Original Investigation
Orijinal Araştırma

DOI: 10.4274/turkderm.galenos.2025.49284
Turkderm-Turk Arch Dermatol Venereol 2025;59(4):125-31

Real-life effectiveness and safety of systemic treatments and phototherapy in pediatric patients with moderate-to-severe atopic dermatitis: Observational study

Orta ve şiddetli atopik dermatitli pediatrik hastalarda sistemik tedavilerin ve fototerapinin gerçek yaşam etkinliği ve güvenliği: Gözlemsel çalışma

Meryem Aktaş, Deniz Yücelten, Ferhan Bulut Demir

Marmara University Faculty of Medicine, Department of Dermatology, İstanbul, Türkiye

Abstract

Background and Design: Systemic therapies are frequently used off-label for the treatment of atopic dermatitis (AD); however, real-world data are limited.
Materials and Methods: This study aimed to evaluate the efficacy and safety of phototherapy and systemic treatments in patients with severe AD aged <18 years using real-world data. The study, designed as a single-center retrospective observational study, evaluated patients who received at least one systemic treatment or phototherapy between 2019 and 2022. Treatment response was assessed using the Physician Global Assessment (PGA) ordinal scale.
Results: This study evaluated 30 patients and 81 treatment courses. The most common treatment was cyclosporine (CSA), administered to 25 (83.3%) patients, followed by systemic corticosteroids (SCS), administered to 18 (60%) patients (treatment course: 21 patients). Azathioprine (AZA) was used in 12 (40%) patients, methotrexate (MTX) in 7 (23.3%) patients, phototherapy in 5 (16.6%, 6 treatment courses), intravenous immunoglobulin (IVIG) in 5 (16.6%), omalizumab in three (10%), dupilumab in one (3.3%), and mycophenolate mofetil in one (3.3%). While all courses of SCS and IVIG resulted in at least a good response (PGA1 or PGA2), the rates of patients with at least a good response to CSA, AZA, MTX, and phototherapy were 92%, 66.7%, 57.1%, and 50%, respectively (p=0.001). The percentage of patients experiencing side effects was 32% (n=8) for CSA, 23.8% (n=5) for SCS, 33.3% (n=4) for AZA, 14.3% (n=1) for MTX, and 33.3% (n=2) for phototherapy. Two patients discontinued CSA treatment due to side effects: one due to nausea and the other due to impetigo and febrile seizure. None of the patients discontinued other treatments because of side effects.
Conclusion: This observational study indicates that classical immunosuppressive treatments are effective alternatives for children with severe AD without serious side effects. However, comprehensive studies involving novel treatment modalities, such as biologics and small molecules, are warranted.
Keywords: pediatric dermatology, atopic dermatitis, therapy

