Original Article

The Efficacy of Adalimumab Treatment in Pediatric Non-Infectious Uveitis: A Retrospective Cohort Study

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Abstract

Objectives: To evaluate the clinical features of pediatric non-infectious uveitis (NIU) patients treated with adalimumab (ADA) and the efficacy of ADA in patients unresponsive to conventional immunosuppressive therapy.

Materials and Methods: The records of 91 NIU patients aged ≤16 years who received ADA therapy were evaluated retrospectively. The patients' demographic and clinical characteristics and treatment approaches were recorded. The efficacy of ADA in patients treated for at least 1 year after failure of conventional immunosuppressive treatment was evaluated by comparing the best corrected visual acuity (BCVA), severity of intraocular inflammation, uveitis flare-ups, topical and systemic corticosteroid (CS) use, and central macular thickness (CMT) values before and after ADA treatment.

Results: The study included 103 eyes of 53 patients, of whom 29 (54.7%) were female. The mean age at presentation was 8.2±3.4 (range: 3-16) years. The mean follow-up period was 41.6±28.2 (range: 18-120) months. Twenty-six patients (49.0%) had anterior uveitis, 22 (41.5%) had intermediate uveitis, and 5 (9.4%) had panuveitis. The mean duration of ADA treatment was 23.0±13.7 (range: 12-60) months. Uveitis flare-ups developed in only 13 patients (24.5%) while on ADA treatment. When pre- and post-treatment periods were compared, the mean number of uveitis flare-ups, intraocular inflammation severity, mean dose of topical and systemic CS, and mean CMT values were significantly lower in the post-treatment period ($p<0.05$). The mean BCVA was significantly improved after 6 and 12 months of ADA treatment compared to the pre-treatment visual acuity ($p<0.05$).

Conclusion: ADA effectively controlled intraocular inflammation, reducing the need for systemic and topical CS and improving visual outcomes in pediatric NIU.

Keywords: Pediatric uveitis, non-infectious uveitis, treatment, adalimumab, tumor necrosis factor alpha

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Introduction

Pediatric uveitis is less common than uveitis in adults, accounting for 5-10% of all uveitis cases.[1] According to data from the Behçet's Uveitis Frequency Screening (BUST) study, children represent approximately 9% of the uveitis patients in our country.[2] Although pediatric uveitis is less common, it is often diagnosed late due to its asymptomatic, insidious course and examination difficulties. In addition, prognosis is quite poor in pediatric uveitis due to chronic recurrent inflammation and the high rate of vision-threatening complications.[1,3] Etiologically, pediatric uveitis is mostly non-infectious, with studies reporting varying rates of pediatric non-infectious uveitis (NIU) ranging from 75% to 95%.[1,4]

A stepwise treatment approach is recommended in pediatric NIU to effectively suppress inflammation and prevent ocular complications.[3,5,6] Topical and systemic corticosteroids (CSs) provide rapid inflammation suppression and are a first-line treatment. However, due to the high side effect profile of systemic CSs, particularly their adverse effects on the growth and development of children, they should only be used in the short term to suppress acute attacks.[3,5] In patients with refractory or CS-dependent chronic uveitis, second-line treatment includes steroid-sparing immunosuppressive agents.[1,6] Biologic therapy

consists primarily of tumor necrosis factor alpha (TNF-α) inhibitors and is used in cases of severe NIU that does not respond to conventional immunosuppressives or threatens vision.[3] Studies show that in pediatric NIU, early and aggressive treatment with conventional immunosuppressives and biologic agents markedly improves the prognosis.[5,6] Therefore, in current practice, these treatment steps are tailored to each individual patient's ocular and systemic condition.[3]

Adalimumab (ADA), a fully human monoclonal TNF-α antibody, is now the only biologic agent approved for use in the treatment of NIU in adults and children.[7,8] Studies have shown ADA to be a safe and effective biologic agent for controlling intraocular inflammation and reducing relapses in the treatment of pediatric NIU.[7,8,9,10,11,12] Experiences with the use and outcomes of ADA in pediatric NIU are steadily increasing. This study aimed to evaluate the clinical characteristics of patients using ADA for pediatric NIU in a tertiary reference center and the effectiveness of ADA in cases refractory to conventional immunosuppressives.

