

The evaluation of dupilumab treatment response in atopic dermatitis patients

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ABSTRACT

OBJECTIVE: This study aims to demonstrate real-life effectiveness of dupilumab treatment in moderate-to-severe atopic dermatitis patients.

METHODS: The 14 patients diagnosed with moderate-to-severe atopic dermatitis were included in this study. All of the patients started dupilumab treatment in our faculty between October 2019 and October 2020. The patients were evaluated at the beginning of the treatment and after 12 weeks of treatments. The baseline scoring atopic dermatitis (SCORAD) scores, the total immunoglobulin E (IgE) levels, and the visual analog scale (VAS) of 0–10 points for itch intensity compared with the post-treatment scores.

RESULTS: The SCORAD scores, the serum total IgE levels, and the VAS itch scores of the patients receiving dupilumab treatment dropped significantly following 12 weeks of dupilumab treatment. No significant correlation was demonstrated between the initial SCORAD scores and the serum total IgE values. Besides, no correlation was shown to exist in the reduction of the SCORAD and the serum total IgE values after dupilumab treatment.

CONCLUSION: Dupilumab treatment showed significant improvement in disease severity with remarkable reduction in serum total IgE levels.

Keywords: Atopic dermatitis; dupilumab; scoring atopic dermatitis.

Cite this article as: Askin O, Yucesoy SN, Serdaroglu S. The evaluation of dupilumab treatment response in atopic dermatitis patients. *North Clin Istanbul* 2021;8(2):145–149.

Atopic dermatitis is a chronic inflammatory skin disease characterized by itchy erythematous papules and plaques. It is very frequently seen as chronic dermatosis (2–10%) in adults [1]. It usually starts in pediatric ages although there are some differences in the clinical presentation. Topical emollients and anti-inflammatory agents including steroids and calcineurin inhibitors are the most widely used treatment options [2]. However, topical agents may fail in moderate-to-severe cases. Systemic immunomodulators and phototherapy are the other treatment options. Cyclosporine is the most widely used immunosuppressive drug in moderate-to-severe atopic dermatitis cases; however, potential toxicity may limit its usage [3].

Dupilumab is a human monoclonal antibody blocking IL-4 and IL-13 signaling pathways [4]. It is approved for the treatment of moderate-to-severe atopic dermatitis cases [5]. This study aims to demonstrate the actual life data of patients who are diagnosed with atopic dermatitis and are under the treatment of dupilumab.

MATERIALS AND METHODS

Fourteen patients diagnosed with moderate-to-severe atopic dermatitis were included in this study. All of the patients started dupilumab treatment in our faculty, between October 2019 and October 2020. The patients in-

Received: May 23, 2020 *Accepted:* November 08, 2020 *Online:* November 25, 2020

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volved in the study were informed beforehand, and their approval forms were taken. The consent of the Medical Faculty Ethics Committee was also taken (February 06, 2020 – 21,295). The patients were evaluated at the beginning of the treatment and after 3 months' of treatments. The initial scoring atopic dermatitis (SCORAD) scores [6], the total immunoglobulin E (IgE) levels, and the visual analog scale (VAS) of 0–10 points for itch intensity compared with the post-treatment scores. All patients were chosen according to the following criteria: Age older than 18, SCORAD score >30, and the treatment failure with topical agents and at least should have used one systemic immunosuppressive therapy.

Statistical Analyses

The Wilcoxon signed-rank test was used to analyze the differences in the SCORAD scores, VAS itch, and total serum IgE levels between the baseline and the 3rd month of treatment. Spearman's correlation test was utilized to show the association between the baseline total serum IgE levels and the SCORAD score as well as reductions in these two parameters from the baseline to the 3rd month of treatment. All statistical analyses were performed with IBM SPSS statistics 21.

