

Effectiveness of Emollients in the Prevention of Atopic Dermatitis in Infants: A Meta-Analysis

Di Xu^a Rainer Stengel^b Pengfei Sun^c

^aDepartment of Dermatology, Zibo Central Hospital, Zibo, China; ^bDepartment of Dermatology, Senior Expert Service, Freiburg, Germany; ^cDepartment of Plastic Surgery, Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Keywords

Atopic dermatitis · Infants · Emollients

Abstract

Background: Atopic dermatitis (AD) is a chronic skin disease characterized by dry skin, severe itching, inflammation and impaired quality of life. Moisturizing is an integral part of treatment for AD, but its potential for prevention of AD is unclear. **Objective:** To evaluate whether the early use of emollients in infancy can prevent later development of AD. **Methods:** We searched Medline, Embase, Web of Science, PubMed, Cochrane Library and other databases to collect randomized controlled trials on early use of emollients in infants for a meta-analysis. **Results:** Nine articles were included. The OR value for incidence rate was 0.7 (95% CI: 0.48–1.01). No significant publication bias was found by Egger's test. The sensitivity analysis indicated that the final conclusion was reliable. **Conclusions:** We found that the difference in incidence rate of AD between the experimental and control groups was not statistically significant. However, due to different methods of using emollients, different follow-up times and different sample sizes included in this meta-analysis, a definitive conclusion could not be reached in this study. In the future, it is still necessary to carry out randomized controlled, multicenter, large-sample trials with

an excellent study design and high methodological quality on early application of emollients in high-risk infants to prevent AD.

© 2021 S. Karger AG, Basel

Introduction

Atopic dermatitis (AD), a chronic inflammatory skin disease, can affect the quality of life of patients and their families. Most children with AD present with pruritus, dry skin, and eczematous rash before they are 1 year old [1]. At present, it is not clear whether early use of skin emollients in infants can effectively prevent AD [2–6]. We therefore carried out a meta-analysis to evaluate whether the use of skin emollients in infants can prevent the later development of AD.

Materials and Methods

This meta-analysis was performed strictly in accordance with the requirements of the PRISMA statement. Medline, Embase, Web of Science, PubMed and Cochrane Library were searched from their inception to October 2020. Among them, the detailed retrieval strategies for PubMed were: ("Emollients"[Mesh]) OR (Emollient)) AND ("Dermatitis, Atopic"[Mesh]) OR (Atopic Der-

