Mini Review
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Omalizumab and sino-nasal allergy treatment

Abstract

Here, recent literature on the use of omalizumab in sino-nasal allergic diseases is reviewed. Omalizumab is an anti-human IgE humanized monoclonal antibody produced against CƐ3 domain of the Fc fragment of IgE molecule. Omalizumab suppresses the effector functions of IgE by preventing binding to high-affinity receptors (FcεR1) on allergy related immune effector cells, blocking mast cell or basophil mediator release. Omalizumab is helpful mainly in ragweed/birch pollen-induced seasonal and perennial allergic rhinitis rather than uncontrolled and concomitant allergic rhinitis and asthma/chronic rhino-sinusitis/nasal polyposis.

Keywords: omalizumab, allergy, sinusitis, rhinitis, polyp

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Introduction

Omalizumab (Omab) has been demonstrated to be safe and effective in the treatment of various allergic disorders other than asthma e.g. allergic rhinitis (AR), allergic conjunctivitis, eczema and food allergy.[1] Use of Omab and other biological agents have been increasing for the last decade.[2,3] Here, we review recently published literature on the use of Omab in sino-nasal allergic diseases.

Mechanisms of Omalizumab in Sino-nasal Allergic Disorders

Omalizumab is an anti-human IgE humanized monoclonal antibody produced against CƐ3 domain of the Fc fragment of IgE molecule. Omalizumab suppresses the effector roles of IgE by preventing binding to high-affinity receptors (FcεR1) on allergy-related immune effector cells and blocking mast cell or basophil mediator release.[4] Based on this mechanism of action, Omab also provides symptomatic relief to allergic patients.

Omalizumab Use in Seasonal and Perennial Allergic Rhinitis

Omalizumab was approved in 2002 by Australian authority and in 2003 by the U.S. Food and Drug Authority for the therapy of persistent allergic asthma.[1–3] In clinical trials, the effects of the Omab seemed to correlate with the reduction in serum IgE, with superior clinical efficiency observed at doses that diminished serum IgE concentrations by 90% or greater.[5] These studies suggest that significant decline in IgE levels are critical to clinical response.

Ragweed pollen-triggered seasonal allergic rhinitis

The initial clinical trial of the Omab in seasonal allergic rhinitis (SAR) was a randomized placebo-controlled double-blinded trials (RPCDBT), for dose-ranging in adolescent as well as adult patients having ragweed-triggered SAR. As reported by Casale et al.[6] the study did not demonstrate a significant reduction in daily SAR symptom scores. This may have been due to less than expected symptom exacerbation during the pollen season, inconsistency in symptom reporting, and fewer patients exhibiting sufficient IgE inhibition.[6] In the second trial by the same group, 536 patients having a 2-year record of moderate to severe ragweed-triggered SAR, with a total IgE level of 30–700 IU/mL were classified into placebo or one of several Omab courses of therapy. Over at least a 12-week period, subcutaneous Omab doses of 50 mg, 150 mg, or 300 mg were given every 3–4 weeks (based on the patient's basal serum IgE level). All patients received an initial Omab dose roughly two weeks ahead of the pollen season. As compared to the placebo group, notably improved results were consistently detected in the group receiving the 300-mg dose for the majority of study parameters over the trial period. The results were variable in groups receiving the 50-mg and 150-mg doses. Among the patients in the 300 mg Omab group, there were noteworthy improvements in nasal and ocular symptom severity scores, need for rescue medications, better treatment effectiveness ratings, Rhinitis Quality of Life (RQoL) scores, and fewer missed work or school days. Although the 300 mg Omab recipients had little alteration in their nasal symptom severity scores during the study, but placebo users suffered from a 50% increase in their scores throughout the peak pollen time of year.[7]

Birch pollen-induced seasonal allergic rhinitis

Omalizumab efficacy has also been assessed by Adelroth et al.[8] in moderate -severe birch pollen-induced SAR patients. Overall 251 patients were treated with either subcutaneous Omab or placebo groups in a 2:1 proportion; 300 mg was given every 3 weeks for 3 doses or every 4 weeks for 2 doses, based on the basal serum IgE levels. Efficacy in birch pollen-induced SAR was comparable to that shown in ragweed pollen-induced SAR.[8]

Omalizumab use with allergen specific immunotherapy in seasonal allergic rhinitis

The benefit of specific immunotherapy (SIT) is the opportunity to modify the disease progression in patients with AR, and to a lesser extent, in patients with asthma. Administration of SIT can produce

life-threatening adverse reactions such as anaphylaxis. However, two studies indicate that the combination of Omab with allergen SIT can improve the safety profile while improving efficacy over individual therapies. Pretreatment with Omab was found to improve the safety and efficacy profile of adults having seasonal AR and treated with ragweed SIT.[9] In a RPCDBT to assess the efficiency and safety of Omab over placebo along with SIT for birch/ grass pollens, the combined Omab therapy decreased symptom score, the total daily symptom severity score, and the need for rescue medication; by nearly 50% over SIT alone.[10] Thus, combined use of Omab and SIT may favorably impact the therapy of allergic diseases, contributing enhanced efficacy, decreased adverse effects (especially anaphylactic reactions in rush protocols of SIT), and deliver potential immune-modifying effects.

