

Emollients improve treatment results with topical corticosteroids in childhood atopic dermatitis: a randomized comparative study

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The aim of the study was to investigate whether adding emollients to the standard topical corticosteroid therapy influences the outcome of children with atopic dermatitis. Fifty-two children aged between 2 and 12 yr were divided randomly in two subgroups consisting of 26 children each. Both groups applied 0.1% methylprednisolone aceponate cream on lesional atopic skin once daily for 2 wk and were observed for another 4 wk after treatment discontinuation. Group B used additionally emollients for the whole study period. Patients were evaluated at days 0 (baseline), 7, 14 (end of therapy), 28 and 42 (follow-up). Both groups demonstrated significant improvement of disease severity according to EASI (Eczema Area and Severity Index) scale (group A: 6.8 ± 3.59 before and 0.87 ± 1.25 after therapy, $p < 0.001$; group B: 9.6 ± 8.39 before and 1.11 ± 2.37 after therapy, $p < 0.001$). Xerosis improved significantly better in group B compared to group A, both clinically (group A: 1.38 ± 0.57 scores before and 1.5 ± 0.58 scores after therapy, $p = 0.11$; group B: 1.62 ± 0.64 scores before and 0.12 ± 0.33 scores after therapy, $p < 0.001$), and by corneometry assessment (group A: 41.7 ± 9.1 units before and 51.3 ± 11.3 units after therapy, $p < 0.001$; group B: 38.9 ± 12.9 units before and 58.2 ± 13.5 units after therapy, $p < 0.001$). A trend towards faster resolving of pruritus in group B (group A: 5.44 ± 2.6 scores before and 3.22 ± 2.31 scores after therapy, $p = 0.001$; group B: 5.87 ± 2.79 scores before and 2.24 ± 1.59 scores after therapy, $p < 0.001$) was also observed. In group B, the improvement was maintained for couple of weeks after treatment discontinuation, while in group A recurrence of the disease was noted (EASI at day 42 in group A vs. group B: 5.29 ± 5.6 vs. 1.25 ± 1.4 , $p = 0.01$). Similar results were also observed for xerosis ($p < 0.001$) and pruritus ($p = 0.002$). Concomitant usage of emollients significantly improves xerosis and pruritus during corticosteroid treatment of atopic dermatitis and enables to maintain clinical improvement after therapy discontinuation.

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Therapies directed towards restoring the impaired barrier function of the epidermis seem to be of significant importance in atopic dermatitis (AD). Emollients, which reconstruct integrity and continuity of stratum corneum, may blockade penetration of air-borne allergens across damaged skin barrier and prevent AD

flares (1). The usage of emollients is also recommended during therapy of AD exacerbations (2, 3). However, only a few randomized studies exist evaluating their efficacy in AD (4–6). Here, we performed a study to investigate whether addition of emollients to the standard topical corticosteroid therapy of

AD would influence the outcome of children with AD.

Materials and methods

Study design

The study consisted of 2 wk of active treatment phase and 4 wk of follow-up period. The total duration of the study was 6 wk. Following criteria had to be fulfilled before inclusion of any patient into the study: patients' age over 2 and below 12 yr (childhood AD) (3), established diagnosis of AD, active stage of AD, patients' parents had to approve the study concept and sign an informed consent. The exclusion criteria were as follows: presence of other skin or systemic disease which could influence the results of the study, known allergy to allergens which could not be avoided during the study, patients were unwilling or unable to participate in all study visits.

All included patients were randomly divided into two groups consisting of 26 children each. Both groups did not differ significantly between themselves according to age and gender as well as regarding any of the analysed parameters (AD severity, itching intensity, clinical severity of skin dryness, electrical capacitance of the epidermis) before inclusion into the study. Group A applied topical corticosteroid (0.1% methylprednisolone aceponate cream) on the lesional atopic skin once daily for the period of 2 wk and was next followed for 4 wk. The usage of any other drugs including also any emollients was not allowed during the study period. Group B additionally to 0.1% methylprednisolone aceponate cream for the period of 2 wk used emollients for the whole study period: a cream (Balneum Baby[®] Cream, Hermal, Reinbek, Germany) was applied in the morning and an oilbath containing mainly soybean oil (Balneum Hermal[®], Hermal, Reinbek, Germany) was added to the bath in the evening. Before entering the study parents had been instructed regarding the usage of the emollients. The cream was applied topically on the whole body surface and during one application about 20 g of the product were used and the oil bath was performed according to manufacturer's instruction.

