

ORIGINAL ARTICLE

Clinical effects of undershirts coated with borage oil on children with atopic dermatitis: A double-blind, placebo-controlled clinical trial

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ABSTRACT

It has been reported that γ -linolenic acid contained in borage oil is effective against atopic dermatitis. The clinical effects of undershirts coated with borage oil rich in γ -linolenic acid on atopic dermatitis were evaluated. Thirty-two children, aged 1–10 years, were involved in the clinical control study. Sixteen had worn undershirts coated with borage oil everyday for 2 weeks, and 16 had worn non-coated undershirts as a placebo. Their symptoms were assessed on a 4-point scale. Those children who had worn undershirts coated with borage oil for 2 weeks showed improvements in their erythema and itch, which were statistically significant. Transepidermal water loss from the back was decreased. In the placebo group, there were no statistically significant differences. The undershirts coated with borage oil were found to be statistically effective, and had no side-effects on children with mild atopic dermatitis.

Key words: atopic dermatitis, borage oil, γ -linolenic acid, transepidermal water loss, undershirts.

INTRODUCTION

Atopic dermatitis (AD) is a common inflammatory skin disorder that is both uncomfortable and distressing to patients as a result of the associated intense itch and unsightly lesions. The majority of cases arise within the first year of life.¹ Patients with AD show a variety of humoral and cell-mediated immune dysfunctions. In the patients with AD, an abnormality in metabolism of polyunsaturated fatty acids (PUFA) is commonly observed.^{2,3} PUFA are structural components of the cell membrane phospholipids, which are important in maintaining membrane fluidity. In the PUFA family, linoleic acid (LA) of the n-6 series and α -linolenic acid (ALA) of the n-3 series are essential fatty acids (EFA) because it is impossible to biosynthesize them within the human body, and so we must absorb them through our diets. EFA

give rise to C₂₀ (eicosanoic) fatty acids which are biosynthetic precursors to a very important group of physiologically and pharmacologically active compounds, the eicosanoids.⁴ Transepidermal water loss (TEWL) has been shown to be increased in the skin of the patients with AD, and it has been suggested that they have a primary defect in the epidermal barrier located in the stratum corneum.⁵

It has been reported that the oral and topical administration of γ -linolenic acid (GLA), which is a metabolite of LA, was effective against AD.^{6–13} The effects of GLA have also been reported for hemodialysis patients with itch and dryness of the skin¹⁴ and on infantile seborrheic eczema.¹⁵ The four main sources of GLA are borage oil, which contains the largest quantity of GLA (24%), black currant seed oil (15%), evening primrose oil (7–9%) and human milk (0.6%).¹⁰ GLA can also be generated within

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the body through the desaturation of LA by the action of the rate-limiting enzyme δ -6-desaturase.³ In our study, to investigate the effects of the topical administration of GLA on AD, we developed the undershirts which were coated with borage oil containing a high dose of GLA, and had children with AD wear them and examined the consequent effects. We had children with AD wear borage oil coated undershirts and non-coated undershirts in a double-blind, placebo-controlled clinical trial. We then compared the effects of borage oil coated undershirts versus non-coated undershirts on the symptoms of AD.

METHODS

The undershirts used in our study were made of pure organic cotton. Borage oil (Fukusen, Wakayama, Japan) was chemically bonded to the cotton fibers of the undershirts. The borage oil was gradually released from the cotton fibers and absorbed into the skin. The borage oil remained on the undershirts even after washing over 60 times. The undershirts were designed such that the sutures did not touch and stimulate the skin directly. Before the study, we performed patch tests with cotton cloths used in this study in 13 subjects with non-atopic healthy adults. The patch test revealed that there were no negative effects (data not shown).

We investigated the effects of undershirts coated with borage oil in a double-blind, placebo-controlled clinical trial. The study consisted of 32 children (21 boys, 11 girls, aged 1–10 years old, mean 5.0) with mild-to-moderate AD as defined by Hanifin and Rajka¹⁶ who visited our department between January and March 2002. The patients with severe symptoms were excluded from the study. The parents of all children as well as the patients gave their informed consent to participation in the study. Undershirts coated with borage oil (including 498 mg of GLA per 100 g of cotton) and non-coated placebo undershirts were provided. The patients were randomly divided into two groups, 16 patients (9 boys, 7 girls, mean 4.44) with undershirts coated with borage oil (BO group) and 16 patients (12 boys, 4 girls, mean 5.56) with non-coated undershirts (placebo group). The patients wore the undershirts for 2 weeks. We gave three undershirts to each patient

