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Blue Cap Is Effective and Safe for the Treatment of Atopic Dermatitis in Children

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Abstract

Background: Atopic dermatitis (AD) is the most common inflammatory skin disease in children. Treatment of AD is based on skin barrier repair and reduction of inflammation. We analyzed the efficacy and safety of activated piroctone olamine (APO)—Blue Cap—in children with AD. **Materials and Methods:** An open-label interventional clinical study was carried out at three clinical centers in Serbia. A total of 58 patients with AD, aged between 3 and 18 years were included and treated with Blue Cap Foam (100 ml; CATALYSIS S.L. Madrid)—Activated Piroctone Olamine—applied twice a day in the affected areas with eczema for 30 days and final assessment at 45 days from baseline. Photographic documentation, clinical evaluation, therapy effectiveness and safety questionnaires were assessed at baseline, 15, 30 and 45 days. **Results:** Our results demonstrated a significant reduction in signs (erythema, scaling, infiltration, excoriations, xerosis) and symptoms (pruritus) at weeks 2 and 4 of the study. At the end of the study, most patients had moderate (28.6%) to great (62.5%) disappearance of manifestations and moderate (25%) to great (71.4%) skin quality improvement. The effect and tolerability of the therapy were evaluated as very good in 66.1 % and 67.9% and good in about 14.3% and 17.9%, assessed by the investigator and patient, respectively. Three patients experienced a burning sensation at the beginning of the study, the side-effects were resolved as the patients continued applying the foam. After two weeks of cessation of the investigated foam, a significant percentage of patients experienced worsening in the final assessment done by the investigator as well as the participant. In the final assessment, a significantly high

percentage (57.1%) of patients had a total reduction of manifestation, and a significant number of participants considered the applied product as treatment success, assessed by the investigator (62.5%) as well as the participants (66.4%). **Conclusions:** Blue Cap is effective and safe in children with AD, although further large-scale randomized controlled trials should confirm our study findings.

Keywords

Pediatric Dermatology, Atopic Dermatitis, Piroctone Olamine, Skin Care

1. Introduction

Atopic dermatitis (AD) is a common chronic inflammatory skin disease. AD usually begins in childhood, but it can also start at any age. Itching is the hallmark symptom of the disease, often unrelenting in severe cases, and leads to sleep disturbance and excoriated infection-prone skin. The distribution of eczematous lesions varies according to the patient's age and disease activity. AD negatively affects quality of life, social interactions, and work productivity, with a high annual cost of living [1].

During infancy, AD is generally more acute and primarily involves the face, the scalp, and the extensor surfaces of the extremities. The diaper area is usually spared. In older children and in those who have long-standing skin disease, the patient develops a chronic form of AD with lichenification and localization of the rash to the flexural folds of the extremities [1].

The pathology behind atopic dermatitis etiology is the loss of the epidermal barrier, which prevents the production of protein filaggrin that can induce T-cell infiltration and inflammation [2].

Treatment of AD depends on the severity of the disease. Mild forms of the disease are mainly treated with local therapy, medium forms with phototherapy, most often narrow-band UVB phototherapy, whereas the most severe cases are treated with systemic therapy. Systemic therapy includes conventional drugs such as methotrexate and cyclosporine. The knowledge of the pathogenesis of AD is leading to the development of new drugs, such as dupilumab, a fully human monoclonal antibody targeting the IL-4 receptor alpha subunit and inhibitors of Janus kinase (JAK)/signal transducers and activators of transcription (STAT) pathway, one of the essential signaling pathways in various inflammatory diseases including AD, such are baricitinib, abrocitinib, upadacitinib. Also, phosphodiesterase 4 (PDE4) inhibitors have been approved for both oral and topical use for inflammatory skin diseases [3] [4] [5].

Treatment of AD is majorly based on skin barrier repair as well as reducing inflammation and itching. They reduce itching and flare-ups, restore the skin barrier and make the patient feel more comfortable [6]. For decades, topical corticosteroids have been the mainstay of treatment for mild-to-moderate AD. One

of the problems is frequent corticophobia in patients with AD and parents of children with AD. Either the severity of AD or parents' fear of chronic corticosteroid treatment has been found to impair the quality of family life [7].