Materials and Methods

This was a retrospective observational study evaluating the records of patients followed up for pediatric NIU and treated with ADA in the uvea department of a tertiary eye hospital between 2010 and 2024. The study was conducted in accordance with the principles of the Declaration of Helsinki and ethics committee approval was obtained from the Ankara Training and Research Hospital Ethics Committee (decision no: 522/2020, approval date: 30.12.2020).

We retrospectively analyzed data from 91 patients with NIU aged ≤16 years who received ADA therapy. The patients' demographic and clinical characteristics and treatment approaches were recorded. Patients with pediatric NIU who used ADA for at least 1 year after non-response to conventional immunosuppressive therapy were included in the study, and the effectiveness of ADA therapy in these patients was evaluated. All patients were diagnosed based on the clinical features of uveitis, ocular examination, and imaging findings, by the same ophthalmologists experienced in the field of uveitis. Infectious causes were excluded with laboratory tests. Systemic investigations and assessments performed during diagnosis and follow-up were carried out in cooperation with pediatric rheumatology specialists.

Demographic data, best corrected visual acuity (BCVA) according to Snellen chart, intraocular pressure (IOP) measured by pneumotonometry, slit-lamp anterior and posterior segment examination findings, follow-up time, and systemic and topical treatment approaches were analyzed. BCVA values were converted to logarithm of the minimum angle of resolution (LogMAR) for analysis. Assessment and classification of ocular inflammation was performed according to the Standardization of Uveitis Nomenclature (SUN) Working Group guideline.[13] Pars planitis was diagnosed using the diagnostic criteria of the SUN Working Group and defined as non-infectious intermediate uveitis not associated with systemic disease, accompanied by vitreous inflammation and snowball and snowbank opacities. For the diagnosis of sarcoidosis-associated uveitis, patients were evaluated in conjunction with pediatric rheumatology based on the SUN criteria and the revised International Ocular Sarcoidosis Workshop criteria for ocular sarcoidosis.[14,15,16] A uveitis attack was defined as a two-grade increase in inflammation (anterior chamber cells and/or vitreous haze) or an increase from grade 3+ to 4+.[13,17] In intermediate and panuveitis patients who had fundus fluorescein angiography data, these findings were taken into account when evaluating the progression of intraocular inflammation and response to treatment.

Indications for initiating ADA (AbbVie Inc., Chicago, USA) included refractory, sight-threatening severe uveitis despite conventional immunosuppressive therapy, CS-dependent recurrent uveitis, and CS-related complications. ADA therapy was initiated subcutaneously at a dose of 20 mg for patients weighing less than 30 kg and 40 mg in those weighing ≥30 kg. It was administered at 2-week intervals from the beginning or after a loading dose consisting of two doses (40 or 80 mg by weight) in week 0 and a single dose (20 or 40 mg) in week 1. Patients who did not respond to the standard dose were switched to a weekly regimen, whereas the frequency of ADA doses was extended to intervals of 3 to 4 weeks for patients with intraocular inflammation control and no new attacks for 2 years. Before treatment, all patients underwent interferon gamma release (Quantiferon) test and chest radiography to exclude tuberculosis, and hepatitis and HIV serology were examined. During treatment, blood biochemistry analyses including regular blood count and liver and kidney function tests were performed every 2 months.

Systemic immunosuppressive treatment approaches before and after initiating ADA and the frequency and duration of ADA use were recorded. The number of uveitis attacks, severity of intraocular inflammation, and topical/systemic CS doses in the 6-month period before ADA therapy, after 6 months of ADA therapy, and between 6 and 12 months of ADA therapy. The severity of intraocular inflammation was determined based on the highest grade (between 0 and 4+) of anterior chamber cells in eyes with anterior uveitis or vitreous haze in eyes with intermediate and panuveitis during the relevant time period. Similarly, topical and systemic CS doses were calculated according to the highest dose used in the relevant time period. The patients' central macular thickness (CMT) on optical coherence tomography and BCVA values were recorded before ADA therapy and at 6 months and 12 months of ADA therapy. The patients' ocular complications at admission and follow-up and the ocular surgeries performed were also noted.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics 22.0 (IBM, Armonk, NY, USA). Descriptive statistics were presented as mean, standard deviation, median, frequency, and percentage. Categorical variables (frequencies and percentages) were compared between dependent groups using the McNemar test.

