

Clinical trial

Efficacy of topical application of human breast milk on atopic eczema healing among infants: a randomized clinical trial

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Conflicts of interest: None.

doi: 10.1111/ijd.12764

Abstract

Infant atopic eczema is an inflammatory lesion usually involving the epidermis of the skin. About 50% of infants are affected by this lesion in the first years of their lives. Studies show human breast milk (HBM) as a preventive measure and effective treatment of some sores and infections. This article evaluates the short-term efficacy of HBM versus hydrocortisone 1% ointment in infants with mild to moderate atopic dermatitis (AD). We conducted a randomized clinical trial among infants with diagnosed AD within a pediatrics unit. The majority of AD cases in both groups were considered moderate severity. There were no significant differences between these two groups at days 0, 7, 14, and 21, and the interventions of both groups were found to have the same effects. The external validity and consequently the ability to generalize the findings may be diminished as this study was conducted in a single site. Owing to HBM and the hydrocortisone 1% ointment providing the same results in the healing of AD, HBM was used because of low cost and accessibility.

Introduction

Atopic dermatitis (AD) is a common chronic skin disease that can involve recurrent skin infections. The disease is characterized by intense pruritus, multiple lesions with erythema, excoriations, and erosions that can be additionally accompanied by exudates, lichens, papules, and dry skin, all of which create a probable interference in most aspects of daily life.¹ Approximately 15–20% of infants are affected by AD in developed countries, and about 50% of them have atopic eczema in the first years of their lives.^{2,3} The prevalence combined with the potentially uncontrollable itching, insomnia, and skin bleeding caused by AD can have a negative effect on the patient's life.⁴ This makes the social and economic effects of the disease, even the acute cases, considerable.

Many factors can cause or aggravate AD symptoms: irritants, allergens, anxiety, stress, humidity, extreme temperatures, or infections such as staphylococcus, streptococcus, and herpes simplex.⁵

Common treatments of AD are based on moisturizing creams or ointments, which supply the skin with the proper moisture¹ and have no side effects. There are other treatments for AD based on topical anti-inflammatory medicines or immunomodulators. Unlike the typical

treatments, these treatments cause several side effects. For example, the frequent use of anti-inflammatory drugs having corticosteroids can make the skin thin and form striae.^{6,7} In addition, the use of immunomodulators can cause local irritation, rash, or itchiness.⁸

Human breast milk (HBM) is the best source of nutrition for infants and protects them from infections. It contains a significant amount of complement components that act as natural antimicrobial agents. It has protective factors as well that provide specific and nonspecific immunity for infants.⁹

Antimicrobial agents in HBM are composed from different materials such as antibodies, lysozymes, polymorphonuclear leukocytes, and bifidus factors.¹⁰ IgA is an immunoglobulin that particularly protects infants from a variety of skin infections.¹¹ Lysozymes kill bacteria such as Enterobacteriaceae and gram-negative bacteria, while the leukocytes have anti-inflammatory effects. The bifidus factor stimulates the production of bacteria beneficial for growth as well as inhibits them to adhere to epithelial cells and compete with cell receptors for binding to pathogens.¹²

Several studies have been recently published about the anti-inflammatory effects of HBM and its wound healing power. These studies analyzed the topical

