ISSN 2658-6630 (Print)
ISSN 2658-6622 (Online)

CONSILIUM MEDICUM

Педиатрия №3 2022

Научно-практический, рецензируемый журнал,
посвящен различным проблемам педиатрии

Pediatrics. Consilium Medicum

OmniDoctor

https://doi.org/10.26442/26586630.2022.3.201825

The results of the study of the effectiveness of the use of emollient in the form of foam, enhanced with ceramides and cholesterol-phytosterol complex, in patients with atopic dermatitis

D.V. Zaslavsky[1], A.N. Barinova[2,3], S.L. Plavinsky[2], M.I. Zelyanina[4], E.S. Menshova[1]
[1]FGBOU VO St. Petersburg State Pediatric Medical University', Ministry of Health of Russia, St. Petersburg, Russia;
[2]FGBOU VO "North-Western State Medical University named after I.I. Mechnikov" of the Ministry of Health of Russia, Saint-Petersburg, Russia;
[3]SPb GBUZ "City Hospital No. 26", St. Petersburg, Russia;
[4]000 Clinic of Skin Diseases of Pierre Wolkenstein", St. Petersburg, Russia

Target. To study the effectiveness of a combined topical agent in the form of foam and the effect of a complex of ceramidamides, a cholesterol-phytosterol complex, bisobolol and pyroctonolamine in its composition on the course of mild and moderate AD.
Materials and methods. A prospective cohort study included 30 children aged 3 to 17 years with mild to moderate AD who applied emollient foam to the affected areas of the skin, surrounding skin and skin with signs of dryness for 4 weeks. The severity of AD was measured in all participants using the SOCARD, EASI, IGA scales, skin pH, skin hydration and transepidermal water loss (TEWL), as well as the severity of itching and xerosis according to visual analogue scales.
Results. The severity of AD in children whose skin was treated with emollient foam decreased by 22.8 points according to the 5!0 .0 index, by 3.1 points according to the EAS1 index (in both cases p<0.001). During the study, skin moisture increased (by 23.5% compared with baseline; p<0.001), while TEWL decreased (by 5.45 g/hm2; p<0.001); Skin pH decreased towards normal by 0.2 units (p=0.002). It has been established that indicators of skin hydration and TEWL correlate with the severity of AD, with a decrease in severity with an increase in moisture and a decrease in TEWL. The smell was rated as good or excellent by 100% (95% confidence interval - CI 88.4-100%) of the respondents, the texture - by 90% (95% CI 73.5-98.0%), and the ease of use - 97% (95% CI 82.8-99.9%) of those surveyed.
Conclusion. A combined topical agent in the form of a foam with ceramides, a cholesterol-phytosterol complex, bisobolol and piroctonolamine is recommended in the treatment of AD.

Key words: atopic dermatitis, emollients plus, skin hydration, corneometry, vapometry
For citation: Zaslavsky D.V., Barinova A.N., Plavinsky S.L., Zelyanina M.I., Manylova E.S. The results of the study of the effectiveness of the use of emollient in the form of foam, enhanced with ceramides and cholesterol-phytosterol complex, in patients with atopic dermatitis. Pediatrics. Consilium Medicum. 2022;3:001:10.26442/26586630.2022.3.201825

Introduction

Atopic dermatitis (AD) is a chronic inflammatory disease that develops in individuals with a genetic predisposition to atopy, which has a relapsing course with age-related clinical manifestations, characterized by increased sensitivity to specific (allergenic) and nonspecific stimuli. AD is considered as a manifestation of the atopic march, which is understood as the typical progression of the clinical symptoms of allergic diseases in childhood. Several studies have shown that AD is positively associated with asthma. It has been shown that the risk of developing bronchial asthma in children with AD is 2 times higher than in children without it [1].

AD is one of the most common diseases of childhood, affecting 15 to 20% of children and 1 to 7% of adults. According to statistics, in 45% of children with AD, symptoms appeared during the first 6 months of life, in 60% - in the first year of life, and in 85% of patients - before the age of 5. The prevalence of the disease in the Russian Federation in children is 11.7 times higher than in adults, the incidence in children is 15.6 times higher than in adults. With such a high incidence and prevalence, the number of dermatological beds for children in the Russian Federation in 2021 was only 1009 (19% of the adult dermatological bed fund - 5062).

According to the annual reports of the dermato-venerological department of the clinic of St. Petersburg State Medical University, presented in Table. 1, it can be seen that the 1st place in the structure of skin diseases in children is occupied by AD with growth dynamics from 46 to 49.6%.

AD is a complex skin inflammatory multifactorial disease involving a complex interplay of epidermal barrier defects, immune dysregulation of both adaptive and innate immunity, and the environment. Debates continue as to whether AD is due to genetic mutations affecting the epidermal barrier (outside-in model) or caused by inflammation that suppresses epidermal differentiation (inside-out model) [2]. Violation of the barrier function of the skin is associated with the state of the microbiota. In the 2018 EADVrecommendations, *Staphylococcus aureus* aggregation is named the main trigger of AD [3], while the long-term use of local antibiotics is not recommended due to the risk of increasing antibiotic resistance and sensitization, the use of local antiseptics is shown, especially in chronic course and reduced response to standard therapy, and local antifungal agents with a predominant lesion of the "head and neck" and in the presence of immunoglobulin E to *Malassezia* ssp.

