

Systematic review and meta-analysis

Omalizumab decreases exacerbation and allows a step down in daily inhaled corticosteroid dose in adults and children with moderate-to-severe asthma

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Commentary on: Normansell R, Walker S, Milan SJ, *et al.* Omalizumab for asthma in adults and children. *Cochrane Database Syst Rev* 2014;1:CD003559.

Context

Asthma is a common chronic disease that affects over 300 million people worldwide. Between 5% and 10% of this population has severe asthma, which often remains uncontrolled despite maximal conventional treatment. Omalizumab is a recombinant humanised monoclonal antibody that binds circulating IgE antibody and decreases allergic, IgE-mediated airway inflammation.¹ In the USA and many other countries, omalizumab is approved 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 (ICS). European approval stipulates that patients should have a history of frequent, severe exacerbations despite receiving ICS in high doses combined with an inhaled long-acting β_2 agonist bronchodilator (LABA). The European license also includes children aged 6–12 years. This systematic review examines the efficacy and safety of omalizumab versus placebo and conventional therapy for asthma in adults and children.

Methods

This was a systematic review and meta-analysis of randomised controlled trials (RCTs) examining omalizumab administered by inhaled, intravenous and subcutaneous injection for any duration. The subcutaneous route of administration is used in clinical practice and was the main focus of the review. The influence of disease severity was examined, classified by forced expiratory volume in 1 s (FEV₁) and baseline therapy.²

Relevant studies were identified in the Cochrane Airways Group Specialised Register of trials, from reference lists of included trials and online trial registries, as well as from drug company websites. The latest search was completed in June 2013.

The primary outcomes were exacerbations as defined by 'events'—such as hospital admissions, emergency room visits, increase in medication—and by the ability to step down or stop ICS or oral corticosteroids.

The results are reported as ORs and 95% CIs. The review adhered to recognised methods for undertaking systematic reviews and meta-analyses.

Findings

Twenty-five RCTs met the inclusion criteria (6382 participants), of which 19 assessed the efficacy of subcutaneous omalizumab. In patients with moderate-to-severe asthma receiving ICS treatment, the addition of subcutaneous omalizumab reduced exacerbations from 26% on placebo to 16% (OR=0.55, 95% CI 0.42 to 0.60), hospital admissions from 3% on placebo to 0.5% (OR=0.16, 95% CI 0.06 to 0.42) and allowed withdrawal (OR=2.50, 95% CI 2.00 to 3.13), or step down in daily ICS dose (−118 μ g beclomethasone dipropionate equivalent per day, 95% CI −154 to −84) over 16–60 weeks of treatment.

The number of patients able to withdraw oral corticosteroid therapy was similar between omalizumab and placebo groups (OR=1.18, 95% CI 0.53 to 2.63; one study). In the subgroup of patients with severe asthma receiving ICS alone or with oral corticosteroids, the efficacy of omalizumab in reducing exacerbations was not demonstrated and there were no data on hospital admissions. Serious adverse events were less with subcutaneous omalizumab (OR=0.72, 95% CI 0.57 to 0.91), although more local injection site reactions occurred (9.1% with omalizumab, 5.6% with placebo).

Commentary

The results confirm and extend the findings of an earlier Cochrane review,³ and suggested that for people with moderate-to-severe asthma receiving ICS, the addition of subcutaneous omalizumab is effective in reducing asthma exacerbations, hospital admissions and the numbers of patients who are able to reduce or withdraw ICS. Apart from local injection site reactions, omalizumab is generally well tolerated.

Both national and international asthma guidelines recommend omalizumab for patients with moderate or severe allergic asthma not controlled with other therapies, which in many severe cases will include high-dose ICS in combination with an LABA.^{3–5} The review does not provide data on the effectiveness of omalizumab in this severe patient group.

The authors highlight the need for further evidence on the effectiveness of omalizumab in children with asthma, on the duration of treatment as well as on thresholds of baseline serum IgE concentrations that warrant treatment. Another unresolved issue regarding the use of omalizumab in the management of allergic asthma is the identification of clinical or immunological biomarkers that predict a good response to omalizumab—an important objective in view of the high costs of treatment.

Competing interests NCT has participated in advisory boards and/or received consultancy fees from Asmacure, Chiesi and Respivert. He has received lecture fees from Boston Scientific, Chiesi, GlaxoSmithKline and Novartis, and industry-sponsored grant funding to the University of Glasgow from AstraZeneca, Boston Scientific, Genentech, GlaxoSmithKline, Novartis, Pfizer and Synairgen for participating in clinical trials.

References

1. Thomson NC, Chaudhuri R. Omalizumab: clinical use for the management of asthma. *Clin Med Insights Circ Respir Pulm Med* 2012;6:27–40.
2. British guideline on the management of asthma. A national clinical guideline. *Thorax* <http://www.sign.ac.uk>, 2012:1–144.
3. Walker S, Montell M, Phelan K, *et al.* Anti-IgE for chronic asthma in adults and children. *Cochrane Database of Syst Rev* 2006;2:CD003559.
4. National Asthma Education and Prevention Program (National Heart, Lung, and Blood Institute). Expert panel report 3: guidelines for the diagnosis and management of asthma. NIH publication no 07-4051 Bethesda, Md: National Institutes of Health National Heart, Lung, and Blood Institute; 2007. <http://www.nhlbi.nih.gov/guidelines/asthma> (accessed 17 Feb 2014).
5. Global Initiative for Asthma (GINA) Report, Global Strategy for Asthma Management and Prevention. www.ginasthma.com (accessed 17 Feb 2014).