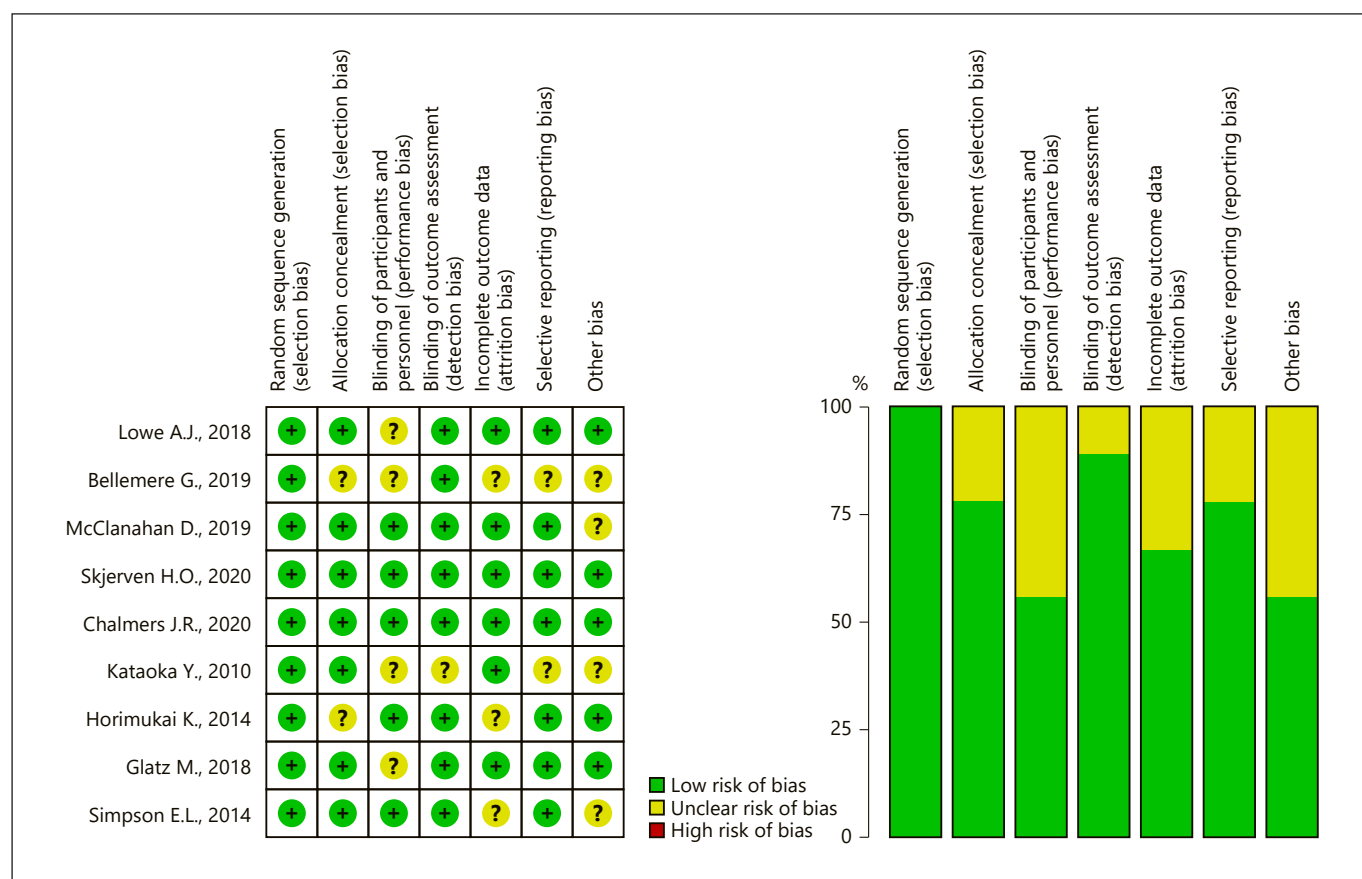


Fig. 1. The Cochrane risk bias assessment.

matitides) OR (Atopic Dermatitis) OR (Dermatitides, Atopic) OR (Neurodermatitis, Atopic) OR (Atopic Neurodermatitides) OR (Atopic Neurodermatitis) OR (Neurodermatitides, Atopic) OR (Neurodermatitis, Disseminated) OR (Disseminated Neurodermatitides) OR (Disseminated Neurodermatitis) OR (Neurodermatitides, Disseminated) OR (Eczema, Atopic) OR (Atopic Eczema) OR (Eczema, Infantile) OR (Infantile Eczema) AND ("Infant"[Mesh]) OR (Infants). No language restrictions were implemented in the literature search. We only extracted available data from published articles.

Inclusion criteria: (1) the type of study: randomized controlled trial (RCT); (2) the subject populations: infants (0–12 months); (3) intervention: the experimental groups were subjected to daily use of emollients, while the control groups received no regular administration of emollients.

Exclusion criteria: (1) any publication type other than RCT; (2) republished papers; (3) the study populations other than infants; (4) papers containing incomplete information.

Two researchers read the abstracts of literature and excluded papers according to the criteria. Papers that met the inclusion criteria were used for further analysis. Consensus was required for inclusion, and in cases of dissenting assessment papers were discussed by all the authors until consensus was reached.

The Cochrane risk of bias assessment tool was used to evaluate the quality of the included literature. There were no significant factors affecting the meta-analysis (Fig. 1).