The agile toxins of *S. aureus* agile toxins are superantigens that cause T-cell activation, expression of anti-staphylococcal antibodies of immunoglobulin E, increase the expression of interleukin-31 receptors, which predisposes to the development of itching. Chronic inflammation, itching and scratching, combined with a deficiency of antimicrobial lipids, play an important role in reducing the colonization resistance of the epidermis of AD patients and form a vicious circle, aggravating the barrier function impairment.

Dry skin is one of the characteristic symptoms of AD. There is now scientific evidence of genetically determined skin barrier abnormalities in humans and mice that facilitate the penetration of the allergen into the skin and predispose to the development of irritation and subsequent inflammation in the skin. Filag green deficiency is the most well-defined anomaly, which leads to a deficiency of molecules formed during the catabolism of filaggrin and having a high hygroscopicity. In addition, the lack of intercellular lipids of the stratum corneum and an inadequate ratio of compounds (cholesterol, essential fatty acids, ceramides) increase transepidermal water loss (TEWL), which contributes to epidermal microdamage. Violation of the skin barrier predisposes to the development of inflammation.

Table 1. The structure of dermatoses in children who were on inpatient treatment in the dermatovenerological department SPb GBUZ clinics from 2019 to 2021.
Table 1.

Diseases	Years					
	2019		2020		2021	
	Abs.	%	Abs.	%	Abs.	%
AD	652	46	492	41,3	1061	49,6
Psoriasis	278	20	240	19,8	506	23,6
Pyoderma	47	3	68	5,7	101	4,7
Seborrheic dermatitis of infants	10	0,71	24	2	7	0,32
Scleroderma	148	10,5	161	11,2	176	8,23
Toxicoderma	60	4,27	123	9,7	69	5,57
Acne	30	2,13	72	5,9	17	0,79
Hair diseasecne	41	2,92	28	2,3	73	3,41
Congenital ichthyosis	–	–	9	0,76	11	0,5

The main therapy is aimed at restoring the impaired barrier function and eliminating triggers. Emollients moisturize the epidermis, create an occlusive layer, and reduce evaporation. Studies have found that the effective and regular use of emollients - emollients - reduces the need for topical corticosteroids, reduces the frequency and severity of exacerbations. For this reason, ***therapy with emollients and moisturizers is the mainstay of AD therapy in children and adults***, it is prescribed to all patients, regardless of severity [4-6]. A comprehensive review of 14 independent published clinical guidelines from around the world (USA, UK, Europe, Japan, Korea, Singapore, Canada, South Africa and selected European countries) showed that daily moisturizing and softening are common recommendations for the treatment of AD [7].

The concept of "moisturizers" includes products that include 3 groups of substances [8] or combinations thereof: occlusives, emollients, moisturizers.

Occlusives include substances that create a hydrophobic barrier on the skin (such as cholesterol), which reduces TEWL. Humectants can increase the transport of moisture from the dermis to the epidermis, from the deep/mid layers of the epidermis to the surface, and in humid conditions they also help the stratum corneum absorb water from the external environment. The most commonly used substances in this group are glycerol and urea. Emollients, usually lipids and carbohydrates, fill the gaps between groups of corneocytes, but do not create a pronounced occlusive effect. Examples of such substances are propylene glycol and isopropyl palmitate. Sometimes the term "emollient" refers to all emollients (because, for example, isopropyl palmitate has both properties), so in this paper the terms "emollients/moisturizers" and "emollients" will be used interchangeably.

Recently, more and more attention has been paid to emo tapes, in which additional components are included to improve their properties [9], for example, ceramides (“emollients plus”). Typically, "emollients" are defined as "topical formulations with carrier-type substances that lack active ingredients", while "emollients plus" refer to "topical formulations with carrier-type substances and additional active, non-pharmacological substances" [3].

Ceramide deficiency appears to be one of the major alterations in AD, and replenishment of this epidermal component through topical application of ceramide-based emollients is safe, well tolerated, and effective [10,11]. For example, treatment with synthetic pseudoceramides has been shown to improve atopic skin by switching the ceramide profile to a healthy skin phenotype. Four weeks of treatment with synthetic pseudoceramides significantly reduced the severity of skin symptoms, which was accompanied by a significant decrease in TEWL and an increase in water content in the stratum corneum [12].

A randomized controlled trial of an emollient with ceramide and filaggrin-associated amino acids for the primary prevention of AD in high-risk children demonstrated that there was a numerical trend in favor of its use across all clinical endpoints, although not statistically significant, probably due to insufficient coverage. AD was diagnosed in 13.2% vs. 25.0% at 12 months (p=0.204) and in 19.4% vs. 31.0% at 2 years (p=0.296) in the intervention group compared to the control group, respectively [13]. In another study, 24 children with AD were recruited.

Of these, 2/3 of the patients reported very good or good tolerance of the lipid ceramide precursor moisturizer, while 1/3 reported fair or poor tolerance. After the use of a ceramide lipid precursor moisturizer, the objective score of Scoppig og Aturyu Vegtatltw (SCORAD - AD index), scores of pruritus, and sleep disturbance scores were lower in the very good/good tolerance group than in the fair/poor tolerance group. The mean objective score of SCORAD improved (from 31.5 to 25.7; p=0.039) and skin hydration improved (from 30.7 to 36.0 c.u.; p=0.021) in the very good/good acceptability group [14]. A cohort study evaluated the efficacy of a twice-daily regimen of ceramide-containing cleanser and moisturizer in men, women, and children with AD. The duration of treatment was 6 weeks. Participants under 12 years of age (n=33) were separated into a separate group. On the 42nd day, the indicators of SCORAD in children showed

https://doi.org/10.26442/26586630.2022.3.201825

a significant improvement (p=0.0001). Similar effects were observed for pruritus, with scores improving from severe pruritus to pruritus only when the skin was moist (p = 0.0001) [15].

