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[Intervention Review]

Specific allergen immunotherapy for the treatment of atopic eczema

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ABSTRACT

Background

Specific allergen immunotherapy (SIT) is a treatment that may improve disease severity in people with atopic eczema (AE) by inducing immune tolerance to the relevant allergen. A high quality systematic review has not previously assessed the efficacy and safety of this treatment.

Objectives

To assess the effects of specific allergen immunotherapy (SIT), including subcutaneous, sublingual, intradermal, and oral routes, compared with placebo or a standard treatment in people with atopic eczema.

Search methods

We searched the following databases up to July 2015: the Cochrane Skin Group Specialised Register, CENTRAL in the Cochrane Library (Issue 7, 2015), MEDLINE (from 1946), EMBASE (from 1974), LILACS (from 1982), Web of Science™ (from 2005), the Global Resource of EczemA Trials (GREAT database), and five trials databases. We searched abstracts from recent European and North American allergy meetings and checked the references of included studies and review articles for further references to relevant trials.

Selection criteria

Randomised controlled trials (RCTs) of specific allergen immunotherapy that used standardised allergen extracts in people with AE.

Data collection and analysis

Two authors independently undertook study selection, data extraction (including adverse effects), assessment of risk of bias, and analyses. We used standard methodological procedures expected by Cochrane.

Main results

We identified 12 RCTs for inclusion in this review; the total number of participants was 733. The interventions included SIT in children and adults allergic to either house dust mite (10 trials), grass pollen, or other inhalant allergens (two trials). They were administered subcutaneously (six trials), sublingually (four trials), orally, or intradermally (two trials). Overall, the risk of bias was moderate, with high loss to follow up and lack of blinding as the main methodological concern.

Our primary outcomes were 'Participant- or parent-reported global assessment of disease severity at the end of treatment'; 'Participant- or parent-reported specific symptoms of eczema, by subjective measures'; and 'Adverse events, such as acute episodes of asthma or anaphylaxis'. SCORing Atopic Dermatitis (SCORAD) is a means of measuring the effect of atopic dermatitis by area (A); intensity (B); and subjective measures (C), such as itch and sleeplessness, which we used.

For 'Participant- or parent-reported global assessment of disease severity at the end of treatment', one trial (20 participants) found improvement in 7/9 participants (78%) treated with the SIT compared with 3/11 (27%) treated with the placebo (risk ratio (RR) 2.85, 95% confidence interval (CI) 1.02 to 7.96; P = 0.04). Another study (24 participants) found no difference: global disease severity improved in 8/13 participants (62%) treated with the SIT compared with 9/11 (81%) treated with the placebo (RR 0.75, 95% CI 0.45 to 1.26; P = 0.38). We did not perform meta-analysis because of high heterogeneity between these two studies. The quality of the evidence was low.

For 'Participant- or parent-reported specific symptoms of eczema, by subjective measures', two trials (184 participants) did not find that the SIT improved SCORAD part C (mean difference (MD) -0.74, 95% CI -1.98 to 0.50) or sleep disturbance (MD -0.49, 95% CI -1.03 to 0.06) more than placebo. For SCORAD part C itch severity, these two trials (184 participants) did not find that the SIT improved itch (MD -0.24, 95% CI -1.00 to 0.52). One other non-blinded study (60 participants) found that the SIT reduced itch compared with no treatment (MD -4.20, 95% CI -3.69 to -4.71) and reduced the participants' overall symptoms (P < 0.01), but we could not pool these three studies due to high heterogeneity. The quality of the evidence was very low.

Seven trials reported systemic adverse reactions: 18/282 participants (6.4%) treated with the SIT had a systemic reaction compared with 15/210 (7.1%) with no treatment (RR 0.78, 95% CI 0.41 to 1.49; the quality of the evidence was moderate). The same seven trials reported local adverse reactions: 90/280 participants (32.1%) treated with the SIT had a local reaction compared with 44/204 (21.6%) in the no treatment group (RR 1.27, 95% CI 0.89 to 1.81). As these had the same study limitations, we deemed the quality of the evidence to also be moderate.

Of our secondary outcomes, there was a significant improvement in 'Investigator- or physician-rated global assessment of disease severity at the end of treatment' (six trials, 262 participants; RR 1.48, 95% CI 1.16 to 1.88). None of the studies reported our secondary outcome 'Parent- or participant-rated eczema severity assessed using a published scale', but two studies (n = 184), which have been mentioned above, used SCORAD part C, which we included as our primary outcome 'Participant- or parent-reported specific symptoms of eczema, by subjective measures'.

Our findings were generally inconclusive because of the small number of studies. We were unable to determine by subgroup analyses a particular type of allergen or a particular age or level of disease severity where allergen immunotherapy was more successful. We were also unable to determine whether sublingual immunotherapy was associated with more local adverse reactions compared with subcutaneous immunotherapy.

Authors' conclusions

Overall, the quality of the evidence was low. The low quality was mainly due to the differing results between studies, lack of blinding in some studies, and relatively few studies reporting participant-centred outcome measures. We found limited evidence that SIT may be an effective treatment for people with AE. The treatments used in these trials were not associated with an increased risk of local or systemic reactions. Future studies should use high quality allergen formulations with a proven track record in other allergic conditions and should include participant-reported outcome measures.

PLAIN LANGUAGE SUMMARY

Specific allergy immunotherapy for the treatment of atopic eczema

Background

At least one in seven children and one in 50 adults suffer from atopic eczema, a skin condition characterised by an itchy red rash. People with atopic eczema are allergic to things in the environment, such as house dust mites, and exposure to what they are allergic to may make their eczema worse. Specific allergen immunotherapy is a treatment that involves a course of injections or drops under the tongue containing the substance to which a person is allergic. The treatment can reduce the severity of a person's allergy and may therefore be able to reduce symptoms of atopic eczema. We evaluated whether specific allergen immunotherapy was better or worse than a standard treatment or placebo at improving disease severity and symptoms as assessed by participants, parents, or investigators.

Review question

Is specific allergen immunotherapy an effective treatment for people with atopic eczema?

Study characteristics

The evidence is current to July 2015. We found 12 studies, with 733 participants, which included both children and adults. Studies were conducted in specialist allergy centres in nine countries. The duration of trials ranged from four months to three years. Immunotherapy was administered to the participants in four different ways. Allergen manufacturers funded seven of the 12 studies.

Key results

We found no evidence from the studies in our review that SIT may be an effective treatment for atopic eczema, as rated by participants or parents for disease severity and symptoms. We found limited evidence that SIT may improve investigator-rated disease severity. Immunotherapy did not cause any more harm than a standard treatment or placebo.

Quality of the evidence

Overall, the quality of the evidence was low. We downgraded quality mainly due to the differing results between studies, lack of blinding in some studies, and that relatively few studies reported outcomes relevant to patients. Future studies should use high quality allergen formulations with a proven track record in other allergic conditions and should include participant-reported outcome measures.