J Pediatr Rev. 2018 January; 6(1):e11507. doi: 10.5812/jpr.11507.

Published online 2017 October 3. **Review Article**

Omalizumab (Xolair) in Children with Atopic Dermatitis: A Review Article

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Received 2017 June 21; **Revised** 2017 July 21; **Accepted** 2017 July 29.

Abstract

Context: Atopic dermatitis is a chronic skin disease in children. The prevalence of eczema is up to 30% in the world. Omalizumab (Xolair) is a monoclonal antibody that blocks the serum IgE. The aim of this study is to review the effect of Xolair in children with atopic dermatitis.
Evidence Acquisition: The data was searched in PubMed, Scopus, and Embase with keywords: atopic dermatitis, eczema, children, pediatrics, Xolair, and Omalizumab. The inclusion criteria included articles related to use of Xolair in children with atopic dermatitis, under the age of 20 years old, as well a both full text and brief articles. The exclusion criteria were purely adult cases who had taken systemic immunosuppressive drugs and abstract article. There was no time limitation for our search.
Results: After evaluating all data and a total of 124 searched articles, we found 8 eligible articles for this review. All of them had severe atopic dermatitis except 2 cases, which had moderate severity. Serum IgE level was increased in all patients. Only one of those studies included a control group. All patients were associated with other allergic disorders such as asthma and allergic rhinitis.
Conclusions: Omalizumab (Xolair) is a safe drug, which decreases serum IgE level, scoring atopic dermatitis, as well as clinical manifestations in all of severe atopic dermatitis. However, in order to approve it, we need future clinical trial studies with control group.

Keywords: Dermatitis, Atopic Eczema, Omalizumab, Child

1. Context

Atopic dermatitis (AD) or atopic eczema is a chronic coetaneous disorder in children. The prevalence of AD is different throughout the world and has decreased in recent decades. The prevalence of AD in children 6-7 and 13 - 14 years old in Iran is 5.99% and 6.52%, respectively (1). Of course, the prevalence of AD is more common in other areas in the world (up to 30%) (1, 2). Genetic and environmental factors contribute to the etiology of AD. Immunological factors such as T cells associated with cytokines and immunoglobulins have a significant role in the pathogenesis of AD. Serum IgE usually increases in about 80% of patients with AD (3). There is no specific test for diagnosis of AD. Atopic dermatitis diagnosed is base on clinical manifestations. The conventional treatments for AD are allergen avoidance, emollients, hydration, antihistamines, and local corticosteroids or calcineurin inhibitors (2, 4). The most mild to moderate AD patients have responded to these treatments. Sometimes a small percent of patients, especially the severe kind, need more effective drugs such as immunosuppressive agents (systemic corticosteroids, Cyclosporine and Mycophenolate mofetil), which induce serious side effects (4). Therefore, use of a drug with a suitable effectiveness and without or low side effects could resolve this problem in severe AD.

Omalizumab or xolair is a monoclonal antibody that connects to free IgE and blocks the IgE to its receptor on the surface of Mast cells, basophiles, and dendritic cells. These actions prevent release of mediators from mentioned cells and resolve the clinical manifestations (4). Xolair is approved by food and drug administration (FDA) for children above 12 years with moderate to severe asthma, of course, in Europe, approved for 6 - 12 years old with the same disease (5, 6). There is a great challenge for use of Xolair in other allergic disorders such as AD. It seems that treatment with Omalizumab may decrease serum IgE level and clinical manifestation of AD.

Usual dose of Xolair is 0.016 to 0.5 mg/kg/IU/mL each, 2 - 4 week subcutaneously. The duration of treatment is dif-

ferent (7). Based on the authors knowledge and searched data, there is no review about Xolair and AD in children. Therefore, the aim of this study is to review of the literatures about xolair use in children with AD.

2. Evidence Acquisition

The data was searched in PubMed, Scopus, and Embase, in English, with the keywords; atopic dermatitis, eczema, children, pediatrics, Xolair, and Omalizumab. The inclusion criteria included articles related to use of Xolair in children with atopic dermatitis, under the age of 20 years, as well as both full and brief articles. The exclusion criteria were purely adult cases who had taken systemic immunosuppressive drugs and abstract article. There was no time limitation for our search.

3. Results

Among total evaluated articles, we found 8 eligible articles for this review. These articles include 4 purely about children, 3 about both the child and adult, and associated with one case report. Two studies included both children and adult population; we could not distinguish how many children were under the age of 21 years (8, 9). Except the 2 cases with moderate severity, all of them had severe AD (10). Serum IgE level was increased in all patients. Only one of those studies included a control group (11). AD were associated with other allergic disorders such as asthma and allergic rhinitis (AR) in all patients (Table 1). All patients had taken Xolair subcutaneously (SC) (3, 8-14).