Öz

Amaç: Sistemik tedaviler atopik dermatit (AD) tedavisinde lisanssız olarak sıklıkla kullanılmalarına rağmen gerçek yaşam verileri kısıtlıdır. Şiddetli AD tanılı 18 yaş altı hastalarda fototerapi ve sistemik tedavilerin etkinlik ve güvenilirliklerini gerçek yaşam verileri üzerinden değerlendirmek.
Gereç ve Yöntem: Tek merkezli retrospektif gözlemsel bir çalışma olarak tasarlanan çalışmada, 2019 ile 2022 yılları arasında en az bir sistemik tedavi veya fototerapi almış hastalar değerlendirildi. Tedavi yanıtı, Hekimin Global Değerlendirmesi (HGD 0-2) sıralı ölçeği kullanılarak değerlendirildi.
Bulgular: Toplam 30 hasta ve 81 tedavi kürü değerlendirmeye alındı. En sık tedavi, 25 (%83,3) hastada kullanılan siklosporin (CSA) olup bunu 18 hastada (60%) sistemik kortikosteroid (SKS) (21 tedavi kürü) takip etti. Azatioprin (AZA) 12 (%40), metotreksat (MTX) 7 (%23,3), fototerapi 5 (%16,6; 6 tedavi kürü), intravenöz immünglobulin (IVIG) 5 (%16,6), omalizumab 3 (%10), dupilumab ve mikofenolat mofetil birer (%3,3) hastada kullanılmıştı. SCS ve IVIG'in tüm kürleri en az "iyi düzeyde yanıtla (HGD1 veya HGD2) sonuçlanırken, CSA, AZA, MTX ve fototerapi için en az "iyi" düzeyde yanıt alan hasta oranları sırasıyla %92, %66,7, %57,1 ve %50 olarak saptandı (p=0,001). Yan etki gözlenen hasta oranları sırasıyla CSA için %32 (n=8), SKS için %23,8 (n=5), AZA için %33,3 (n=4), MTX için %14,3 (n=1), fototerapi için %33,3 (n=2) olarak saptandı. İki hastada CSA tedavisi yan etki nedeniyle sonlandırıldı: bir hastada bulantı, bir hastada impetigo ve febril nöbet. Diğer tedavi gruplarında yan etki nedeniyle tedavisi sonlandırılan hasta olmadı.
Sonuç: Çocukluk çağı şiddetli AD tedavisinde konvansiyonel sistemik tedaviler, güvenli ve etkili tedavi seçenekleri olarak görünmektedir ancak biyolojikler ve küçük moleküller gibi yeni tedavi yöntemlerini de içeren kapsamlı çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: pediatrik dermatoloji, atopik dermatit, tedavi

Address for Correspondence/Yazışma Adresi: Meryem Aktaş MD, Marmara University Faculty of Medicine, Department of Dermatology, İstanbul, Türkiye
E-mail: meryemaktas72@gmail.com **ORCID:** orcid.org/0000-0002-0157-0748
Received/Geliş Tarihi: 16.12.2024 **Accepted/Kabul Tarihi:** 12.12.2025 **Publication Date/Yayınlanma Tarihi:** 30.12.2025

Cite this article as/Atıf: Aktaş M, Yücelten D, Bulut Demir F. Real-life effectiveness and safety of systemic treatments and phototherapy in pediatric patients with severe atopic dermatitis: observational study. Turkderm-Turk Arch Dermatol Venereol. 2025;59(4):125-31

Turkderm - Turk Arch Dermatol Venereol
2025;59(4):125-31

Introduction

Atopic dermatitis (AD) is a chronic inflammatory disease affecting up to 20% of children[1]. Topical anti-inflammatory medications, along with emollients and allergen avoidance, are the first steps in the AD treatment algorithm[2]. Systemic corticosteroids (SCS) are recommended only as salvage therapy in acute flares; high-dose and long-term use is associated with side effects, in addition to the risk of rebound exacerbation[3]. Although cyclosporine (CSA) is approved for the treatment of AD in patients over the age of 16 years, it is often used as a first-line systemic treatment in children. Phototherapy, especially ultraviolet A1 and narrowband ultraviolet B, is recommended as a second step in the treatment of moderate-to-severe AD. Azathioprine (AZA), methotrexate (MTX), and mycophenolate mofetil (MMF) are other systemic agents used off-label in pediatric AD[2]. The efficacy of omalizumab in AD is controversial; however, it has been reported to be effective in the pediatric age[4]. The approval of dupilumab for 6-month-old and abrocitinib and upadacitinib for adolescents is promising; however, many patients do not have access to these treatments because of a lack of insurance coverage[5]. Intravenous immunoglobulin (IVIG), which can provide significant improvement in pediatric AD, is recommended in advanced stages due to the inconvenience of administration and high cost[6].

Although conventional systemic therapies and phototherapy (narrow-band UVB) are frequently used off-label in pediatric AD, real-life data are scarce[7]. In this study, we aimed to evaluate the efficacy and safety of phototherapy and systemic treatments in patients with moderate-to-severe AD aged <18 years.

