Short Research Article

The comparative study of Atopic dermatitis and Chronic hand eczema clinical course in adults after acute relapse treatment

ABSTRACT

Aims: To evaluate Atopic dermatitis (AD) and Chronic hand eczema (CHE) course in adults after discontinuation of acute or sub acute relapse treatment.
Study design : three groups of adult patients that finished standard treatment for relapse of AD and CHE were followed up within 24 weeks of period to check disease severity, itch intensity and skin management effectiveness.
Place and duration of study sample: population of Ivano-Frankivsk region of Ukraine September 2015 – May 2021.
Methods: 155 patients (51 females and 104 males; age between 20 and 50 years) with AD or CHE were enrolled in the study. The patients were randomized into three study groups depending on diagnosis. SCORAD index was used to assess disease severity, visual analog scale (VAS) was used to assess skin itch intensity. Frequency of disease treatment re-start with topical or systemic anti-inflammatory drugs as well as patients'sintention to ask for a treatment were calculated.
Results : Results of our study have shown that cases of new disease worsening occured within nearest 24 weeks after AD and CHE aggravation treatment discontinuation and are quite frequent despite appropriate skin care.
Conclusion: part of adult patients continues suffering from skin itch or mild skin lesions within nearest 24 weeks after discontinuation of intensive treatment of AD or CHE relapse. Prescription of antihistamines and/or topical anti-inflammatory treatment in addition to generally recommended skin care with emollients is crucial for patients with new worsening of the disease. Among patients with a new signs of worsening a part would unlikely ask for a new treatment immediately unless this worsening is moderate or severe.

Keywords: Atopic Dermatitis, Chronic Hand Eczema, Treatment, Follow-Up.

1. INTRODUCTION

Atopic dermatitis (AD), also known as atopic eczema, is a multifaceted, chronic relapsing inflammatory skin disease that is commonly associated with other atopic manifestations such as food allergy, allergic rhinitis, and asthma [1, 2]. In the last Last decadit affects approximately 15% to 20% of children and 1% to 3% of adults [3, 4]. Approximately 90% patients have experienced first symptoms of the disease within the first 5 years of life [5] and approximately 17% of adults have AD experience onset soon after adolescence [6, 7]. It is used to think that in many cases AD mostly resolves by the time a child reaches adulthood; however, approximately 10% to 30% of adult patients still have symptoms of disease [8]. Severity of AD course and frequency of acute relapses in adults are not so well investigated for different reasons and self-management of skin problems by adults seems to be the most influencing reason. Controversial data are available for AD

course in adults. Results of different AD studies present us different information: on one hand, at any age 80% of participants with ≥5 years of follow-up continued to have symptoms or had continued using medications for their AD [10], on the other hand only 20% of childhood AD persisted 8 years after onset and there is a median duration of 3 years for AD persistence [11]. A fact that big portion of adult AD patients stay of ten behind statistical analysis was supported a 2007 US based study that estimated 17.8 million persons with AD mostly undiagnosed [9]. The clinical presentation of AD varies based on the age of the individual affected [12]. In adulthood, xerosis is prominent and lesions are more diffuse with underlying erythema. Anatomically, the face is commonly involved, lichenification may also be present [1]. There are some differences in AD course in adults depending on sex and age of the disease onset: AD was shown to be more persistent in males, in patients with late-onset disease, and in those with severe cases of the disease [11]. Individuals with AD were formerly referred to as individuals having eczema. However, the word “eczema” is a broad term that refers to various conditions causing inflammation of the skin [1]. Hand dermatitis or eczema is considered as a sign or complication of AD in adults [5, 9, 13]. But in a more wider population, it may be a separate chronic skin disease with estimated 10% prevalence in the general population [14, 15]. If itchy lesions affect mostly hands of an adult patient, it may not be easy to differentiate CHE from AD without precise examination and following-up a patient. Probably due to that available statistical data often provide us with common figures on eczema frequency in adults without differentiation between AD and chronic eczema [16]. Taking in account that AD may be considered as diverse disease with different intensity of skin barrier and immune dysfunction [17], and different age the disease onset it looks even more difficult to diagnose AD in adults, prognose the disease course and treatment efficacy for relapses. The aim of the study to evaluate Atopic dermatitis (AD) and Chronic hand eczema (CHE) course in adults after discontinuation of acute or sub acute relapse treatment.