Normality of the data was evaluated using visual (histogram and probability) and analytical methods (Shapiro-Wilk test). Friedman test was used to compare repeated measures in dependent groups. For variables with significant results, Bonferroni-corrected Wilcoxon's signed-rank test was used in post-hoc pairwise comparisons to determine the sources of the differences. P<0.05 was set as the level of statistical significance.

Results

Of 91 pediatric NIU patients who received ADA therapy during the study period, 53 patients (103 eyes) treated with ADA for at least 1 year after non-response to conventional immunosuppressive therapy were included in the study. Thirty-eight patients (41.8%) who received biologic agents as first-line treatment were excluded. The demographic and clinical characteristics of all pediatric NIU patients evaluated within the scope of the study are summarized in Table 1. Of the 53 patients included in the study, 29 (54.7%) were female and 24 (45.3%) were male. The mean age at admission was 8.2±3.4 years (range, 3-16 years) and the mean follow-up period was 41.6±28.2 months (range, 18-120 months). The mean LogMAR visual acuity of the patients at admission was 0.22±0.28 (range, 0.0-1.51) (Table 2).

For systemic treatment, all patients received systemic CS and/or conventional immunosuppressive therapy, followed by ADA therapy. ADA was administered at the standard dose every 2 weeks in 50 patients (94.3%), while 3 patients (5.7%) started with a weekly regimen. The mean duration of ADA use in all patients was 23.0±13.7 months (range, 12-60 months). Only 13 patients (24.5%) developed new uveitis attacks while receiving ADA therapy; the mean time to the first attack in these patients was 4.9±2.4 months (range, 1-9 months). Nine patients (16.9%) received ADA every 2 weeks for a mean of 12.6±10.6 months (range, 4-48 months) before switching to a weekly regimen. The mean duration of use in patients using ADA weekly was 9.4±2.9 months (range, 6-13 months). In 4 patients (7.5%) receiving ADA every 2 weeks for a mean of 12.5±5.0 months (range, 6-18 months), the dosing schedule was extended to 3-week intervals for a mean of 7.7±3.3 months (range, 4-12 months), then to 4-week intervals. The systemic CS and immunosuppressive therapy received by the patients before ADA initiation and at the last visit after ADA treatment are summarized in Table 3.

Systemic CS was used by 50 patients (94.3%) before ADA therapy and 11 patients (20.7%) after ADA therapy (p<0.001). The systemic CS dose was reduced (<5 mg/day) in 8 (72.7%) of the patients receiving CS therapy. After ADA treatment, the dose of methotrexate (MTX) (Koçak Pharmaceuticals, İstanbul, Türkiye) was reduced in 27 patients (50.9%), and cyclosporine-A (Novartis, Basel, Switzerland) was discontinued in 2 patients (3.7%). Tocilizumab (Roche, Basel, Switzerland) and infliximab (Shering-Plough Pharma, Berlin, Germany) were each initiated in 1 patient (1.9% each) who had refractory uveitis despite weekly ADA (after 10 months and 15 months of use, respectively). In addition, 1 patient (1.9%) received mycophenolate mofetil (Roche, Basel, Switzerland) due to elevated liver enzymes secondary to MTX therapy, and 1 patient (1.9%) received azathioprine (Aspen Farma, Durban, South Africa) due to MTX-related gastrointestinal adverse effects. In all 4 patients whose ADA treatment was extended to 4-week intervals, MTX was tapered and discontinued, and ADA was also discontinued in 2 (50.0%) of these patients after a mean of 5.0±1.4 months (range, 4-6 months) (Table 3). None of the patients developed serious adverse effects due to ADA use during follow-up.

