Original paper

Comparative efficacy of combined antihistamine and montelukast therapy in adult patients with atopic dermatitis

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Adv Dermatol Allergol 2024; XLI (1): 32–40
DOI: https://doi.org/10.5114/ada.2023.135759

Abstract

Introduction: Atopic dermatitis (AD) is one of the most common chronic skin conditions affecting about 20% of children and 5% of adults. However, the studies assessing novel therapies for AD have been focused mainly on paediatric patients and only few studies have involved adult participants.
Aim: To compare the treatment outcomes between the antihistamine monotherapy and combined intervention with an antihistamine agent and a cysteinyl leukotriene receptor antagonist in adult patients with atopic dermatitis.
Material and methods: Patients were randomized into two groups to receive 5 mg oral desloratadine or the combined therapy with 5 mg oral desloratadine and 10 mg montelukast. Both groups were also administered topical treatment using the same protocol (topical Elocon and moisturizer). To estimate the efficacy of the implemented therapy methods, different skin health scores (SCORAD, GISS, EASI, PPNRS and DLQI) and skin functional assessment outcomes (corneometry, pH and transepidermal water loss) were evaluated before and after the treatment.
Results: Significant differences were revealed in compared measurement results for scales of the Extent and Severity of Eczema assessment, Global Individual Signs Score, Eczema Area and Severity Index, Pruritus Numerical Rating Scale, Dermatology Life Quality Index and Skin Functional Properties ($p > 0.05$).
Conclusions: Comparison of data presenting the therapy outcomes in two groups showed that administration of the combined therapy was significantly more effective compared to the antihistamine monotherapy. The results revealed considerable efficacy of the combined therapy reinforced by the use of cysteinyl leukotriene receptor antagonist, montelukast.

Key words: atopic dermatitis, adult patients, viral complication, antihistamine, montelukast, combined, treatment.

Introduction

Atopic dermatitis (AD) is one of the most common chronic skin conditions worldwide [1, 2] affecting about 20% of children and 5% of adults [1–5]. However, based on data provided by different investigators, the epidemiologic studies and clinical trials assessing novel therapies for the AD have been focused mainly on paediatric patients and a small number of studies involved adult participants [6]. The patient characteristics, including both the demographic and clinical variables are rather different between the paediatric and adult patient categories, hence requiring a special approach when the study participants are past childhood [7–9]. A recent study attempted to identify the distinct lifespan prevalence of clinically confirmed AD and the obtained results revealed high rates of the condition in older adults [10]. Limited evidence is collected presenting the "senile" AD, without filling the gap in the epidemiological description of AD in this category of patients [9, 11, 12].

Severe or persistent AD significantly affects the health-related quality of life in majority of patients [2, 13, 14]. Additionally, the condition imposes a heavy economic burden on patients and families [15, 16]. There is strong evidence showing the association of AD with many clinical subtypes of hypersensitivity, like the food allergy, bronchial asthma and allergic rhinitis [17–21].

The problem of treating AD goes far beyond the competence of doctors of one specialty. Patients with AD

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Received: 13.09.2023, **accepted:** 4.10.2023, **online publication:** 28.02.2024.

usually seek medical treatment at different specialized clinics. The condition is usually managed by the dermatologists, paediatricians or clinical immunologists. The pathophysiology of AD has shown genetic predisposition to this condition, characterized with a relapsing course of exudative or lichenoid skin rashes, increased serum IgE levels, hypersensitivity to specific or nonspecific allergens and showing age-related features of clinical manifestations [22]. The pathogenesis includes hypersensitivity-induced inflammation causing increased proliferation and impaired differentiation of the epidermal cells, changes in the proteins of the horny envelope (involucrin, loricrin and filaggrin), alterations in the composition of lipids, resulting in disruption of the epidermal barrier capacities [4, 23–26]. In patients with AD the compromised epidermal barrier makes the skin vulnerable to viruses. One of the common dermal conditions resultant of recurrent viral complication in individuals with AD is eczema herpeticum (EH) produced by herpes simplex viruses (HSV) [27]. Other potential viral agents complicating the are molluscum contagiosum, eczema coxsackium and rarely the small pox vaccination agent [28].

