Omalizumab reduced inhaled corticosteroid use and exacerbations in childhood allergic asthma

Milgrom H, Berger W, Nayak A, et al. **Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab).** Pediatrics. 2001 Aug;108:e36.

QUESTION

In children with moderate-to-severe allergic asthma who require daily inhaled corticosteroid (ICS) treatment, is omalizumab (anti-immunoglobulin E [anti-IgE] antibody) more effective than placebo for reducing steroid use and asthma exacerbations?

DESIGN

Randomized {allocation concealed*}†, blinded (clinicians, patients, {outcome assessors, and statisticians}†),* placebo-controlled trial with 34-week follow-up.

SETTING

Research centers in 12 U.S. states and in Washington, D.C.

PATIENTS

334 asthmatic patients who were 6 to 12 years of age (mean age 9 y, 69% boys) and whose asthma was well controlled with ICSs (beclomethasone dipropionate [BDP] and bronchodilator therapy) for ≥ 3 months before randomization. Other inclusion criteria were allergic asthma for ≥ 1 year; positive skin prick test result to ≥ 1 of house dust mite, cockroach, dog, or cat; total serum IgE level between 30 and 1300 IU/mL; body weight < 90 kg; FEV_1 ≥ 60% of predicted normal; ≥ 12% increase in FEV_1 from baseline within 30 minutes of taking albuterol; and stable asthma. Exclusion criteria were previous treatment with omalizumab; sinusitis, respiratory tract infection, or lung disease within 1 month or systemic disease within 3 months of randomization; abnormal findings on an electrocardiogram or a chest radiograph or abnormal laboratory values; or elevated serum IgE levels for reasons other than atopy. All patients were analyzed for the stable steroid phase and the steroid reduction phase.

INTERVENTION

Patients were allocated to subcutaneous omalizumab, 150 or 300 mg every 4 weeks; omalizumab, 225, 300, or 375 mg every 2 weeks (minimum dose 0.016 IU/mL per 4 wk) (n = 225); or placebo (n = 109). For 16 weeks, the baseline BDP dose was maintained; during the next 8 weeks, BDP was reduced stepwise to establish an effective minimum dose.

MAIN OUTCOME MEASURES

Reduction of BDP dose and asthma exacerbations.

MAIN RESULTS

More patients who received omalizumab reduced the BDP dose than did patients who received placebo (P = 0.002) (Table). Asthma exacerbations occurred in fewer patients receiving omalizumab (P < 0.001) (Table), and the mean number of exacerbations per patient was lower in omalizumab recipients (0.42 vs 0.72, P < 0.001).

CONCLUSION

In children with moderate-to-severe allergic asthma requiring daily inhaled corticosteroids, omalizumab reduced corticosteroid use and asthma exacerbations.

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*See Glossary.

†Information provided by author.

Omalizumab vs placebo for childhood allergic asthma‡

Outcomes	Omalizumab	Placebo	RBI (95% CI)	NNT (CI)
75% to 100% reduction in BDP dose at 34 wk	65%	50%	32% (8 to 65)	7 (4 to 23)
			RRR (CI)	
Asthma exacerbations at 12 wk	18%	39%	53% (32 to 67)	5 (4 to 10)

‡BDP = beclomethasone dipropionate. Other abbreviations defined in Glossary; RBI, RRR, NNT, and CI calculated from information provided by author.

COMMENTARY

The study by Milgrom and colleagues is their second on the use of omalizumab (anti-IgE antibody) in the treatment of asthma and the third published in the past 3 months that addresses treatment with anti-IgE in large, multicenter asthma studies. Concurrent studies by Busse and colleagues (1) and Soler and colleagues (2) included > 500 adult patients aged 12 to 75 years and used medium- to high-dose inhaled steroids (500 to 1200 µg/d of beclomethasone). They used a design similar to that of Milgrom and colleagues and achieved similar results in terms of steroid reduction and decreases in exacerbations. These studies, along with an earlier publication by Milgrom and colleagues (3), make a case for anti-IgE antibodies as adjunctive treatment for steroid-dependent patients with asthma.

The advantages of anti-IgE over conventional therapies include once- or twice-monthly subcutaneous injections and its tolerability with infrequent side effects. However, many questions remain. Although the association between asthma and elevated IgE is well established, the actual mechanism by which anti-IgE improves asthma is not known. Whether a role exists for anti-IgE in patients who do not have positive skin test results but who do have elevated IgE—as is commonly seen in asthma patients—is also unclear. The high placebo response role in these studies needs to be reconciled. Longer-term studies (≥ 12 mo) must be done to establish whether anti-IgE has a lasting effect on steroid use, enabling steroids to be used either intermittently or not at all. Such studies must also determine whether anti-IgE can be used as initial anti-inflammatory therapy for patients with mild asthma or whether a patient must be stabilized with corticosteroids before being treated with anti-IgE therapy.

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References

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3. **Milgrom H, Fick RB, Jr., Su JQ, et al.** N Engl J Med. 1999;341:1966-73.