In 2021, the state registration in the Russian Federation and the countries of the EAEU received a moisturizing and nourishing foam for dry sensitive skin BLUE CAP of the company CATALYSIS, S.L.(Madrid, Spain), which contains as active ingredients ceramides (NRP, AP, EOP), phytosphingosine, cholesterol, glycerin, bisobolol and piroctonolamine, *as well as other substances belonging to all three groups of substances for emollient hearts* such as, propylene glycol, isopropyl palmitate and diethylhexyl carbonate. In other words, the emollient is enhanced with ceramides and a cholesterol-phytosterol complex. Phytosphingosine, bisobolol and piroctonolamine, which are part of the product, are important for the normalization of the microbiota and suppression of growth of *S. aureus* and yeast-like fungi.

It has been proven that sphingosines also have activity against *S. aureus* and *Candida albicans* [16], bisobolol is not only an excellent natural antiseptic, but also has an anti-inflammatory [17] effect, since it reduces the production of pro-inflammatory cytokines, and piroctonolamine has a high antifungal activity against the fungi *Malassezia* [18].

Such a tool can be attributed to the group of "emollients plus", therapeutic moisturizers [19]). For the use of drugs in pediatric practice in children with AD, it is desirable to have data on the tolerability and effectiveness of these drugs, the composition of which corresponds to the basic principles of therapy aimed at restoring the impaired skin barrier function and eliminating triggers.

An important advantage of the BLUE CAP foam is also the shape of the preparation *drug form*. First: the foam has a light, airy texture that spreads very easily over the surface (literally with a few light movements) and is quickly absorbed, which minimizes skin contact during application, which is especially important for children. Secondly: hermetic packaging, which excludes bacterial contamination and oxidation of the contents, ensures the constancy of the composition and microbiological purity. This is an important advantage of the remedy, since in the recommendations of EADV 2018 "Consensus-based European guidelines for tratment of atopic eczema (atopic dermatitis) in adults and children", data are provided that creams and ointments that patients use become bacterially contaminated in 53% of cases, in 25% of cases they are contaminated with *S. aureus* [3,20].

The purpose of the study was to study the effect of a multicomponent emollient foam on the course of AD of mild and moderate severity.

To achieve the goal, the following tasks were set: to evaluate the dynamics of changes in the severity of AD during treatment using a combined foam emollient for moisturizing; evaluate the dynamics of skin hydration, TEWL and skin pH; to study the relationship between changes in the severity of AD and indicators of the barrier function of the skin during the use of the drug; analyze the assessment by patients and / or their legal representatives of the organoleptic properties and ease of use of the drug.

Materials and methods

The study included 30 patients with mild to moderate AD, aged 3 to 17 years. The inclusion criteria were a confirmed (on the basis of the criteria HnSn and IC'ka [21]) diagnosis of AD with the values of the SCORAD index less than 50 points; exudative, erythematous-squamous with/without lichenification or lichenoid clinical and morphological form of AD in the stage of exacerbation of the underlying disease with severe clinical manifestations without oozing and secondary infiltration of the skin or the stage of incomplete remission with a limited localized prevalence of the skin process. Also, patients/legal representatives were required to agree not to use illegal drugs for the duration of the study. Prohibited drugs included any other cosmetics or topical moisturizing drugs (emollients), topical in-calcineurin inhibitors, any local and systemic glucocorticosteroids, any systemic immunosuppressants, systemic antibacterial and antiviral drugs, systemic antihistamines. Phototherapy with ultraviolet radiation was also prohibited during the study.

Information on the conduct of the local ethical committee (LEK). French Clinic of Skin Diseases Pierre Wolkenstein, St. Petersburg, session LEC 05/2022 dated 03/15/2022, protocol BLC-2022. The study was conducted from 03/25/2022 to 05/27/2022. All study participants or their legal representatives gave informed consent to participate prior to inclusion in the study.

Used moisturizing and nourishing foam for dry sensitive skin BLUE CAP - hereinafter referred to as foam. The mode of use included application to the affected areas, the skin surrounding them, and skin with signs of dryness. The drug was applied to well-cleansed and dry skin, at least 1 time per day for 4 weeks.

During participation in the study, 3 visits were provided - the initial visit, the intermediate visit in the middle of the study and the end of the study visit. The total time of participation in the study ranged from 26 to 31 days. At all visits, the severity of the disease was assessed according to the SCORAD and E8AI indices, as well as the overall assessment of the severity of AtD by the investigator (IAS); xerosis intensity and pruritus intensity were analyzed using a visual analogue scale (VASH-K and VASH-3, respectively). At each visit, objective indicators of the skin barrier function were measured in the form of skin moisture (corneometry method), TEWL (te-vametry/vapometry method) and pH using the Multiskin Test Center MC750. Upon completion of the use of the drug, the organoleptic properties of BLUE CAP foam, and satisfaction with its use were evaluated.

