# Comparing the combination of copper, zinc, and sucralfate (Cicalfate®) with white soft paraffin in the treatment of cracked nipples

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**Background:** Cracked nipples represent the most common complication of breastfeeding. This study aimed to compare the therapeutic effect of the Cicalfate® commercial cream (containing copper, zinc, and sucralfate) with white soft paraffin in treating cracked nipples.

**Methods:** This study was a double-blind clinical trial conducted on 115 patients with cracked nipples. Patients were randomly divided into two case and control groups. The case group received the Cicalfate® cream and the control group received white soft paraffin. After a period of one to two weeks of treatment, all patients were re-examined and the severity and rate of their recovery were recorded. Data were analyzed using SPSS version 15.

**Results:** In this study, 68 patients were in the case group and 47 were in the control group. The comparison of the two groups in terms of improvement of the right nipple with the removal of other variables showed that the degree of cracking reduction in the case group was 3.3 times that of the control group (OR = 3.3; CI = 1.3-8.3). Also, the comparison of the two groups in terms of improvement of the left nipple with removing the effect of other variables showed that the degree of cracking reduction in the case group was 5.3 times that of the control group (OR = 5.3; CI = 2.0-14.1).

**Conclusion:** The results of this study showed that the therapeutic effect of Cicalfate® is more than that of white soft paraffin.

**Keywords:** breastfeeding, cracked nipples, treatment

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## INTRODUCTION

The best nutrition for infants is breast milk, which is associated with a unique emotional impact on both the mother and baby [1]. The results of studies showed that breastfeeding can lead to high intelligence and prevent the child from having diabetes, obesity, infections, and dental malocclusion. It can also significantly reduce the risk of breast cancer, ovarian cancer, and type 2 diabetes in breastfeeding mothers [2]. However, due to complications from breastfeeding such as nipple trauma, many mothers refuse to breastfeed their infants in the very first months after childbirth [3]. Nipple trauma leads to the development of redness, edema, ecchymosis, abrasions, cracks, and blisters on the nipples' skin [4] due to various reasons such as improper attachment of the baby's mouth to the breast, inappropriate positioning of the baby, contamination with *Candida albicans* [5-8], inappropriate sucking of the baby due to oral problems and abnormalities, the use of nipple

shields [9], and the use of pacifiers and breast pumps [10,11]. The most common time for nipple trauma is usually between the third and seventh days following childbirth, sometimes lasting for up to six weeks after delivery [12]. Nipple fissures or cracked nipples are among the main causes of nipple trauma, representing the most common problem associated with breastfeeding [13]. The prevalence rate of this complication varies from 34 to 96%, comprising the second leading cause of early termination of breastfeeding [5,14,15]. Studies show a 2.4-fold increase in early termination of breastfeeding due to nipple fissures [16]. This condition is characterized by transverse and stellate ulcers in the nipples of breastfeeding women, usually associated with pain, inflammation, and secretion [17,18]. Untreated fissures can cause anatomical complications such as edema, turgidity, decreased flexibility, and flat nipples [19], and may also increase the risk of mastitis, pain, and bleeding [20,21].

Various pharmacological and non-pharmacological treatments are used to treat cracked nipples and improve their associated complications. The most common treatments are phototherapy [22], silver cap [23], hydrogel dressing [24], tea bags and warm compresses [25], menthol essential oil [12], Calendit-E cream [26], aloe vera gel [18], antimicrobial and antifungal ointments [27], lanolin ointment, breast milk [5,28], and white soft paraffin [29]. Nowadays, studies have demonstrated the therapeutic and anti-inflammatory effects of copper, zinc, and sucralfate in the treatment of dermatological lesions [30-33]; these elements are combined in the Cicalfate® commercial cream, which can be used to treat cracked nipples.

Due to the undeniable role of breastfeeding in the nutrition and health of infants, and considering the negative effects of cracked nipples on the physical and mental health of breastfeeding mothers and the production of milk by mammary glands, this study aimed to compare Cicalfate® cream with white soft paraffin in terms of treating cracked nipples and minimizing its complications.