Materials and Methods

This retrospective study included 30 patients aged <18 years who received at least one systemic treatment or (narrow-band UVB) for moderate-to-severe AD between 2019 and 2022. At our institution, pediatric patients with AD are referred to the pediatric dermatology unit when topical treatments, including wet wrap application, are insufficient. Consistent with the stepwise treatment approach for AD[2], patients received phototherapy or systemic therapies.

Data on patient demographics, clinical and treatment characteristics, treatment outcomes, and post-treatment remission duration were collected by reviewing electronic medical records. A systemic corticosteroids (CS) regimen shorter than 2 weeks was considered as short-course rescue therapy, whereas an SCS regimen >2 weeks, >2 mg/kg/day, or >20 mg/day prednisolone or its equivalent was considered as systemic immunosuppressive therapy[8]. Treatment outcomes were evaluated using the Physician Global Assessment (PGA) scale (PGA 0-poor: inadequate response, no reduction in clinical signs and symptoms; PGA 1-good: moderate reduction in clinical signs and symptoms; PGA 2-significant: complete or almost complete improvement). The combined response rates for PGA 1 and 2 indicated overall effectiveness.

This research was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee with protocol no.: 09.2021.1199, date: 05.11.2021.

Statistical Analysis

Statistical analyses were conducted using SPSS version 26 (IBM). Categorical data were compared using chi-square analysis, Fisher's exact test, and Z test in the presence of more than two groups with Bonferroni correction. The Mann-Whitney U test was used to compare continuous data between the two groups. The Kruskal-Wallis H analysis of variance was employed to compare continuous data from more than two independent groups. The treatment response comparison was made on a total of 76 treatment courses, including 25 courses of CSA, 7 of MTX, 12 of AZA, 21 of SCS, 6 of phototherapy, and 5 of IVIG. Good and significant responses (PGA 1 and 2) were collectively evaluated for overall effectiveness. The factors influencing treatment response were examined using the chi-square test, Mann-Whitney U test, and correlation analyses. Statistical significance was set at $p<0.05$.

Results

The study evaluated 30 patients who underwent 81 treatment courses. At data lock, the median age was 12 [interquartile range (IQR): 8] years, while the median age at disease onset was 12 (IQR: 55) months. Seven patients had food allergies, six of whom were allergic to eggs, and 12 patients had mite allergies. Of all patients, 43.3% (13) had atopic comorbidity and 46.7% (14) had non-atopic comorbidity, the most frequent being primary immunodeficiency (PID, n=4, Table 1).

CSA was the most frequently administered treatment and was administered to 25 (83.3%) patients. SCS was administered to 18 patients (60%) in 21 treatment sessions. Other treatments included AZA (n=12, 40%), MTX (n=7, 23.3%), phototherapy (n=5, 16.6% over 6 treatment courses), IVIG (n=5, 16.6%), omalizumab (n=3, 10%), dupilumab (n=1, 3.3%), and MMF (n=1, 3.3%). Twelve short courses of SCS were administered as rescue therapy for severe exacerbations in six patients. All patients continued to receive topical anti-inflammatory treatment. The characteristics of the treatments are summarized in Table 2.

Four (16%) patients with CSA and one each treated with SCS (4.8%), phototherapy (16.6%), AZA (8.3%), and omalizumab (33.3%) showed a significant response (p=0.689). The overall effectiveness of SCS, IVIG, CSA, AZA, MTX, and phototherapy was 100%, 100%, 92%, 66.7%, 57.1%, and 50%, respectively (p=0.001; Figure 1). It was found that SCS was significantly more effective than MTX and phototherapy. However, no significant differences were observed among the other treatments. One dupilumab-treated and one MMF-treated patient achieved PGA0.

No significant correlation was found between treatment response and age at treatment initiation, onset of AD, allergy, or sex. No treatments were discontinued due to side effects, except for two patients who had to discontinue CSA treatment due to nausea, seizures, and impetigo. The pediatric department classified the seizure as a febrile seizure, and no further treatment was indicated. Table 3 presents the side effects experienced by patients and their corresponding management strategies.

At data lock, six patients were lost to follow-up. Eleven patients remained in remission following topical treatment. Six patients remained on CSA, four on MTX (one in combination with IVIG), two on omalizumab, and one on dupilumab.