Table 1. Concomitant treatment of the patients

Treatment	BO group	Placebo group
Topical corticosteroids		
Mild class	9	4
Strong class	4	3
Very strong class	1	2
Emollients	11	10
Antihistamines	8	8

Values indicate numbers. BO group, patients wearing undershirts coated with borage oil; placebo group, patients wearing non-coated undershirts.

and instructed them to change their undershirt and wash it everyday. We assessed the clinical activity objectively at the beginning of the study and after 2 weeks. The clinical symptoms of AD, erythema, itch, papules, erosion, scaling and lichenification were all scored on a 4-point scale (0–3, representing grades of “none”, “mild”, “moderate” and “severe”). All clinical evaluations were performed by the same clinician in a blind fashion. Furthermore, TEWL from the back was measured at the beginning and after 2 weeks with DermaLab (Cortex Technology, Hadsund, Denmark). The parents of the patients assessed their overall impression at the end of study in three degrees: “improved”, “unchanged” and “worse”. We permitted no changes in concomitant treatment before the study and during the study, except in the quantity and frequency of topical corticosteroid application, which could be decreased if the symptoms were improved during the study. Table 1 shows concomitant treatment. No patients received systemic corticosteroid therapy.

Statistical analysis was performed with the Wilcoxon matched-pairs signed-rank test. $P < 0.05$ was considered to be statistically significant.

RESULTS

No patients withdrew from the study. The results are shown in Tables 2 and 3 and Figure 1. In the BO group, statistically significant improvements were observed for the symptoms of itch ($P = 0.033$) and erythema ($P = 0.033$) (Table 2). Papules, erosion, scaling and lichenification revealed no statistically significant differences in the BO group. There were no statistically significant differences in the placebo group for all clinical symptoms. Table 3 shows the

Table 2. Changes of scores of the clinical symptoms before and after wearing undershirts

Symptoms	BO group (<i>n</i> = 16) Duration of treatment (week)		Placebo group (<i>n</i> = 16) Duration of treatment (week)	
	0	2	0	2
Itch	1.44 ± 0.51	0.94 ± 0.57*	1.31 ± 0.60	1.06 ± 0.57
Erythema	0.81 ± 0.83	0.31 ± 0.48*	0.75 ± 0.77	0.50 ± 0.63
Papules	0.94 ± 0.77	0.56 ± 0.63	0.81 ± 0.54	0.69 ± 0.70
Erosion	0.13 ± 0.34	0.00 ± 0.00	0.06 ± 0.25	0.06 ± 0.25
Scaling	0.06 ± 0.25	0.00 ± 0.00	0.13 ± 0.34	0.06 ± 0.25
Lichenification	0.06 ± 0.25	0.00 ± 0.00	0.13 ± 0.34	0.06 ± 0.25

Numbers indicate means ± standard deviation (SD). **P* < 0.05 (Wilcoxon matched-pairs signed-rank test).

Table 3. Overall assessments of response by children's parents

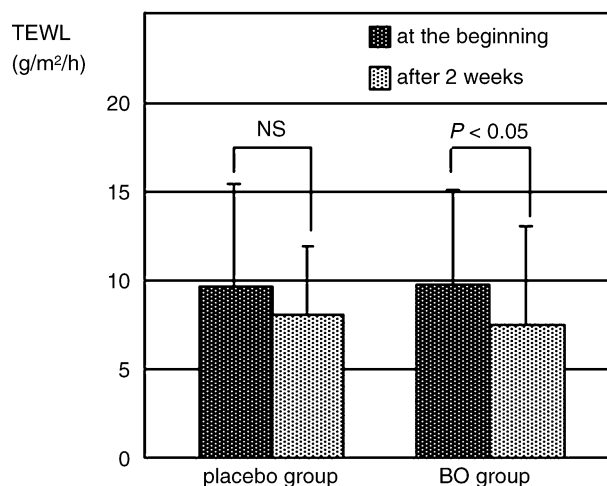
	BO group (<i>n</i> = 16)	Placebo group (<i>n</i> = 16)
Improved	12 (75.0)	9 (56.2)
Unchanged	4 (25.0)	7 (43.8)
Worse	0 (0.0)	0 (0.0)

Values indicate numbers (percentages).

assessments of the overall response to the undershirts by the children's parents. In the BO group, 75% of children's parents believed that the clinical symptoms were improved by wearing the undershirts, versus 56.2% in the placebo group. TEWL from the back before and after 2 weeks are shown in Figure 1. In the BO group, there was a statistically significant decrease in TEWL between before and after 2 weeks (*P* = 0.0480). However, there was no statistically significant difference in the placebo group (*P* = 0.1026). In the study, no side-effects were noted.