We used STATA version 14.0 to calculate a 95% confidence interval (CI) for the incidence of AD of the included patients. The heterogeneity of the literature was tested according to the Cochrane Handbook requirements, and an $I^2 > 50\%$ was considered indicative of high heterogeneity. If the heterogeneity was high, we would use the random-effect model for the meta-analysis. Conversely, we would use the fixed-effect model for the meta-analysis. We used Egger's test to assess publication bias. Sensitivity analysis was realized by a one-by-one exclusion method. For analysis of combined effects, $p < 0.05$ was used to indicate significant differences between the experimental and control groups.

Results

A total of 1,606 papers were retrieved. After screening, 9 papers meeting the inclusion criteria were included [7–15]. The basic information of the included articles is shown in Table 1, and the specific paper screening pro-

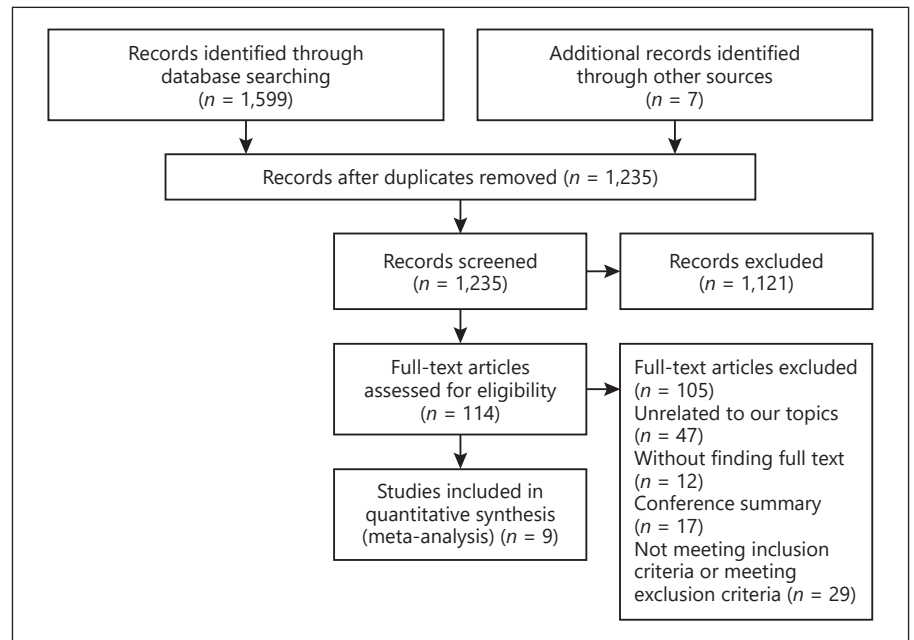


Fig. 2. Article screening flow diagram.

Table 1. The information table for the articles

| Author | Year | Country | Trial type | Number of subjects | Number of AD in treated/ placebo group | Intervention | Follow- up | Conclusion |
|------------------------|------|------------------|------------|----------------------------|--|--------------|------------|--|
| Kataoka et al. [7] | 2010 | Japan | RCT | 35 treated 32 placebo | 5/6 | Emollients | 6 months | The application of emollients in infants cannot reduce the incidence of AD |
| Horimukai et al. [8] | 2014 | Japan | RCT | 59 treated 59 placebo | 19/28 | Emollients | 32 weeks | The application of emollients in infants can reduce the incidence of AD |
| Simpson et al. [9] | 2014 | USA | RCT | 53 treated 55 placebo | 12/24 | Emollients | 6 months | The application of emollients in infants can reduce the incidence of AD |
| Lowe et al. [10] | 2017 | Australia | RCT | 38 treated 37 placebo | 2/6 | Emollients | 12 months | The application of emollients in infants can reduce the incidence of AD |
| Glatz et al. [11] | 2018 | USA | RCT | 11 treated 12 placebo | 1/3 | Emollients | 24 weeks | The application of emollients in infants can reduce the incidence of AD |
| Bellemere et al. [12] | 2019 | France | RCT | 60 treated 60 placebo | 6/11 | Emollients | 24 months | The application of emollients in infants can reduce the incidence of AD |
| McClanahan et al. [13] | 2019 | USA | RCT | 54 treated 46 placebo | 8/12 | Emollients | 12 months | The application of emollients in infants can reduce the incidence of AD |
| Chalmers et al. [14] | 2020 | UK | RCT | 598 treated 612 placebo | 139/150 | Emollients | 2 years | The application of emollients in infants cannot reduce the incidence of AD |
| Skjervén et al. [15] | 2020 | Norway Sweden | RCT | 575 treated 596 placebo | 64/48 | Emollients | 12 months | The application of emollients in infants cannot reduce the incidence of AD |