Besides topical corticosteroids, there are several remedies available for the treatment of AD, such as Janus kinase inhibitors (dergocitinib, ruxolitinib, tofacitinib), calcineurin inhibitors (tacrolimus, pimecrolimus), and phosphodiesterase-4 inhibitors (crisaborole) [3] [5] [8] [9].

However, all of the treatments aforementioned report some degree of toxicity. In children, the efficacy and safety of topical drugs have not been studied as they are considered as high-risk population. Therefore, conditions such as atopic dermatitis, "cradle cap" or "nappy rash" are often successfully treated with baby shampoos and creams enriched with emollients and plant oils.

Effective treatment of atopic dermatitis therefore requires the development of novel, effective and reliable therapies. New therapies with functional dermocosmetic treatment schemes to help control inflammatory processes and skin damage as well as AD-associated symptomatology have been developed in recent years. One of these, and the subject of this study, is piroctone olamine [10] [11] [12] [13]. Piroctone olamine has been studied in skin and scalp damage and inflammation processes since the 1970s and has been used in various commercial preparations up to the present day. In 2022, the product Blue Cap, whose main ingredient is activated piroctone olamine (CATALYSIS S.L., Madrid), was evaluated with a high degree of satisfaction with no adverse effects reported in the treatment of symptoms associated with psoriasis and seborrheic dermatitis in patients aged 15 to 60 years [14].

Thus, due to the results obtained and the safety of this ingredient in pediatrics, in the present study we are going to evaluate the efficacy and safety of the product Blue Cap Foam whose main ingredient is activated piroctone olamine in atopic dermatitis in children between 3 and 18 years of age.

2. Materials and Methods

2.1. Product under Study

In this trial, Blue Cap® Foam label 100 mL (CATALYSIS S.L., Spain) was the study product used, twice a day for 30 days.

2.2. Study Population

This is a proof-of-concept open-label single-arm clinical interventional study that included children from 3 to 18 years of age diagnosed with AD in varying areas and of varying extent. The study was conducted at two University clinical centers and City Institute for Skin and Venereal Diseases between 2022 and 2023. A total of 58 patients were enrolled in the trial according to the inclusion and exclusion criteria as follows:

Inclusion criteria

- Confirmed diagnosis of AD affecting different areas of the body in varying

extent.

- Outpatient status.
- Age of 3 to 18 years, male, female.
- Voluntary participation in the trial.
- Signed informed patient consent form (parents, legal tutor, or individual) with a one-time participation in the trial.

Exclusion criteria

- Concurrent usage of other systemic and/or topical preparations that might influence the final assessment (natural preparations, physical therapy).
- known allergy to the tested preparation.
- Disease focus infection manifestations (superinfection requiring therapy).
- Immunosuppressive therapy.
- Prior or current diagnosis of malignancies.
- Alcohol and/or drug abuse.
- Participation in another clinical trial within the past 30 days.
- Restricted ability of the patient to follow therapy instructions.
- Other physical or mental disorders disturbing the trial plan.
- Possible consent withdrawal.
- Presumed patient unreliability.

2.3. Ethics Committee

This study was conducted following the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The protocol trial "BC_SERBIA_2022" with ClinicalTrials.gov ID: NCT06361992 was approved by three independent ethics committees at the study sites Ethics committee of University of Belgrade Faculty of Medicine, University Clinical Center of Serbia with approval number: 1100/3-A, from 25.11.2022; Ethics committee of University of Niš Faculty of Medicine, University Clinical Center of Niš with approval number: 35797/15 , from 01.12.2022; Ethics committee of City Institute for Skin and Venereal Diseases Belgrade with approval number: 1861/2 from 26.12.2022.

Investigators were responsible for data collection, data collation, and analysis. All authors had full access to study data, participated in drafting the manuscript, approved its submission for publication, and vouched for the accuracy and completeness of the data and the fidelity of the trial to the protocol. Parents were involved in the informed consent approval process. The sponsor (Catalysis. SL) was not involved in the trial design.

2.4. Clinical Trial Design

Blue Cap foam 100 ml, Activated Piroctone Olamine (Foam, label 100 ml), Catalysis S.L. Madrid applied twice a day on all affected areas by eczema. The application is to be continued for 30 days, after which the patients stop using the foam until the final assessment at day 45.

Information on the application of the investigation product and the application technique were provided by the doctor specialist orally and in writing.