Discussion

In this study, we present systemic treatment data for pediatric patients with moderate-to-severe AD who were followed up at a third-line referral center. Response rates to treatment with SCS have been reported to be as high as 84%, with rebound exacerbation rates ranging from 26.7% to 47.6%[3]. Although our study observed high overall response rates, the low significant response rates were attributed to the termination of treatment to prevent possible side effects after the severe symptoms subsided in 95% (n=20) of the patients. Response rates to CSA range from 40% to 95% in retrospective cohort studies, with excellent response rates of up to 80%[9]. Although the overall effectiveness of CSA was similar to that in previous studies, the significant response rate of 16% (n=4) was lower than that reported[6,10,11]. The outcome may have been influenced by possible selection bias or varying response-assessment criteria. The CSA discontinuation rate due to side effects in our study was consistent with that reported in the literature[9].

In this study, lower than recommended doses of AZA[6] were administered due to the inability to measure Thiopurine S-methyltransferase (TPMT) activity levels in our hospital. This may have resulted in lower significant response rates than those reported in the literature[12,13]. In fact, 41.7% (n=5) of treatment sessions were replaced because the treatment response did not reach the intended level, which could have been improved by increasing the dose according to the TPMT activity. Side effects were lower than those previously reported, possibly due to the low treatment doses[12,13]. Similarly, the MTX dose was lower than the recommended dose of 0.3-0.4 mg/kg/week. Although the overall response rates were comparable to those reported in the literature[2,14], the lower rate of significant response in the study may be attributed to the use of lower than recommended doses or the administration of treatment in advanced stages in patients who were resistant to other treatments Table 4.

Response rates to phototherapy in pediatric AD have been reported to range between 60% and 90% in the literature[2,15-18]. Although the number of treatment courses was limited, the clinical response and side effect results obtained with phototherapy were consistent with those of previous studies.

Following skin infections, the most common skin finding in PID is AD, with an incidence of 13% to 22%. Conversely, in a study of 75 patients diagnosed with severe AD, 7.9% were subsequently diagnosed with PID[19], which supports the high PID rate observed in our cohort.

Although studies have shown a lack of response in adult patients, IVIG treatment has achieved a response rate of 60-90% in pediatric AD[7,20]. All patients who received IVIG in this study had a good response. They had significantly elevated serum IgE levels, with a mean of 39311 international unit/mL (±34079). These findings align with previous research indicating a correlation between high serum IgE levels and a positive response to IVIG treatment[20]. However, the low treatment doses and concomitant PID in 80% of the patients may have reduced the significant response rates.

Table 1. Baseline characteristics of the study population

Characteristics (n)		Median (IQR) / n (%)
Age (n=30)		12 (8)
Onset of disease (month, n=27)		12 (55)
Duration of disease until systemic treatments (months, n=27)		39 (66)
Baseline serum total IgE levels (IU/ml) (n=18)		3230.5 (15815.5)
Gender (n=30)	Female	14 (46.7)
	Male	16 (53.33)
Family history of atopy (n=30)		9 (26.5)
Food allergy (n=30)		7 (23.3)
Atopic comorbidities (n=30)	None	17 (58.8)
	Allergic rhinitis	1 (3.3)
	Asthma	13 (43.3)
Comorbidities (n=30)	None	16 (53.3)
	Psoriasis	2 (6.6)
	Lichen planus	2 (6.6)
	Immunodeficiency	4 (13.3)
	Prurigo nodularis	2 (6.6)
	Cataract	1 (3.3)
	GH deficiency	1 (3.3)
	Coffin-Siris syndrome	1 (3.3)
	ADHD	1 (3.3)
	Thalassemia trait	1 (3.3)
	Epilepsia	1 (3.3)
	Pectus excavatum	1 (3.3)

n: Number, IQR: Interquartile range, ADHD: Attention deficit hyperactivity disorder, GH: Growth hormone, IVIG: Intravenous immunoglobulin, IU: International unit

Turkderm - Turk Arch Dermatol Venereol
2025;59(4):125-31

Omalizumab has been shown to significantly reduce disease severity and the need for topical CS in pediatric patients with severe AD[21]. Systematic reviews have reported treatment response rates of 70-74% and noted that lower serum IgE levels may be associated with a better response[4,22,23]. Although our sample size was small, our treatment responses were consistent with those reported in the literature. Dupilumab, recommended for patients with severe AD over the age of six[6], is not reimbursed for pediatric patients in our country. Only one patient received dupilumab, and no response was observed.

