

Allergen-specific immunotherapy improves asthma symptoms compared with placebo, but the possibility of adverse effects should be considered

Rabia Rashid,¹ Anthony J Frew¹

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Commentary to: **Abramson MJ**, Puy RM, Weiner JM. Injection allergen immunotherapy for asthma. *Cochrane Database Syst Rev* 2010;**8**:CD001186.

¹Department of Allergy & Respiratory Medicine, Royal Sussex County Hospital, Brighton, UK

Correspondence to:

Anthony J Frew
Department of Allergy & Respiratory Medicine, Royal Sussex County Hospital, Brighton BN2 5BE UK;
anthony.frew@bsuh.nhs.uk

Context

Asthma affects millions of people worldwide. Current drug treatments for asthma relieve bronchospasm and airway inflammation but do not offer a cure, and symptoms return when treatment is stopped. In many parts of the world, allergen-specific immunotherapy is used to treat asthma; it is the only treatment option that targets the underlying disease process, by modulating the immune response. However, immunotherapy can induce severe adverse reactions including anaphylaxis and death, especially in people with asthma, which has led to restrictions on its use, particularly in the UK.¹ In a previous systematic review, Abramson and colleagues² included 75 trials of allergen immunotherapy in asthma published between 1954 and 2001. This review concluded that immunotherapy significantly reduced asthma symptoms, medication requirements and bronchial hypersensitivity. The authors have now updated their analysis, including 13 new trials published between 2001 and 2005.

Methods

The Cochrane Airways Group Trials Register was used to identify relevant studies up to 2005. Dissertation abstracts and Current Contents were searched to identify newer published and unpublished studies. Non-English studies were also included. Three authors independently assessed suitability of studies for inclusion. Two authors independently assessed the methodological quality of the studies. Only randomised controlled trials (RCTs) assessing the use of allergen-specific subcutaneous immunotherapy in subjects with asthma and reporting at least one clinical outcome were included.

Meta-analysis was used with fixed-effect models to evaluate the overall efficacy of allergen immunotherapy on categorical and continuous outcomes. Heterogeneity between studies was assessed by χ^2 tests. Random-effect models were applied to recalculate efficacy when significant heterogeneity was identified.

The main objectives of the review were to estimate the overall efficacy of allergen-specific immunotherapy on asthmatic symptoms, asthma medication usage, lung function, non-specific bronchial hyper-reactivity and allergen-specific bronchial hyper-reactivity. Secondary outcomes comprised local and systemic reactions to immunotherapy.

Findings

A total of 88 trials were included in the review (41 trials of house dust mite immunotherapy, 27 pollen allergy, 10 animal dander, 2 *Cladosporium* mould allergy, 2 latex allergy and 6 trials involving multiple allergens). Overall, immunotherapy reduced asthma symptoms, medication usage and allergen-specific bronchial hyper-reactivity, with a lesser effect on non-specific bronchial hyper-reactivity. No effects were demonstrated on lung function parameters. Asthma symptom scores were significantly better with immunotherapy (standardised mean difference -0.59, 95% CI -0.83 to -0.35). The number needed to treat to avoid one deterioration in asthma symptoms was 3 (95% CI 3 to 5). The number needed to treat to prevent one person requiring increased medication was 4 (95% CI 3 to 6). One patient would be expected to develop a local adverse reaction out of every 16 patients treated with immunotherapy, and one out of every nine would be expected to develop systemic side effects of any severity.

Commentary

This review is a useful update of the earlier meta-analysis, including 13 additional RCTs. The conclusions remain consistent with the previous review. Overall, this is a high-quality review with clear objectives and sound methodology. However, there are significant limitations. The methodological quality of the included trials was only moderate and concealment of allocation was assessed adequate in only 16/88 trials. Furthermore, there was substantial heterogeneity in symptom and medication scores between the studies. In part, this reflects lack of standardisation of scoring systems. Publication bias may also be an issue.

The reported incidence of local side effects was similar to previous literature, but the incidence of systemic reactions is far greater, implying that these may have previously been under-reported.

With regard to clinical practice, this review supports the use of immunotherapy in patients with asthma to improve symptoms and use of medication. Patients with extrinsic allergic asthma may also profit from the beneficial effects on allergen-specific bronchial hyper-reactivity. The risks of using immunotherapy to treat asthma need to be considered with respect to the following: all such therapy should be supervised by experienced medical personnel with close monitoring for possible side effects

and full resuscitation facilities available to deal with possible anaphylaxis. An area that remains unexplored is the size of the effect compared with other asthma treatments such as inhaled corticosteroids, and this could be the subject of future trials and reviews. Finally, despite the positive findings of this review, further large-scale RCTs in immunotherapy in asthma are still required, both for the standard subcutaneous route and sublingual immunotherapy.

Competing interests None.

References

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