After signing the participation consent, patients were photographed emphasizing the notable affected areas with eczema. The pictures were taken on the initial visit (visit 1), as well as on days 15 (visit 2), 30 (visit 3) and 45 (end of study).

Besides photographic documentation, on every visit, all patients were examined by a dermatology specialist, regarding the topographic region that is affected, as well as the type of lesion that is present on every visit. Every patient was followed-up by the same specialist.

2.5. Test Analysis

The effects and potential side/effects of the applied Blue Cap foam were rigorously assessed by investigators as well as the participants' points of view. Assessment of therapy effectiveness made by the investigator was to be graded on a scale 1 - 4:

1) Excellent (80 - 100% improvement in skin quality—excellent aesthetic effect).

2) Satisfactory (up to 60% improvement in skin quality—satisfactory aesthetic and cosmetic effect).

3) Insignificant improvement (30% improvement in skin quality—dissatisfactory aesthetic and cosmetic effect).

4) Unsatisfactory condition (finding in original extent, so no clinical change from baseline).

The subjective assessment of the effect of the test product therapy on skin healing in patients was quantified on a scale of 1 to 4:

1) Excellent aesthetic and cosmetic effect, no undesired effects.

2) Satisfactory aesthetic effect.

3) Insignificant improvement, unsatisfactory effect.

4) Unsatisfactory effect.

Tolerability assessment by both the investigator and the patient was carried out using a 1 - 4 scaled questionnaire:

1) Excellent.

2) Very good.

3) Good.

4) Intolerance.

2.6. Statistical Methodology

Results are presented as count (%), means ± standard deviation depending on the data type. Measurements were compared using non-parametric (Wilcoxon signed ranks test, McNemar test). All p-values less than 0.05 were considered significant. All data were analyzed using R 4.3.0 (R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL (https://www.R-project.org/).

3. Results

The study included 58 patients with AD. All patients were included in the safety

analysis (n = 58) whereas 2 patients were excluded from the efficacy analysis due to follow-up loss. The distribution of patients (safety analysis) regarding general characteristics (anamnestic data) is presented in Table 1. Most participants are females, with normal constitutions for their age. Extremities are the most dominant place of skin changes. Half of the participants were previously treated, dominantly with local corticosteroid therapy.

Most skin signs significantly decreased from the baseline to the end of the study. A significant reduction from baseline to end of study is observed for all clinical signs (all p values are less than 0.001). A significant decrease is observed in visit 2, and from visit 2 significant decreases continue to visit 3. On the last visit, a slight increase in symptoms and signs was observed, but still significantly lower compared with baseline and mostly from visit 2 (Table 2). Statistical comparisons between measurements (before and after) are performed with and without Bonferroni corrections, and both approaches are presented in Tables 2-4, Figure 1 in superscripts, next to percentages.

Most patients had moderate to great disappearance of manifestations, skin quality, and total improvement on the second visit (Table 3). Compared to visit 2, the fading of manifestations and improvement continues in visit 3 where the dominant category is "Great" in all variables. At the end of the study, slight worsening is observed compared to visit 3, but still significantly better compared to visit 2. Most of the participants still have a "Great" grade as the dominant category at the end of the study.

Efficacy and tolerability assessed by the investigator were dominantly graded as very good or good on visit 2. By the end of the study, minor improvement or no improvement was observed in efficacy assessed by the investigator and the patient as well as in tolerability assessed by the investigator and the patient compared to visit 2 (Table 4).

Table 1. General characteristics.

	N (%); mean ± sd
Age (yrs)	8.9 ± 4.9
Gender female	36 (62.1%)
BMI (kg/m^2)	17.4 ± 3.0
Area	
Scalp	14 (24.1%)
Upper extremities	50 (86.2%)
Lower extremities	39 (67.2%)
Torso	20 (34.5%)
Perigenital area	2 (3.4%)
Previous th	30 (51.7%)
Corticoid local	29 (51.8%)
Systemic	2 (3.6%)
Other	6 (10.7%)

Table 2. Clinical assessment of symptoms and sings (Efficacy population, n = 56).

