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## **Immunotherapy in children and adolescents with allergic rhinoconjunctivitis: a systematic review**

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### **CRD summary**

The review investigated whether immunotherapy was beneficial for symptoms or medication use in children and adolescents with allergic rhinoconjunctivitis. The studies included were limited in quality and had often inconsistent results. The authors concluded, appropriately, that there was insufficient evidence to establish whether or not immunotherapy had a beneficial effect.

### **Authors' objectives**

To evaluate the effect of immunotherapy with inhalant allergens on symptoms and medication use in children and adolescents with allergic rhinoconjunctivitis.

### **Searching**

An electronic search of MEDLINE, EMBASE and the Cochrane Controlled Trials Register was performed by one reviewer in June 2006. Search terms were given in the review. Bibliographies of recent reviews and trials were handsearched. No language restriction was applied. Only full text articles were eligible for inclusion.

### **Study selection**

Randomised controlled trials (RCTs) of children aged up to 18 years with allergic rhinoconjunctivitis that compared immunotherapy with placebo or symptomatic treatment, or those which compared different administration forms of immunotherapy, were eligible for inclusion. RCTs that compared different doses of the same product were not eligible. To be included, studies had to report sensitivity to the administered allergen confirmed by either a positive skin test and/or serum allergen-specific IgE (immunoglobulin E). Outcome inclusion criteria were at least one of a rhinoconjunctivitis symptom score, an anti-allergic medication score and/or a composite symptom-medication score.

In the included studies, the children were aged between three and 18 years. Where stated, between 31 per cent and 88 per cent of the participants were male; overall, more boys than girls were included. Immunotherapy was subcutaneous, nasal, oral or sublingual. Treatment lasted from one to 36 months. Most studies were placebo-controlled, although some compared immunotherapy to symptomatic treatment and one of the included studies was a comparison of oral immunotherapy to subcutaneous immunotherapy. The main allergen was grass pollen (other allergens used were: house dust mite, olive pollen, mould, ragweed pollen, birch pollen or parietaria pollen).

Two reviewers independently performed the study selection. Disagreements were resolved by consensus.

### **Assessment of study quality**

Two reviewers independently assessed the methodological quality using the Delphi list (a nine-point validity scale). Two additional points relating to drop-out rate were added to the list. Trials with a score  $\geq 6$  (out of 11) were considered high quality.

### **Data extraction**

Two reviewers independently extracted data on a standardised form. If a rhinitis score was absent, a total symptom score including a rhinitis score was extracted. If a composite symptom-medication score was absent, an overall evaluation of the treatment was extracted (if presented). Where possible, data for the last treatment period were extracted, unless the data for this period were insufficient or a control group was no longer present.

### **Methods of synthesis**

The heterogeneity between study outcomes and poor reporting of individual study results meant that results could not be pooled statistically. The number of studies reporting positive effects of the interventions was summarised according to type of immunotherapy.

### Results of the review

Twenty-eight RCTs (1,619 participants) were included in the review. Most trials were small; only four had over 100 participants. Study quality scores ranged from 2 to 9; 11 of the studies were of high quality. There were 11 trials supported by a pharmaceutical company, four of which had the study drugs supplied by the manufacturer.

Subcutaneous immunotherapy (six trials): Two trials reported a positive effect on symptoms, none a positive effect on rescue medication and none a positive effect on symptom-medication score.

Nasal immunotherapy (four trials): One trial and subgroup analyses from two other trials reported a positive effect on symptoms. The subgroups were grass pollen (positive effect) versus ragweed pollen (no effect) and nasal administration (positive effect) versus oral administration (effect not stated). Two trials reported a positive effect on rescue medication and one a positive effect on symptom-medication score.

Oral immunotherapy (seven trials): No trials reported a positive effect on symptoms or rescue medication. One trial and a subgroup analysis from one other trial reported a positive effect on symptom-medication score. The subgroups were nasal administration (positive effect) versus oral administration (effect not stated).

Sublingual immunotherapy (11 trials): Two trials and a subgroup analysis from one other trial reported a positive effect on symptoms. The subgroups were nasal administration (positive effect) versus oral administration (effect not stated). Two trials reported a positive effect on rescue medication and no trial reported a positive effect on symptom-medication score.

### Authors' conclusions

There was insufficient evidence that immunotherapy in any administration form had an effect on symptoms and/or medication use in children and adolescents with rhinoconjunctivitis.

### CRD commentary

The authors addressed a specific research question with clear inclusion/exclusion criteria. The search strategy was adequate (it involved more than one database and handsearching). Since only full text articles were eligible, and no attempt to locate unpublished data was reported, the results could be affected by publication bias. Although the authors did not apply a language barrier to their search, some articles were excluded following identification because of the language of publication. The authors acknowledged that this could have resulted in language bias.

The quality of the included studies was assessed and full results were reported. The authors decided not to conduct a meta-analysis, and their analysis was based on counting positive findings, which has several limitations.

The conclusions were sufficiently cautious to be likely to be reliable.

### Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: Optimal doses of subcutaneous immunotherapy and sublingual immunotherapy need to be determined using randomised placebo-controlled dose-finding studies. Following this, well-conducted trials should be used to investigate efficacy, quality of life, compliance and cost-effectiveness.

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### Bibliographic details

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