RESULTS

The characteristics of patients are shown in Table 1. The study included a total of 14 patients, 6 females and 8 males, all diagnosed with atopic dermatitis and received dupilumab. Following a 600 mg loading dose, these 14 patients received a biweekly 300 mg subcutaneous treatment regularly for at least 3 months. All patients included in the study were selected from patients diagnosed with moderate-to-severe atopic dermatitis either who had shown resistance to the oral or topical corticosteroids and cyclosporine treatments or whose treatments had been interrupted due to side effects. During the course of the study, all patients were allowed to use topical moisturizers and topical steroids in their flaring periods while one patient received one dose of IM betamethasone dipropionate and betamethasone sodium phosphate treatments to suppress the attack in the beginning of the treatment. All patients were advised that they can use artificial eye tear agents during the course of the study.

The mean SCORAD scores, VAS itch scores, and the serum total IgE levels at the beginning of the treatment and after 3 months' of treatments are shown in Table 2. Although the variations in the upper limit

Highlight key points

- Atopic dermatitis is a chronic skin disease which is characterized by itchy inflammatory plaques and xerosis.
- Dupilumab is a monoclonal antibody which targets IL-4 and IL-13 signalling pathways.
- dupilumab treatment improved the disease severity, the itch scores which affect the quality of life, and the serum total IgE levels in patients diagnosed with the atopic dermatitis.

TABLE 1. Characteristics of 14 patients with atopic dermatitis

Age at diagnosis, years, mean (min–max)	16.8 (1.0–49.0)
Age at dupilumab initiation, years, mean (min–max)	37.7 (18.0–61.0)
Sex, %	
Female	42.8
Male	57.2
Duration of disease, years, mean (min–max)	16.8 (1.0–58.0)
Min: Minimum; Max: Maximum.	

TABLE 2. Data of patients at baseline and follow-up after 3 months

	Baseline	3-month follow-up	p
SCORAD			
Mean (min–max)	50.9 (35–74.5)	20.56 (7–37)	0.001
Itch (VAS)			
Mean (min–max)	8.07 (7.9)	2.64 (1–4)	0.001
Serum total IgE			
Mean (min–max)	3577.8 (115–19 157)	774.4 (47–2638)	0.01

SCORAD: Scoring atopic dermatitis; Min: Minimum; Max: Maximum; VAS: Visual analog scale; IgE: Immunoglobulin E.

of normal serum total IgE have been reported, the accepted upper limit is between 100 and 300 UI/ml [7]. Whereas the average value for initial SCORAD score was 50.9, at the 3rd month of the treatment, it was 20.56, and this drop was of significance statistically ($p < 0.05$). Whereas the average value for the initial VAS itch score was 8.07, the evaluation at the 3rd month of the treatment yielded a score of 2.64. This drop also was of significance statistically ($p < 0.05$). Moreover, whereas the average serum total IgE value

TABLE 3. Correlation between baseline and decrement levels of SCORAD and serum total IgE levels

	Sig. (two tailed)
Baseline SCORAD value	0.97
Baseline serum total IgE value	
Reduction in SCORAD	0.47
Reduction in serum total IgE	

SCORAD: Scoring atopic dermatitis; IgE: Immunoglobulin E.

measured at the beginning of the treatment was 3577.8 UI/ml, the value measured at the 3rd month of

the treatment was 774.4 UI/ml, and this decrease was also statistically significant ($p < 0.05$).

On the other hand, no significant correlation was observed between the initial SCORAD scores and serum total IgE levels of the patients ($p = 0.97$) and between the reductions in the SCORAD scores and the serum total IgE levels from baseline to the 3rd month of the treatment ($p = 0.47$) (Table 3).

Ten out of 14 patients showed approximately 50% reduction in VAS itch score following loading dose of dupilumab treatment at follow-up visit 2 weeks later. Only 1 patient (7.1%) developed the conjunctivitis during the treatment period. Other than the conjunctivitis, the patients did not develop any side effects.



FIGURE 1. (A–C) A 45-year-old female patient with severe atopic dermatitis before treatment, scoring atopic dermatitis (SCORAD) score of 67.5. (D–F) a 45-year-old female patient with severe atopic dermatitis after 12 weeks of dupilumab treatment, SCORAD score of 24.45.