Although this study found that SCS was significantly more effective than MTX and phototherapy, it is important to note that the latter two are preferred for different clinical scenarios. Systemic CS is often used for short-term treatment during acute flares, whereas MTX and phototherapy are preferred for long-term disease control. According to a 2020 meta-

Table 2. Characteristics of the treatment courses (n=81)

	Treatment course/ patient n (%)	Female (n) / male (n)	Age at the treatment onset median (IQR) (year)	Treatment duration median (IQR) (month)	Dosage median (IQR)	Overall effectiveness n (%)	Side effect n (%)	Reason to terminate the treatment
Cyclosporine	25 (31.3)/25(71.4)	12/13	9.3 (8.7)	10 (11)	3.52 (1.2) (mg/kg/day)	23 (92)	8 (32)	2-side effects 2-unresponsiveness 6-ongoing treatment 2-loss of follow-up 7-to prevent to presumed side effects 1-decision of PAID 1-patient decision 4-remission
Systemic corticosteroid	21 (26.3)/18 (60)	11/10	10.5 (9.2)	50 (41.5)+	0.59 (0.42) (mg/kg/day)	21 (100)	5 (23.8)	20-to prevent to presumed side effects 1-remission
Azathioprine	12 (15)/12 (40)	6/6	10.9 (4.3)	5 (20.5)	1.25 (0.75) (mg/kg/day)	8 (66.7)	4 (33.3)	4-unresponsiveness 2-loss of follow-up 5-treatment alteration due to insufficient response 1-remission
Methotrexate	7 (8.8)/7(23.3)	5/2	9.6 (9.9)	7 (10)	0.26 (0.1) (mg/kg/ week)	4 (57.1)	1 (14.3)	2-unresponsiveness 1-loss of follow-up 4-ongoing treatment
Phototherapy (narrow-band UVB)	6 (7.5)/5(16.7)	1/5	5.7 (7)	3 (3)	N/A	3 (50)	2 (33.3)	2-maximum possible responses[a] 3-unresponsiveness 1-remission
IVIG	5 (6.3)/5(16.7)	2/3	5.9 (6.4)	35 (55.3)	0.4-0.5 g/ kg/3 weeks	5 (100)	-	1-ongoing treatment 4-decision of PAID
Omalizumab	3 (3.8)/3(10)	2/1	11	4	300 mg/ month	3 (100)	-	2-ongoing treatment 1- replacing with dupilumab
Dupilumab	1 (1.25)/1(3.3)	1/0	11.5	5	400 mg loading, 200 mg/2 weeks	0 (0)	-	1-financial reasons
Mycophenolate mofetil	1 (1.25)/1(3.3)	1/0	10.5	4	635 mg/m²/ day	0 (0)	1 (100)	1-unresponsiveness
p*		0.675	0.487			0.001*	0.746	

*Statistical analyses were performed for the treatments with at least five courses. P<0.05 is considered statistically significant.
+duration of the treatment measured in days, [a]The maximum attainable response was achieved, and no further improvement was obtainable. IQR: Interquartile range, N: Number, N/A: Not available, PAID: Pediatric allergy and immunology department, IVIG: Intravenous immunoglobulin

analysis, CSA was more effective than MTX and AZA in treating AD[24]. In our study, we observed higher response rates for CSA than for MTX and AZA, although the difference was not statistically significant.

