The sublingual allergen immunotherapy

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The immunologic changes associated with immunotherapy are complex, and the exact mechanism or mechanisms responsible for its' clinical efficacy are continually being elucidated. Data support the concept that successful immunotherapy is associated with a change to a Th1 cytokine profile. Data indicate that increased production of IL-12, a strong inducer of Th1 responses, contributes to this shift. Clinically successful immunotherapy has been reported to be associated with immunologic tolerance, which is defined as a relative decrease in antigen specific responsiveness, immune deviation, or anergy. Successful immunotherapy results in generation of a population of T regulatory cells, which are CD4+CD25+ T lymphocytes producing IL-10, TGF-b, or both. Regulatory T-cell release has been described in allergen immunotherapy with Hymenoptera venom, grass pollen extract, and house dust mites. IL-10 reduces B-cell antigen-specific IgE and increases IgG4 levels; reduces proinflammatory cytokine release from mast cells, eosinophils, and T cells; and elicits tolerance in T cells by means of selective inhibition of the CD28 costimulatory pathway. Allergen immunotherapy has been shown to block both the immediate and late-phase allergic response. Clinical improvement in many patients develops before decreases in their IgE antibody levels occur or in other patients whose IgE antibody levels never decrease, thereby demonstrating that efficacy is not dependent on reductions in specific IgE levels. However, the relationship between these immunologic changes and immunotherapy efficacy is not completely understood. Sublingual allergen immunotherapy (SLIT) studies have evaluated house dust, olive pollen, grass pollen, ragweed, birch, cat, latex, Alternaria species, and Parietaria judaica. SLIT has been shown to be effective in patients sensitized to 2 non–cross-reacting allergens, grass and birch. It has been noted that the allergen is not degraded by saliva and that there is no direct sublingual absorption of allergen. Radiolabeled allergen has been detected after 48 hours in the sublingual region. Alternative protocols, such as rush and ultrarush (20 minutes) sublingual swallow and no induction (build-up) phase, have been studied. Several studies have suggested a relationship between dose and efficacy with sublingual immunotherapy, but a consistent relationship among allergen dose, treatment duration, and clinical efficacy has not been established. The majority of sublingual studies have

demonstrated some evidence of clinical efficacy in the form of either improved symptom scores, medication scores, or both, but approximately 35% of the randomized, double blind, placebo-controlled studies did not demonstrate efficacy in either parameter during the first year of treatment. Further studies are needed to confirm the optimal dose for sublingual immunotherapy. One of the potential advantages of sublingual immunotherapy is that it appears to be safe, even at very high doses (up to 500 times the usual monthly subcutaneous dose), and to be associated with a lower incidence of serious side effects. This appears to apply to young children (<5 years), for whom there are prospective safety data and a post-marketing survey. There have been no SLIT-related fatalities, but there have been 3 case reports of anaphylaxis caused by sublingual immunotherapy. There is currently no FDA-approved formulation for sublingual immunotherapy in the United States at this time, and this modality should be considered investigational. In this presentation, we will report our experience in a double-blind randomized controlled study in childhood allergic asthma in Taiwan.