DISCUSSION

The study which we conducted demonstrated that the SCORAD scores, the serum total IgE levels, and the VAS itch scores of the patients receiving dupilumab treatment dropped significantly after the treatment (Fig. 1, 2). No significant correlation was found between the initial SCORAD scores and the serum total IgE values. In addition, no correlation was shown to exist in the decrement levels of the SCORAD and the serum total IgE values after dupilumab treatment.

Olesen et al. [8] demonstrated that for the patients who were diagnosed with atopic dermatitis and received dupilumab treatment, the eczema area and severity index (EASI), VAS itch, and VAS-sleep scores before, after the 1st, and the 3rd month of treatments showed significant drops in the 1st and the 3rd months' values as compared to the initial ones, whereas no significant difference was recorded in the parameters between the 1st and 3rd months of treatments. In this study, the drops in the EASI score and the VAS itch score after the 3rd month of treatment were 76.7% and 67.5% as compared to the initial scores, respectively, while in our study, the drops in the SCORAD score and the VAS itch score were 58% and 67%, respectively. The study carried out by Olesen et al. [8] demonstrated that the dupilumab effect exhibited itself primarily in the 1st month and that its effect continued in the same manner for at least 3-month period. No correlation could be detected between the baseline EASI score and the serum total IgE levels and the drops in these parameters after the 3rd month of treatment. However, there existed a positive correlation between the drop in the serum LDH level, which was another parameter, and the drop in the EASI scores after the 3rd month of treatments. Aside from conjunctivitis which was reported with 18.4% of the patients and which receded with the topical treatment, no side effect was recorded. In our study, nonetheless, the rate of conjunctivitis was 7.1%.

In another multicentric research carried out by Fagnoli et al. [9], the patients diagnosed with atopic dermatitis and received dupilumab treatments were evaluated. The evaluation showed that in the 4th and 16th weeks of the follow-up, there were significant drops in the EASI, the itch and sleep NRS, and the DLQI scores as compared to the beginning levels. The 16th week of the treatment also recorded significant drops in these parameters in comparison with the 4th week's levels. This study revealed that the dupilumab effect continued for at least 4 months. The study also demonstrated that the EASI score dropped by 72.3% from the baseline value in

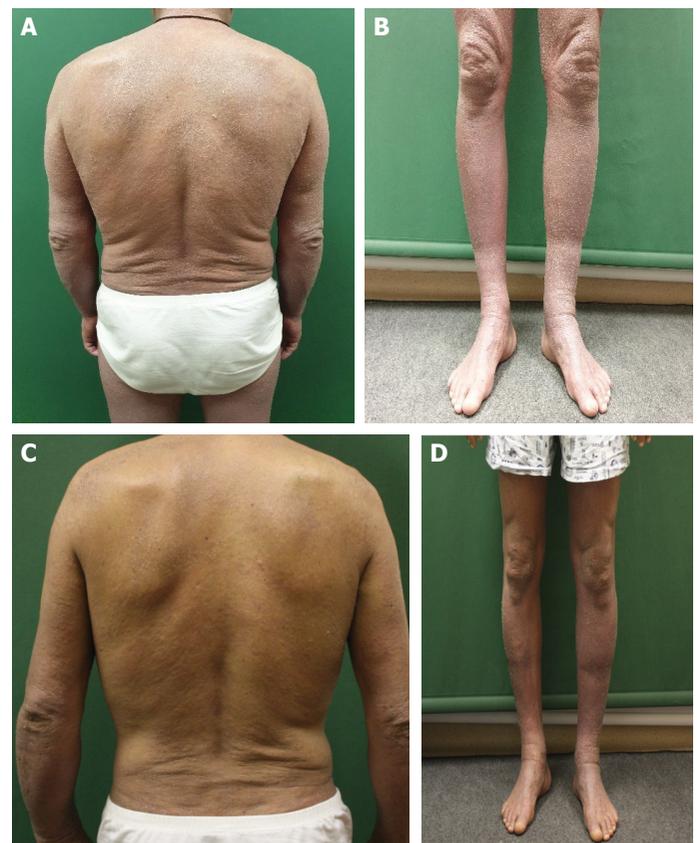


FIGURE 2. (A, B) A 64-year-old male patient with severe atopic dermatitis before treatment, scoring atopic dermatitis (SCORAD) score of 74.5. **(C, D)** a 64-year-old male patient with severe atopic dermatitis after 12 weeks of dupilumab treatment, SCORAD score of 20.95.

