IMMUNOTHERAPY

484
Allergen Standardisation in Allergens and Allergoids—Challenges and Considerations

Murray Skinner, PhD, Alan Bullimore, Simon Hewings, and Nicola Swan, MSc. R&D. Allergy Therapeutics, Worthing, United Kingdom.

Background: The range of therapeutics and dosing schedules for allergen preparations and allergoids produced and used clinically are considerable. Standardisation of allergy immunotherapies is considered a positive step; however there are difficulties in identifying universal metrics for standardisation. Many advocate the use of major allergen content whilst others advocate total allergenicity. Additionally as a compounding argument, where major allergen is used, many disagree on what the major allergen is for certain species.

Methods: Major allergen content measurement allows a consistent recognised measure, and IgE responses of a serum pool are often dominated by IgE against major allergens. However issues such as specificity of different assays toward isoforms and other variants of single allergens often results in diverging allergen contents that can cause unexpected and misleading disparity. Other aspects that increase complication are the relevance to modified allergens, use of adjuvants and differing dosing regimes.

Results: The major allergen content of key products in different therapeutic formats has been measured.

Conclusions: This has been performed in conjunction with techniques such as total allergenicity, as allergy treatments and therapeutics require careful characterisation to allow supply of consistent, safe and efficacious products.

485
Therapeutic Effect and Safety of Tropical Mite Allergen Vaccines by Subcutaneous Route in Allergic Asthmatics Patients

Raúl Lázaro Castro Almarales, MD,1 Mercedes Ronquillo, MD,2 Mirta Alvarez Castello, MD,3 José Rodríguez, MD,4 Mayda González, MD,5 Alexis Labrada, PhD,6 Bárbara I Navarro Viltres, MD,7 Yunia Oliva Díaz,8 and Maytee Mateo9.1 National Center of Bioproducts (BIOCEN), WAO Member, Cuban Society of Allergy Member, Cuban Society of Immunology Member, Cuban Society of Family Medicine Member, Mayabeque, Cuba; 2Allergy Service, University Hospital General Calixto García, WAO Member, Cuban Society of Allergy Member, Cuban Society of Immunology Member, Havana, Cuba; 3Allergy Department, University Hospital General Calixto García, WAO Member, Cuban Society of Allergy Member, Cuban Society of Immunology Member, Havana, Cuba; 4Docent Policlinic Pedro Fonseca, Cuban Society of Family Medicine Member, Mayabeque, Cuba; 5Allergy Department, WAO Member, Cuban Society of Immunology, Havana, Cuba; 6Allergist, Universidad de La Habana, Havana, Cuba; 7Docent Policlinic Pedro Fonseca, Cuban Society of Family Medicine Member, Mayabeque, Cuba; 8Member of Cuban Society of Immunology, Havana, Cuba; 9Member of Cuban Society of Immunology, Mayabeque, Cuba.

Background: Allergen-specific subcutaneous immunotherapy (SCIT) is presently recognized as a biological response modifier, as it is the only available treatment able to influence the natural course of allergic disease. Extensive clinical evidence supports its efficacy. Safety concerns are related to the risks of anaphylactic reactions during treatment. Standardization of allergen vaccines in terms of allergenic activity allows a more precise control over the administered doses and can be, therefore, very relevant for both efficacy and safety of SCIT. House Dust Mites (HDM), particularly Dermatophagoïdespteronyssinus (Dp), Dermatophagoïdes siboney (Ds) and Blomia tropicalis (Bt) have been described as very relevant allergen sources in Cuba, with a strong association to respiratory allergy symptoms.

Objective: To assess the efficacy and safety of standardized allergen vaccines of these 3 mite species (Valeragen, Biocen, Cuba) in Cuban asthmatic patients.

Methods: Three Double-Blind Placebo-Controlled clinical trials were performed in 40 patients each, showing asthmatic symptoms and positive predominant Skin Prick Test (SPT) to each mite, respectively. Half of patients received the active treatment consisting of subcutaneous injections with increasing doses, up to 6000 BU.

Results: The total 1 year cumulative dose was 63035 BU, in an average of 20.5 injections. The treatment was effective in the reduction of clinical symptoms (up to 32%, 95%CI: 28-36%; P = 0.0006) and medication intake (23%, 95%CI:18-28%), as compared to control treatment. The skin sensitivity to the allergens decreased significantly (P = 0.0001), with regard to the beginning of the treatment. The allergen amount needed to induce a positive SPT increased 297-fold. An improvement of the lung function was observed, expressed in a modest Peak-Expiratory-Flow increase (P < 0.05) and reduction of PEF daily variability. SIT was considered effective in 71% of patients. The frequency of local adverse reactions was 2.4 % of injections.

Conclusions: The results indicate that immunotherapy, using standardized House Dust Mite vaccines, including tropical species, is effective and safe for the control and amelioration of the asthma in our population.

486
Therapeutic Effect and Security in Asthmatics Adult Patients Treated with Dermatophagoïdes Pteronyssinus Allergen Sublingual Immunotherapy

José Rodríguez, MD,1 Raúl Castro, MD,2 Alexis Labrada, PhD,3 Mirta Alvarez, MD,4 Mercedes Ronquillo, MD,5 Mayda González, MD,6 Bárbara Navarro, MD,7 Maytee Mateo8 Yunia Oliva,9 Iris García, MD,1 and Irene Enríquez, MD,1.1 Allergy Department, University Hospital Calixto Garcia, Havana City, Cuba; 2Allergens, National Center of Bioproducts, Havana City, Cuba; 3Allergens, National Center of Bioproducts, Mayabeque, Cuba; 4Pedro Fonseca Docent Policlinic, Havana City, Cuba.