DISCUSSION

Essential fatty acids have important roles in the structure and physiology of the skin. Many studies have shown that there are abnormal metabolisms of EFA in many tissues in patients with AD.² Because of the deficiency in the activity of δ -6-desaturase, LA cannot be converted into GLA in the patients with AD.¹⁷ As a result, GLA, dihomo- γ -linolenic acid (DGLA), and arachidonic acid (AA), which are metabolites of LA, are decreased in many tissues of AD patients.¹⁷⁻²¹ Several clinical studies have confirmed that the oral and topical administration of GLA has beneficial effects

**Figure 1.** Changes of transepidermal water loss (TEWL) from the back at the beginning and after 2 weeks. In the group with undershirts coated with borage oil (BO group), there was a statistically significant decrease (*P* = 0.0480). However, there was no difference in the placebo group (*P* = 0.1026).

on AD. By administering GLA, the δ -6-desaturase block in AD patients is bypassed,²² and DGLA level is increased. DGLA is converted into prostaglandin E1 (PGE1) and 15-hydroxy-DGLA which have anti-inflammatory properties.² PGE1 activates adenylate cyclase, which increases the intracellular cyclic adenosine monophosphate (AMP) levels of mast cells and basophils, thereby leading to a dose-dependent inhibition of histamine release.²² Itch is the symptom that seems to respond best to GLA.^{8,10,23} This might be explained by the fact that PGE1 mediates the inhibition of histamine release from mast cells and basophils.^{22,23} Moreover, cyclic AMP can inhibit

phospholipase A2, an enzyme important in releasing AA during inflammation.³ 15-Hydroxy-DGLA can also inhibit the 5- and 12-lipoxygenase systems which generate pro-inflammatory metabolites such as leukotriene B4 from AA.^{24,25}

There are some studies about the effects of topical administration of GLA on patients with AD.^{9,12} AD has a basic problem of pathogenic significance due to the impaired epidermal barrier function, which can be documented as increased TEWL.¹² It has been suggested that there are abnormalities in epidermal lipid metabolism in patients with AD.² This would lead to a defective structure of the intercellular multiple-lipid bilayer constituting the water barrier in the stratum corneum, and subsequently to an increased evaporative water loss and dry skin.² Dry skin and itch are typical of patients with AD, and dry skin correlates with a disturbed epidermal barrier function. Hartop indicated that LA and GLA are important in maintaining the barrier function of the epidermis. In their studies of EFA-deficient rats, TEWL was restored toward normal when LA and GLA were applied topically to the skin.²⁶ Beside the anti-inflammatory effects of GLA on skin epidermis, it might play a physical structural role in the stability of the skin.

In our study, we investigated the effects of undershirts coated with borage oil on mild-to-moderate AD. We excluded severe AD patients from the study because they needed to be given potent topical steroids. Horrobin indicated powerful corticosteroids interfere with the ability to show an effect of GLA.²⁷ We considered that wearing the undershirts coated with borage oil had the similar effects to the topical application of borage oil. It was showed that there were statistically significant improvements in both erythema and itch, which are often found in mild-to-moderate AD patients. A decreased TEWL means an improvement in the barrier function of the stratum corneum. The effect of GLA on itch has been particularly remarkable in the past studies.^{8,10,23} Scratching is one of the important factors exacerbating AD. The reduction of itch by borage oil coated undershirts may prevent an exacerbation of AD due to scratching. In addition, there may also be a significant reduction in the need for corticosteroids. In the placebo group, there were no statistically significant differences in the clinical symptoms. However, 56.2% of the

patients regarded their clinical symptoms as improved. Because the undershirts used in this study were made of pure organic cotton and were of very high quality, it seemed that those patients wearing placebo undershirts also improved in their clinical symptoms to some degree. In our study, the observation periods were short, so the long-term beneficial effects of undershirts coated with borage oil should be evaluated further.

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