When the severity of intraocular inflammation before and after ADA therapy was evaluated, the mean anterior chamber reaction severity was significantly lower after 6 months and 6-12 months of ADA treatment than before treatment in eyes with anterior and panuveitis (p<0.05 for all). In the eyes with intermediate and panuveitis, the mean vitreous haze severity was also significantly lower after 6 months and 6-12 months of ADA treatment compared to before ADA treatment (p<0.05 for all) (Table 4).

When uveitis attacks before and after ADA therapy were evaluated, the number of uveitis attacks observed after 6

Table 1. Demographic and clinical characteristics of all patients with pediatric non-infectious uveitis treated with adalimumab

Sex	**Patients, n (%)**
Female	41 (45.1)
Male	50 (54.9)
Age, years, mean±SD (range)	9.3±3.6 (3-16)
Ocular involvement	
Unilateral	6 (6.6)
Bilateral	85 (93.4)
Anatomical and etiological uveitis classification	
Anterior uveitis	44 (48.3)
JIA-associated anterior uveitis	24 (26.4)
Chronic anterior uveitis	18 (19.7)
Sarcoidosis-associated anterior uveitis	1 (1.1)
FMF-associated anterior uveitis	1 (1.1)
Intermediate uveitis	34 (37.4)
Pars planitis	34 (37.4)
Panuveitis	13 (14.3)
Chronic (late-stage) VKH	6 (6.6)
Idiopathic	5 (5.5)
Acute (early-stage) VKH	1 (1.1)
Sarcoidosis-associated panuveitis	1 (1.1)
First-line systemic therapy	
Conventional immunosuppressive followed by ADA	53 (58.2)
Conventional immunosuppressive with ADA	38 (41.8)

SD: Standard deviation, JIA: Juvenile idiopathic arthritis, FMF: Familial Mediterranean fever, VKH: Vogt-Koyanagi-Harada disease, ADA: Adalimumab

months and 6-12 months of ADA treatment was found to be significantly lower than before ADA treatment (p<0.001 for all). However, no difference was observed between the number of uveitis attacks after 6 months and 6-12 months of ADA treatment (p=0.842) (Table 4). Comparison of mean topical and systemic CS doses before and after ADA therapy showed that CS doses were significantly lower after 6 months and 6-12 months of ADA treatment compared to before ADA treatment (p<0.01 for all). There was no difference in topical or systemic CS doses after 6 months and 6-12 months of ADA treatment (p=1.0 for all) (Table 4).

When CMT was evaluated before and after ADA treatment, the mean CMT values after 6 months and 12 months of ADA treatment were significantly lower than before treatment (p<0.05 for all) (Table 5). Comparison of mean LogMAR BCVA values before and after ADA therapy revealed a significant increase in BCVA after 6 and 12 months of ADA treatment (p=0.003 and p=0.002, respectively). Mean LogMAR BCVA values at 6 and 12 months were similar (p=1.0) (Table 5).

At least one ocular complication was observed at admission in 53 eyes (51.4%). The most common ocular complications at admission were posterior synechiae (25 eyes, 24.2%), cataract (12 eyes, 11.6%), and cystoid macular edema (CME) (11 eyes, 10.6%). The most common ocular complications observed during follow-up were steroid-induced IOP elevation (20 eyes, 19.4%), cataract (18 eyes, 17.4%), and posterior synechiae (14 eyes, 13.5%) (Figure 1). IOP was controlled with antiglaucoma therapy in 19 (79.1%) of the 24 eyes with IOP elevation. Antiglaucoma therapy was discontinued in 14 eyes (58.3%) after ADA treatment. However, the other 5 eyes (20.8%) required glaucoma surgery, with trabeculectomy performed in 3 eyes (12.5%) and Ahmed valve tube implantation surgery in 2 eyes (8.3%). Phacoemulsification and intraocular lens implantation surgery were performed in 8 eyes (7.7%) with cataract during follow-up. The mean LogMAR BCVA of the patients at the last examination was 0.08±0.2 (range, 0.0-1.0), which was a significant improvement compared to BCVA at admission (p<0.001).