cess is shown in Figure 2. The comparison results of the incidence rate of AD between the experimental and control groups are shown in Figure 3. The odds ratio (OR) value for the incidence rate was 0.7 (95% CI: 0.48–1.01). The difference between the experimental and control

groups was not statistically significant ($z = 1.90$, $p = 0.057$). No significant publication bias was found by Egger's test ($p > 0.05$). We used the one-by-one exclusion method to perform the sensitivity analysis, which proved that the final conclusion was reliable (Fig. 4).

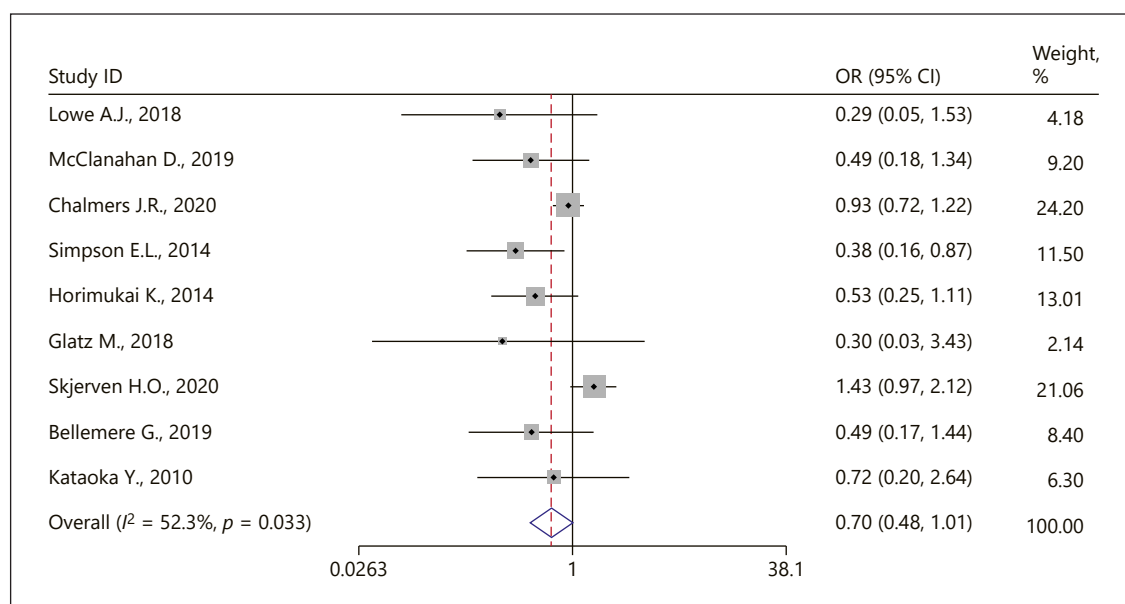


Fig. 3. Results of meta-analysis.

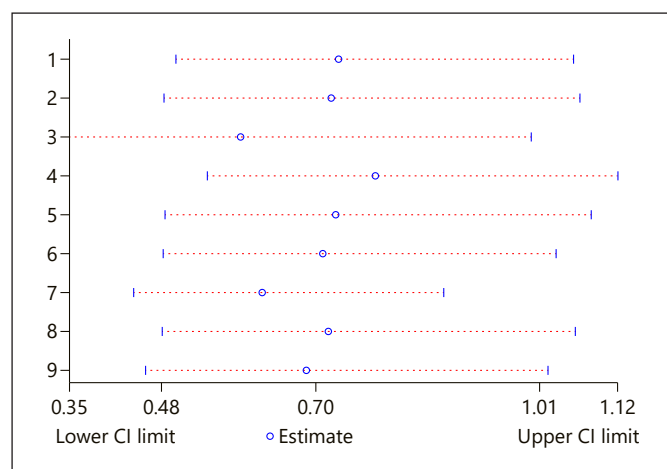


Fig. 4. Results of sensitivity analysis.