Management of AD includes multifaceted strategy based on the severity of the condition. Variety of topical agents including ointments of corticosteroids and calcineurin inhibitors have been estimated as effective therapeutic means. Oral antihistamine agents are effective in AD therapy, yet they do not reduce pruritus in moderate and severe dermatitis [28]. A promising option for the AD therapy is molecules antagonizing the proinflammatory mediators. The leukotrienes are 5-lipoxygenase pathway pro-inflammatory mediators involved in the inflammatory phase of atopic dermatitis. Research data have shown the participation of cysteinyl leukotrienes in the pathogenesis of AD and the suppression of this pathway by pharmacological agents could be an effective strategy to manage AD [29]. A case report presented by Angelova-Fischer *et al.* has demonstrated successful management of severe AD with a cysteinyl leukotriene receptor antagonist, montelukast [29]. Leukotrienes participate in both pathways of the inflammatory process triggered by the immune and infectious mechanisms. The accumulated research evidence indicates that viral infections can alter the course of allergic diseases suggesting the montelukast as a therapeutic option with anti-inflammatory rather than anti-allergic properties, which supposedly may produce an antiviral effect. However, the relationship between the use of montelukast and management of viral infection has not yet been documented [30].

Aim

This study aimed to compare the treatment outcomes between the traditional antihistamine therapy and combined therapeutic intervention with antihistamine and a cysteinyl leukotriene receptor antagonist in AD patients.

Material and methods

Study participants

This randomized clinical trial was completed during February 2021–March 2023. Patients who received treatment provided by the Dermatology Clinic of Erebuni Medical Center and the specialized service of Helios Clinic in Yerevan (Armenia) were included in this study.

Ninety-one participants diagnosed with complicated AD were involved in two interventional study groups. Forty-seven patients were included in Group I and received anti-histamine therapy (AH) with 5 mg oral desloratadine, while 44 patients in Group II had undergone administration of combined therapy with 5 mg oral desloratadine and cysteinyl leukotriene receptor antagonist, montelukast (AH-ALTM). Patients were adults (age 21–37 years) diagnosed with moderate-to-severe AD previously controlled by isolated therapy with anti-histamine drugs.

To assess the functional outcomes of therapy a third group (control group) of patients was formed including 40 patients with AD meeting all other criteria for inclusion.

The inclusion criteria for patients were as follows: chronic AD diagnosed at least 3 years before the study; Eczema Area and Severity Index (EASI) score 16, AD involvement in 10% of body surface area (BSA); Investigator's Global Assessment (IGA) score 3 at baseline; pruritus Numerical Rating Scale (NRS) average score for maximum itch intensity 3 at baseline; and documented recent history (within 6 months) of inadequate response (partial or non-response) to antihistamine therapy.

The exclusion criteria of the study included confirmed diagnosis of any disorder contraindicating the perception of the therapy compounds, pregnancy, breastfeeding period, intolerance to therapy compounds, oncological diseases, presence of prosthetic valves or other implants, previous therapy with anti-leukotriene agents and surgery performed within 6 months prior to the study.

Treatment protocols

Patients were randomized to receive antihistamine drug (5 mg oral desloratadine) or a combined therapy with 5 mg oral desloratadine and 10 mg cysteinyl leukotriene receptor antagonist, montelukast. Randomization was stratified according to disease severity (IGA 3 versus 4) [31] and affected skin region.

The 5 mg of desloratadine was administered to patients in group I. Patients in group II received a combined therapy with 5 mg of the antihistamine agent and 10 mg of montelukast to match the loading AH dose in Group I. o maintain blinding, coded kits containing desloratadine or combined agents were used to mask treatment assignment. Concomitant topical therapy of AD included application of a topical corticosteroid Elocon (Organon Pharma, UK) twice daily, with 12 h' interval (morning and evening applications). In both groups, the topical corticosteroid was used with 1-month duration. Twice daily,

in the period between the steroid applications a special moisturizer, Topicrem DA (La Roche) was used topically. Additionally, patients of both groups were administered thrice per day with a probiotic, *Lacto G* (GM Pharmaceuticals) for 4 weeks. The clinical parameters were evaluated in all groups before and after the treatment using different therapy outcomes. The treatment outcomes were assessed after a 12-week therapy period.