Table 2. Demographic and clinical characteristics of study group patients who started adalimumab after conventional treatment

Sex	**Patients, n (%)**
Female	29 (54.7)
Male	24 (45.3)
Age, years, mean±SD (range)	8.2±3.4 (3-16)
Follow-up time, months, mean±SD (range)	41.6±28.2 (18-120)
Ocular involvement	
Unilateral	3 (5.7)
Bilateral	50 (94.3)
Anatomical and etiological uveitis classification	
Anterior uveitis	26 (49.0)
JIA-associated anterior uveitis	16 (30.2)
Chronic anterior uveitis	9 (16.9)
Sarcoidosis-associated anterior uveitis	1 (1.9)
Intermediate uveitis	22 (41.5)
Pars planitis	22 (41.5)
Panuveitis	5 (9.4)
Late-stage VKH	2 (3.7)
Idiopathic	2 (3.7)
Sarcoidosis-associated panuveitis	1 (1.9)
Visual acuity, LogMAR, mean±SD (range)	0.22±0.28 (0.0-1.51)

SD: Standard deviation, JIA: Juvenile idiopathic arthritis, VKH; Vogt-Koyanagi-Harada disease, LogMAR: Logarithm of the minimum angle of resolution

Table 3. Systemic treatment received by study patients before and after adalimumab therapy

Systemic therapies before ADA initiation	**Patients, n (%)**
Systemic CS+MTX	45 (84.9)
Systemic CS+MTX+CSA	3 (5.7)
MTX	3 (5.7)
Systemic CS	2 (3.7)
Systemic therapies at the last visit after ADA treatment	
ADA+MTX	35 (66.0)
ADA+MTX+systemic CS	10 (18.9)
ADA	2 (3.7)
ADA+MTX+CSA+systemic CS	1 (1.9)
ADA+AZA	1 (1.9)
TCZ+MMF	1 (1.9)
IFX+MTX	1 (1.9)

ADA: Adalimumab, CS: Corticosteroid, MTX: Methotrexate, CSA: Cyclosporine A, AZA: Azathioprine, TCZ: Tocilizumab, MMF: Mycophenolate mofetil, IFX: Infliximab

Discussion

This study evaluated the effectiveness of ADA therapy in pediatric patients with NIU and showed that ADA use in children was effective in improving visual acuity as well as controlling intraocular inflammation, which reduced the need for topical and systemic steroids.

Many studies in the literature have demonstrated the effectiveness of ADA therapy in children with chronic NIU refractory to conventional immunosuppressive therapy.[7,8,9,10,11,12,18,19] In the SYCAMORE randomized controlled trial, the addition of ADA to MTX therapy in children and adolescents with juvenile idiopathic arthritis (JIA)-associated uveitis was reported to reduce treatment failure.[7] In ADJUVITE, another important randomized controlled trial conducted in children with JIA-associated uveitis, successful outcomes were reported with ADA therapy in patients with chronic uveitis who showed an inadequate response to topical therapy and MTX.[8] In addition to non-infectious anterior uveitis, ADA therapy has also been shown to be effective in the treatment of intermediate uveitis, posterior uveitis, and panuveitis in children.[12,18,19] Based on these studies, ADA is now accepted as the first choice of

Table 4. Comparison of intraocular inflammation severity and corticosteroid doses of the study patients before and after adalimumab therapy

	Before ADA Mean±SD Median (range)		After ADA Mean±SD Median (min-max)				p^a
		p^b	6 months	p^c	6-12 months	p^d	
Anterior chamber cells (31 patients/59 eyes)	2.1±0.9 0.5 (1-4)		0.89±0.7 0.5 (0-3)		0.42±0.7 0 (0-3)		<0.001
		<0.001		0.023		<0.001	
Vitreous haze (26 patients/52 eyes)	2.16±0.7 2.0 (1-3)		0.55±0.4 0.5 (0-2)		0.14±0.22 0 (0-1)		<0.001
		<0.001		0.024		<0.001	
Systemic steroid dose (mg/day)	13.4±11.3 10.0 (0-40)		1.0±2.0 0 (0-10)		0.68±1.5 0 (0-8)		<0.001
		<0.001		1.00		<0.001	
Topical steroid (drops/day)	3.5±4.2 3.0 (0-16)		0.67±1.5 0 (0-8)		0.62±1.58 0 (0-8)		<0.001
		0.003		1.00	0.016	0.001	
Uveitis attack (53 patients/103 eyes)	1.5±0.7 1.0 (0-3)		0.23±0.4 0 (0-1)		0.05±0.2 0 (0-1)		<0.001
		<0.001		0.842		<0.001	

