The Role of Omalizumab in Treatment of Severe Asthma[1]

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ABSTRACT

Omalizumab, also known as Xolair, is a medication used primarily for the treatment of moderate-to-severe allergic asthma that does not respond well enough to other treatments such as inhaler corticosteroids or leukotriene modifiers. This drug has been found effective in reducing symptoms related to asthma including wheezing, coughing, shortness of breath, chest tightness, and nighttime awakenings due to asthma attacks. The mechanism behind its effectiveness lies in blocking IgE, which is a type of antibody involved in allergic reactions but can also be associated with certain types of asthma. By preventing IgE from binding to mast cells, it prevents histamine release leading to bronchoconstriction during an asthmatic episode. Asthma affects millions worldwide, causing significant morbidity and mortality rates globally. In addition to physical manifestations like difficulty breathing, there are psychological aspects that need consideration too. Omalizumab helps alleviate these issues by significantly decreasing the frequency of exacerbations and improving lung function in patients suffering from severe persistent asthma despite standard therapy. Studies have shown promising results wherein patients experienced fewer hospitalizations, emergency room visits, and improved quality of life after starting omalizumab treatment compared to those on placebo. However, despite these advantages, some concerns exist regarding the use of omalizumab. One major concern relates to potential side effects. Common adverse events include fatigue, headache, rashes, arthralgia (joint pain), sore throat, dizziness, and flushing. Serious complications such as hypersensitivity reactions and immune system disorders may occur in rare cases. Therefore, close monitoring during the initial stages of treatment is crucial to identify any possible adverse effects promptly. In conclusion, while omalizumab offers substantial benefits for individuals struggling with severe asthma who haven't responded adequately to conventional treatments, careful evaluation of individual patient factors is necessary before initiating this medication. It should only be considered when other options have proven insufficient or ineffective. Continued research into alternative forms of therapy will undoubtedly contribute to better management strategies for asthma sufferers around the globe.

Keywords: *Asthma; Inflammation; Omalizumab; Monoclonal antibody.*

INTRODUCTION

Asthma is a very common chronic disease of the airways that is originate mainly from complex interactions between genetic and environmental factors and it is usually characterized by chronic airway inflammation. Asthma can be confirmed by the history of respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough [1].

About 300 millions of persons around the world have asthma [2]. The prevalence of severe allergic asthma is increased significantly in the recent years, and patients with severe allergic severe asthma are often associated with increased both morbidity and mortality. These complications of severe asthma lead to increase rates of hospitalization after an emergency department visit, longer periods in hospital, higher rates of readmission, and impaired lung function [3]. These progressions of severe asthma may be due to several multiple factors such as under treatment, poor adherence with treatment, delayed symptoms recognition, concomitant use of medications, lack of response to treatment and other possible differences in airway inflammation with aging [4].

Most patients with asthma can get good control of their disease by using inhaled medications which include β2 agonists and corticosteroids which recently added to inhaled anticholinergic bronchodilator and oral drugs leukotriene inhibitors [5]. Despite of optimal therapies for patients with severe asthma, inadequate control of respiratory symptoms may occur in addition to recurrence exacerbations of disease therefore, we need an adjunctive biological treatment for further control of asthma and Omalizumab is an example of biological treatment [6].

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The World Health Organization (WHO) suggests that severe asthma includes three groups: first: untreated asthma; second: incorrectly treated asthma and third: difficult to-treat asthma We also need to distinguish between severe asthma in which the patients need medium to high doses of inhaled corticosteroids in combined with long acting B2 agonist and uncontrolled asthma which result from inappropriate therapy or persistent problems with adherence or comorbidities [2].

OMALIZUMAB

Omalizumab is a recombinant DNA-derived humanised monoclonal antibody that selectively binds to human IgE. Omalizumab has been shown to reduce the number of asthma exacerbations, the dose of inhaled corticosteroid and use rescue medication in both adults and children with moderate to severe allergic asthma [7]. In addition, omalizumab was the first anti-immunoglobulin (Ig)E humanized antibody and for a long time was the only biological drug available in clinical practice for the add-on therapy of uncontrolled asthma [8]. Therapeutic effect of omalizumab is depending on the functions that exerted by IgE in the pathobiology of allergic asthma [9]. The main distinguishing features of allergic asthma is remarked by increasing production of IgE directed against inhaled antigens, which known as atopy and occur in atopic patients [10].

Omalizumab was approved by the FDA in 2003 for the treatment of moderate to severe allergic asthma in adult and children aged 12 years and above and the dose is measured by patient's body weight (kg). According to this calculation, omalizumab is given at a dose of 150 to 375 mg by subcutaneously every 2 or 4 weeks. Omalizumab is contraindicated when there is past history of a severe hypersensitivity reaction to omalizumab. There is limited data about the efficacy of omalizumab in active cigarette smokers with severe allergic asthma; as a result, these groups are usually excluded from clinical trials of omalizumab, although it is likely that the efficacy will be similar to that reported in non-smokers with allergic asthma [11]. Cardiopulmonary exercise testing has been measured as an additional method to detect and confirm the clinical response to omalizumab in patients with severe allergic asthma [12].

MECHANISM OF ACTION OF OMALIZUMAB

Immunoglobulin E (IgE) play an important role in the pathogenesis of allergic asthma and the level of IgE in the circulation to common inhalant allergens is a strong risk factor for emergency admissions with asthma [13]. Specific IgE allergen is binds to high affinity receptors FCεRI on mast cells and basophils result in inducing an allergic reaction by releasing a wide range of inflammatory mediators including histamine, tryptase and arachidonic acid metabolites [14]. High affinity receptors are also expressed on other inflammatory cells including dendritic cells, monocytes and eosinophils. Omalizumab is a recombinant humanized monoclonal antibody that binds to the FC portion of the IgE antibody. By forming complexes with circulating IgE antibody it reduces the levels of free IgE and prevents the binding of IgE to high-affinity IgE receptors on mast cells and basophils and the sub-sequent release of inflammatory mediators induced by allergen exposure [15].