Data on the persistence of disease beyond adolescence are inconsistent, ranging from 8% to 70%, with disease severity being a risk factor[25,26]. At data lock, 11 (36.7%) patients had discontinued systemic treatment, whereas 13 (43.3%) were still receiving it. This finding is reasonable, given their age at the time and the fact that all patients had severe AD.

The study reflects real-life patient and disease characteristics with disease management by the same physician.

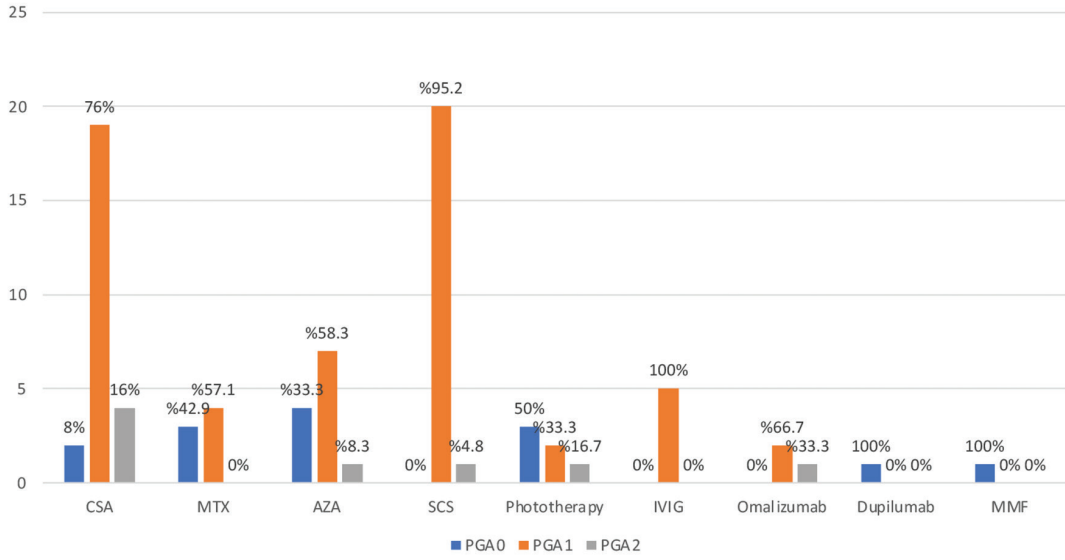

Figure 1. Treatment response rates

PGA: Physician Global Assessment, MMF: Mycophenolate mofetil, CSA: Cyclosporine, AZA: Azathioprine, IVIG: Intravenous immunoglobulin, MTX: Methotrexate, SCS: Systemic corticosteroids

Table 3. Side effects and their management

Treatment	Side effects (n)	Management
Cyclosporine	Herpes virus skin infection (2) Increase in serum creatinine level (2) Nausea Impetigo (2) Hypertrichosis Lymphopenia Seizure (3 years of age, febrile)	Antiviral treatment Normalized at control test Treatment termination Systemic antibiotics No intervention Normalized at follow-up Treatment termination
Systemic corticosteroids	Acneiform eruption Herpes labialis Leukocytosis (2) Abdominal pain Arthralgia Osteopenia	Topical treatment Topical treatment Normalized at follow-up Improved without intervention PTRD consultation Calcium replacement
Azathioprine	Abdominal pain AST/ALT increase Verruca vulgaris Pain at lower extremities	Improved without intervention Normalized at follow-up Surgical excision No intervention
Methotrexate	Increased LDL level	Normalized at follow-up
Phototherapy	Xerosis Aggravation of disease	Emollients Dose modification
IVIG	None	-
Omalizumab	None	-
Dupilumab	None	-
Mycophenolate mofetil	Abdominal pain	Improved without intervention

n: Number (side effects were indicated when they occurred more than once), PTRD: Physical Therapy and Rehabilitation Department, AST/ALT: Aspartate transaminase/alanine transaminas, LDL: Low-density lipoprotein, IVIG: Intravenous immunoglobulin