Table 2. Interpretation of skin moisture indicators [23]
Table 2.

Meaning	Humidity level	Detailed information	
45–99,9	Very tall	45–99,9	Very tall
30–44,9	Normal	40,1–44,9	High normal
		35,1–40	Medium normal
		30–35	Low normal
0–29,9	Short	20,1–29,9	Short
		Below 20	Very low

TEWL<25 g/hcm2 and skin pH 4.5-5.5 were used as reference values. To interpret the degree of skin moisture (since the method of corneometry is semi-quantitative [22]), the limits given in Table 1 were used. 2.

The severity of the disease was established on the basis of the value of the SCORAD index [24]: mild - less than 25 points, moderate - from 25 to 50 points, severe - more than 50 points. The EA8I score ranges from 0 to 72 [25]: 0 indicates clear skin or no eczema; 0.1 to 1.0 indicates almost complete absence of eczema; 1.1 to 7 indicates mild disease; 7 1 to 21 is moderate disease, 21.1 to 50 is severe disease, and more than 51 is very severe disease. As auxiliary indicators, the indices SCORAD 25, SCORAD 50 and SCORAD 100 were calculated, which means an improvement in scores by 25, 50 and 100%, respectively.

For statistical data analysis, non-parametric statistics methods were used due to the small size of the group and the impossibility to exclude deviations from the normal distribution, as well as the semi-quantitative nature of a number of variables. Statistical processing of the results included the calculation of the median of changes in the values of quantitative indicators and their interquartile distance, as well as the assessment of the median and interquartile distances for visits. To assess the significance of changes between visits 1 and 3, the scores were compared using a paired Wilcoxon test. Relationships between objective indicators of skin barrier function and AD severity indices were studied based on Spearman's rank correlation coefficients. When conducting a qualitative assessment of objective indicators of the barrier function of the skin and global indices, the proportion of patients in certain groups was calculated and the exact 95% confidence interval (CI) for the proportion (Klopper-Pearson) was calculated. A Type I error level of 5% was chosen as the boundary value for deciding whether to reject the null hypothesis, about the absence of significant dynamics or differences in proportions (i.e., to reject the null hypothesis, p<0.05 was required). Statistical data processing was performed in the K system (version 3.5).

Results

The main results of assessing changes in measured indicators during the study are given in Table. 3.

As can be seen from Table. 3, during the study there were significant changes in all measured indicators. The SCORAD index decreased by 22.8 points - from 34.5 to 12.2 points (p<0.001), EASI - by 3.1 points - from 5.1 to 2 points (p<0.001). VASH scores for pruritus and xerosis decreased by 4 points (out of 10 possible) (p<0.001 in both cases). TEWL decreased by 5.5 g/hcm2 (p<0.001) and skin hydration increased (by 23.5% of the original). Significantly decreased, by 0.2 units, and skin pH (p = 0.002), however, the median value for the group is (**See Table 3**).

At the 2nd visit, all patients showed clinical improvement: SCORAD 25 achieved 73.3% (95% CI 57.7-90.1%) of patients, SCORAD 50 - 13.33% (95% CI 3.7-30 .7%). At the final visit, SCORAD 100 and SCORAD 75 reached 20 (95% CI 7.7-20.6%) and 36.7% (95% CI 19.9-56.1%) patients, respectively (p<0.01); rice. 1, the EASI index also improved.

In percentage terms, improvements in skin hydration, TEWL, and pH were smaller, so the proportion of people with an improvement of at least 10% was calculated for them, but data for improvements of 100 and 75% are not provided (Fig. 2, 3).

The figures show Clopper-Pearsons, since they are determined at zero values, there are no columns at the corresponding positions, but there is an interval (at 0, the upper limit is at the level of 11.6%).

Thus, significant favorable changes in indicators were identified, but a more detailed qualitative analysis was required to determine how clinically significant they were. The results of this analysis are presented in Table 4.

As can be seen from Table. 4, the greatest positive dynamics was noted for the SCORAD index: if at the visit of inclusion in the study 87% (95% CI 69-96%) of all patients had index values exceeding 25 (moderate severity of the disease), then by the visit of the completion of treatment there were only 10% (95% CI 2.1-26.5%). Since the CIs did not overlap, this means that the proportion of people with moderate severity of the disease

Table 3. Changes in the main indicators for the period of treatment with Blue Cap foam.
Table 3.

Index	Median (IQR), values			Median change, visit 1-3 (IQR)	p according to the Wilcoxon test
	Visit 1	Visit 2	Visit 3		
SCORAD	34,45 (15,78)	22,15 (14,48)	12,2 (13,53)	22,8 (7,65)	<0,001
EASI	5,05 (2,38)	3,55 (2,47)	2 (2,13)	3,1 (1,8)	<0,001
IGA	2 (1)	2 (1)	1 (1)	1 (0)	<0,001
VASH-3	6 (2)	4 (3)	2 (1,75)	4 (1,75)	<0,001
VASH-K	6 (1)	5 (1,75)	3 (2)	4 (2,75)	<0,001
TEWL (vapometry, g/hm^2)	33,55 (3,95)	29,95 (3,73)	28,95 (4,65)	5,45 (3,53)	<0,001
Humidity (corneometry)	21,05 (5,83)	24 (4,79)	25,95 (3,13)	-4,95 (4,48)	<0,001
pH	5,9 (0,4)	5,5 (0,75)	5,7 (0,48)	0,2 (0,68)	0,002

Note. IQR - interquartile distance.