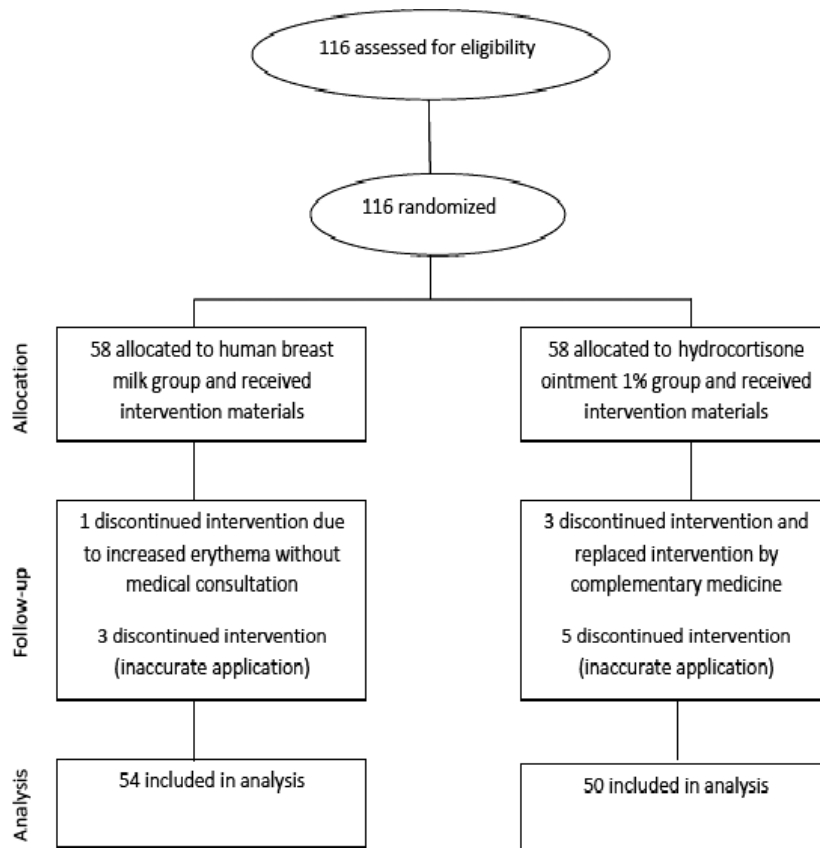


Figure 1 The enrollment of participants into two groups of human breast milk and 1% hydrocortisone ointment

application of HBM on bacterial colonization, separation time of the umbilical cord,¹³⁻¹⁵ conjunctivitis caused by *Chlamydia*, severe eye dryness and eye lesions,¹⁶ and sore nipples;¹⁷⁻¹⁹ however, to the best of our knowledge, there is no study that compares HBM with other atopic eczema treatments. HBM is the most accessible treatment to all mothers and does not have any cost in comparison with other eczema treatments. This study is designed to assess the healing effect of the topical application of HBM and 1% hydrocortisone ointment on atopic eczema among infants.

Methods

Trial design

This study was conducted as a controlled two-arm study among infants at a referral center (Paediatric Unit, Amir Kabir Hospital, Arak, Iran) in the period between April 2011 and March 2012. Infants who met the entry criteria were randomly assigned to either the topical application of HBM or the 1% hydrocortisone ointment (made by Aburaihan Pharmacology Company, Tehran, Iran) by the toss of a coin. It was not possible to perform a double blind study, but the investigator, study coordinator, statistical analyzer, and other personnel who assisted with this study were not aware of the treatment used for each infant.

The study was approved by the university ethics committee (Arak University of Medical Sciences, Arak, Iran) and complied with the Helsinki Declaration. Moreover, the parents of the infants involved in the study were fully informed and provided signed consent preceding the study.

Participants

In this study, patients were <20 months of age and diagnosed with AD based on Hanifin and Rajka's criteria.²⁰ According to the criteria of Oranje and Kunz,^{21,22} the patients were selected with mild, moderate, and severe AD.

These infants were selected based on criteria of not having any diagnosed diseases such as skin diseases, congenital anomalies, and oral or genital thrushes. In addition, they did not have an allergy to hydrocortisone and did not use any medications that might affect the results of the study.

Interventions

In one group, the treatment was a thin layer of 1% hydrocortisone ointment that was applied twice a day to all areas of the actively diseased skin, as defined by the investigator at the baseline. In the other group, subjects' mothers were recommended to rub the hind milk twice a day (at the end of breastfeeding) on the affected area. All parents also received a general instruction about the infants' atopic eczema care, such as using perfume-free baby

soaps, preventing woolen and synthetic fabrics from contacting the diseased skin, using 100% cotton fabrics, keeping nails short to minimize skin scratching, and avoiding extreme temperature environments.

Efficiency of the treatment was defined by complete healing of the diseased area. The study interventions of both groups were used for the full 21 days.

Outcomes

The infants were evaluated on the first day (baseline) and days 7, 14, and 21 of the treatment. Severity of AD was measured using the objective SCORAD severity index (O-SSI) and the Patient-Oriented SCORing Atopic Dermatitis (PO-SCORAD) index. The O-SSI score, at baseline and at the end of the intervention (day 21), was calculated with the formula:

$$A/5 + 7 \times B/2 \quad (1)$$

In this formula, *A* represents the extent (within a range of 0–100, determined by the rule of nines applied to a front-back drawing of the infants' inflammatory lesions), and *B* represents the intensity, which is the sum of six factors: erythema, edema/papulation, excoriations, lichenification, oozing/crusts, and dryness (each ranging from 0 to 3). The maximum objective SCORAD score is 83.²³

The PO-SCORAD index, widely used and validated in many publications,²⁴ is a self-assessment scale that allows the patients to evaluate the severity of AD by using subjective and objective criteria derived mainly from the SCORAD.