2. MATERIAL AND METHODS

2.1 Subjects

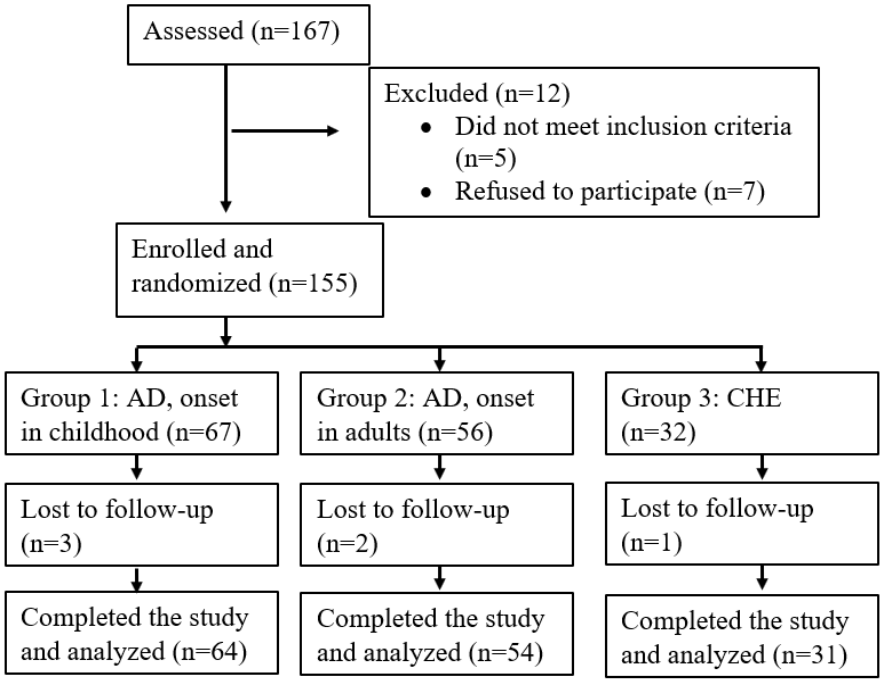
The study comprised 155 consecutive adult patients who were observed after treatment discontinuation for acute/subacute relapse of AD or CHE between September 2015 – May 2021. Figure 1 summarizes the flowchart regarding patients' enrollment. The study protocol was approved by the local ethics committee.

2.2 Inclusion criteria

Inclusion criteria were as follows: aged 20–50 years, discontinued treatment for acute/subacute relapse of AD or relapse of CHE, significant improvement of the disease clinical course at treatment discontinuation.

2.3 Exclusion criteria

Subjects with the presence of any of the following were excluded: AD and CHE cases complicated with erythroderma or skin infections, discharge and\or treatment discontinuation due to other reasons then significant improvement of the disease course, current treatment of skin disease or concomitant illness with systemic and\or topical anti-inflammatory medications, corticosteroid-dependent cases of the diseases, pregnant or breastfeeding mothers.



AD: Atopic dermatitis **CHE:** Chronic hand eczema

Fig. 1. Flowchart diagram for participants who were randomized into three groups of the study

2.4 Duration of the study

All subjects were followed up within 24 weeks after inclusion with every 4th week phone interview or visit for examination whenever necessary and obligatory visits for examination on 1st day (baseline), end of week12 and week24 of observation.

