

Efficacy and safety of omalizumab in pediatric patients with high immunoglobulin E levels: A case series

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ABSTRACT

Background: The efficacy and safety of omalizumab has been demonstrated in children as young as 6 years of age. Omalizumab is currently approved for a range of immunoglobulin E (IgE) levels that differ by age. In patients with IgE levels higher than the indicated therapeutic window, only a few studies have demonstrated the efficacy and safety of its use. Specifically, no reported studies exist to describe the use of omalizumab in pediatric patients with asthma ages <12 years and with high IgE levels.

Objective: We reported a series of pediatric patients who were initiated on omalizumab despite an IgE level higher than the age-indicated therapeutic windows and aimed to describe whether omalizumab was safe and improved asthma outcomes.

Methods: Patients who initiated omalizumab in our pediatric allergy clinic between January 2008 and December 2015, with serum IgE levels higher than the age-indicated therapeutic ranges were included. Patient charts were reviewed to determine the number of asthma-related events in the 12 months before and after initiation of omalizumab and the Asthma Control Test™ scores at the time of initiation and at 12 months of therapy.

Results: Eleven patients were identified with pretreatment IgE levels higher than the age-approved thresholds. Five patients were ages <12 years, and six patients were ages >12 years. For all but one patient, the maximum recommended dose of 375 mg every 2 weeks was effective in reducing the need for corticosteroids, emergency department visits, or hospitalizations in the year after initiation of therapy. During the period of therapy, there were no reports of severe reactions.

Conclusion: Despite a small study group, our results indicated that omalizumab may be safely used in pediatric patients with IgE levels higher than the indicated therapeutic windows.

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Omalizumab is a recombinant, humanized monoclonal antibody that acts to attenuate the airway inflammatory response to inhaled allergen in patients with allergic asthma, and its safety and efficacy have been demonstrated in children as young as 6 years of age.^{1–3} The dose and frequency of omalizumab administration are determined by using a dosing chart that takes into account the patient's pretreatment serum immunoglobulin E (IgE) level and body weight. The current dosing chart covers serum IgE levels between 30 and 1300 IU/mL for patients ages 6–12 years, and serum IgE levels between 30 and 700 IU/mL for patients ages ≥12 years, to a maximum drug dose of 375 mg every 2 weeks.⁴ It is pertinent to note that, in the United Kingdom, omalizumab has been approved for a wider therapeutic window in pediatric patients, up to

1500 IU/mL and to a maximum drug dose of 600 mg every 2 weeks.⁵ For patients with IgE levels higher than the indicated therapeutic window, treatment may still be beneficial, although only a few studies examined the efficacy and safety of its use.^{6–8} We reported on a series of pediatric patients who were initiated on omalizumab, despite an IgE level higher than the age-indicated therapeutic windows, and aimed to describe whether omalizumab was safe and improved asthma outcomes.

METHODS

The study protocol (IRB 14–011104) was approved by the institutional review board of the Children's Hospital of Philadelphia. Patients with inadequately controlled moderate-to-severe allergic asthma who initiated omalizumab in our pediatric allergy clinic between January 2008 and December 2015 with serum IgE levels higher than the age-indicated therapeutic ranges were included. Patients or legal guardians signed informed consent for treatment at the initiation of therapy. We reviewed patients' electronic medical records to determine the number of asthma-related events (corticosteroid requirement, emergency department visits, and hospitalizations) in the 12 months before and after initiation of omalizumab. In addition,

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Table 1 Summary of patient demographics and asthma outcomes