## PARTICIPANTS AND METHODS

### Sample size

The required sample size was calculated using the formula below based on the results of the study of Guerrero *et al.*, in which there was an 80% and 43% treatment effect in the intervention and control groups, respectively. The study power and P-value were set at 80% and 0.05, respectively. A minimum sample size of 26 was obtained [30].

$$n = \frac{(Z_{1-\frac{\alpha}{2}} + Z_{\beta})^2 \times \left(\left(p_1 q_1\right) + \left(p_2 q_2\right)\right)}{(p_1 - p_2)^2}$$

### Methods

This study was a double-blind clinical trial conducted on 115 patients with cracked nipples referred to the dermatology clinic of Shahid Beheshti Hospital in Kashan, Iran. These patients were randomly divided into two groups of cases and controls according to their ID numbers. To ensure the similarity of the study groups, the demographic characteristics of the participants were checked using statistical tests, revealing no significant differences. Patients in both groups received an informed consent form and they were able to withdraw from the study at any time. Subsequently, after the examination of patients by a dermatologist at the hospital clinic for the severity and extent of nipple cracking, all characteristics of patients were recorded in the relevant forms. These forms included questions such as the name of the questionnaire, the questionnaire number, the age of the mother, the age of the baby (in days), the frequency of breastfeeding per day, the duration of breastfeeding in one day, the type of study group (case or control), the severity of nipple cracking before treatment, the severity of nipple cracking after treatment, the duration of crack healing after treatment, and the rate of recovery from the disease after treatment. Then, the case group received Cicalfate® cream, while the control group received white soft paraffin as prescribed. Cicalfate® cream is a commercial cream made by the Avene company, France. It is fat-based and used to moisturize and heal skin wounds and abrasions. Cicalfate® cream is composed of substances such as copper sulfate, magnesium stearate, zinc sulfate, caprylic triglyceride, glycerin, hydrogenated vegetable oil, zinc oxide, propylene glycol, and aluminum sucrose, and is used twice a day. For the sake of blinding, both creams were

poured into similar containers; moreover, during the study period, the dermatologist was blinded regarding the prescribed creams.

All patients were reexamined by a dermatologist one and two weeks after starting the treatment and the severity and extent of crack healing were recorded. The severity of nipple cracking was determined as follows according to a reference book on breastfeeding [34]:

- Grade 1: Only pain and itching with redness in the area without skin damage.
- Grade 2: Pain with a superficial ulcer, abrasion, and possibly the presence of a blister.
- Grade 3: Deeper ulcers with the splitting of the epidermis.
- Grade 4: Injury to the dermis, associated with a complete loss of part of the nipple skin.

Shifting from a higher grade to a lower grade was considered a positive therapeutic effect. Nipple cracking was scored ordinally from 1 to 5. The highest score was for cured cases and the lowest one was for grade 4 cracks. After checking the similarity of the study groups, the effect of treatment was assessed using ordinal regression, with the independent t-test and Chi-squared tests being used to compare groups. As a repeated measure of outcome across time, the Generalized Estimating Equation (GEE) approach was applied in the used model. The analysis was conducted in SPSS version 15 with a significance level of 0.05.

This study was approved by the Ethics Committee of Kashan University of Medical Sciences under the registration number: IRCT138901283734N1.

## RESULTS

Of 115 participants in this study, 68 were in the case group (59.1%) and 47 (40.9%) were in the control group. The demographic characteristics of all participants are presented in Table 1. There was a significant difference between the two groups in terms of the mean age of neonates and the mean duration of breastfeeding ($P < 0.05$); therefore, the effects of these variables were controlled in the analysis. Tables 2 and 3 show changes in nipple cracking in the study groups during the study period.

Before the main analysis, the proportional odds assumption was checked with the score test. The results of ordinal regression analysis using the GEE approach for the right nipple revealed that the intervention group had a 3.3 (CI; 1.3-8.3) times chance of a lower grade compared with the control group at the end of the study ($P < 0.05$); this value was 5.3 (CI; 2.0-14.1) for the left nipple ($P < 0.05$) (Table 4). These results showed a significant effect

**Table 1.** Descriptive characteristics of the study participants

| Variable | Study group | | *P*-value |
|---|---|---|---|
| | Case (n = 68) mean ± SD | Control (n = 47) mean ± SD | |
| Mother's age (years) | 27.6 ± 4.4 | 27.7 ± 4.7 | 0.85 |
| Infant's age (days) | 139.5 ± 170.2 | 46.6 ± 52.9 | <0.001 |
| Frequency of breastfeeding (times/day) | 10.0 ± 3.0 | 11.0 ± 3.9 | 0.17 |
| Duration of breastfeeding (min/day) | 174.0 ± 90.5 | 217.0 ± 103.2 | 0.02 |
| Duration of right wound (days) | 34.7 ± 32.0 | 35.7 ± 31.7 | 0.88 |
| Duration of left wound (days) | 33.7 ± 32.3 | 34.4 ± 31.5 | 0.90 |

Abbreviations: min, minute; SD, standard deviation.