2.5 Outcome measures

Outcome measures were SCORing Atopic Dermatitis (SCORAD) index [18], skin itch intensity assessment with visual analog scale (VAS), number of cases of return to active anti-inflammatory or anti-itch treatment due to worsening of the disease, as well as number of cases where such treatment was prescribed mostly due to obligatory scheduled study visit to a dermatologist.

2.6 Skin management and treatments

All subjects were recommended to use moisturizers for previously/currently affected and dry skin regions on regular base through the study duration. In case of reappearance of inflammatory lesions and\or increase of itch intensity topical calcineurin inhibitors or mild topical corticosteroids were prescribed alone or in combination with antihistamines.

2.7 Statistical results

Statistical analysis was performed with Statistica 13.2 version. While the differences among the groups for continuous data were compared using Kruskal–Wallis test, Student's t test, or Mann–Whitney U test. When the *p* value from the Kruskal–Wallis test statistics was statistically significant, Conover's nonparametric multiple comparison test was used to determine which group differed from which others. Categorical data were analyzed using chi-square or Fisher's exact test, where applicable. Odds ratios are expressed with 95% confidence intervals. A *p* value less than 0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

Detailed Demographic features of the subjects are given in Table 1. All groups were similar with respect to age and sex. Side of skin involvement in patients with childhood-onset AD (ADc) was similar to late-onset AD group (ADl). Part of the patients from these groups had signs of hand dermatitis accompanied by other symptoms of AD in adults. No meaningful differences existed between two AD groups at baseline in terms of SCORAD values and itch intensity scores. CHE group SCORAD index at baseline slightly but not significantly differed from AD groups due to limitation of affected areas with hands only (**Table 1)**.

Table 1. The demographic characteristics, clinical outcome measures of the groups at baseline

VARIABLES	*ADc group (n=64)*	*ADl group (n=54)*	*CHE group (n=31)*
Sex (n)			
Female	20	13	14
Male	44	41	17
Age	26,85±6,73	29,48±6,15	34,83±7,57
SCORAD	12,69±3,06	10,43±1,95	10,02±1,94
skin itch by VAS	2,31±0,85	2,27±0,73	2,25±0,72

Values presented as mean ± standard deviation or *n* (number)

Values of diseases severity measured with SCORAD index are given in **Table 2.** From 64 adult patients with childhood-onset AD worsening was detected in 11 patients by week 12 and in 10 patients by week 24. In total 21 patients from the group (32, 8%) were prescribed anti-inflammatory topical treatment alone or in combination with antihistamines in addition to moisturizers. Among this 21 only 11 patients (52,4%) would apply for new treatment for worsening if not being in the study. The rest 10 patients would do nothing in addition to moisturizers waiting for improvement.

Table 2. SCORAD index in groups during observation period

Groups of observation	*baseline*	*Week 12*	*Week 24*
ADc group (n=64)	12,69±3,06	10,03±3,21^{A}	7,95±2,31^{AB}
ADl group (n=54)	10,43±1,96	9,92±2,98	7,89±2,15^{AB}
CHE group (n=31)	10,02±1,94	4,17±1,34^{A}	4,15±1,33^{B}

Values presented as mean ± standard deviation.
A-significant difference to value of previous visit
B- significant difference to value at baseline

On the contrary to childhood-onset, AD patients those who had first episodes in adulty did not show significant improvement within 12 weeks after the treatment discontinuation. Moreover, 15 of them (27, 8%) had signs of worsening of different degree by week 12 and received additional anti-inflammatory treatment. By week 24, mean SCORAD index value decreased significantly comparing to baseline but 10 more patients (18, 5%) had signs of worsening and received

new treatment. In total, 25 patients of the group (46, 3%) had episodes of worsening while stopped any treatments except moisturizers within observation period. Among this 25 patients, only 16 individuals(64%) would disturb their dermatologist for new treatment.