Patient No.	Sex	Age at Initiation, y	Pretreatment IgE Level, IU/mL	% Adherence	Smoke Exposure	Monthly Rate of Steroid Course		% Change	Monthly Rate of Emergency Department Visit		% Change	Monthly Rate of Hospitalizations		% Change	ACT Score	
						12 months Pre-therapy	12 months Post-therapy		12 months Pre-therapy	12 months Post-therapy		12 months Pre-therapy	12 months Post-therapy		At Initiation	12 months Post-therapy
1	M	10	1380	50	No	0.42	0	-100	0.25	0	-100	0.17	0	-100	12	24
2	M	10	1740	54	No	0.58	0.58	0	0.25	0.17	-33	0.25	0.08	-67	10	12
3	F	10	2510	58	No	0.75	0.08	-89	0.33	0	-100	0.33	0	-100	11	19
4	M	10	4320	45	Passive	0.58	0	-100	0.08	0	-100	0	0	0	12	20
5	F	11	1830	45	No	0.33	0.17	-50	0.25	0.17	-33	0.17	0	-100	14	22
6	M	12	1990	58	Passive	0.08	0.08	0	0.08	0.08	0	0.08	0	-100	18	16
7	M	13	2130	67	No	0.33	0	-100	0.17	0	-100	0	0	0	22	22
8	F	15	1380	50	No	0.25	0	-100	0.17	0	-100	0.17	0	-100	8	18
9	F	17	892	50	No	0.17	0.08	-50	0.17	0.08	-50	0.08	0.08	0	16	20
10	M	17	903	50	Passive	0.25	0.58	+133	0.17	0.17	0	0.17	0.25	+50%	10	15
11	F	17	2120	100	No	0.92	0.50	-45	0.17	0.17	0	0.08	0	-100	10	24

IgE = Immunoglobulin E; ACT score = Asthma Control Test Score.

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the Asthma Control Test™ (ACT) scores were collected at the time of initiation and at 12 months of therapy. Demographic data, adherence to injections, and adverse events were noted.

RESULTS

In total, we reviewed 49 pediatric patients who initiated omalizumab during this time period and identified 11 patients with pretreatment IgE levels above the age-approved thresholds. Five patients were ages <12 years and 6 patients were ages ≥12 years. All the patients received the maximum recommended dose of 375 mg every 2 weeks. Baseline characteristics and asthma outcomes before and after initiation of omalizumab are detailed in Table 1. The mean serum IgE level in the group ages 6–12 years was 2356 IU/mL (range, 1380–4320 IU/mL), and, in the group ages ≥12 years, this was 1569 IU/mL (range, 892–2130 IU/mL). During the 12-month period before therapy with omalizumab was initiated, the study group experienced asthma flares that required 56 courses of corticosteroids, 25 emergency department visits, and 18 hospitalizations. During the 12-month period after initiating treatment, the study group as a whole experienced fewer flares, leading to a reduction of 31 courses of corticosteroids (–55%), 15 emergency department visits (–60%), and 13 hospitalizations (–72%). At the time of initiation, the mean ACT score was 13, which increased to mean score of 19 (+46%) after a year of therapy. All but one patient had reduction in at least one asthma-related event, and all but two patients had improvement in ACT scores. During the period of therapy, there were no reports of severe reactions. One patient had headache and dizziness but was able to continue therapy without further adverse events.

DISCUSSION

For our pediatric population with high IgE levels who initiated omalizumab for allergic asthma, in all but one patient, the maximum recommended dose of omalizumab was effective in reducing the need for corticosteroids, emergency department visits, or hospitalizations in the year after initiation of therapy. We noted one patient with unchanged or worsening outcomes, which may have been due in part to his poor adherence and passive smoke exposure. There was a report of one adverse effect, but subsequent doses of omalizumab were administered without additional symptoms.

Our findings corroborated the limited studies that describe the efficacy of omalizumab in patients with IgE levels higher than the indicated thresholds.^{6–8} Masselli *et al.*⁶ demonstrated that omalizumab was as effective in reducing asthma symptoms, corticosteroid requirements, and emergency department visits in

adult patients with IgE levels >700 IU/mL compared with matched control patients with IgE levels of 30–700 IU/mL. Vennera *et al.*⁸ found that improvement in ACT scores and exacerbations in patients ages ≥12 years with IgE levels >700 IU/mL were similar when compared with patients with IgE levels of <700 IU/mL. Although our study group was small and there were no matched controls, to our knowledge, this study was the first report of safety and efficacy of omalizumab use in patients ages <12 years and with elevated IgE levels. Another limitation was that adherence to prescribed inhaled medications was not assessed, which may have confounded the degree of improvement in asthma outcomes.

CONCLUSION

Our results indicated that omalizumab may be safely used in pediatric patients with IgE levels above the indicated therapeutic windows and offers another option in patients in whom asthma cannot be controlled with other therapies.

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