

Effect of allergen specific immunotherapy on allergic inflammation in the upper and lower airways

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Experimental allergen challenge is widely used in diagnostic practice and research in allergy, but its relationship to environmental exposures is not clarified. Both models of allergic diseases have been used in order to examine the effects of allergen specific immunotherapy (SIT). Placebo-controlled studies have demonstrated the clinical efficacy of this treatment. However, long-term placebo-controlled studies with standardized birch pollen extract were lacking and the effect on early and late asthmatic reactions had not been examined in birch pollen-allergic patients.

The aims of this thesis were (I) to investigate the relationship between experimental and environmental bronchial challenge; (II) to examine the early kinetics of skin and mucosal sensitivity following rush immunotherapy (rapid up-dosing schedule); (III) to evaluate the effect of immunotherapy with standardized birch pollen extract on airway symptoms and use of medication in birch pollen-allergic patients in a placebo-controlled study and; (IV) to examine the effect of specific immunotherapy with standardized birch pollen extract on early- and late-phase asthmatic reactions in asthmatic patients.

Sixty-two patients with cat-induced asthma underwent an experimental allergen bronchial challenge followed by an environmental challenge. Thirty-four percent (21/62) of the patients developed a late response in both challenge models and 31% (19/62) failed to develop a late response in either model. Thus, consistency in development of a late response was found in 65% of the patients. Twelve cat- and five birch pollen-allergic patients received rush immunotherapy and underwent allergen challenges to skin and conjunctiva plus methacholine tests of lower airways and blood cell counts before and after 3 days, 1 week, 3 weeks and 12 weeks of therapy. Treatment significantly reduced skin and conjunctival sensitivity after three weeks, while transient increases in eosinophil numbers and bronchial hyperreactivity were seen after one week. In a 2-year placebo-controlled immunotherapy 49 patients with a history of birch pollen allergy symptoms involving the upper and lower airways were included and treated with a standardized birch pollen extract. A significant reduction in symptoms and use of medication was demonstrated in the treatment group compared to the placebo. In a further placebo-controlled study including 19 birch pollen asthmatic patients, a significant decrease in early and late asthmatic responses was seen following allergen bronchial challenge after one year of birch SIT.

In conclusion: The results show that environmental bronchial challenges may be replaced by experimental challenges for studies of the late phase reaction in allergic asthma. Rush immunotherapy was found to significantly reduce the skin and conjunctival sensitivity while transient increases in eosinophil numbers and bronchial hyperreactivity were seen. Allergen specific immunotherapy with birch pollen extract was shown to be a clinically effective and safe treatment. An attenuation of the early and late phase reactions in lower airways of birch pollen asthmatic patients was also observed following SIT.

Key words: birch pollen allergy, cat allergy, specific immunotherapy, rush immunotherapy, experimental allergen challenge, environmental allergen challenge, late asthmatic response