CHE patients demonstrated the most evident improvement within 12 weeks after the treatment discontinuation when all patients had clinical improvement in comparison to baseline. Next 12 weeks demonstrated eczema signs stability and even worsening of different degree for 11 (35,5%) patients. Among them, only 7 (63,6%) would apply for new treatment due to worsening clinical condition. Itching is the major symptom associated with impact on quality of life. Values of skin itch intensity in study patients are given in Table 3. We observed gradual significant decrease of itch intensity in ADc patients only. In case of adult-onset AD significant lowering of itch severity was partially caused by additional treatment that 27, 8% of the group were receiving from week 12. In case of CHE patients significant reduction of skin itch was observed together with general improvement by week 12 and no more significant changes within next 12 weeks (**Table 3**).

Table 3. Skin itch intensity (VAS values) during observation period

Groups of observation	***baseline***	***Week 12***	***Week 24***
ADc group (n=64)	2(2;3)	1(1;2)^{A}	1(1;2)^{AB}
ADl group (n=54)	2(2;3)	2(2;3)	1,5(1;2)^{AB}
CHE group (n=31)	2(2;3)	1(1;1)^{A}	1(1;1)^{B}

Values presented as median (lower quartile; upper quartile).
A-significant difference to value of previous visit
B- significant difference to value at baseline

Areas of disease burden most impacted by AD include overall quality of life and the social, academic, and occupational realms [2]. The burden of AD is not limited to just the patient, because AD is a chronic relapsing skin disease that can persist into adulthood and burden of disease is frequently experienced by the patient's family [1]. Chronic hand eczema mostly affects adults and the disease psychosocial burden, and the functional impairment have been identified as a major cause of morbidity and employment-related financial hardships [19].

Current treatment strategy for chronic skin problems like AD and CHE usually divided into treatment of a disease aggravation followed by skin, dietary, hygiene and occupational measures to prevent new worsening and allow a patient to have the highest quality of life among possible with the disease. Current dermatology is armed with different potent medications and other treatments to fight against severe aggravations but in practice the less controlled period of the diseases starts just after active treatment discontinuation. "Hidden" inflammation may easily return to "visible" stage unless it is under the control till the final disappearance. Results of our study have shown that cases of new disease worsening within nearest 24 weeks after AD and CHE aggravation treatment discontinuation are quite frequent despite appropriate skin care with moisturizers. Significant part of AD and CHE patients do require additional topical anti-inflammatory treatment or antihistamines to suppress "new wave" of skin inflammation and itch. AD is a chronic relapsing inflammatory skin condition with different pathophysiology mechanisms involved. As s results we used to observe different clinical variants of the disease with different sensitivity to treatments and prognosis [20]. Our results show that early follow up of adult AD patients who stopped active therapy differs depending on age of AD onset. In case the disease started in adulthood early follow-up period would be more often associated with stable presence of the disease symptoms rather than continuous improvement. For CHE patient's discontinuation of treatment is less probably causes aggravation within nearest 12 weeks, but later period is often connected with worsening of eczema for some reasons. Dermatologic patients may demonstrate different types of disease coping that influences both treatment effectiveness and cooperation with medical team. As our results demonstrated within 24 weeks period after treatment discontinuation part of patients would not attend dermatologists again despite some worsening of the disease. This fact may explain why statistics data on AD and eczema course in adults differs from study to study showing opposite trends.

4. CONCLUSION

End of AD or CHE aggravation treatment may be connected with probability of new disease worsening within nearest 24 weeks despite good previous clinical results. Moisturizers used for skin care allow to control the disease not for all patients. The worsening is more probable for AD patients with onset in adulthood during all 24 weeks. In case of hand eczema period from 12 till 24 weeks is riskier for new worsening. Follow-up of AD and CHE patients helps to identify early signs of worsening and prescribe adequate treatment to control the disease. Scheduled visits to dermatologists during follow-up may help to identify patients with worsening who would neglect it for different reasons.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to

use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, respondents' written consent has been collected and preserved by the authors.