Assessment of the extent and severity of eczema

The SCORing Atopic Dermatitis (SCORAD) is an AD assessment tool used by clinicians to standardize the assessment data presenting the severity and the extent of the skin condition. The tool targets three different domains in AD including the affected body surface area (BSA), symptoms and severity of clinical manifestations. The affected BSA is measured as a percentage of the defined body area and reported as the sum of all areas (scoring 0–100). Using a four-point scale (none = 0, mild = 1, moderate = 2, severe = 3) the SCORAD targets severity of six specific symptoms of AD (redness, swelling, oozing/crusting, excoriation, skin thickening/lichenification, dryness) with a maximum possible total score of 18 points. The itch and sleeplessness were recorded by the patient or caregiver using a visual analogue scale, ranging from 0 (no symptoms) to 10 (the worst imaginable symptom), with a maximum possible score of 20. The SCORAD score is the sum of all three above presented component scores. The maximum possible total score is 103; higher scores indicate more severe condition [31].

Global Individual Signs Score

The Global Individual Signs Score (GISS) is a cumulative score of ratings for individual components of lesions associated with AD (erythema, infiltration or papulation, excoriations, and lichenification); the cumulative score ranges from 0 to 12, with higher scores indicating greater severity; the MCID for this scale has not been determined [32].

Eczema Area and Severity Index

The general eczema area and severity index (EASI) score is the summation of the 4 regional scores, ranging from 0 to 72. A score of 0 indicates clear or no eczema, 0.1 to 1.0 indicates almost clear, 1.1 to 7 indicates mild disease, 7.1 to 21 indicates moderate disease, 21.1 to 50 indicates severe disease, and greater than 51 indicates very severe disease [33–36].

Pruritus Numerical Rating Scale

The itch severity was assessed by the Peak Pruritus Numerical Rating Scale (PPNRS). The scale is a validated tool assessing the patient-reported outcome (PRO) of itch severity. Using the tool the patients report the intensity of itch based on a daily recall period. Participants were asked to rate the itch score (average) and maximum intensity of itch experienced during the past 24 h on a scale from 0 to 10 (0 = no itch and 10 = worst itch imaginable) [35–37].

Dermatology Life Quality Index

The dermatology life quality index (DLQI) is represented by the sum of points for each question (maximum of 30 and a minimum of 0). The higher score indicates poor quality of life. If the score is higher than 10 the patient's health related quality of life is severely affected by the skin condition. The level of DLQI was calculated based on questionnaire results [32].

Skin Functional Properties

Assessment of skin functional properties was conducted using the multi-parameter skin analysis system, Dermalab Combo SkinLab (DermaLab® COMBO SkinLab, Denmark). Corneometry (determination of the degree of hydration of the epidermis), TEWL-metry (determination of the level of transepidermal water loss), pH-metry (evaluation of skin acid-alkaline balance) were performed. The study environment was designed according to research protocol requirements to ensure high accuracy of obtained data: the testing of the patient was performed in a special room (with a temperature of 24 ±2.00°C and a relative humidity of 50 ±10%). The patients spent at least 20 min in the room before the procedure, and had not applied any topical cream on the skin within the preceding 2 h prior to the tests.

Statistical analysis

Statistical data processing was performed using the statistical software package SPSS 23 (Statistical Package for Social Sciences 23) to determine any significant difference in post-interventional scores between the groups. For a comparative analysis of the group results (between the interventional and control groups) obtained before and after the intervention the Kolmogorov-Smirnov test was used revealing the pattern of data distribution, followed by the Student's parametric test for the comparison of group means. When using the Student test for independent samples, the calculation depended on the statistical significance of differences in the variance of the compared groups.

Ethical approval

The study protocol conforms to the ethical guidelines of the 2013 Declaration of Helsinki as reflected in the approval by the human research committee. All participants gave written informed consent to participate in the trial and to use their data. The protocol was approved by the Ethics Committee of National Institute of Health, RA MOH (Yerevan, Armenia).