Patients were examined before treatment (Day 0), as well as every 1 wk during active phase of the study (Day 7 and Day 14), and every second week during the follow-up period (Day 28 and Day 42). The study was approved by the local ethic committee (decision KB 224/2006).

Patients

Fifty-two children suffering from AD: 25 (48.1%) males and 27 (51.9%) females were included into the study. Theirs age ranged between 2 and 12 yr (mean 5.9 ± 2.8 yr, median 6 yr). None of the included patients suffered simultaneously from any other skin or systemic disorders. The AD severity before inclusion, assessed according to EASI (Eczema Area and Severity Index), ranged between 1.4 and 39.7 points (mean 8.2 ± 6.5 points). All parents approved the study concept and signed the informed consent regarding the participation of their children in the study.

Assessment of studied parameters

The severity of AD was assessed according to EASI scale (3). Itching intensity was evaluated by the 10-point visual analogue scale (VAS), where 0 points referred to none itching, and 10 points referred to the worst itching. The clinical severity of skin dryness was scored according to the 5-point scale, as described previously (7). The skin hydration was also assessed by the electrical capacitance measurements of the outer layers of epidermis by Corneometer CM 820[®] (Courage-Khazaka electronic GmbH, Cologne, Germany). In every patient involved skin within the flexural area of forearm, and uninvolved skin in the same location were chosen for measurements. The same areas were assessed each time. The measurements were always performed after 10-min rest in sitting position, at the same time, at constant room temperature (20–22°C) and relative humidity (40–50%).

Results

Severity of atopic dermatitis

All patients in both groups finished the active phase treatment (first 2 wk of the study). However, only 17 (65.4%) participants from group A lasted out to the latest follow-up visit (Day 42) compared to 22 (84.6%) subjects from group B ($p = 0.1$). The reasons for discontinuation in group A were AD exacerbation and in group B, AD exacerbation in three (11.5%) patients and mother request in one (3.8%) patient. The treatment was well tolerated in both study groups. Except the disease worsening mentioned above, we did not observe any significant side effects.

Both groups demonstrated significant improvement of disease severity according to

EASI scale during the active treatment phase ($p < 0.001$) (Table 1, Fig. 1a). No significant difference was noted between group A and group B regarding the disease severity at Day 14 ($p = 0.71$). However, in group B, the improvement was maintained for couple of weeks after treatment discontinuation, while in group A recurrence of the disease was noted ($p = 0.01$) (Table 1, Fig. 1b). The disease severity in group A at Day 42 did not differ from baseline ($p = 0.15$), in contrast to group B where patients at Day 42 had still significantly less severe AD compared to Day 0 ($p < 0.001$) (Table 1, Fig. 1b). At Day 42, the responders ratios in group A were also significantly lower compared to group B ($p < 0.01$) (Fig. 1c).

Itching intensity

A significant improvement of itching intensity was noted in both groups during active treatment phase (group A: $p = 0.001$, group B: $p < 0.001$) (Table 1, Fig. 1d). Despite a trend towards faster resolving of pruritus in group B, the difference at Day 14 between group A and group B was not significant ($p = 0.13$) (Fig. 1d). However, itching intensity increased significantly in group A after treatment discontinuation ($p < 0.001$) and at the end of the study did not differ from the baseline visit ($p = 0.75$) (Table 1, Fig. 1e). In contrast, the itching intensity during follow-up period remained significantly reduced in group B compared to baseline ($p < 0.001$) (Table 1, Fig. 1e).