**Table 2.** Distribution of the grades of right nipple cracking across time

| Grade | Study group | | | | | |
|---|---|---|---|---|---|---|
| | Case Number (%) | | | Control Number (%) | | |
| | Time 1 | Time 2 | Time 3 | Time 1 | Time 2 | Time 3 |
| Grade 1 | 15 (65.2) | 16 (80.0) | 5 (71.4) | 8 (34.8) | 4 (20.0) | 2 (28.6) |
| Grade 2 | 14 (77.8) | 10 (50.0) | 3 (42.9) | 4 (22.2) | 10 (50.0) | 4 (57.1) |
| Grade 3 | 16 (42.1) | 10 (55.6) | 5 (41.7) | 22 (57.9) | 8 (44.4) | 7 (58.3) |
| Grade 4 | 18 (60.0) | 6 (37.5) | 2 (22.2) | 12 (40.0) | 10 (62.5) | 7 (77.8) |
| Improved | - | 14 (56.0) | 38 (69.1) | - | 11 (44.0) | 17 (30.9) |

**Table 3.** Grades of left nipple cracking across time

| Grade | Study group | | | | | |
|---|---|---|---|---|---|---|
| | Case Number (%) | | | Control Number (%) | | |
| | Time 1 | Time 2 | Time 3 | Time 1 | Time 2 | Time 3 |
| Grade 1 | 15 (68.2) | 12 (66.7) | 6 (75.0) | 7 (31.8) | 6 (33.3) | 2 (25.0) |
| Grade 2 | 18 (69.2) | 14 (58.3) | 7 (53.8) | 8 (30.8) | 10 (41.7) | 6 (46.2) |
| Grade 3 | 13 (43.3) | 10 (55.6) | 1 (16.7) | 17 (56.7) | 8 (44.4) | 5 (83.3) |
| Grade 4 | 18 (56.3) | 7 (43.8) | 1 (14.3) | 14 (43.8) | 9 (56.3) | 6 (85.7) |
| Improved | - | 16 (66.7) | 40 (72.7) | - | 8 (33.3) | 15 (27.3) |

**Table 4.** Ordinal regression analysis results

| Parameter | Hypothesis Test | | | OR | 95% CI | |
|---|---|---|---|---|---|---|
| | Wald Chi-Square | df | Sig. | | Lower | Upper |
| **Right nipple** | | | | | | |
| Threshold | | | | | | |
| Grade 1 | 1.74 | 1 | 0.18 | 10.6 | 0.3 | 352.1 |
| Grade 2 | 3.64 | 1 | 0.05 | 31.7 | 0.9 | 1104.5 |
| Grade 3 | 4.49 | 1 | 0.03 | 45.2 | 1.3 | 1535.2 |
| Grade 4 | 5.48 | 1 | 0.01 | 65.4 | 1.9 | 2169.0 |
| Intervention group | 6.65 | 1 | 0.01 | 3.3* | 1.3 | 8.3 |
| Control group | - | - | - | 1 | - | - |
| Mother's age | 5.14 | 1 | 0.02 | 1.1 | 1.0 | 1.3 |
| **Left nipple** | | | | | | |
| Threshold | | | | | | |
| Grade 1 | 0.97 | 1 | 0.32 | 7.0 | 0.1 | 344.8 |
| Grade 2 | 1.73 | 1 | 0.18 | 14.2 | 0.2 | 748.2 |
| Grade 3 | 3.02 | 1 | 0.08 | 34.6 | 0.6 | 1886.4 |
| Grade 4 | 3.87 | 1 | 0.04 | 54.6 | 1.0 | 2938.0 |
| Intervention group | 11.60 | 1 | 0.00 | 5.3 | 2.0 | 14.1 |
| Control group | - | - | - | 1 | - | - |
| Mother's age | 3.19 | 1 | 0.07 | 1.14 | 0.9 | 1.3 |

*The higher grade has a lower score, therefore, for instance, the chance of moving to a higher score in the intervention group is 3.3 times the control group for the right nipple.
**Abbreviations:** CI, confidence interval; df, degrees of freedom; OR, odds ratio; Sig, statistical significance.

of the treatment on reducing the grade of nipple cracking.

## DISCUSSION

The findings of the present study showed that the effect of the combination of copper, zinc, and sucralfate in the commercial Cicalfate® cream was far greater than that of white soft paraffin, which is used as a common treatment for cracked nipples. This is consistent with the results of the study by Cuerrero *et al.* [30], which compared the therapeutic effect of white soft paraffin with the combination of copper, zinc, and sucralfate (Cicalfate®) on blisters and skin wounds in six healthy volunteers in Spain. The results of that study showed that the strongest therapeutic effect (80%) was associated with the combination of the three elements of copper, zinc, and sucralfate. However, the therapeutic effect of white soft paraffin at the highest concentration (5%) was only 43%. Also, the results of a study by Markham *et al.* showed that topical treatment with white soft paraffin and sucralfate has a significant effect on the treatment of severe secondary dermatitis and skin inflammation [31], which is consistent with the results of the present study. However, in a study by Mohammadzadeh *et al.* on nipple fissures, no significant difference in treatment effect was observed between lanolin oil and white soft paraffin [29].