Results

According to the study results the clinical manifestations of AD documented in patients had improved after the conducted therapies showing reliable changes in all assessed clinical parameters. Tables 1 and 2 show the shifts in EASI, GISS, SCORAD, and PPNRS in both intervention groups before and after the AH and AH-ALTM combined therapies (mean ± SD and CV coefficient of variation were estimated) respectively.

In both groups, changes in scores of investigated parameters were revealed after the therapeutic interventions compared with the pre-treatment examination scores. Mean EASI scores of treatment groups were similar at baseline ($p = 0.278623$) before treatment and decreased in both groups after the therapeutic interventions. Group I patients demonstrated less decline in the EASI mean scores (AH therapy vs AH-ALTM scores were –10.36% and 32%, respectively). As anticipated, the mean difference between the scores obtained from groups after treatment was significant ($p < 0.001$).

The other clinical scores were also improved in both groups, including GISS, SCORAD and PPNRS. The initial assessment did not reveal significant discrepancy in SCORAD scores between the groups ($p = 0.16632$). The percentage of deviation after treatment was –11.4% and –27.36% in group I and group II, respectively. The statistical analysis showed that post-treatment mean values of SCORAD assessment were significantly different ($p < 0.001$).

GIS scores showed the same between group pattern at baseline ($p = 0.12961$), but were altered after the applied therapy in both interventional groups. The reduction was significantly different in both groups ($p = 0.0004629$). The values of GIS Scoring after treatment were decreased in group I and group II by 16.31% and 29.44%, respectively.

No significant between group difference was observed in mean values of PPNRS before the treatment ($p = 0.542603$). Relatively less decline was observed in group 1 (AH therapy) patients (–28.1% vs. –47.3%), and statistically significant between-group difference was detected after the therapy completion ($p < 0.001$).

The evaluation of treatment results was performed using the DLQI to estimate the overall skin condition 12 weeks after the intervention baseline. Results of conducted evaluation are presented in Table 3. The data presented in Table 3 demonstrate the significant difference between treatment results in groups I and II ($p < 0.001$).

To estimate the efficacy of the implemented therapy methods (AH vs. AH-ALTM), the comparison of data from final measurements in groups was performed. Significant differences were revealed in compared measurement results ($p < 0.05$ in all parameters).

The data showing changes in the functional state of the skin in patients treated with AH and combined therapy are presented in Tables 4 and 5. Analysis of data derived from these two tables suggests that the combined therapy resulted in a significant improvement of studied outcome parameters.

The initial results of corneometry, TEWL and pH in patients of group I were significantly similar to the same parametric values in patients of group II ($p = 0.014$, $p = 0.14$ and $p = 0.099605$, respectively). The measurement data revealed significant decrease of the corneometry results compared with the control patient data ($p < 0.001$). At the same time the results of TEWL ($p < 0.001$) and pH ($p < 0.001$) were reliably increased (by 35.53% and +10.98%, respectively). The AH therapy resulted in elevation of corneometry scores (by 41.45%) and reliable decrease of TEWL by 14.72% and pH by 7.37% respectively ($p < 0.001$). However, the difference in results, compared to the same parameters of the control group, still continued to remain significant in the combined therapy group (for corneometry, TEWL and pH, $p < 0.001$).

In patients of group II, the baseline value of skin humidity with 95% probability was decreased (SD 46.86% with 95% probability) compared to the control group. The test results of trans-epidermal water loss (TEWL) and pH-metry were higher at study baseline compared with

Table 1. Descriptive statistics data on dynamic changes of parameters in patients with complicated AD treated with anti-histamine monotherapy and combined AH-ALTM therapy

Variables	AH therapy (*N* = 47)		Combined AH + ALT therapy (*N* = 44)	
	Before treatment (mean ± SD) CV (%)	After treatment (mean ± SD) CV (%)	Before treatment (mean ± SD) CV (%)	After treatment (mean ± SD) CV (%)
EASI	81.67 ±3.83 1.09%	73.21 ±5.02 1.44%	82.55 ±3.85 1.14%	56.09 ±4.37 1.29%
GISS score, median (IQR)	18.98 ±1.24 0.35%	15.89 ±3.82 1.09%	18.26 ±2.87 0.85%	12.88 ±4.14 1.22%
SCORAD total score, median (IQR)	58.37 ±2.41 0.69%	51.79 ±3.8 1.09%	57.68 ±2.26 0.67%	48.61 ±3.05 0.9%
Pruritus NRS	8.22 ±1.44 0.44%	5.91 ±1.25 0.36%	8.03 ±1.63 0.48%	4.22 ±1.34 0.40%