	Baseline (1)	Visit 2 (2)	Visit 3 (3)	End of study (4)	p value (Overall)
Erythema	55 (98.2%)[2,3,4]	31 (55.4%)[1,3,4]	4 (7.1%)[1,2,4a]	16 (28.6%)[1,2,3a]	<0.001[b]
Scaling	48 (85.7%)[2,3,4]	13 (23.2%)[1,3a]	1 (1.8%)[1,2a]	7 (12.5%)[1]	<0.001[b]
Infiltration	29 (51.8)[2,3,4]	9 (16.1%)[1,3a]	1 (1.8%)[1,2a]	7 (12.5%)[1]	<0.001[b]
Excoriations	38 (67.9%)[2,3,4]	15 (26.8%)[1,3a]	4 (7.1%)[1,2a]	12 (21.4%)[1]	<0.001[b]
Lichenification	43 (76.8%)[2a,3,4]	33 (58.9%)[1a,3,4]	6 (10.7%)[1,2]	14 (25.0%)[1,2]	<0.001[b]
Xerosis	44 (78.6%)[2,3,4]	21 (37.5%)[1,3,4a]	0[1,2]	8 (14.3%)[1,2a]	<0.001[b]
Pruritus	46 (82.1%)[2,3,4]	12 (21.4%)[1,3a]	2 (3.6%)[1,2a]	7 (12.5%)[1]	<0.001[b]

In superscript, the number represents the significant difference between examined visit and number visit in superscript. [a]Significant difference only without Bonferroni correction (not significant on 0.008 level). [b]Cochrane Q test.

Table 3. Clinical improvement.

	Visit 2 (2)	Visit 3 (3)	End of study (4)	p value (Overall)
Disappearance of manifestations				<0.001[c]
None	1 (1.8%)[3,4]	0[2]	1 (1.8%)[2]	
Slight	6 (10.7%)	4 (7.1%)	4 (7.1%)	
Moderate	31 (55.4%)	5 (8.9%)	16 (28.6%)	
Great	18 (32.1%)	47 (83.9%)	35 (62.5%)	
Skin quality improvement				<0.001[c]
None	0[3,4]	0[2]	0[2]	
Slight	4 (7.1%)	0	2 (3.6%)	
Moderate	31 (55.4%)	8 (14.3%)	14 (25%)	
Great	21 (37.5%)	48 (85.7%)	40 (71.4%)	
Assessment of total improvement				<0.001[c]
None	0[3,4]	0[2]	1 (1.8%)[2]	
Slight	3 (5.4%)	3 (5.4%)	2 (3.6%)	
Moderate	33 (58.9%)	6 (10.7%)	14 (25%)	
Great	20 (35.7%)	47 (83.9%)	39 (69.6%)	

In superscript, the number represents the significant difference between examined visit and number visit in superscript. [c]Friedman test.

Table 4. Efficacy and tolerability by investigator and patient.

	Visit 2	Visit 3	End of study	p value (Overall)
Efficacy				
By investigator				0.008[c]
Very good	30 (53.6%)[3a]	44 (78.6%)[2a]	37 (66.1%)	
Good	17 (30.4%)	6 (10.7%)	8 (14.3%)	
Satisfactory	8 (14.3%)	6 (10.7%)	8 (14.3%)	
Without changes	0	0	1 (1.8%)	
Aggravation	1 (1.8%)	0	2 (3.6%)	

Continued

By patient				0.012[c]
Very good	37 (66.1%)	48 (85.7%)	38 (67.9%)	
Good	15 (26.8%)	5 (8.9%)	10 (17.9%)	
Satisfactory	3 (5.4%)	3 (5.4%)	5 (8.9%)	
Without changes	0	0	1 (1.8%)	
Aggravation	1 (1.8%)	0	2 (3.6%)	
Tolerability				0.368[c]
By investigator				
Very good	51 (91.1%)	52 (91.1%)	50 (89.3%)	
Good	2 (3.6%)	3 (5.4%)	3 (5.4%)	
Satisfactory	3 (5.4%)	1 (1.8%)	1 (1.8%)	
Without changes	0	0	0	
Aggravation	0	0	2 (3.6%)	
By patient				0.368[c]
Very good	51 (91.1%)	53 (94.6%)	51 (91.1%)	
Good	3 (5.4%)	2 (3.6%)	2 (3.6%)	
Satisfactory	2 (3.6%)	1 (1.8%)	1 (1.8%)	
Without changes	0	0	0	
Aggravation	0	0	2 (3.6%)	

In superscript, the number represents the significant difference between examined visit and number visit in superscript; [a]Significant difference only without Bonferroni correction (not significant on 0.016 level). [c]Friedman test.