[1]Certificate of state registration of products RU.77.01.34.001.R..002994.11.21 dated 11/30/2021, Expert opinion on product compliance with the technical regulations of the Customs Union 77.01.12.P.004324.11.21 dated 11/03/2021.

https://doi.org/10.26442/26586630.2022.3.201825

Table 4. Qualitative assessment of objective indicators of skin barrier function and global indices by visits
Table 4.

Index	Detailed information		
	Abs. (p); 95% GO		
	Visita 1	Visita 2	Visita 3
Humidity (low)	100 (30); 88,4–100	93,3 (28); 77,9–99,2	86,7 (26); 69,3–96,2
TEWL (increased)	100 (30); 88,4–100	100 (30); 88,4–100	100 (30); 88,4–100
pH (abnormal)	86,7 (26); 69,3–96,2	56,7 (17); 37,4–74,5	63,3 (19); 43,9–80,1
SCORAD (>25)	86,7 (26); 69,3–96,2	46,7 (14); 28,3–65,7	10,0 (3); 2,1–26,5
EASI (>1)	100 (30); 88,4–100	96,7 (29); 82,8–99,9	63,3 (19); 43,9–80,1
IGA (>1)	93,3 (28); 77,9–99,2	53,3 (16); 34,3–71,7	46,7 (14); 28,3–65,7

has significantly decreased. Looking at the EASI index, at visit 1 all patients had values greater than 1, i.e. had at least a mild illness. By the end of the study visit, 63% remained (95% CI 44-80%), again the decrease was significant, and in fact, in 37% of patients the skin was practically cleared (less than 1 EASI point is received by patients with clear skin and/or no eczema). or almost complete absence of eczema). At the same time, the dynamics of objective indicators in the qualitative interpretation was less pronounced.

In order to understand in more detail the relationships between disease severity indices and objective indicators of the skin barrier function, a rank correlation analysis was performed, the results of which are presented in Table 5.

As can be seen from Table 5, skin hydration significantly correlated with both SCORAD and EASI. The only exception was the relationship between moisture content at the 1st visit and the SCORAD index at the 3rd one, although even here there was an approach to the limit of significance ($p = 0.051$). The degree of relationship with the values of the SCORAD index was moderate for moisture content at the 1st visit (about 0.36-0.45) and pronounced for the moisture index at the 3rd visit (0.65-0.76). The same was true for the EASI index. At the same time, as expected, the correlation was negative, indicating that higher SCORAD and EASI scores are associated with less skin moisture. Interestingly, TEWL at all visits was strongly associated with AD severity score (correlation coefficients 0.5-0.7; $p<0.05$ in all cases). It should be noted that the correlation matrix included a large number (54) of correlation coefficients, and it could be argued that the assessment of the relationship reliability at the level of 0.05 overestimates the type I error. However, if we use the Bonferroni correction (reduce the significance level by the number of comparisons), then the marginal significance level for the correlation coefficients becomes equal to 0.0009, and, as can be seen in Table 5, in most cases, the correlation coefficients of TEWL and the severity score of AD had a significance below even this extremely conservative limit. Therefore, it could be argued that the severity of AD is associated with TEWL (the stronger, the higher the score) and moisture (the higher, the lower the score), and if we take into account the fact that the relationship was stronger for the indicators at the 3rd visit (at the end of treatment), it can be assumed that the initial severity of the disease was associated with the degree of restoration of the barrier function under the influence of the use of the BLUE CAP foam .

As can be seen from Table. 5, skin pH was not associated with AD severity scores at any of the visits, showing that, at least in this small sample, there is little relationship between pH and AD severity as it changes over the course of follow-up.

A correlation also existed between skin hydration and pruritus (VASH-3) and xerosis (VASH-K) scores, especially at visit 3, although the relationship was weaker for VASH-K at visit 3. TEWL at visits 1, 2, and 3 was associated with VAS-K at visit 3. TEWL at visits 1 and 2 were associated with VAS-3, but for TEWL at visit 3, the relationship was weaker.

In addition to the assessment of the indicators described above, at the end of the study, the opinion of patients / their legal representatives about the drug itself was assessed. Odor was rated "excellent" by 57% (95% CI 37.4-74.5%) of patients and "good" by 43% (95% CI 25.5-62.6%). There were no satisfactory and unsatisfactory ratings. Consistency was rated "excellent" by 57% (95% CI 37.4-74.5%), "good" by 33% (95% CI 17.3-52.8%) and "satisfactory" by 10%. (95% CI 2.1-26.5%) of respondents. There were no "unsatisfactory" ratings. Ease of use was rated "excellent" by 67% (95% CI 47.2-82.7%), "good" by 30% (95% CI 14.7-49.4%) and "satisfactory" by 3 % (95% CI 0.1-17.2%) of respondents. It can be stated that the organoleptic properties and ease of use are highly rated. According to the study, once a day (less than in the instructions for use), the foam was used from 3.1 to 18.7% of patients, 2 times a day - from 7.9 to 48.4% of patients, 10.1-63.1% applied it 3 times a day. It is for further study how much more standardization of the frequency of application of foam can contribute to the normalization of the barrier function of the skin. All patients were given recommendations on diet and treatment, since, according to our data, 40.1% of adolescents and 38.2% of parents prefer not to tell the doctor about violations of the diet and treatment [26-29].

https://doi.org/10.26442/26586630.2022.3.201825

Fig. 1. Improvement of the SCORAD and EASI indices on the 2nd and 3rd visits.
Fig. 1.