Table 2. Data for different parameters produced by statistical analysis of results in patients with severe AD treated with AH or combined AH-ALTM therapy

Variable			Before treatment group I vs. Before treatment group II	Before treatment vs. After treatment group I	Before treatment vs. After treatment group II	After treatment group I vs. After treatment group II
EASI		*t* value	–1.0900738	9.194027902	30.13779958	17.3815663
		P-value	0.2786232	0.0007 1.98116E-14	0.0000 3.79788E-47	0.001 2.3486E-30
		Mean ± SD	81.67 ±3.83 82.553.85	81.67 ±3.83 73.21 ±5.02	82.55 ±3.85 56.09 ±4.37	73.21 ±5.02 56.09 ±4.37
		95% CI	1.09% 1.14%	1.09% 1.44%	1.14% 1.11%	1.44% 1.11%
		%	N/A	–10.36%	–32.05%	–23.38%
GISS	score, median (IQR)	*t* value	1.53749	5.44794364	7.082724519	3.64112432
		P-value	0.12961	1.1792E-06	5.79346E-10	0.0004629
		Mean ± SD	18.98 ±1.24 18.26±2.87	18.98 ±1.24 15.89 ±3.82	18.26 ±2.87 12.88 ±4.14	15.89 ±3.82 12.88 ±4.14
		95% CI	0.35% 0.85%	0.35% 1.09%	0.85% 1.22%	1.09% 1.22%
		%	N/A	–16.31	–29.44	–18.89
SCORAD		*t* value	1.395555	10.01191472	22.89260498	12.3774289
		P-value	0.16632	1.19672E-15	2.16858E-33	6.9177E-21
		Mean ± SD	58.37 ±2.41 57.68 ±2.26	58.37 ±2.41 51.79 ±3.8	57.68 ±2.26 48.61 ±3.05	51.79 ±3.8 48.61 ±3.05
		95% CI	0.69 0.67	0.69 1.09%	0.67 0.9%	1.09 0.9%
		%	N/A	–11.26%	–28.1%	–19.9%
Pruritus NRS		*t* value	0.611316	8.302453515	11.91974	6.205284603
		P-value	0.542603	9.67E-13	1.14E-19	1.79613E-08
		Mean ± SD	8.22 ±1.44 8.03 ±1.63	8.22 ±1.44 5.91 ±1.25	8.03 ±1.63 4.22 ±1.34	5.91 ±1.25 4.22 ±1.34
		95% CI	0.41% 0.48%	0.41% 0.36%	0.48% 0.4%	0.36% 0.40%
		%	N/A	–28.1%	–47.3%	–28.57%

the similar data of the control group (34.7% and 11.38% (SD) with 95% probability). Results of humidity (corneometry), TEWL and pH measurements were relatively improved by the therapy (increase of the corneometry level (SD with 95% probability) with the simultaneous decrease in the levels of the TEWL and pH (SD –14.72% and –9.37% with 95% probability) in interventional group II.

However, results of corneometry and pH from the patients of group II after treatment with AH-ALTM were considerably similar to the results obtained from the control group participants ($p = 0.14$ and $p = 0.31759$), but still showing a significant difference in the same parameters of patients from group ($p < 0.001$ for both corneometry and pH).

Discussion

AD is a persisting condition that can lead to serious complications. The research evidence indicates that patients with AD have higher baseline disease severity and health related quality of life scores (assessed with EASI, IGA and DILQI scores) compared with the overall population. The 47 adult patients with AD treated for 12 weeks with the combined interventional strategy (topical agents and AH-ALTM) showed statistically significant improvements in therapeutic outcomes, including the AD signs, pruritus, quality of life (DLQI), and skin parameters compared to the group treated with AH strategy. Improvements in majority of the observational outcomes were registered in the early stage of therapy

(3–4 weeks of therapy). The novelty of the presented study was the combined use of antihistamine and antileukotriene therapy to manage AD. The systemic use of AH and ALTM was supplemented with topical use of a corticosteroid ointment and a special skin moisturizer. To reduce the risk of adverse reactions the patients were additionally administered probiotics.