EFFICACY OF OMALIZUMAB IN SEVERE ALLERGIC ASTHMA

Omalizumab is the first biologic medication that was globally approved for the treatment of moderate to severe allergic asthma and treatment of severe allergic asthma, which is given subcutaneously every two or four weeks at a dose determined according to the patient's body weight and serum total IgE levels (30-1500 IU/ml), as a result, each single dose can ranged from 75 to 600 mg. Omalizumab provides a number of benefit effects that include improvement in quality of life, improvement in pulmonary function and reduction symptoms and exacerbations of asthma, asthma, in addition to decrease of doses of corticosteroid inhaler. Several studies found that the doses of oral corticosteroid can be reduces after omalizumab treatment. Some studies demonstrate that omalizumab can reduce severe allergic asthma exacerbations by 43% [16, 17].

In addition to that other studies found that a greater reduction in exacerbation rates of severe allergic asthma can be seen after treatment with omalizumab in patients with more frequent history of emergency asthma treatment, severer airflow limitation, and higher daily doses of corticosteroids inhaler. As a result of long-term treatment with omalizumab, when asthma exacerbations were occur after discontinuation of omalizumab, an increase in blood eosinophil counts was seen in these patients as compared with those who were free from exacerbations (18)

ADVERSE EFFECTS OF OMALIZUMAB

Omalizumab seems to be a safe and well-tolerated medication. Few adverse effects have been reported and most of them are minor. The most common adverse effects which may appear after administration of omalizumab were urticarial and skin reactions at site of injection. 40% of patients may demonstrate different types of skin reactions including pruritus, erythema, swelling, and pain [19].

The most serious adverse effect of omalizumab was anaphylaxis which firstly started in 0.2% of 57,300 Patients receiving omalizumab in the company's Pivotal studies conducted between 2003 and 2006 [20]. OJTF issued a five-step recommendations including 1.obtaining informed consent, 2.delivery of anaphylaxis education, 3. availability epinephrine auto injector, 4. pre-injection health assessment and 5.a waiting period of 30 minutes after each injection (with an extended waiting period after the first 3 injections to 2 hours). In 2011, the OJTF published their second report examining additional 77 patients with possible anaphylaxis from the post-marketing survey by Genentech/Novartis. By using the recommendations in the first report, approximately 77% of the anaphylactic reactions would have been encountered in a medical facility and thus being adequately treated [21].

Also, omalizumab appears to be safe for the cardiovascular system. A careful analysis of eight controlled trials comprehensively including more than 3000 participants, showed that the omalizumab-related cardiovascular risk was similar to that one observed in patients undergoing treatment with placebo [22].

Meta-analysis of seven controlled trials with omalizumab has confirmed the clinically significant effect of therapy of severe asthma – results demonstrated reduced rate of exacerbations by 38% in comparison with placebo, in spite of reduced overall corticosteroid dose. Furthermore, it was indisputably found that severe asthmatic patients who treated with omalizumab experience decrease in rates of physician visit, stay in the emergency room and hospital admissions due to exacerbations [23].

SPECIAL POPULATIONS

There are no clear studies about the safety of omalizumab during pregnancy, although animal studies in monkeys have not reported adverse effects. Therefore, the risk and benefits of treatment with omalizumab during pregnancy should be done by the Physicians[24].

There is limited data about the efficacy and safety of omalizumab in elderly patients. Since omalizumab prevents seasonal peaks in asthma exacerbations it has been suggested that a seasonal course of treatment in individuals at high risk should be studied, as this approach would reduce the cost of treatment [25].

CONCLUSION

Omalizumab is a recombinant humanized monoclonal antibody that binds circulating IgE antibody. It is approved in the US and Europe, as well as many other countries, for the treatment of adults and adolescents aged 12 years and above with moderate to severe persistent allergic asthma, whose symptoms are poorly controlled with inhaled corticosteroids, plus in Europe patients should also be receiving inhaled long-acting β2 agonist bronchodilators. In Europe, the license also includes children aged 6 to, 12 years as an add-on treatment for poorly controlled asthma in patients with severe persistent allergic asthma. Both national and international guidelines recommend omalizumab for patients with severe allergic asthma that is not controlled with other therapies. Better clarification of asthma endotypes will likely improve the accuracy of predicting response. Currently available biomarkers are limited in number and precision, but are of value. The combination of a history of frequent exacerbations, decreased FEV1; Presence of total serum IgE within dosing range (30–700 IU/ mL in adolescents and adults and 30–1,300 IU/mL in childrenaged 6–12 years), allergen-specific IgE, increased FeNO, and increased blood eosinophils are associated with greater likeli- Hood of response to omalizumab (Figure 3). Persistent increase of eosinophils during therapy or an increase in FeNO following discontinuation may predict the need for continued therapy. Endotype recognition and associated markers will advance personalized asthma care to move beyond the one-size-fits-all or trial-and-error approach.

The main adverse effect of omalizumab is anaphylaxis, although this occurs infrequently. Preliminary data from a five year safety study raised concerns about increased cardiovascular events and a final report is awaited. Clinical trials are in progress to determine whether omalizumab has efficacy in the treatment of non-allergic asthma.

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