The distribution of patients regarding the activated piroctone olamine (APO) during the trial, assessed by the patient, is presented in Table 5. Very good and good are dominant or only categories, both on visit 2, visit 3, and at the end of the study. Improvement from visit 2 to the end of the study is small and even overall statistical significance is present in feeling on the skin and staining after application, post hoc analysis revealed no significant differences between measurements with and without p-value correction. The change between visits 2, 3, and 4, even if significant, is clinically small. The overall variability might be different, but comparing each measurement reveals no statistical significance.

In the final assessment (Table 6), the grading of the treatment revealed significant healing and reduction of manifestations, nearly 50% reduction at the end of the study. Three patients had adverse effects, all at the beginning of the study (all had a burning sensation). Tolerability assessed by the patient and investigator revealed very good and good results at the beginning of the study and by the end of the study with no significant difference from visit 2 to the end. Therapy success assessed by the investigator and patient was dominantly graded as excellent and very good, both on visit 2 and at the end of the study (Table 4, Figure 1).

Table 5. APO during trial assessed by the patient.

	Visit 2	Visit 3	End of study	p value (Overall)
Scent				0.097[c]
Very good	43 (76.8%)	43 (76.8%)	45 (80.4%)	
Good	11 (19.6%)	12 (21.4%)	11 (19.6%)	
Satisfactory	2 (3.6%)	1 (1.8%)	0	
Sufficient/Unsat/Insuff	0	0	0	
Easy to apply				0.135[d]
Very good	48 (85.7%)	50 (89.3%)	50 (89.3%)	
Good	8 (14.3%)	6 (10.7%)	6 (10.7%)	
Satisfactory	0	0	0	
Sufficient/Unsat/Insuff	0	0	0	
Texture				0.368[c]
Very good	45 (80.4%)	46 (82.1%)	46 (82.1%)	
Good	10 (17.9%)	9 (16.1%)	9 (16.1%)	
Satisfactory	1 (1.8%)	1 (1.8%)	1 (1.8%)	
Sufficient/Unsat/Insuff	0	0	0	
Absorption rate				0.074[c]
Very good	46 (82.1%)	48 (85.7%)	47 (83.9%)	
Good	8 (14.3%)	8 (14.3%)	8 (14.3%)	
Satisfactory	2 (3.6%)	0	1 (1.8%)	
Sufficient/Unsat/Insuff	0	0	0	
Feeling on the skin after application				0.050[c]
Very good	42 (75%)	43 (76.8%)	44 (78.6%)	
Good	9 (16.1%)	9 (16.1%)	9 (16.1%)	
Satisfactory	5 (8.9%)	4 (7.1%)	3 (5.4%)	
Sufficient/Unsat/Insuff	0	0	0	
Staining after application				0.011[c]
Very good	40 (71.4%)	42 (75.0%)	44 (78.6%)	
Good	12 (21.4%)	11 (19.6%)	10 (17.9%)	
Satisfactory	4 (7.1%)	3 (5.4%)	2 (3.6%)	
Sufficient/Unsat/Insuff	0	0	0	

Scoring range from 1—insufficient to 6—very good; No significant differences between measurements in posthoc analysis have been observed and no superscript numbers are presented. [c]Friedman test. [d]Cochrane Q test.

Table 6. Final assessment.