The anti-inflammatory role of "zinc" has been demonstrated in a study by Lang *et al.* on animal samples. In that study, using a particular concentration of zinc solution, the inflammation

of the airways of the studied rats was significantly reduced over a period of one year [35], which is partially consistent with the results of our study. In addition to its anti-inflammatory role, the zinc element can also be effective in repairing damaged skin layers. The results of Ebrahimi *et al.*'s study showed that zinc oxide nanoparticles offer a beneficial effect on the healing of burned skin layers and hair follicles [36]. The results of that study are in line with the results of the present study.

Soltani *et al.* demonstrated the therapeutic effect of the zinc element on the healing of skin lesions. The results of this study showed that dressing with zinc oxide ointment helps speed up the healing of chronic and acute wounds [37]. In a double-blind clinical study conducted by Tumino *et al.* on 50 patients in Rome, Italy, the effect of sucralfate on the healing of chronic venous ulcers was compared against a placebo, indicating a 95.6% effect of sucralfate on the improvement of chronic venous ulcers [33]. The results of the two above-mentioned studies are consistent with the results of the current study. Also, in a study by Bo *et al.*, which aimed to measure the effect of oral and parenteral copper on inflammation, it was found that copper has a very good effect on reducing the inflammatory factors in the body [32], which is consistent with the results of the present research.

## CONCLUSION

According to the results obtained from this study, the therapeutic effect of copper, zinc, and sucralfate combined in Cicalfate® commercial cream is better relative to routine treatment of cracked nipples with white soft paraffin. Therefore, the use of this drug combination is recommended for treating cracked nipples and averting its complications.

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**Conflict of Interest:** None declared.

## REFERENCES

1. Levinienė G, Tamulevičienė E, Kudzytė J, et al. Factors associated with breastfeeding duration. Medicina (Kaunas). 2013;49(9):415-21.
2. Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. The Lancet. 2016;387(10017):475-90.
3. Thompson R, Kruske S, Barclay L, et al. Potential predictors of nipple trauma from an in-home breastfeeding programme: A cross-sectional study. Women Birth. 2016;29(4):336-44.
4. Ghwass MM, Ahmed D. Prevalence and predictors of 6-month exclusive breastfeeding in a rural area in Egypt. Breastfeed Med. 2011;6(4):191-6.
5. Asaadi N, Kariman N, Shahrahmani H, et al. A systematic review of clinical trials in the treatment of sore nipple and nipple pain in breastfeeding women. Iran J Obstet Gynecol Infertil. 2016; 19(6):22-33.
6. Tafazoli M, Ebrahimi A, Mohammad Zadeh A, et al. Effect of breastfeeding technique modification on prevention of nipple sore. Iran J Obstet Gynecol Infertil. 2015;17(138):10-17.
7. Buck ML, Amir LH, Donath SM. Topical treatments used by breastfeeding women to treat sore and damaged nipples. Clin Lact. 2015;6(1):16-23.
8. Amir LH, Donath SM, Garland SM, et al. Does candida and/or staphylococcus play a role in nipple and breast pain in lactation? a cohort study in Melbourne, Australia. BMJ open. 2013;3(3):e002351.
9. Perrella SL, Lai CT, Geddes DT. Case report of nipple shield trauma associated with breastfeeding an infant with high intra-oral vacuum. BMC Pregnancy Childbirth. 2015; 15(1):155.
10. Vieira GO, Martins CD, Vieira TD, et al. Factors predicting early discontinuation of exclusive breastfeeding in the first month of life. J Pediatr (Rio J). 2010;86(5):441-4.
11. Qi Y, Zhang Y, Fein S, et al. Maternal and breast pump factors associated with breast pump problems and injuries. J Hum Lact. 2014;30(1):62-72.
12. Akbari SA, Alamolhoda SH, Baghban AA, et al. Effects of menthol essence and breast milk on the improvement of nipple fissures in breastfeeding women. J Res Med Sci. 2014;19(7):629.
13. Da Silva Santos KJ, Santana GS, De Oliveira Vieira T, et al. Prevalence and factors associated with cracked nipples in the first month postpartum. BMC Pregnancy Childbirth. 2016;16(1):209.
14. Abou-Dakn M, Fluhr JW, Gensch M, et al. Positive effect of HPA lanolin versus expressed breastmilk on painful and damaged nipples during lactation. Skin Pharmacol Phys. 2011;24(1):27-35.
15. Roohi M. Maternal morbidity within 45 days after delivery. Iran Journal of Nursing. 2005;18(41):145-52.
16. Vieira TO, Vieira GO, de Oliveira NF, et al. Duration of exclusive breastfeeding in a Brazilian population: new determinants in a cohort study. BMC Pregnancy Childbirth. 2014;14(1):175.
17. Cunningham F, Leveno K, Bloom S, et al (Eds). Williams