p^a: Friedman test, three-group comparison (before, 6 months after, 12 months after ADA initiation), p^b: Wilcoxon signed-rank test, two group comparison (before and 6 months after ADA initiation), p^c: Wilcoxon signed-rank test, two-group comparison (6 months and 12 months after ADA initiation), p^d: Wilcoxon signed-rank test, two-group comparison (before and 6-12 months after ADA initiation), ADA: Adalimumab, SD: Standard deviation, min: Minimum, max: Maximum

Table 5. Comparison of central macular thickness and visual acuity results of study patients before and after adalimumab therapy

	Before ADA Mean±SD Median (range)		After ADA Mean±SD Median (range)				p^a
		p^b	6 months	p^c	12 months	p^d	
CMT (µm)	307.1±47.5 311 (223-437)		282.8±37.7 281 (214-358)		273.3±39.2 270 (224-339)		<0.001
		<0.001		0.034		<0.001	
BCVA (LogMAR)	0.16±0.27 0.1 (0.0-1.51)		0.11±0.25 0.0 (0.0-1.40)		0.11±0.26 0.0 (0.0-1.0)		<0.001
		0.003		1.00		0.002	

p^a: Friedman test, three-group comparison (before, 6 months after, 12 months after ADA initiation), p^b: Wilcoxon signed-rank test, two-group comparison (before and 6 months after ADA initiation), p^c: Wilcoxon signed-rank test, two-group comparison (6 months and 12 months after ADA initiation), p^d: Wilcoxon signed-rank test, two-group comparison (before and 12 months after ADA initiation), ADA: Adalimumab, SD: Standard deviation, CMT: Central macular thickness, BCVA: Best corrected visual acuity

biologic agent for children with chronic NIU. In our study, we evaluated the outcomes of ADA treatment in patients with recurrent non-infectious anterior, intermediate, and panuveitis refractory to conventional immunosuppressive therapy and determined that only a quarter of the patients developed a new uveitis attack after starting ADA therapy. The standard dosing regimen for ADA is every 2 weeks. Studies have shown that weekly ADA administration is effective in children with severe uveitis that cannot be controlled with the standard dose.[3,9,10] In our study, the majority of patients received ADA at the standard dose, while 22% received ADA weekly. ADA was found to be effective in controlling intraocular inflammation in 83% of patients on a weekly regimen.

In a study by Sonmez et al.[20] including pediatric patients with NIU of varying etiology, ADA therapy was found to be effective in the control of anterior and posterior segment inflammation and there was a significant reduction in CMT values from the second week, but the decrease leveled off after 12 weeks. In our study, CMT values decreased significantly after 6 and 12 months of treatment. Tao et al.[18] found that ADA improved visual acuity in the long term and was effective in controlling ocular inflammation in children with non-infectious posterior and panuveitis. The authors reported a significant reduction in uveitis attacks in children using ADA compared to those using conventional therapy, but the use of ADA had no superior advantage in terms of systemic CS cessation.[18]

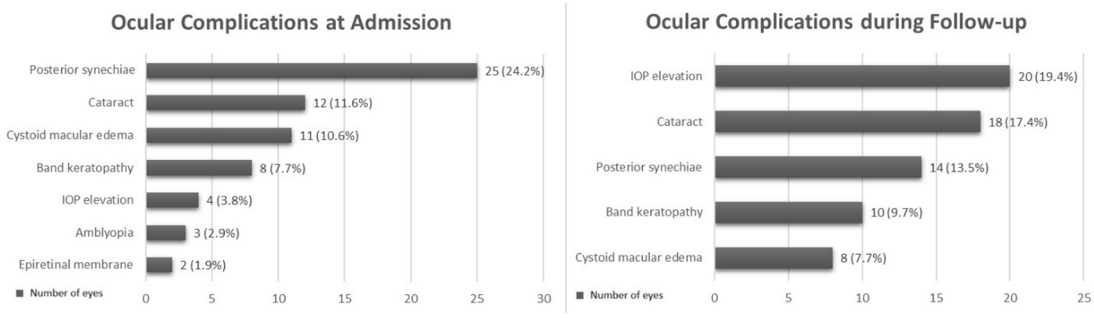

Figure 1. Distribution of the study patients' ocular complications at presentation and during follow-up
IOP: Intraocular pressure