Turkderm - Turk Arch Dermatol Venereol
2025;59(4):125-31

Table 4. Sequence of treatment for each patient

Patient number	Order of treatment
1	CSA, AZA
2	IVIG, phototherapy, CSA, SCS, AZA, MTX, omalizumab
3	SCS, AZA, CSA, omalizumab
4	CSA
5	SCS, AZA
6	SCS, phototherapy, CSA, phototherapy
7	CSA
8	IVIG, MTX
9	Phototherapy, CSA, SCS, AZA
10	CSA
11	SCS, CSA
12	SCS, CSA
13	SCS
14	IVIG, MTX
15	CSA
16	SCS, CSA, IVIG, SCS, AZA
17	Phototherapy, CSA
18	CSA
19	SCS, CSA
20	CSA
21	CSA, MTX
22	SCS
23	SCS, AZA, SCS, CSA
24	SCS, CSA
25	SCS, phototherapy, CSA, AZA
26	SCS, AZA, CSA, MTX
27	CSA, SCS, AZA
28	AZA, CSA, MTX, MMF, omalizumab
29	IVIG, CSA, AZA, SCS, dupilumab, SCS, MTX
30	SCS, CSA

CSA: Cyclosporine, AZA: Azathioprine, IVIG: Intravenous immunoglobulin, MTX: Methotrexate, MMF: Mycophenolate mofetil: SCS: Systemic corticosteroids

Study Limitations

The study's limitations include its retrospective design, the limited number of patients, the limited post-treatment follow-up time, and the absence of objective scoring systems.

Conclusion

In conclusion, it can be stated that classical immunosuppressive therapies remain effective and safe treatment options in real-life situations, particularly when used by experienced physicians with appropriate patient selection. It is important to recognize the significance of escalating the dosage to the recommended levels, in conjunction with the provision of essential patient monitoring, to achieve optimal treatment outcomes. Although more recent therapies, such as dupilumab and JAK inhibitors, show promise, limited access due to financial constraints remains a challenge. To develop more comprehensive and widely accepted algorithms for managing AD in pediatric patients, future studies must analyze real-life data and long-term treatment outcomes of novel therapies in addition to conventional systemic treatments.

Ethics

Ethics Committee Approval: This research was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee with protocol no.: 09.2021.1199, date: 05.11.2021.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.A., D.Y., F.B.D., Concept: M.A., D.Y., F.B.D., Design: M.A., D.Y., F.B.D., Data Collection or Processing: M.A., F.B.D., Analysis or Interpretation: M.A., D.Y., F.B.D., Literature Search: M.A., D.Y., F.B.D., Writing: M.A., D.Y.

Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study received no financial support.