Cysteinyl leukotrienes (CysLTs) are proinflammatory mediator molecules representing the 5-lipoxygenase pathway. They exert pharmacological effects interacting with different receptors, CysLT1 and CysLT2. There is accumulated evidence that the manifestations of atopy-related asthma or rhinitis are mediated by the cysteinyl leukotriene 1 receptor subtype. By competitive binding to the CysLT1 receptor, leukotriene receptor antagonists (LTRAs) block the effects of cysteinyl leukotrienes and alleviate the symptoms of these conditions. Because of the common association of AD with allergic asthma and rhinitis, improvement of atopic eczema was anecdotally reported in patients receiving LTRAs to control the manifestations of airway disease. These observations have been confirmed in studies in small groups of paediatric and adult patients with AD [29]. Some controversial results regarding the effectiveness of montelukast in the management of AD were published before in earlier investigations [38, 39].

Similar results were obtained with another pro-inflammatory mediator molecule. Adult AD patients treated with dupilumab had demonstrated similar improvements in observational and serological marker outcomes of the therapy [40, 41].

In our study, the safety profile of montelukast did not show any substantial shifts from other reported trials [42]. Overall, montelukast was well tolerated, with only a small percentage (13.6%) of mild adverse reactions. Permanent or temporary discontinuation of the drug was not registered. The most frequent adverse events in montelukast-treated patients were conjunctivitis and nasopharyngitis. The higher incidence of conjunctivitis in patients with AD in comparison with the overall population is consistent with previous findings supporting an association between higher AD severity in adults and an increased risk of conjunctiva inflammation [43, 44].

Integration of montelukast in the therapy program is a proper extension to the steroid therapy with a complimentary purpose to minimize the sequela of the viral infection. Therapeutic action of the cysteinyl leukotriene receptor antagonist is via the common anti-inflammatory and potential antiviral influences, providing with a possible clue to resolve the mechanism underlying the treatment efficacy.

This work also has limitations. The population of patients with AD involved in the study group was not large and the number of patients that experienced therapy complications was small and not proportional with the high rate of adverse reactions presented in the published studies [45, 46]. The latter limitation is most likely explained by the small number of the study group par-

Table 3. Evaluation of therapy results in all patients according to DLQI Scale. Analysis performed using the two-sample *t*-test (assuming equal variances)

Variable	Combined therapy *N* = 44	AH *N* = 47
Mean	13.167384615	24.476315789
Variance	3.47993957	3.47993957
Observations	44	47
Pooled variance	2.83866319 69	
Hypothesized mean difference	0	
d*f*	89	
t Stat	31.9992703	
P(T<=t) one-tail	6.64219E-51	
t Critical one-tail	1.665425373	
P(T<=t) two-tail	1.32844E-50	
t Critical two-tail	1.9869787	

Table 4. Descriptive statistics data on dynamics of changes for skin functional parameters in patients with complicated atopic dermatitis treated with anti-histamine therapy and combined AH-ALTM therapy

Variable	Control	AH therapy (*N* = 47)		Combined AH + ALTM therapy (*N* = 44)	
		Before treatment (mean ± SD) CV (%)	After treatment (mean ± SD) CV (%)	Before treatment (mean ± SD) CV (%)	After treatment (mean ± SD) CV (%)
Corneometry [μS]	339.9 ±8.7 (3.81287305)	182.52 ±2.51 1.3150946	258.3 ±3.64 (1.4) 1.04064007	180.6 ±4.29 (2.4) 1.267	331.41 ±17.25 (2.1)5.06445329
TEWL [g/m²/h]	13.9 ±1.42 (9.2) 0.6135658	18.88 ±1.13 (5.8) 0.314479143	16.45 ±0.77 (4.41) 0.023963838	19.15 ±0.58 (3.1) 0.171375899	14.7 ±1.45 (9.8) 0.428439748
pH	5.56 ±0.089 (1.6)	6.17 ±0.07 (1.1)	5.71 ±0.12 (1.0)	6.19 ±0.05 (0.8)	5.60 ±0.07 (1.3)