Table 1. Comparison of disease severity, itching intensity, skin dryness and stratum corneum hydration between group A and group B

	Day 0	Day 7	Day 14	Day 28	Day 42	p^*
Disease severity – EASI (points)						
Group A (n = 26)	6.8 ± 3.59	2.46 ± 2.26	0.87 ± 1.25	–	–	<0.001
Group B (n = 26)	9.6 ± 8.39	2.7 ± 5.34	1.11 ± 2.37	–	–	<0.001
$p^\dagger$	0.37	0.18	0.71	–	–	–
Group A (n = 17)	6.38 ± 3.6	2.29 ± 2.45	0.72 ± 1.36	4.33 ± 5.95	5.29 ± 5.6	<0.001 ‡
Group B (n = 22)	8.06 ± 5.54	1.45 ± 1.54	0.55 ± 0.67	0.87 ± 0.93	1.25 ± 1.4	<0.001
$p^\dagger$	0.51	0.28	0.98	0.004	0.01	–
Pruritus – VAS (points)						
Group A (n = 26)	5.4 ± 2.6	3.6 ± 2.5	3.2 ± 2.3	–	–	0.001
Group B (n = 26)	5.9 ± 2.8	3.2 ± 2.3	2.24 ± 1.6	–	–	<0.001
$p^\dagger$	0.57	0.53	0.08	–	–	–
Group A (n = 17)	4.72 ± 2.82	3.01 ± 2.45	2.64 ± 2.13	4.07 ± 2.37	4.95 ± 2.28	<0.001 §
Group B (n = 22)	6.13 ± 2.71	3.3 ± 2.27	2.18 ± 1.58	3.0 ± 1.64	2.52 ± 2.19	<0.001
$p^\dagger$	0.12	0.7	0.44	0.1	0.002	–
Skin dryness – clinical assessment (points)						
Group A (n = 26)	1.38 ± 0.57	1.38 ± 0.57	1.5 ± 0.58	–	–	0.11
Group B (n = 26)	1.62 ± 0.64	0.56 ± 0.65	0.12 ± 0.33	–	–	<0.001
$p^\dagger$	0.31	<0.001	<0.001	–	–	–
Group A (n = 17)	1.36 ± 0.57	1.36 ± 0.57	1.48 ± 0.59	1.6 ± 0.71	1.35 ± 0.61	0.9
Group B (n = 22)	1.55 ± 0.51	0.48 ± 0.51	0.05 ± 0.21	0.05 ± 0.21	0.05 ± 0.21	<0.001
$p^\dagger$	0.25	<0.001	<0.001	<0.001	<0.001	–
Skin hydration – electrical capacitance – lesional skin (AU)						
Group A (n = 26)	41.7 ± 9.1	50.9 ± 8.5	51.3 ± 11.3	–	–	<0.001
Group B (n = 26)	38.9 ± 12.9	58 ± 13.9	58.2 ± 13.5	–	–	<0.001
$p^\dagger$	0.25	0.05	0.05	–	–	–
Group A (n = 17)	43.1 ± 9.8	53.0 ± 8.8	54.2 ± 11.2	48.8 ± 10.1	44.8 ± 10.1	0.02 §
Group B (n = 22)	38.3 ± 12.7	57.9 ± 12.2	58.5 ± 11.0	63.7 ± 9.7	60.1 ± 10.3	<0.001
$p^\dagger$	0.15	0.22	0.31	<0.001	<0.001	–
Skin hydration – electrical capacitance – non-lesional skin (AU)						
Group A (n = 26)	61.9 ± 9.7	61.5 ± 7.1	61.8 ± 6.7	–	–	0.74
Group B (n = 26)	58 ± 8.4	66.3 ± 8.7	68 ± 8.8	–	–	<0.001
$p^\dagger$	0.09	0.01	0.001	–	–	–
Group A (n = 17)	62.4 ± 9.7	62.8 ± 6.8	62.4 ± 6.6	61.9 ± 7.4	61.5 ± 9.2	0.91
Group B (n = 22)	58.1 ± 7.8	66.8 ± 7.1	68.9 ± 6.2	72.7 ± 4.6	73.3 ± 5.0	<0.001
$p^\dagger$	0.09	<0.05	0.002	<0.001	<0.001	–

All results are presented as mean values ± standard deviations.

EASI, eczema area and severity index; VAS, visual analogue scale; AU, arbitral units.

*According to Friedman analysis of variance.

†According to Mann–Whitney *U*-test.