The PO-SCORAD index was used by parents for evaluating AD on days 7 and 14. The current study evaluated the objective criteria only and omitted the subjective criteria.²⁵

During the first visit with the parents, they were trained how to properly fill out the questionnaire assessing the PO-SCORAD index, demographic data, mother and infant health, as well as breastfeeding status.

The research assistant who assessed the AD result was "blind" to the interventions used on the affected area. Parents were asked to return the questionnaire completed on days 7 and 14 at the end of intervention (day 21) and to bring their infants for clinical reassessment.

Sample size

As there are no known studies to date that provide a comparison of HBM and hydrocortisone treatment, we have designed our trial based on the Pocock method. This method necessitates a sample size of 100 to achieve a fair assessment; therefore, 50 participants were selected for each trial condition.

Statistical analysis

The differences between the topical application of human milk and 1% hydrocortisone ointment were assessed using the chi-squared test on nominal and ordinal data and the independent

samples *t*-test for quantitative data if distributions were found to be normal according to the Kolmogorov–Smirnov test. The objective SCORAD index scores from the baseline were non-parametric. These were analyzed by performing the Mann–Whitney *U* test to compare groups at each reference time and Friedman's one-way analysis of variance to compare change over time in each group. We calculated a *post hoc* pairwise comparison with the Wilcoxon signed-rank test when $P < 0.05$ was in the analysis of variance. Statistical analyses were performed using SPSS version 20 software. $P < 0.05$ was considered statistically significant for analyses.

Results

Demographics and baseline characteristics of infants

A total of 104 infants were enrolled in the trial and randomly distributed into two groups to receive the topical application of HBM ($n = 54$) or 1% hydrocortisone ointment ($n = 50$). During the trial, eight infants were excluded from the hydrocortisone group and three infants from the HBM group due to the parents' failure to follow the assigned intervention properly. In addition, one participant in the hydrocortisone ointment group exhibited

Table 1 Demographics and baseline characteristics of study participants and comparisons between topical application of HBM and 1% hydrocortisone ointment groups

	Topical application of HBM group ($n = 54$)	1% Hydrocortisone ointment group ($n = 50$)	<i>P</i> value ^b
Gender, <i>n</i> (%)			
Male	29 (53.7)	32 (64)	0.32
Female	25 (46.3)	18 (36)	
Age (month), mean (SD)	4.73 (4.51)	4.34 (5.22)	0.14
Ethnicity			
Fars	33 (61.1)	29 (58)	0.53
Turk	7 (13)	5 (10)	
Kurd	6 (11.1)	6 (12)	
Lor	6 (11.1)	8 (16)	
Other	2 (3.7)	2 (4)	
Objective SCORAD, mean (SD)	15.62 (3.89)	17.76 (5.32)	0.8
Severity of AD, ^a <i>n</i> (%)			
Mild	21 (38.89)	14 (28)	0.24
Moderate	33 (61.11)	36 (72)	
Severe	0 (0)	0 (0)	
Exposure to day care, mean (SD)	0.074 (0.26)	0.04 (0.19)	

AD, atopic dermatitis; HBM, human breast milk.

^aSeverity of AD defined according to the objective SCORAD index: mild <15, moderate 15 to <40, severe >40.^{24,27}

^b $P < 0.05$ is significant.

an exacerbation of AD signs and so was excluded from the study (Fig. 1).

There was no significant difference between the topical application of HBM and the 1% hydrocortisone ointment groups in any of the demographic or baseline characteristics (Table 1).

Table 2 Comparison of the severity of atopic dermatitis between topical application of HBM and 1% hydrocortisone ointment groups in days 0, 7, 14, and 21

	Topical application of HBM group (n = 54)	1% Hydrocortisone ointment group (n = 50)	P value ^a
Day 0, mean (SD) ^b			
Total score ^c	15.62 (3.89)	17.76 (5.32)	0.8
Extent	6.4 (2.38)	7.5 (5.6)	0.53
Intensity	4.05 (1.07)	4.5 (1.23)	0.092
Day 7, mean (SD)			
Total score ^d	4.3 (5.05)	7.2 (6.97)	0.28
Extent	2.36 (3.02)	4.43 (6.23)	0.056
Intensity	1.09 (1.3)	1.8 (1.73)	0.038
Day 14, mean (SD)			
Total score ^d	1.94 (3.65)	3.7 (5.5)	0.83
Extent	0.95 (1.8)	2.7 (5.1)	0.055
Intensity	0.5 (0.94)	0.9 (1.32)	0.098
Day 21, mean (SD)			
Total score ^c	1.25 (3.3)	1.61 (3.32)	0.43
Extent	0.75 (1.83)	1.77 (4.5)	0.36
Intensity	0.48 (1.67)	0.37 (0.72)	0.48

HBM, human breast milk.

