0.001, t = 8.52
	lanolin	0		
baseline Eighth day	Purslane cream	0.58	0.1	P < 0.001, t = 5.67
	lanolin	-0.76	0.14	
baseline		0.23	0.09	P = 0.001, t = 2.06

Table 4

Comparison of research units according to the status of the left nipple fissure in the studied groups before the intervention, on the third day and the eighth day.

time	groups		Mann-Whitney Test Result
	Purslane cream Mean ± SD	lanolin Mean ± SD	
baseline	3.02 ± 0.83	2.90 ± 0.77	Z = 0.494, P = 0.685
Third day	0.15 ± 0.36	1.65 ± 1.09	P < 0.001, Z = 6.17
Eight day	0.00 ± 0.0	0.80 ± 0.91	P < 0.001, Z = 5.07
Changes between of the third day and baseline	2.87 ± 0.75	1.25 ± 0.92	P < 0.001, Z = 6.37
Changes between of the eight-day and baseline	3.02 ± 0.83	2.10 ± 0.92	P < 0.001, Z = 4.15
P ¹	χ ² = 76.76, P = 0.001	χ ² = 68.17, P = 0.001	

P¹ denotes nonparametric repeated measurement (Friedman test).

demonstrated that the repairing and epithelialization of the purslane may be through increasing the fibroblast proliferation and maturation.⁴⁴ In another study, Eldeighdye et al. (2016) stated that the purslane extract increases the levels of VEGF 160.6%, antioxidant 45% on a diabetic ulcer in rats compared to the group who received no treatment. They also explained its protective effects regarding the presence of flavonoids in purslane leading to an elevation in the levels of VEGF and antioxidant. These factors are effective in accelerating epithelialization, producing the granular tissue and increasing the angiogenesis in wound healing and repair.⁴⁵ In the present study, we standardized the hydro-ethanolic extract of purslane using the total phenolic compound. We achieved that the extract contains high levels of phenolic compounds about 10 mg GAE/g dried extract, and these compounds probably are responsible for the protection and healing effects.

In our study, the effect of using both lanolin and modifying the correct lactation technique was indicated on the nipple fissure. The results of some studies regarding the effect of lanolin on repairing the nipple fissure are not consistent with our research. In the study of Riordan, each research unit randomly used lanolin or tea bag on the right or left breast after delivery, and no treatment was performed on the other breast. The results showed no significant difference between two groups.⁴⁶ The simultaneous use of several treatments in one group can have a negative effect on each intervention. In our study, we used two independent groups to examine treatment interventions.

Table 5

Comparison of changes of the left nipple fissure in the studied groups.

Time		β	SE	repeated measures Test Result
Third day	Purslane cream	-1.55	0.16	P < 0.001, t = 9.48
	lanolin	0		
baseline Eighth day	Purslane cream	0.46	0.1	P < 0.001, t = 4.5
	lanolin	-0.82	0.14	
baseline		0.22	0.08	P = 0.001, t = 2.52

Some studies have pointed out multiple complications of lanolin, including burns, pruritus, and nipple fissure infection. In our clinical trial, two cases were excluded from the study due to the breast fissure infection, but no complications were found regarding the use of the purslane cream. Some limitations of the present study were the individual and genetic differences, the impossibility of monitoring how to use cream and personal hygiene. However, we tried to decrease them by the training and providing the maternal pamphlets which included the information. The use of standard tools for assessing the nipple fissure and examining two types of treatment in separated groups are considered the strengths of the present study. Considering the promising and repairing effects of purslane cream, it can be suggested that further studies with larger sample size be conducted to evaluate the

effect of purslane on other wounds.

5. Conclusion

In summary, we showed that the use of purslane cream without any complications could accelerate the repairing of nipple fissure. Based on this clinical trial, purslane cream (2% w/w) can be used as an accelerator for improving the nipple fissure in lactating women.

Authors' contributions

Conceptualization, Hassan Rakhshandeh, and Vahid Reza Askari; Formal analysis, Habibollah Esmaily; Investigation, Azin Niazi, Sedigheh Yousefzadeh and Hassan Rakhshandeh; Methodology, Habibollah Esmaily, and Vahid Reza Askari; Supervision, Sedigheh Yousefzadeh, Hassan Rakhshandeh, and Vahid Reza Askari; Writing – review & editing, Vahid Reza Askari.

Competing interests

All contributed authors declare no conflict of interest to perform and publishing of this study.

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