	Visit 2 (2)	Visit 3 (3)	End of study (4)	p value (Overall)
Healing and reduction of manifestations				
None	0	0	1 (1.8%)	
Partial	47 (83.9%)	22 (39.3%)	22 (39.3%)	
Total	9 (16.1%)	34 (60.7%)	33 (58.9%)	
Total reduction of manifestations	10 (17.9%)[3,4]	34 (60.7%)[2]	32 (57.1%)[2]	<0.001[d]
Adverse effects (n = 58 patients)	3 (5.2%)	0	0	0.368[d]
Tolerability by investigator				0.097[c]
Very good	51 (87.9%)[4a]	53 (94.6%)	54 (96.4%)[2a]	
Good	5 (8.6%)	3 (5.4%)	2 (3.6%)	
Satisfactory	1 (1.7%)	0	0	
Moderate improvement	1 (1.7%)	0	0	
Aggravation	0	0	0	
Tolerability by patient				0.097[c]
Very good	52 (89.7%)[4a]	55 (98.2%)	54 (96.4%)[2a]	
Good	4 (6.9%)	1 (1.8%)	2 (3.6%)	
Satisfactory	2 (3.4%)	0	0	
Moderate improvement	0	0	0	
Aggravation	0	0	0	
Th success by investigator				<0.001[c]
Excellent	24 (42.9%)[3,4]	44 (78.6%)[2,4a]	35 (62.5%)[2,3a]	
Very good	27 (48.2%)	8 (14.3%)	12 (21.4%)	
Good	5 (8.9%)	4 (7.1%)	8 (14.3%)	
Intolerance	0	0	1 (1.8%)	
Th success by patient				<0.001[c]
Excellent	26 (46.4%)[3,4]	44 (78.6%)[2]	37 (66.4%)[2]	
Very good	26 (46.4%)	9 (16.1%)	13 (23.2%)	
Good	4 (7.1%)	3 (5.4%)	5 (8.9%)	
Intolerance	0	0	1 (1.8%)	

In superscript, the number represents the significant difference between examined visit and number visit in superscript; [a]Significant difference only without Bonferroni correction (not significant on 0.016 level). [c]Friedman test. [d]Cochrane Q test.