‡Significant difference compared to Day 0 only at Day 7, Day 14 and Day 28.

§Significant difference compared to Day 0 only at Day 7 and Day 14.

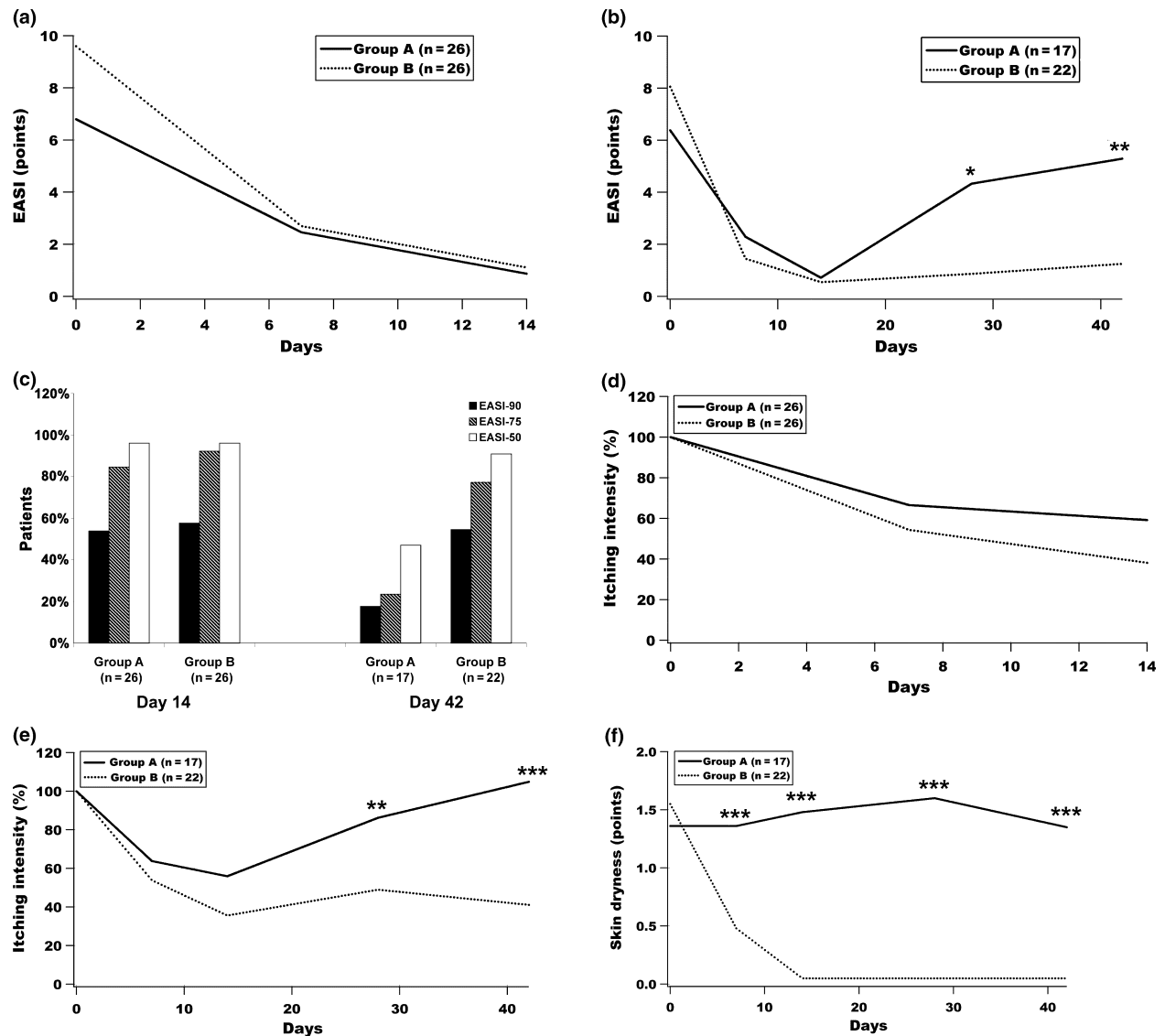


Fig. 1. Comparison of atopic dermatitis improvement between group A using topical corticosteroids and group B using combination of topical corticosteroids and emollients. (a) Mean Eczema Area and Severity Index (EASI) scoring during active phase treatment. (b) Mean EASI scoring during active phase treatment and follow-up period. (c) Comparison of atopic dermatitis improvement between group A and group B at Day 14 ($p = 0.78$) and Day 42 ($p < 0.01$) demonstrated as $\geq 90\%$ (EASI-90), $\geq 75\%$ (EASI-75) and $\geq 50\%$ (EASI-50) reduction of EASI scoring. (d) Comparison of itching intensity assessed according to 10-point Visual Analogue Scale (VAS) during active phase treatment (results demonstrated as percentage of itching intensity at baseline visit). (e) Comparison of itching intensity during active phase treatment and follow-up period (results demonstrated as percentage of itching intensity at baseline visit). (f) Comparison of clinical severity of skin dryness assessed according to 5-point scale during active phase treatment and follow-up period (comparison of group A vs. group B on A,B,D,E,F: Mann-Whitney U -test: * $p = 0.004$, ** $p = 0.01$, *** $p < 0.001$).

Skin dryness

No significant improvement of clinically rated skin xerosis was observed in group A at any point of the study ($p = 0.9$, $n = 17$) (Table 1, Fig. 1f). On the other hand, a rapid improvement of skin dryness was found in group B, which was noted as quick as at Day 7 ($p < 0.001$) and this enhancement of skin moisture was maintained during the whole follow-up period (Table 1, Fig. 1f). Regarding electrical capacitance mea-

surements, a significant improvement of skin dryness was noted in group B, both within lesional and non-lesional skin (Table 1). However, we also found significant increase of skin moisture in patients belonging to group A at Day 7 and Day 14. This improvement was limited only to lesional atopic skin (Table 1). Discontinuation of the treatment resulted in significant worsening of skin hydration in this group of patients (Table 1). Comparison of electrical capacitance between group A and group B

revealed that the improvement of skin dryness was significantly better in patients additionally applying emollients (Table 1).

Discussion