Perennial allergic rhinitis

The primary published study of Omab in perennial allergic rhinitis (PAR) was a RPCDBT by Chervinsky et al.[11] Where 289 patients having moderate-severe PAR over a 2 year period, a positive skin prick test to a perennial allergen (mites, dog, or cat allergen), and a total serum IgE level of 30–700 IU/mL were given 4 months of subcutaneous placebo or Omab. Doses were given once or twice monthly to provide at least 0.016 mg/kg of Omab per IU of IgE/mL per 1 month. Omalizumab recipients had lower daily nasal severity score, needed less rescue medication, and more patients had an important clinical improvement in their RQoL score. Post-hoc analyses of subgroups that had been previously unresponsive to allergen immunotherapy or intranasal steroids demonstrated that these patients showed considerable improvement.[11]

Omalizumab Use in Concomitant Asthma and Perennial allergic rhinitis

Because allergic asthma and AR share pathophysiology, it is predicted that patients having these disorders could achieve relief from symptoms with Omab therapy.[12,13] Vignola et al. assessed the efficiency of Omab in a RPCDBT (SOLAR study) including 405 adults and adolescents with simultaneous allergic asthma and PAR. Enrollment criteria consisted of an IgE level of 30–1300 IU/mL, a positive skin-prick test to an indoor allergen, and a record of moderate-to-severe PAR for ≥2 years, asthma requiring inhaler steroid therapy. After conversion to budesonide inhaler therapy, patients were categorized into subcutaneous Omab (≥0.016 mg/kg per IU of IgE/mL per month) or placebo for 7 months. Outcome comparisons of treatment compared to placebo showed that the mean rate of exacerbations was lower, showed important declines in their asthma and rhinitis symptom scores, large improvements in their quality of life, and asthma and rhinitis therapy efficacy were rated by more patients and researchers as excellent or good.[14]

Omalizumab for uncontrolled allergic rhinitis: a systematic review and meta-analysis

A meta-analysis of eleven studies including 2870 patients was performed to assess the efficiency and safety of Omab in uncontrolled moderate-to-severe AR.[15] A statistically significant decline in the daily nasal symptom severity score and a significant reduction in the requirement for daily nasal rescue medication were observed. There was no statistically significant difference for any adverse event between the Omab treated and groups not receiving Omab. Omalizumab was notably linked with symptomatic relief, diminished need for rescue medication, and an upgrade in the quality of life in patients with uncontrolled allergic rhinosinusitis.[15]

Omalizumab Use in Concomitant Asthma/Allergic Rhinitis and Chronic Rhino-sinusitis

The benefit of Omab was more likely to be experienced in asthma patients with chronic rhino-sinusitis (CRS) than in patients without CRS.[13] Furthermore, patients having refractory AR and eosinophilic CRS appear to have a more significant improvement from Omab, which supports the premise that disease endotype influences the therapeutic response and that there is no etiology common to asthma and CSR patients.[16] Omalizumab could be a likely add-on in the treatment of intractable allergic fungal rhino-sinusitis (AFRS) in patients with moderate or severe asthma,[17] as first demonstrated by Evans and Coop in a patient with unmanageable AFRS in 2014.[18]

Omalizumab use in chronic rhinosinusitis: a systematic review

Quite a few therapeutic options exist for CRS, but control of the disorder continues to elude most patients. Lately, data has accumulated indicating the potential for Omab use for CRS. Omab therapy has been compared to placebo in two studies.[19,20] Although there was an important distinction in Lund-McKay score, there was no difference in percent opacification on computed tomography. At 4 months, Omab therapy produced a reduction in clinical polyp score. No important difference was observed in quality of life (total nasal symptom severity; sinonasal outcome test,[20] and no significant complications were seen in either study. However, there is presently inadequate clinical data on the efficacy of Omab in the therapy of CRS to recommend routine use.[19]

Omalizumab Use in Nasal Polyposis

Like asthma, nasal polyposis related to eosinophilia at the nasal mucosa is inclined to be steroid responsive. However, constant nasal tissue eosinophilia is connected with reappearance of nasal polyps.[21] Augmented IgE levels and secretion from local polyclonal IgE production in nasal polyp tissue have been demonstrated in a few studies and linked with disease severity.[22] As nasal polyposis is an example of Th2-type dominant disorder, proof-of-concept trials and case reports investigating the Omab effects on nasal polyps are of interest. In a RPCDBT by Gevaert et al.[23] as performed in 24 allergic and nonallergic patients having nasal polyps and concomittant asthma, Omab considerably reduced total nasal polyp scores, sinus opacification, nasal and asthma symptoms scores including anosmia, while it improved quality-of-life for both diseases. Regardless of this and anecdotal case reports implying the Omab efficiency in nasal polyps, it is uncertain whether Omab will achieve endorsement for this indication.

Conclusion

While Omalizumab is indicated for the treatment of persistent allergen-driven asthma, it has also begun to be demonstrated as an effective agent for relieving sino-nasal allergy symptoms in clinical trials. In light of these studies, the latest reported position paper on pediatric allergic rhinitis by the European Academy for Allergy and Clinical Immunology (EAACI) suggest Omab as a possible

therapeutic form in AR and moderate to severe asthma patients when other treatments are unsuccessful.[20] In summary, recent literature shows Omab use in seasonal as well as perennial allergic rhinitis to be effective. However, the effect of Omab use in concomitant allergic rhinitis and asthma/chronic rhino-sinusitis/nasal polyposis needs to be proven with further studies.

Acknowledgment

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Conflicts of interest

None.

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