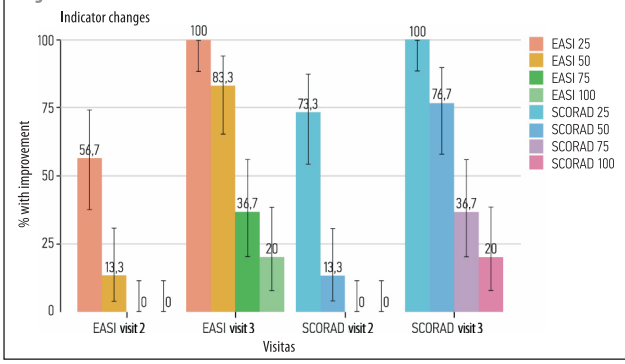


Fig. 2. Improvement in skin moisture at 2nd and 3rd visits from baseline.
Fig. 2.

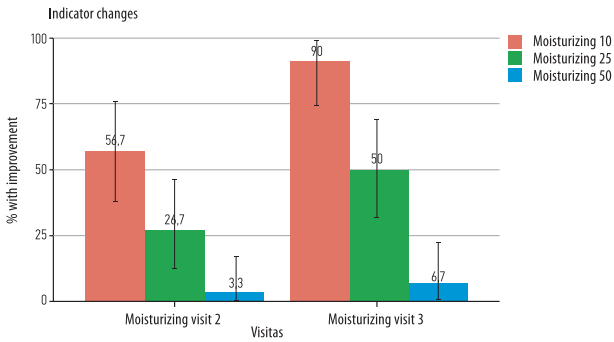
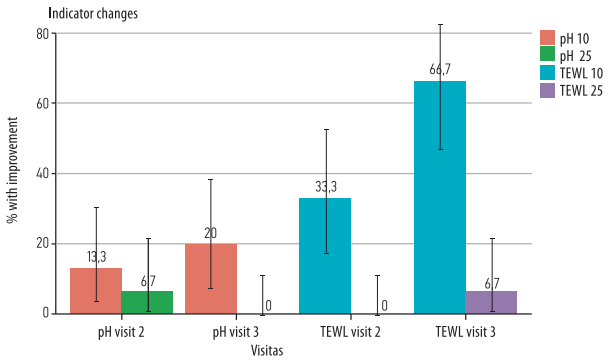


Fig. 2. Improvement (decrease) in TEWL and pH depending on the initial level. Since there was no 50% improvement, data are not shown.
Fig. 2.



https://doi.org/10.26442/26586630.2022.3.201825

Table 5. Relationship between objective indicators of the skin condition and total severity indices of AD
Table 5.

Indicators	Visit	Spearman correlation coefficients, N=30; p score					
		SCORAD			EASI		
		Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3
Humidity	Visit 1	-0,41704; 0,0219	-0,45117; 0,0123	-0,35934; 0,0511	-0,44057; 0,0148	-0,43532; 0,0162	-0,45532; 0,0115
	Visit 2	-0,52632; 0,0028	-0,42279; 0,0199	-0,48839; 0,0062	-0,57001; 0,0010	-0,50212; 0,0047	-0,55901; 0,0013
	Visit 3	-0,75769; <,0001	-0,64766; 0,0001	-0,72392; <0,0001	-0,76719; <0,0001	-0,67194; <0,0001	-0,75328; <0,0001
TEWL	Visit 1	0,68024; <0,0001	0,53461; 0,0023	0,62132; 0,0002	0,64585; 0,0001	0,65134; <,0001	0,64052; 0,0001
	Visit 2	0,76927; <0,0001	0,62287; 0,0002	0,66324; <0,0001	0,76217; <0,0001	0,74663; <0,0001	0,66995; <0,0001
	Visit 3	0,60134; 0,0004	0,49054; 0,0059	0,50537; 0,0044	0,58239; 0,0007	0,49432; 0,0055	0,51018; 0,0040
pH	Visit 1	-0,11711; 0,5377	0,04094; 0,8299	-0,07611; 0,6894	-0,08708; 0,6473	-0,20652; 0,2736	-0,06985; 0,7138
	Visit 2	-0,08792; 0,6441	-0,00357; 0,9850	-0,08388; 0,6595	-0,18060; 0,3396	-0,28013; 0,1338	-0,12175; 0,5216
	Visit 3	-0,17462; 0,3560	-0,16399; 0,3865	-0,24562; 0,1908	-0,17837; 0,3456	-0,01353; 0,9434	-0,14574; 0,4422

Thus, the use of BLUE CAP foam in the treatment of mild to moderate AD in children was well tolerated and was associated with a pronounced improvement in the course of the disease, as well as positive changes in objective indicators of the skin barrier function.

Conclusion

1. The severity of AD in children whose skin was treated with BLUE CAP foam decreased: by SCORAD index - by 22.8 points, by EASI index - by 3.1 points (in both cases p<0.001).
2. Skin hydration increased (by 23.5% compared to baseline), TEWL decreased (by 5.45 g/chm^2) - in both cases p<0.001; Skin pH decreased towards normal by 0.2 units (p=0.002).
3. Indicators of skin hydration and TEWL correlate with the severity of AD with a decrease in severity with an increase in hydration and a decrease in TEWL.
4. The 97% patient/guardian rating of "excellent" or "good" for ease of use confirms the benefit of the foam form, which minimizes skin contact upon application, providing speed, comfort and minimal risk of irritation, which is especially important for children.
5. On the basis of these results, BLUE CAP foam is recommended as standard therapy for AD in children.