^aBy using Mann–Whitney *U*-test and Bonferroni correction, $P < 0.0125$ is significant.

^bValues are presented as mean (SD).

^cObjective SCORAD.

^dPO-SCORAD.

Effect of human breast milk on the extent and severity of atopic dermatitis

No significant differences were found between the total O-SSI scores, extent, or intensity of either group before intervention ($P = 0.8$). In addition, there were no significant differences found in the between-group comparisons for all reference times (days 7, 14, and 21), which were assessed using Mann–Whitney *U*-test and Bonferroni correction (Table 2).

There were significant differences in the total score, extent, and intensity over time in both groups ($P < 0.001$, using Friedman's analysis of variance). When reference times were compared, significant differences were yielded as well ($P < 0.001$ and Wilcoxon signed-rank test). The results showed the frequency of severity of atopic eczema in the aspect of total score for the topical application of HBM and 1% hydrocortisone ointment groups at days 0, 7, 14, and 21 (Fig. 2).

The frequency of healed infants was 81.5% and 76% in HBM and 1% hydrocortisone groups on day 21 respectively.

Discussion

This is the first study that shows the benefits of the topical application of HBM for infants with mild to moderate AD. Through this study, it has been shown that the topical application of HBM has a role in the treatment of this condition. We have also provided evidence that HBM is as effective in healing infants' AD as 1% hydrocortisone. The degree of improvement in the infants' skin condition was similar between the two groups at days 7, 14, and 21.

There is no research regarding the efficacy of HBM in infants with AD that allows or facilitates a comparison of findings. Most studies exploring the treatment of AD have compared immunosuppressive drugs.

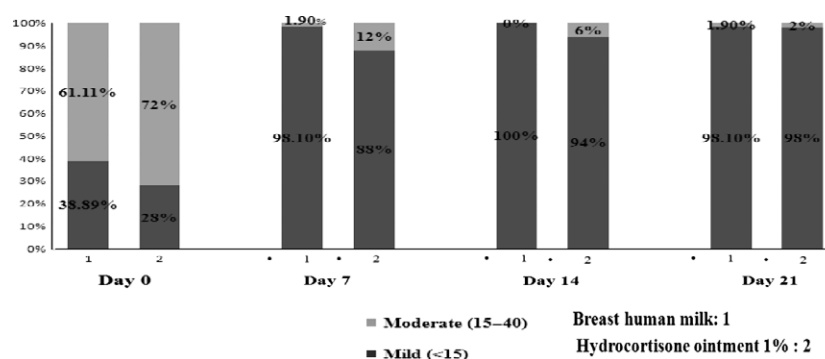


Figure 2 Comparison of frequency of severity of atopic eczema in aspect of total score between topical application of HBM and 1% hydrocortisone ointment groups at days 0, 7, 14, and 21

HBM has many immunologic and anti-infective agents that act as natural antimicrobials. It also contains protective factors that provide specific and nonspecific passive immunity.²⁶

Breast milk had no side effects, and its immunologic and anti-infective agents were examined in several studies. Our results satisfy those from previous studies in this regard. Pishva *et al.* indicated the topical application of HBM as having beneficial effects on the prevention of neonatal conjunctivitis.²⁷ Mohammadzadeh *et al.* showed the therapeutic effect of HBM and lanolin on sore nipples. HBM was found to heal nipples faster than using lanolin.¹⁷

Ahmadpour and his colleagues compared the effects of topical HBM to ethyl alcohol 96%, dry care, and silver sulfadiazine groups on the umbilical cord separation time. They showed that the mean cord separation time in the HBM group was significantly shorter than the other groups.¹⁴

Penjvini *et al.* reported that the topical application of HBM was an effective treatment for the healing of diaper rash. They showed that there were no significant differences between the HBM and zinc oxide groups with respect to lesion size, inflammation, and intense erythema.²⁸

The results of the present study suggest that the HBM can improve infant atopic eczema with the same results as 1% hydrocortisone ointment. We recommend the use of HBM for curing infant atopic eczema due to its healing effect and availability.

Acknowledgments

This research was supported by the research grant no. 637 from Arak University of Medical Sciences and registered to IRCT201208313869N5 in the Iran Randomized Clinical Trial (IRCT) center. The author would like to thank Prof. Arnold P. Oranje, pediatric dermatologist, in the pediatric dermatology unit at the Erasmus University Hospital Rotterdam, for his constructive help, Kayla J. Power for valuable assistance in English language editing of the article, and the mothers and their infants who participated in this study.

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