obstetrics. New York: McGraw Hill; 2010, 872.

18. Tafazoli M, Saeedi R, Gholami Robatsangi M, et al. *Aloe vera* gel vs. lanolin ointment in the treatment of nipple sore: a randomized clinical trial. Tehran Univ Med J. 2010;67(10): 699-704.
19. Coca KP, Gamba MA, Silva RS, et al. Factors associated with nipple trauma in the maternity unit. J Pediatr (Rio J). 2009;85(4):341-5.
20. Mediano P, Fernández L, Rodríguez JM, et al. Case–control study of risk factors for infectious mastitis in Spanish breastfeeding women. BMC Pregnancy Childbirth. 2014;14(1):195.
21. Melli MS, Rashidi MR, Delazar A, et al. Effect of peppermint water on prevention of nipple cracks in lactating primiparous women: a randomized controlled trial. Int Breastfeed J. 2007;2(1):7.
22. Chaves ME, Araújo AR, Santos SF, et al. LED phototherapy improves healing of nipple trauma: a pilot study. Photomed Laser Surg. 2012;30(3):172-8.
23. Marrazzu A, Sanna MG, Dessole F, et al. Evaluation of the effectiveness of a silver-impregnated medical cap for topical treatment of nipple fissure of breastfeeding mothers. Breastfeed Med. 2015;10(5):232-8.
24. Brent N, Rudy SJ, Redd B, et al. Sore nipples in breast-feeding women: a clinical trial of wound dressings vs conventional care. Aech Pediat Adol Med. 1998;152(11):1077-82.
25. Lavergne NA. Does application of tea bags to sore nipples while breastfeeding provide effective relief? Jognn-J Obst Gyn Neo. 1997;26(1):53-8.
26. Kazemirad M. Comparison of calendit-e cream versus expressed breast milk. Adv Nurs Midwifery. 2014;23(80):1-9.
27. Dennis CL, Schottle N, Hodnett E, et al. 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.
28. Vieira F, Bachion MM, Mota DD, et al. A systematic review of the interventions for nipple trauma in breastfeeding mothers. J Nurs Scholarsh. 2013;45(2):116-25.
29. Mohammad Zadeh A, Farhat A.Sh, Esmaeili H, et al. Effect of lanolin on sore nipples. Iran J Obstet Gynecol Infertil. 2003;2(6):95-2.
30. Guerrero D, Mengeaud V, Verriere F, et al. Efficacité et tolérance d'une association cuivre, zinc et sucralfate en dermatologie. Nouv Dermatol. 2002;21:20-3.
31. Markham T, Kennedy F, Collins P. Topical sucralfate for erosive irritant diaper dermatitis. Arch Dermatol. 2000;136(10):1199-200.
32. Bo S, Durazzo M, Gambino R, et al. Associations of dietary and serum copper with inflammation, oxidative stress, and metabolic variables in adults. Nutr J. 2008;138(2):305-10.
33. Tumino G, Masuelli L, Bei R, et al. Topical treatment of chronic venous ulcers with sucralfate: a placebo controlled randomized study. Int J Med Microbiol. 2008;22(1):17-23.
34. Lauwers J, Swisher A (Eds). Counseling the Nursing Mother. Burlington, MA: Jones & Bartlett Learning; 2015, 386.
35. Lang C, Murgia C, Leong M, et al. Anti-inflammatory effects of zinc and alterations in zinc transporter mRNA in mouse models of allergic inflammation. Am J Physiol-Lung C. 2007;292(2):L577-84.
36. Ebrahimi S, Hayati Roodbari N, Parivar K, et al. Investigation of the effect of nano zinc oxide on skin burns in adult female mouse. Medical Sciences. 2015; 25(4):257-62.
37. Soltani S, Naghedinia H, Ghorbani R. Evaluation effect of topical zinc oxide ointment on healing of the open wounds due to surgery of pilonidal sinus. Med J Mashhad Uni Med Sci. 2010;53(1):48-52.