Pros and cons on sublingual immunotherapy in children allergic to house dust mites

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Allergic asthma is a common pathology in children and house dust mites are the most frequent indoor allergens implicated 1. The Global Initiative for Asthma (GINA) guidelines has defined the management of allergic asthma, which recommends the association of allergen avoidance, pharmacologic treatment and allergen immunotherapy, when indicated 2.

Immunotherapy is a specific therapeutic approach in the treatment of allergic airway disease and insect venom allergy and has been utilized for decades: it is therefore recommended to start it as soon as possible in allergic children to modify the natural course of respiratory allergy. Specific immunotherapy (SIT) has been shown to be effective in reducing asthma symptoms, medication use and bronchial hyper-responsiveness 3-4. Additionally, it has been recently shown that specific immunotherapy can be also used to prevent the occurrence of new sensitizations to airborne allergens in children exclusively sensitized to house dust mites 5-6. However, subcutaneous administration of SIT is inconvenient, time and resource consuming and is likely not to be effective in cases where the sensitization is due to allergic rhinitis 7. The use of sublingual immunotherapy (SLIT) is therefore becoming more popular, in particular in pediatric patients, due to the convenience of the administration, the safety profile and the long-term efficacy 8-9.

Mechanisms of SLIT. The mucosal antigen presenting cells pick up the allergen in the oral mucosa 10. After the application of SIT, a rise in serum IgG4 and IgE, but lower than that observed in SCIT, and a down-regulation of Th-1 type responses have been reported 11-12 in patients treated with SLIT 13-14-15. Moreover, in paediatric patients affected by allergic rhinitis SLIT was found to be clinically effective with pollens but not with mites 16. Conversely, when administered to children suffering from allergic asthma, it was found that SLIT with mites extracts has a clinically effective and safe profile in children 17-18-19. Specifically, SLIT has been demonstrated in adults, particularly in pollen-allergic rhinoconjunctivitis 10-11-12. Due to methodological problems, studies are not comparable as they were performed using different products, allergen concentrations, doses and duration of the treatment.

Efficacy in allergic asthma

The induction of tolerance is thought to be mediated by Treg cells and IL-10 20. A recent study reports that IL-18 and signalling lymphocytic activation molecule are up-regulated during SLIT suggesting that the Th2 type inflammatory response is down-regulated by an increase Th1 type response 21. According to this, Barbieri et al. reported that 2-year SLIT is capable of inducing immunologic hyporeactivity to mites with a significant IL-10 increase and an important decrease of Th2-dependent pro-inflammatory cytokines 22. Another study showed that after 12 months of SLIT, mature dendritic cells derived from SLIT-treated patients showed a statistically significant defect of CD86 up-regulation, an increase of IL-10, and a reduction of IL-12 production. SLIT induces changes in DCs functions that might be responsible for an impairment of T cell activation or drive T cells towards a regulatory activity, thus restoring immune tolerance to allergens 23.

Efficacy in allergic rhinitis

Most of the data on the efficacy of SLIT has been generated in adults and safety and tolerability data seem to be convincing for grass pollen tablet. The efficacy for other allergens is not as well proven. A Cochrane review has been published on SLIT in patients with allergic rhinitis 24. It concluded that SLIT is a safe treatment, which significantly reduces allergic rhinitis symptoms and medication requirements in pollen-induced rhinitis, but there is less significant efficacy in house dust mites-induced rhinitis and the degree of this benefit compared to other available therapies such as SCIT is not clear. Two paediatric meta-analyses 11-27 suggest that SLIT is more effective than the placebo, with significant reductions in symptoms and medication use. However, a third meta-analysis has demonstrated only a small improvement on asthma severity 14. Also two trials demonstrated improvement to bronchial challenge 34-36, but two did not 37-38. Another trial failed to show any effect in 92 mite-sensitive asthmatic children 39. In a recent meta-analysis on paediatric allergic asthma it was concluded that SLIT reduces both symptom score and rescue medication use when compared to placebo 10. The effect was found particularly with house dust mite allergen extracts.

More recent studies comparing SLIT and SCIT have been published. Two studies, in which the combination of SLIT and SCIT have been analysed, concluded that this option may produce a better efficacy than SCIT alone in the improvement of symptoms and pulmonary function and it successfully combines the advantages of the 2 alternatives: rapid onset and potency in SCIT and safety and avoidance of injections in SLIT 40.

In the matter of preventive effects of SLIT in children sensitized to house dust mites, a recent non-randomized parallel group open study with SLIT for 5 years indicated a preventive effect of SLIT as regards development of new sensitivities 41.

Conclusion

Immunotherapy is indicated for patients with IgE-mediated allergy to house dust mites confirmed by a specific diagnosis such as Skin Prick Test and/or specific IgE dosage, because of its immunological influence demonstrated by deviation of the immunological response to allergens toward production of T-reg dependent cytokines, such as IL-10 and the TGF-β. The role of IL-10 in the efficacy of SLIT in children population due to the modest level of methodological quality together with the publication bias, the high inter-study heterogeneity, the different doses administrated and the small sample size, represent the main interfering factors in this evaluation.

More data in children population are needed about SLIT’s efficacy, before this treatment can be strongly recommended.

References