References

1. Ramírez-Marín HA, Silverberg JI: Differences between pediatric and adult atopic dermatitis. Pediatr Dermatol. 2022;39:345-53.
2. Wollenberg A, Kinberger M, Arents B, et al: European guideline (EuroGuiDerm) on atopic eczema: Part I - systemic therapy. J Eur Acad Dermatol Venereol. 2022;36:1409-31.
3. Yu SH, Drucker AM, Lebwohl M, Silverberg JI: A systematic review of the safety and efficacy of systemic corticosteroids in atopic dermatitis. J Am Acad Dermatol. 2018;78:733-40.e11.
4. Wang HH, Li YC, Huang YC: Efficacy of omalizumab in patients with atopic dermatitis: A systematic review and meta-analysis. J Allergy Clin Immunol. 2016;138:1719-22.e1.
5. Flohr C: How we treat atopic dermatitis now and how that will change over the next 5 years. Br J Dermatol. 2023;188:718-25.
6. Wollenberg A, Barbarot S, Bieber T, et al: Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: Part I. J Eur Acad Dermatol Venereol. 2018;32:657-82.
7. Slater NA, Morrell DS: Systemic therapy of childhood atopic dermatitis. Clin Dermatol. 2015;33:289-99.
8. Wang X, Patel C, Giles ML, et al: Glucocorticoid dosing and implications for vaccination: Evolution of global definitions. Clin Infect Dis. 2025;80:998-1004.
9. Sibbald C, Pope E, Ho N, Weinstein M: Retrospective review of relapse after systemic cyclosporine in children with atopic dermatitis. Pediatr Dermatol. 2015;32:36-40.
10. Beaumont DR, Arkwright PD: Factors determining the effectiveness of oral ciclosporin in the treatment of severe childhood atopic dermatitis. J Dermatolog Treat. 2012;23:318-22.
11. Sarıcaoğlu H, Yazici S, Zorlu Ö, Bülbül Başkan E, Aydoğan K: Cyclosporine-a for severe childhood atopic dermatitis: Clinical experience on efficacy and safety profile. Turk J Med Sci. 2018;48:933-8.
12. Murphy LA, Atherton D: A retrospective evaluation of azathioprine in severe childhood atopic eczema, using thiopurine methyltransferase levels to exclude patients at high risk of myelosuppression. Br J Dermatol. 2002;147:308-15.
13. Caufield M, Tom WL: Oral azathioprine for recalcitrant pediatric atopic dermatitis: clinical response and thiopurine monitoring. J Am Acad Dermatol. 2013;68:29-35.
14. Taieb Y, Baum S, Ben Amitai D, Barzilai A, Greenberger S: The use of methotrexate for treating childhood atopic dermatitis: A multicenter retrospective study. J Dermatolog Treat. 2019;30:240-4.
15. Dayal S, Pathak K, Sahu P, Jain VK: Narrowband UV-B phototherapy in childhood atopic dermatitis: Efficacy and safety. An Bras Dermatol. 2017;92:801-6.
16. Jury CS, McHenry P, Burden AD, Lever R, Bilsland D: Narrowband ultraviolet B (UVB) phototherapy in children. Clin Exp Dermatol. 2006;31:196-9.
17. Clayton TH, Clark SM, Turner D, Goulden V: The treatment of severe atopic dermatitis in childhood with narrowband ultraviolet B phototherapy. Clin Exp Dermatol. 2007;32:28-33.
18. Wollenberg A, Kinberger M, Arents B, et al. European guideline (EuroGuiDerm) on atopic eczema - part II: Non-systemic treatments and treatment recommendations for special AE patient populations. J Eur Acad Dermatol Venereol. 2022;36:1904-26.
19. Aghamohammadi A, Moghaddam ZG, Abolhassani H, et al. Investigation of underlying primary immunodeficiencies in patients with severe atopic dermatitis. Allergol Immunopathol (Madr). 2014;42:336-341.
20. Zhang Z, Chen J, Yang Y, et al: Intravenous immunoglobulin therapy in children with severe atopic dermatitis. Dermatol Ther. 2022;35:e15947.
21. Chan S, Cornelius V, Cro S, Harper JI, Lack G: Treatment effect of omalizumab on severe pediatric atopic dermatitis: The ADAPT randomized clinical trial. JAMA Pediatr. 2020;174:29-37.
22. Holm JG, Agner T, Sand C, Thomsen SF: Omalizumab for atopic dermatitis: case series and a systematic review of the literature. Int J Dermatol. 2017;56:18-26.
23. Nečas M, Vašků V, Březinová E: Lack of omalizumab efficacy in severe atopic dermatitis with extremely elevated IgE levels: two case reports and a literature review. Acta Dermatovenerol Alp Pannonica Adriat. 2019;28:89-92.
24. Drucker AM, Ellis AG, Bohdanowicz M, et al: Systemic immunomodulatory treatments for patients with atopic dermatitis: A systematic review and network meta-analysis. JAMA Dermatol. 2020;156:659-67.
25. Kim JP, Chao LX, Simpson EL, Silverberg JI: Persistence of atopic dermatitis (AD): A systematic review and meta-analysis. J Am Acad Dermatol. 2016;75:681-7.e11.
26. Wüthrich B: Clinical aspects, epidemiology, and prognosis of atopic dermatitis. Ann Allergy Asthma Immunol. 1999;83:464-70.