In another study evaluating 59 patients with pars planitis, most (87%) of whom were children, ADA was found to be highly effective in cases refractory to conventional immunosuppressive therapy, with ADA use enabling discontinuation of systemic CS therapy in 70% of patients.[12] In our study, there was a reduction in uveitis attacks with ADA use in children with non-infectious anterior, intermediate, and panuveitis, and the need for topical and systemic CS use also decreased substantially. In addition, a significant improvement in BCVA was observed in our patients after ADA treatment.

There is still insufficient evidence in the literature on how long biologic therapy should be used and when it should be discontinued in children with NIU.[1,21] In a recent study, ADA dose reduction and discontinuation was associated with a high risk of relapse in children with NIU.[21] Another study indicated that gradual tapering of ADA treatment in pediatric NIU was linked to a low relapse rate.[22] In our study, the ADA dose was reduced in only 4 patients (8%) by extending to 3-week and then 4-week intervals, and discontinuation of ADA was possible in 2 (50%) of these patients.

Serious, sight-threatening ocular complications are common in pediatric uveitis, both at the time of diagnosis and during follow-up.[3,5,20,21,22,23,24,25] Ekici Tekin et al.[26] reported that 74% of pediatric NIU patients had ocular complications at the time of admission. Numerous studies have demonstrated posterior synechiae, CME, and cataract as the most common complications at diagnosis in pediatric uveitis.[12,18,19,24,25,26] In our study, at least ocular complication was detected in 51% of patients at admission. Consistent with the literature, the most common complications in our study included posterior synechiae (22%), cataract (11%), and CME (10%). Pediatric patients are more susceptible than adults to ocular complications secondary to topical CS use, with high doses and long-term use of topical CSs shown to increase the risk of cataract development and IOP elevation.[3,27,28] In our study, the main complications seen during follow-up were steroid-induced IOP elevation (19%) and cataract development (17%). After ADA treatment, antiglaucoma therapy was discontinued in more than half (58%) of the eyes with IOP elevation, and IOP control was achieved without medication. This shows the importance of steroid-sparing systemic immunomodulatory therapy for children with chronic NIU. ADA therapy is highly effective in the management of steroid-related ocular complications in pediatric NIU.

Study Limitations

The main limitations of our study include the retrospective design, limited sample size, heterogeneity of our patient group, and varying follow-up times. Due to the differences in follow-up periods, ocular complications at admission and during follow-up were evaluated separately, so the effect of ADA use on the development of ocular complications could not be evaluated. In this regard, comparative and prospective studies with larger and homogeneous patient groups and standard follow-up periods may be beneficial.

Conclusion

Pediatric uveitis is a difficult disease group to manage due to challenges in its diagnosis and treatment, as well as the high complication rates and risk of vision loss. ADA is effective in improving visual outcomes and controlling intraocular inflammation in pediatric NIU, as well as reducing the need for systemic and topical CS treatment.

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Ethics

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki and ethics committee approval was obtained from the Ankara Training and Research Hospital Ethics Committee (decision no: 522/2020, approval date: 30.12.2020).

Informed Consent: Retrospective study.

Declarations

Authorship Contributions

Surgical and Medical Practices: P.Ç.Ö., Y.Ö.E., K.Ö.Y., Concept: K.Ö.Y., P.Ç.Ö., Y.Ö.E., Design: K.Ö.Y., P.Ç.Ö., O.Ö., Data Collection or Processing: K.Ö.Y., P.Ç.Ö., Y.Ö.E., Analysis

or Interpretation: K.Ö.Y., P.Ç.Ö., Literature Search: K.Ö.Y., P.Ç.Ö., Writing: K.Ö.Y., P.Ç.Ö.

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