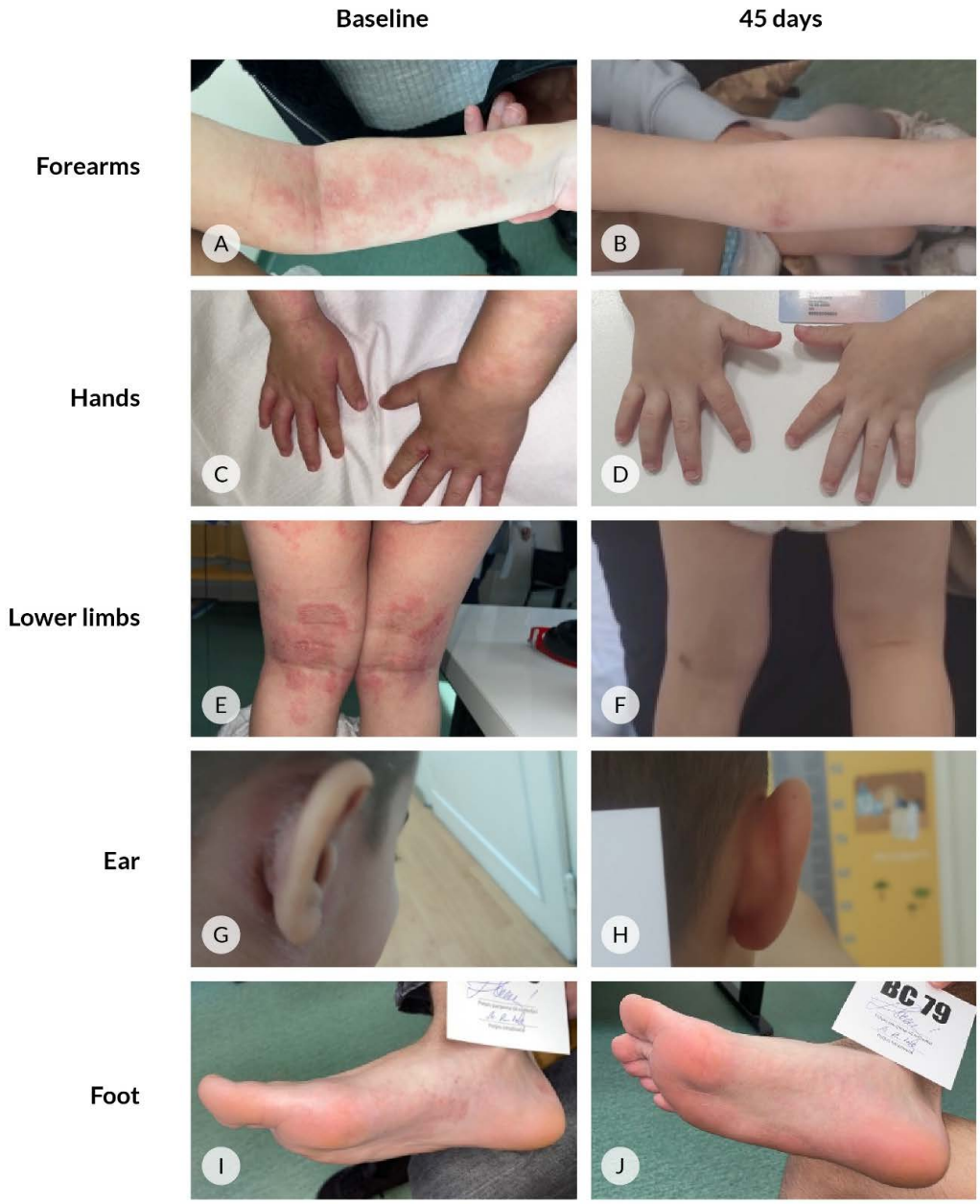

Figure 1. Photo documentation of the visual clinical evolution of the pediatric patients included in the clinical study affected by atopic dermatitis at different body areas: forearm (A, B); hands (C, D); lower limbs (E, F); ear (G, H); and foot (I, J), at baseline and after 45 days of follow-up after using Blue Cap Foam respectively.

4. Discussion

Piroctone olamine (PO)—the main chemical ingredient of Blue Cap—has been widely used in the treatment of facial and hair seborrheic dermatitis. The action mechanism of PO consists of selective inhibition in the cellular uptake of essential substances for the metabolism and development of fungal cells such as potassium ions, phosphates, and amino acids. Also, PO is concentrated inside the fungal cell where it binds irreversibly to certain structures and organs such as the

cell wall and membrane, mitochondria, ribosomes, and microsomes fortifying its fungistatic effect [15] [16].

Besides its fungistatic effect, PO expresses anti-inflammatory properties by lowering free radical concentration, as well as inhibiting the WTN signaling pathway which leads to lower cell differentiation, migration, and hyperplasia [17].

Through these properties PO has been proven efficacious in the treatment of seborrheic dermatitis as well as positive adjuvant effects in the treatment of psoriasis [18], its effect has not been investigated in the treatment of atopic dermatitis yet.

First-line therapy for acute management of AD includes topical therapies such as corticosteroids, calcineurin inhibitors, and phosphodiesterase inhibitor crisaborole, as well as a tendency to explore the efficacy and safety of topical JAK inhibitors. Topical agents have remained the mainstay therapy for decades. However, there has been a longstanding need for topical therapies with high efficacy and low risk of adverse effects with long-term use [19].

Evidence shows that 42.5% of the caregivers of children with atopic dermatitis had used alternative therapies, most commonly due to fears of topical steroid side effects and dissatisfaction with conventional treatment [20].

Our results show that patients treated twice daily with only Blue Cap foam had a significant improvement in skin lesions as well as subjective symptoms of their AD. In the examined group during the first month of the study, none of the patients had the necessity of additional application of topical steroids, and most of them reported high tolerability of the applied product.

Upon cessation of application of the investigated product (Blue Cap foam), a significant percentage of patients experienced a relapse of AD, nevertheless in most cases not in the severity before the study inclusion. Given the high tolerability and efficacy during the application phase, these findings endorse the investigation of continuous and frequent use of Blue Cap foam as a non-steroidal alternative topical treatment of AD.

The Blue Cap foam represents a unique product, that accentuates the antioxidative and anti-inflammatory effects of piroctone olamine by distributing it in its activated form. With this method, we are strengthening the antioxidant potential of molecules, and therefore we can donate more electrons and neutralize a larger number of free radicals, prevent and reduce the risk of developing an acute disease, or stabilize a chronic disease.

5. Conclusion

In this study, we demonstrated that Blue Cap foam is a safe and effective treatment option for pediatric patients with AD, who desire an alternative treatment approach or who are unable to use standard treatment. Since the incidence rise of this global disease and an increase of patients and parents/caregivers that insist on a non-steroidal topical treatment, such product should be evaluated in further large and placebo-controlled studies and potentially find itself in future

treatment protocols.

Author Contributions

Mirjana Gajić-Veljić and Jovan Lalošević: Crucial contribution to the article conception. Obtaining and interpretation of results. Design and review of manuscript. Final revision of the manuscript, being prepared for publication. All others: Obtaining and interpretation of results.

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Conflicts of Interest

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