Discussion

Studies have found that regular use of emollients can alleviate clinical symptoms in patients with AD, delay flares, and reduce the dosage of topical corticosteroids [16–20]. At present, however, it is not clear whether early use of skin emollients in infants can effectively prevent AD.

We included 9 RCTs in this meta-analysis (1,483 patients in the intervention group and 1,509 in the control

group), and found the OR = 0.7 (95% CI: 0.48–1.01). The results of this meta-analysis suggest that the use of emollients in early life (before 1 year) in high-risk infants does not significantly prevent the development of AD. However, this result needs to be further verified by high-quality RCTs.

Of the 9 studies included, 6 supported the early use of emollients while 3 did not. The 3 studies that did not support the prevention of AD by early use of emollients, namely the studies by Chalmers et al. [14], Kataoka et al. [7], and Skjerven et al. [15], were more rigorous in design but lacked detailed information on the specific amount and frequency of emollient use in the experimental groups. The 6 studies supporting the prevention of AD by early use of emollients shared the common limitations of small sample size and short follow-up time. We believe that increasing the sample size and extending the follow-up time may ultimately lead to a conclusion that does not support the prevention of AD by early use of emollients. However, due to different methods of using emollients, different follow-up times and different sample sizes included in this meta-analysis, a definitive conclusion could not be reached in this study.

Heterogeneity in meta-analyses should always be paid attention to. In this study, the heterogeneity of the included literature was not high ($I^2 = 52.3\%$). The heterogeneity included the small sample sizes of most included studies, and different evaluated outcomes. The sensitivity test indicated that our conclusion was reliable.

At present, there are only few published papers in this field, and the conclusion of our study is therefore likely to be influenced by potential publication biases. We included articles written in English only because there were few articles on this topic written in other languages. However, in this meta-analysis, no significant publication bias was found by Egger's test, and the stable OR value of our sensitivity test suggested that our final conclusion is reliable.

This study also has some limitations: not all the included articles mentioning random grouping provide the specific randomization methods. The subject populations of the included articles come from different regions, and the sample sizes of the included articles vary greatly. Different amounts and administration methods of the emollients were used in the included studies.

In conclusion, in the future, it is still necessary to carry out randomized controlled, multicenter, large-sample trials with an excellent study design and high methodological quality on the early application of emollients in high-risk infants to prevent AD. It is better to conduct a comprehensive study with a fixed type of emollients, a fixed amount of emollients, a fixed frequency of emollient administration, and multiple outcome evaluation indicators.

Key Message

This meta-analysis shows that the application of emollients does not significantly reduce the later development of infantile AD.