the 16th week of the treatment while the drop in the itch score was 69.5%. The drop in the EASI score was higher in comparison with our study while the decline in the itch score was similar. In this study by Fagnoli et al. [9], positive correlations were reported between the initial EASI and serum total IgE values and between the drops in the EASI and serum total IgE values, while our study yielded no significant correlation. Whereas their study reported conjunctivitis to be the most frequent side effect (11%), injection site reaction, fatigue, and folliculitis were among the other seldom seen adverse effects. All conjunctivitis cases were receded with the topical treatment.

In the SOLO 1 and SOLO 2 which are placebo-controlled randomized Phase 3 studies, as compared to the placebo groups, a significant drop was recorded in the EASI scores in both groups who received the dupilumab treatment on a weekly and biweekly basis [10]. While the dupilumab treatment was demonstrated to cause significant drops in the itch, anxiety, and the depression scales,

conjunctivitis and injection site reactions were reported to be among the most frequent side effects.

In their multicentric research, Faiz et al. [11] recorded that of the patients who had been diagnosed with the atopic dermatitis and given the dupilumab treatments, 16.6% and 48.8% yielded the SCORAD-75 and EASI-75 responses, respectively, in the average 3rd month of their follow-up. The most prevalent side effect in that study was conjunctivitis in 38.2% of the patients. In another study by Armario-Hita et al. [12], in which both the SCORAD and the EASI scoring systems were used in the evaluations, the follow-up responses of 70 patients who had been diagnosed with the atopic dermatitis and given the dupilumab treatments revealed score drops of 79.3% in the EASI, 69.3% in the SCORAD, and 69.9% in the VAS itch. In our study, improvement in VAS itch score was similar while the reduction in mean SCORAD value was 58%.

The international consensus advises that the EASI and SCORAD scoring systems are basically used in the scoring of the severity of atopic dermatitis and in the evaluation of treatment responses. The comparison of the two scoring systems reveals that xerosis and oozing/weeping used in the SCORAD scoring are not used in the EASI scoring system. This results in the SCORAD scores being higher as a ratio than the EASI scores. It is our observation that xerosis still continues in many patients even after the treatment albeit not as an active lesion. Taking the SCORAD scoring parameters into account, this condition may constitute a factor for the SCORAD treatment response in our study to be a bit lower as compared to other studies. Another important difference in the EASI and SCORAD scoring systems is that, while the SCORAD may score higher in localized severe cases, the EASI may end up lower [13]. We presume that this phenomenon might be another factor in the explanation of the difference between the EASI and SCORAD treatment responses. Conjunctivitis, being the most observed side effect in the studies, was relatively less encountered in our study. Moreover, we believe that the leading cause for this was that the patients in our study were advised to use artificial eye tear agents.

Conclusion

This study supports the view that the dupilumab treatment when given to patients who had been diagnosed with the atopic dermatitis led to appreciable drops in the disease severity, the itch scores which affect the quality of life, and the serum total IgE levels. However, no correlation could be found between the disease severity and the serum total IgE levels.

Ethics Committee Approval: The Cerrahpasa University, Faculty of Medicine Clinical Research Ethics Committee granted approval for this study (date: 06.02.2020, number: 21295).

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – OA, SNY, SS; Design – OA, SNY, SS; Supervision – OA, SNY, SS; Fundings – OA, SNY, SS; Materials – OA, SNY; Data collection and/or processing – OA, SNY, SS; Analysis and/or interpretation – OA, SNY, SS; Literature review – OA, SNY, SS; Writing – OA, SNY, SS; Critical review – OA, SNY, SS.

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