Table 5. Summary of statistical results for skin assessment in AD patients treated with AH and AH-ALTM therapy

Variable	Before treatment group I vs. Before treatment group II	Before treatment group I vs. Control group	Before treatment group II vs. Control group	After treatment group I vs. Control group	After treatment group II vs. Control group	Before treatment vs. After treatment group I	Before treatment vs. After treatment group II	After treatment group I vs. After treatment group II
Corneometry [μS]								
t value	2.52	–79.56	–77.73	–40.46	–2.65	–117.68	–56.27	–27.51
P-value	0.014	1.69E–26	2.36453E–29	3.77E–22	0.01	3.23E–93	1.74E–45	1.26E–30
Mean ± SD	182.52 ±0.51 180.65 ±4.29	182.52 ±2.51 339.89 ±8.7	180.65 ±4.29 339.9 ±8.7	258.3 ±3.64 339.9 ±8.7	331.34 ±17.25 339.9 ±8.7	182.52 ±2.51 258.3 ±3.64	180.65 ±4.29 331.34 ±17.25	258.33 ±3.64 331.34 ±7.25
95% CI	(0.72–1.27)	(0.72–3.81)	(1.27–3.81)	(1.04–3.81)	(5.09–3.81)	(0.72–1.04)	(1.27–5.09)	(1.04–5.09)
%	N/A	– 46.30%	–46.86%	–24.00%	–6.34%	+41.45%	+83.50%	N/A
TEWL [g/m^2/h]								
t value	–1.51	13.32	15.32	6.91	1.49	12.18	18.98	–7.12
P-value/	0.14	3.97E–14	3.2009E–13	3.84E–07	0.14	5.21E–20	4.52E–26	1.06E–09
Mean ± SD	18.88 ±1.13 19.15 ±0.58	18.88 ±1.13 13.93 ±1.42	19.15 ±0.58 13.93 ±1.42	13.9 ±1.42 16.45 ±0.77	14.71 ±1.45 13.93 ±1.42	18.88 ±1.13 16.45 ±0.77	19.15 ±0.58 14.71 ±1.45	16.45 ±0.77 14.71 ±1.45
95% CI	0.32 0.17	0.32 0.62	0.17 0.62	0.22 0.62	0.43 0.62	0.32 0.22	0.17 0.43	0.22 0.43
%	N/A	+35.53%	+37.47%	+18.13%	+5.57%	+14.72%	–23.21%	N/A
pH								
t value	–1.66517	26.75	29.18	4.95	2.25	20.25	44.72	3.99
P-value	0.099605	1.72016E–22	7.81929E–21	7.54E–06	0.031759	9.31E–31	7.13E–59	0.000168
Mean ± SD	6.17 ±0.07 6.19 ±0.05	6.17 ±0.07 5.56 ±0.09	6.19 ±0.053 5.56 ±0.09	5.71 ±0.14 5.56 ±0.09	5.61 ±0.07 5.56 ±0.09	6.17 ±0.07 5.71 ±0.14	6.19 ±0.05 5.61 ±0.07	5.71 ±0.14 5.61 ±0.07
95% CI	0.02 0.015	0.02 0.04	0.015 0.04	0.04 0.04	0.02 0.04	0.02 0.04	0.015 0.02	0.04 0.02
%	N/A	+10.98 %	+11.38%	+2.81%	–0.94%	–7.35%	–9.37%	N/A

ticipants. Another limitation is that data from the study subgroups might not be reflective of overall population of AD patients and needs further investigation.

Conclusions

The results of the conducted studies allow to conclude that the administration of the combined AH-ALTM therapy is significantly more effective compared to the monotherapy with AHs which is reflected in data presenting the therapy outcomes. The data showed a significant improvement in different assessment scales of patients treated with AH-ALTM. Additionally the skin morphofunctional data supplement the obtained evidence. Both the corneometry and pH parameters in patients who received AH-ALTM therapy were considerably improved. The results demonstrate the efficacy of a new approach to manage AD revealing the advantage of combining ALTM agent with AHs, supposedly backed by the dual action of the montelukast – anti-inflammatory and antiviral.

Conflict of interest

The authors declare no conflict of interest.

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