REFERENCES

1. Avena-Woods C. Overview of atopic dermatitis. Am J Manag Care. 2017;23(8 Suppl):S115–123.
2. Drucker AM, Wang AR, Li W-Q, Sevetson E, Block JK, Qureshi AA. The burden of atopic dermatitis: Summary of a report for the national eczema association. J Invest Dermatol. 2017;137(1):26–30. doi: 10.1016/j.jid.2016.07.012.
3. Nutten S. Atopic dermatitis: global epidemiology and risk factors. Ann Nutr Metab. 2015;66(1):S8-16. doi:10.1159/000370220.
4. Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014;70(2):338–351. doi: 10.1016/j.jaad.2013.10.010.
5. Williams HC, Strachan DP. The natural history of childhood eczema: observations from the British 1958 birth cohort study. Br J Dermatol. 1998;139(5):834-839.
6. Ozkaya E. Adult-onset atopic dermatitis.J Am Acad Dermatol. 2005;52(4):579-82.
7. Ellis CN, Mancini AJ, Paller AS, Simpson EL, Eichenfield LF. Understanding and managing atopic dermatitis in adult patients.Semin Cutan Med Surg. 2012;31(suppl 3): S18-S22. doi: 10.1016/j.sder.2012.07.006.
8. Hanifin JM, Reed ML; Eczema Prevalence and Impact Working Group. A population-based survey of eczema prevalence in the United States. Dermatitis. 2007;18(2):82-91.
9. Margolis JS, Abuabara K, Bilker W, Hoffstad O, Margolis DJ. Persistence of mild to moderate atopic dermatitis. JAMA Dermatol. 2014;150(6):593-600. doi: 10.1001/jamadermatol.2013.10271.
10. Kim JP, Chao LX, Simpson EL, Silverberg JI. Persistence of atopic dermatitis (AD): a systematic review and meta-analysis. J Am Acad Dermatol. 2016;75(4):681-7.e11. doi: 10.1016/j.jaad.2016.05.028.
11. Weissler A. Atopic dermatitisa new dawn. Physician Assistant Clin. 2016;1(4):661-682. doi: http://dx.doi.org/10.1016/j.cpha.2016.06.004.
12. Siegfried EC, Hebert AA. Diagnosis of atopic dermatitis: mimics, overlaps, and complications. J Clin Med. 2015;4(5):884-917. doi: 10.3390/jcm4050884.
13. Lee GR, Maarouf M, Hendricks AK, Lee DE, Shi VY. Current and emerging therapies for hand eczema.Dermatol Ther. 2019;32(3):e12840. doi:10.1111/dth.12840
14. Coenraads PJ. Hand eczema. N Engl J Med. 2012;367(19):1829–37. doi:10.1056/NEJMcp1104084
15. Silverberg JI, Garg NK, Paller AS, Fishbein AB, Zee PC. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. J Invest Dermatol. 2015;135(1):56-66. doi: 10.1038/jid.2014.325.
16. Silverberg NB, Silverberg JI. Inside out or outside in: does atopic dermatitis disrupt barrier function or does disruption of barrier function trigger atopic dermatitis? Cutis. 2015;96(6):359-361.
17. Rishi Chopra, Jonathan I. Silverberg. Assessing the severity of atopic dermatitis in clinical trials and practice. Clinics in Dermatology. 2018;26(5):606-15. Doi:10.1016/j.clindermatol.2018.05.012.
18. Agner T, Andersen KE, Brandao FM, et al. Hand eczema severity and quality of life: a cross-sectional, multicentre study of hand eczema patients. Contact Dermatitis. 2008;59(1):43–47. doi:10.1111/j.1600-0536.2008.01362.x
19. Cabanillas B, Brehler AC, Novak N. Atopic dermatitis phenotypes and the need for personalized medicine. Curr Opin Allergy Clin Immunol. 2017;17(4):309–315. doi: 10.1097/ACI.0000000000000376