4. Discussion

There is not a significant and appropriate study regarding the effect of Xolair on children with AD. However, all of the patients, except 2 cases in this review had severe AD, which were resistant to the routine treatment. Criteria for severe AD included; scoring atopic dermatitis (SCORAD) > 45, no response or partial response to the routine treatment including; emollients, antihistamines, antileukoterians, local steroids, and calicinurin inhibitors, as well as irritant or allergen avoidance. Some of these cases used systemic drugs such as steroid, Cysclosporine, and mycophenolate mofetil (12). We could not find an appropriate clinical trial study. The number of cases was small ranging from 1 to 11 (3, 8). Therefore, the size of the sample was so small that we cannot make a clear analysis or met analysis. The IgE level increased in all patients with a variable range. We did not find a study with pure AD cases. All patients had other allergic diseases such as allergic rhinitis and/or asthma. Furthermore, many of these patients had positive skin prick test to food and/or aeroallergens extracts. Perhaps, the positive effects of Xolair may be due to AR or asthma. Omalizumab should only be used in patients with increased serum IgE levels. Cases had taken the drug for 2 or 4 weeks SC. The drug dosage was different in these studies, from 150 mg, 150 mg to 375 mg, 225 mg to 375 mg, and 300 mg to 375 mg (9, 11-13). The reason for this difference is because of the difference in weight of the patients and baseline IgE. Lacombe selected 0.001 to 0.002 mg/iu and Anne used 0.001 to 0.005 mg/kg/iu (12). Therefore, there is not a fixed dose for Xolair. The variable doses in these studies were not significant because all patients had responses. It seems that the dose of the drug could be adjusted based on the patient's response. The duration of treatment was different from 12 weeks, 20 weeks, 24 weeks, and 12 to 67 months (9, 11-13). Serum IgE level decreased in 100% of the studies (3, 8-14). It seems that Xolair could be effective in decreasing IgE levels in different doses and durations of the treatment, although, the decrease of IgE level is not important on its own. Some studies showed that the decrease of IgE did not associate with clinical resolutions (9, 11). Clinical manifestations improved in all of the studies (3, 8-14) except one, other researches had no control group. In a case-control study, there was no significant resolution between 2 groups (11). Of course, due to a small sample size in this study, the valuability of the study was low. Other reasons for failure of treatment may be hereditary factor and lesser age in the case group treated with Xolair (11). After treatment, the SCORAD decreased gradually in all of the reviewed studies (3, 8-14). Two cases in Belloni's study had increase SCORAD after treatment and we did not know whether these cases were children or adults (9). It should be mentioned that omalizumab could improve clinical manifestation of other allergic disorders such as AR and asthma (3). All of these studies showed that the Xolair had no significant, serious side effects or complications (3, 8-14). Therefore, at present, the Xolair is a safe drug. The limitations of these studies in children were; no control group and low sample size.

4.1. Conclusion

Omalizumab is a safe drug that decreases serum IgE level and SCORAD in all of severe AD. This drug also causes resolution of clinical manifestations in all patients. However, based on evidence-based medicine, these studies were weak and therefore, we need further clinical trials with bigger sample size. However, we concluded that in a case with severe AD that does not response to routine treatment, Xolair could be used.

Table 1. Number, Age, Serum IgE, Xolair Dose / Duration of Treatment and Resolution of All Patients

Author/Date	No. of Cases	IgE Level	Associated Disorder(s)	Dose of Xolair	Duration of Treatment (Week or Months)	Reference	Resolution	SCORAD
Ramirez del Pozo/ 2011	11 (12 - 54 y)	NA	NA		10 m	8	Yes	43 - 103
Caruso/ 2010	1 (15 y)	107 iu/mL to 318	AR and asthma	300 mg q4w sc	8 m	3	Yes	55 to 9
Lane/ 2006	3 (10 - 13 y)	1990 - 6120 iu/mL	Aeroallergen Skin test positive	150 - 450 mg q2w sc	3 m	14	Yes	NA
Belloni/ 2007	11 (14 - 64 y)	> 1000 iu/mL	AR and or asthma	150 mg q2w sc	5 m	9	Yes	NA
Lacombe/ 2013	7 (6 - 19 y)	7520 - 35790 iu/L to 6610	AR and asthma	225 - 375 mg q2w sc	12 - 67 m	12	Yes	75.4 to 30
Iyenger/ 2013	8(4 - 22 y)	375 - 1890 iu/mL	AR and asthma	150 - 375 mg Q2-4w sc	Over 24 w	11	No significant	NA
Vigo/ 2006	2 (7 and 13 y)	1375, 2020 iu/L	AR and asthma	375 mg Q2w	7 m	10	Yes	NA
Amrol/ 2010	2	NA	AR and asthma	300 - 375 mg q2w sc	3 and 18 m	13	Yes	NA

Abbreviations: AR, Allergic Rhinitis; IgE, Immunoglobulin E; NA, No Accessible; Q2w, Each 2 Weeks; SC, Sub Cutaneous.

Footnotes

Conflict of Interests: None declared.

Funding/Support: None declared.

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