One of the most widely used treatment modalities of AD is the usage of emollients. However, the efficacy of this therapy in AD has not been yet well proven well. Grimalt et al. (4) observing nearly 200 infants with AD for 6 wk noted, that the usage of emollient containing oat extracts as addition of the standard topical corticosteroid treatment reduced the total high-potency topical corticosteroid consumption. Despite similar decrease of AD severity and itching in both groups, patients applying emollients demonstrated significantly better improvement of skin dryness and sleeping disturbances (4). In another study evaluating the usage of emollients in combination with twice daily applications of desonide 0.05% lotion in children with mild-to-moderate AD (6) it was documented, that application of emollients trice-daily as addition to corticosteroid therapy for 3 wk resulted in significantly greater improvement of disease severity, pruritus and skin dryness compared to corticosteroid treatment without any additional moisturizers. Emollients were also shown to significantly decrease the risk of irritant contact dermatitis, both in AD and non-AD subjects, while added to a propanol-based hand rub for skin disinfection (8). Although in our study we did not notice significant differences regarding disease severity among patients applying corticosteroids alone or corticosteroids in combination with emollients, similar trend towards greater improvement was also observed in the group using emollients. In our opinion, the slight discrepancies between our results and the study by Hanifin et al. (6) may reflect differences in the initial disease severity, usage of different corticosteroid (methylprednisolone aceponate vs. desonide) and different scheme of emollients usage. Nevertheless, we documented that additional usage of emollients during AD flares significantly improves skin dryness and enables to maintain the achieved remission in the majority of patients. It was also shown, that the risk of AD recurrence could be further diminished by the addition of topical corticosteroids twice weekly to the maintenance therapy with emollients or the use of special silk clothes (5, 9). Among many available products restoring the altered AD epidermis, a recently developed ceramide-dominant, barrier repair

emollient seems to be of special interest as it was demonstrated that stratum corneum in AD has reduced ceramide content (10).

Another important point of AD care is an education of patients and their families. It was clearly documented, that an educational training of AD children's parents improves the regular use of emollients, use of antiseptics and topical steroids in the event of exacerbation, and leads to the reduction in the use of unconventional therapies.

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