References

- 1 Roduit C, Frei R, Depner M, et al. Phenotypes of atopic dermatitis depending on the timing of onset and progression in childhood. *JAMA Pediatr.* 2017;171(7):655–62.
- 2 Egawa G, Kabashima K. Multifactorial skin barrier deficiency and atopic dermatitis: essential topics to prevent the atopic march. *J Allergy Clin Immunol.* 2016;138(2):350–e1.
- 3 Kelleher M, Dunn-Galvin A, Hourihane JO, et al. Skin barrier dysfunction measured by transepidermal water loss at 2 days and 2 months predates and predicts atopic dermatitis at 1 year. *J Allergy Clin Immunol.* 2015;135(4):930–5.e1.
- 4 van Zuuren EJ, Fedorowicz Z, Arents BWM. Emollients and moisturizers for eczema: abridged Cochrane systematic review including GRADE assessments. *Br J Dermatol.* 2017;177(5):1256–71.
- 5 Flohr C, Ahmed A. New evidence challenges use of bath emollients for children with eczema. *BMJ.* 2018;361:k1791.
- 6 Santer M, Ridd MJ, Francis NA, et al. Emollient bath additives for the treatment of childhood eczema (BATHE): multicentre pragmatic parallel group randomised controlled trial of clinical and cost effectiveness. *BMJ.* 2018;361:k1332.
- 7 Kataoka Y, Yoshida N, Nishino H, et al. Can skin care from neonatal period prevent the onset of atopic dermatitis? *Allergo J.* 2010;19(5):338–9.
- 8 Horimukai K, Morita K, Narita M, et al. Application of moisturizer to neonates prevents development of atopic dermatitis. *J Allergy Clin Immunol.* 2014;134(4):824–30.e6.
- 9 Simpson EL, Chalmers JR, Hanifin JM, et al. Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention. *J Allergy Clin Immunol.* 2014;134(4):818–23.
- 10 Lowe AJ, Su JC, Allen KJ, et al. A randomized trial of a barrier lipid replacement strategy for the prevention of atopic dermatitis and allergic sensitization: the PEBBLES pilot study. *Br J Dermatol.* 2018;178(1):e19–e21.
- 11 Glatz M, Jo JH, Kennedy EA, et al. Emollient use alters skin barrier and microbes in infants at risk for developing atopic dermatitis. *PLoS One.* 2018;13(2):e0192443.
- 12 Bellemere G, Boyer G, De Belilovsky C, et al. Prevention of atopic dermatitis using emollients for 6 months – follow-up for 24 months. *J Invest Dermatol.* 2019;139(5):S97.
- 13 McClanahan D, Wong A, Kezic S, et al. A randomized controlled trial of an emollient with ceramide and filaggrin-associated amino acids for the primary prevention of atopic dermatitis in high-risk infants. *J Eur Acad Dermatol Venereol.* 2019;33(11):2087–94.

Statement of Ethics

No ethical approval was needed because data in our study came from previously published studies in which informed consent was obtained by the original investigators.

Conflict of Interest Statement

The authors have no conflicts of interest.

Funding Sources

No funding was received for this study.

Author Contributions

R.S. contributed to the conception of the study. X.D. and S.P. were responsible for data analysis and writing the first draft of the manuscript. All coauthors contributed to the writing of the manuscript. All coauthors have provided important intellectual input and approved the final version of the paper.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

- 14 Chalmers JR, Haines RH, Bradshaw LE, et al. Daily emollient during infancy for prevention of eczema: the BEEP randomised controlled trial. *The Lancet*. 2020(10228):395.
- 15 Skjerven HO, Rehbinder EM, Vettukattil R, et al. Skin emollient and early complementary feeding to prevent infant atopic dermatitis (PreventADALL): a factorial, multicentre, cluster-randomised trial. *The Lancet*. 2020; 395(10228):951–61.
- 16 Perrett KP, Peters RL. Emollients for prevention of atopic dermatitis in infancy. *Lancet*. 2020;395(10228):923–4.
- 17 Tiplica GS, Boralevi F, Konno P, et al. The regular use of an emollient improves symptoms of atopic dermatitis in children: a randomized controlled study. *J Eur Acad Dermatol Venereol*. 2018;32(7):1180–7.
- 18 Lindh JD, Bradley M. Clinical effectiveness of moisturizers in atopic dermatitis and related disorders: a systematic review. *Am J Clin Dermatol*. 2015;16(5):341–59.
- 19 Tiplica GS, Kaszuba A, Malinauskienė L, et al. Prevention of flares in children with atopic dermatitis with regular use of an emollient containing glycerol and paraffin: a randomized controlled study. *Pediatr Dermatol*. 2017;34(3):282–9.
- 20 Tiplica GS, Boralevi F, Konno P, et al. The regular use of an emollient improves symptoms of atopic dermatitis in children: a randomized controlled study. *J Eur Acad Dermatol Venereol*. 2018;32(7):1180–7.

Copyright of Dermatology (10188665) is the property of Karger AG and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.