Applications

Photos of patients before and after 4 weeks of study medication.

Fig. 4. Patient A., AD, moderate severity before (a) and after 4 weeks of use of the study drug (b).

Fig. 4.

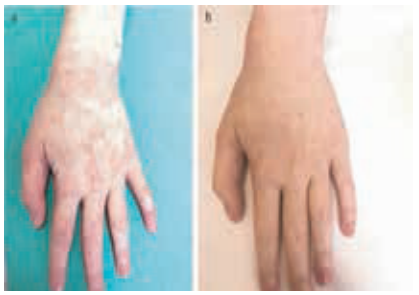


Fig. 5. Patient B., AD, moderate severity before (a) and after 4 weeks of use of the study drug (b).

Fig. 5.

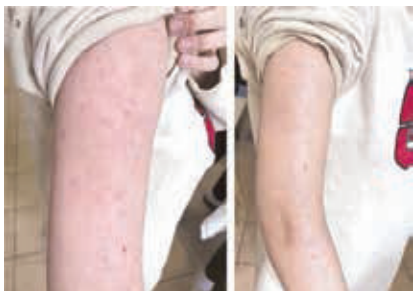
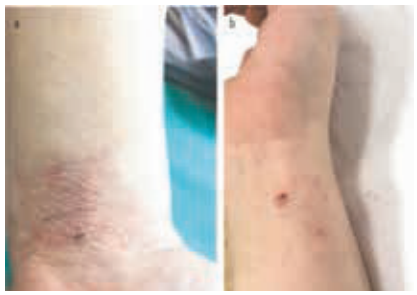


Fig. 6. Patient C, AD, moderate severity before (a) and after 4 weeks of study medication (b).

Fig. 6.



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. Saini S, Pansare M. New Insights and Treatments in Atopic Dermatitis. *Pediatr Clin North Am.* 2019;66(5):1021-33.
3. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. *J Eur Acad Dermatol Venereol.* 2018;32(6):850-78. DOI:10.1111/jdv.14888
4. Lewis-Jones S, Mugglestone MA. Management of atopic eczema in children aged up to 12 years: summary of NICE guidance. *BMJ.* 2007;335(7632):1263-4.
5. Strathie Page S, Weston S, Loh R. Atopic dermatitis in children. *Aust Fam Physician.* 2016;45(5):293-6.
6. Атопический дерматит. Клинические рекомендации, 2021. Режим доступа: https://cr.minzdrav.gov.ru/recomend/265_2. Ссылка активна на 15.06.2022 [Atopicheskii dermatit. Klinicheskie rekomendatsii, 2021. Available at: https://cr.minzdrav.gov.ru/recomend/265_2. Accessed: (in Russian)].
7. LePoidevin LM, Lee DE, Shi VY. A comparison of international management guidelines for atopic dermatitis. *Pediatr Dermatol.* 2019;36(1):36-65.
8. Заславский Д.В., Баринова А.Н. Микробиом кожи при атопическом дерматите и особенности различных средств базисного ухода за кожей. *Медицинский совет.* 2018;(2):170-6 [Zaslavskii DV, Barinova AN. Mikrobiom kozhi pri atopicheskom dermatite i osobennosti razlichnykh sredstv bazisnogo ukhoda za kozhei. *Meditsinskii sovet.* 2018;(2):170-6 (in Russian)].
9. Заславский Д.В., Баринова А.Н. Новая стратегия базовой увлажняющей терапии при атопическом дерматите – «эмоленты плюс». *Дерматовенерология. Косметология.* 2019;5(1):69-79 [Zaslavskii DV, Barinova AN. Novaia strategiia bazovoi uvlazhniaiushchei terapii pri atopicheskom dermatite – „emolenty plius". *Dermatovenerologiia. Kosmetologiia.* 2019;5(1):69-79 (in Russian)].
10. Pacha O, Hebert AA. Treating atopic dermatitis: safety, efficacy, and patient acceptability of a ceramide hyaluronic acid emollient foam. *Clin Cosmet Investig Dermatol.* 2012;5:39-42.
11. Fujii M. The Pathogenic and Therapeutic Implications of Ceramide Abnormalities in Atopic Dermatitis. *Cells.* 2021;10(9):2386. DOI:10.3390/cells10092386
12. Ishida K, Takahashi A, Bito K, et al. Treatment with Synthetic Pseudoceramide Improves Atopic Skin, Switching the Ceramide Profile to a Healthy Skin Phenotype. *J Invest Dermatol.* 2020;140(9):1762-70.
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.
14. Hon KL, Pong NH, Wang SS, et al. Acceptability and efficacy of an emollient containing ceramide-precursor lipids and moisturizing factors for atopic dermatitis in pediatric patients. *Drugs R D.* 2013;13(1):37-42.
15. Lynde CW, Andriessen A. A cohort study on a ceramide-containing cleanser and moisturizer used for atopic dermatitis. *Cutis.* 2014;93(4):207-13.
16. Fischer CL, Drake DR, Dawson DV, et al. Antibacterial activity of sphingoid bases and fatty acids. *Biol Chem.* 2010;391(1): 65-71.
17. Maurya AK, Singh M, Dubey V, at al. α-(-)-bisabolol Reduces Pro-inflammatory Cytokine Production and Ameliorates Skin Inflammation. *Curr Pharm Biotechnol.* 2014;15(2):173-81. DOI:10.2174/1389201015666140528152946
18. Youn HJ, Kim SY, Park M, et al. Efficacy and Safety of Cream Containing Climbazole/Piroctone Olamine for Facial Seborrheic Dermatitis: A Single-Center, Open-Label Split-Face Clinical Study. *Ann Dermatol.* 2016; 28(6):733-739. DOI:10.5021/ad.2016.28.6.733
19. Hebert AA, Rippke F, Weber TM, Nicol NH. Efficacy of Nonprescription Moisturizers for Atopic Dermatitis: An Updated Review of Clinical Evidence. *Am J Clin Dermatol.* 2020;21(5):641-55.
20. Chiu LS, Chow VC, Ling JM, Hon KL. Staphylococcus aureus carriage in the anterior nares of close contacts of patients with atopic dermatitis. *Arch Dermatol.* 2010;146:748-52.
21. HanifIn JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol.* 1980;92(Suppl.):44-7.
22. Панова О.С., Губанова Е.И., Лапатина Н.Г., и др. Современные методы оценки гидратации и биомеханических свойств кожи. *Вестник дерматологии и венерологии.* 2009;(2):80-7 [Panova OS, Gubanova EI, Lapatina NG, et al. Sovremennye metody otsenki gidratatsii i biomekhanicheskikh svoistv kozhi. *Vestnik dermatologii i venerologii.* 2009;(2):80-7 (in Russian)].
23. Пинсон И.Я., Верхогляд И.В. Клиническая оценка эффективности радиочастотного фракционного воздействия при инволюционных изменениях кожи. *Российский журнал кожных и венерических болезней.* 2017;20(5):297-304 [Pinson IIa, Verkhogliad IV. Klinicheskaia otsenka effektivnosti radiochastotnogo fraktsionnogo vozdeistviia pri involiutsionnykh izmeneniiakh kozhi. *Rossiiskii zhurnal kozhnykh i venericheskikh boleznei.* 2017;20(5):297-304 (in Russian)].
24. Oranje AP. Practical issues on interpretation of scoring atopic dermatitis: SCORAD Index, objective SCORAD, patient-oriented SCORAD and Three-Item Severity score. *Curr Probl Dermatol.* 2011;41:149-55.
25. Hanifin JM, Baghoomian W, Grinich E, et al. The Eczema Area and Severity Index-A Practical Guide. *Dermatitis.* 2022;33(3):187-92.
26. Юрьев В.К., Заславский Д.В., Моисеева К.Е. Методика расчета и анализ показателей деятельности учреждения здравоохранения. Учебно-методическое пособие для самостоятельной работы студентов. СПб., 2009 [Iur'ev VK, Zaslavskii DV, Moiseeva KE. Metodika rascheta i analiz pokazatelei deiatel'nosti uchrezhdeniia zdravookhraneniia. Uchebno-metodicheskoe posobie dlia samostoiatel'noi raboty studentov. Saint Petersburg, 2009 (in Russian)].
27. Заславский Д.В., Харбедия Ш.Д., Хведелидзе М.Г., и др. Результаты оценки пациентами деятельности медицинского персонала. В: Новые горизонты: инновации и сотрудничество в медицине и здравоохранении. Материалы IX российско-немецкой научно-практической конференции Форума им. Р. Коха и И.И. Мечникова. Под ред. О.В. Кравченко, Г. Хана. 2010; 28-9 [Zaslavskii DV, Kharbediia ShD, Khvedelidze MG, et al. Rezul'taty otsenki patsientami deiatel'nosti meditsinskogo personala. In: Novye gorizonty: innovatsii i sotrudnichestvo v meditsine i zdravookhranenii. Materialy IX rossiisko-nemetskoi nauchno-prakticheskoi konferentsii Foruma im. R. Kokha i I.I. Mechnikova. Pod red. O.V. Kravchenko, G. Khana. 2010; 28-9 (in Russian)].
28. Мурашкин Н.Н., Иванов А.М., Заславский Д.В., Камилова Т.А. Вопросы эффективности и безопасности применения системных ретиноидов в терапии акне у подростков. *Вестник дерматологии и венерологии.* 2010;(5):112-6 [Murashkin NN, Ivanov AM, Zaslavskii DV, Kamilova TA. Voprosy effektivnosti i bezopasnosti primeneniia sistemnykh retinoidov v terapii akne u podrostkov. *Vestnik dermatologii i venerologii.* 2010;(5):112-6 (in Russian)].
29. Юрьев В.К., Заславский Д.В., Витенко Н.В., и др. Некоторые результаты оценки пациентами качества медицинской помощи. *Ученые записки СПбГМУ им. акад. И.П. Павлова.* 2010;17(2):5-7 [Iur'ev VK, Zaslavskii DV, Vitenko NV, et al. Nekotorye rezul'taty otsenki patsientami kachestva meditsinskoi pomoshchi. *Uchenye zapiski SPbGMU im. akad. I.P. Pavlova.* 2010;17(2):5-7 (in Russian)].