Background: The specific active immunotherapy, employing vaccine of allergen of mite is a treatment considered as effective for the respiratory allergy and asthma. The sublingual route has minor risk of systematisations reactions. The objective of this study was to determine the therapeutic effect and security of sublingual immunotherapy (ITSL) employing the standard vaccine VALERGEN-DP (BIOCEN, CUBA) in a population of asthmatic Cuban patients.

Methods: A phase II Clinical Trials double blind, placebo controlled in a total of 40 adult patients with mild or moderate asthma and specific sensitivity preponderant to this mite. Half of patients received drops by sublingual route with growing doses up to 2000 UB.

Results: The treatment was effective in the reduction of clinical symptoms and medication intake as compared to conventional treatment in control group. The cutaneous sensibility to this mite was significant reduced, increasing in 1.9 log; the amount of necessary allergen to provoke a positive Prick Test. An improvement of the lung function was observed with a significant reduction (P < 0.05) of expiratory pick flow variability. The frequency of local reactions were only 0.58% of administration.
Conclusions: The VALERGEN-DP vaccine is an effective treatment and profitable against asthma in our population and guarantee its generalization in the Allergy Services of our health system.

487 Safety of Sublingual Immunotherapy with Standardized Vaccines of Domestic Mites

Mirta Alvarez, MD,1 Raúl Castro, MD,2 Daniel Gutierrez, MD,1 Alexis Labrada, PhD,2 Irene Enriquez, MD,1 Mercedes Ronquillo, MD,1 José Rodriguez, MD,1 and Iris García, MD1

Background: Allergen-specific immunotherapy consists of administering gradually increasing doses of the allergen, to which the patient is sensitized, aiming at achieving tolerance to it and decreasing clinical symptoms. The sublingual immunotherapy (SLIT) was introduced as an alternative to subcutaneous route. Its use is being increased in the world and in Cuba, using standardized vaccines owing to greater safety. The objective of this study was to determine the safety of sublingual standardized vaccines of 3 domestic mite species (Valeragen, Cuba) and its adverse events in allergic patients from the Calixto Garcia University Hospital in Havana, as well as the frequency of its prescription.

Methods: Descriptive and cross-sectional study design, which included 130 patients with treatment of SLIT with VALERGEN-DP (Dermatophagoides pteronyssinus), VALERGEN-DS (D. siboney) and VALERGEN-BT (Blomia tropicalis) (BIOCEN, Cuba), who attended the Allergy Service in the period January-September 2010. Age distribution: mean 19.6 years (range 1–75), 40.7% was younger than 18 years.

Results: The multi-allergen vaccine was the type of vaccine most used (63.8%). The most common allergen was D. pteronyssinus followed by B. tropicalis. 71.55% of administered allergens vaccines were in maintenance phase. We found 4 adverse events (3.1% of patients), all local, mild, and not requiring treatment or change of vaccination dosing schedule.

Conclusions: The Valeragen vaccines by sublingual route are safe and well tolerated in Cuban allergic patients.

488 The Effect of Specific Immunotherapy on the Clinical Response in Patients with Grass-pollen Induced Rhinoconjunctivitis

Zoran Arsovski, MD, MSC,1 Biserka Jovkovska Kaeva, MD, PhD,2 Miroslav Gavrilovski, MD, PhD,2 Toma Stefanovski, MD, PhD,2 Sava Pejkovska, MD,2 Suzana Arbutina, MD,2 Irfan Ismaili,2 Tatjana Caparoska, MD, PhD,2 and Dejan Doci, MD, PhD2

Background: Specific immunotherapy (SIT) has a significant potential in the treatment of allergic rhinitis and allergic conjunctivitis. The aim of the study was to evaluate the effect of specific immunotherapy (SIT) in patients with grass-pollen-induced allergic rhinitis and allergic conjunctivitis.

Methods: Twenty-six patients with pollen induced rhinoconjunctivitis and positive history for more than 2 years were included in our study. They had skin prick test of ≥ 5 mm, age range from 18 to 44 years and all underwent conjunctiva provocation tests before and after 1 year of SIT. Clinical severity score of nasal and conjunctiva symptoms during the season was assessed by 4-point arbitrary rating scale from 0 to 3. Conjunctiva provocations were performed out of the season until allergic symptoms occurred, achieving the allergen threshold dose (ATD).

Results: After 1 year of SIT, we have noticed reduction of clinical symptoms present in allergic conjunctivitis: burning, itching, lacrimation and hyperemia (P < 0.05). We have found also reduction in clinical symptoms of allergic rhinitis: secretion, irritation, itching and nasal blockade (P < 0.01). The patients tolerated significantly higher allergen doses in provocation tests after 1 year of SIT, reaching new ATD.

Conclusions: SIT reduces the clinical symptoms of allergic rhinoconjunctivitis and modifies the inflammatory response after specific allergen challenge.

489 Does Sublingual Immunotherapy Work with an Immune Deviation Mechanism?

Laura Giovanna Sensi, MD, Elisa Panfili, Arianna Latini, Francesco Marcucci, and Giuseppe Di Cara, MD. Medical-Surgical Specialties and Public Health, University of Perugia, Perugia, Italy.

Background: We aimed at finding out the immunological mechanisms of SLIT by studying the activity of IgE specific for the epitopes of Phleum in patients treated with SIT for grass allergen and in a control group.

Methods: 30 patients allergic to grass were included in the study:
- 15 patients carried out a pre-seasonal SIT for 2 years with the 5 grass mix extract from Stallergenes.
- 15 patients were not treated with SIT.

Eligible patients: Clear symptoms of seasonal rhinoconjunctivitis during the past year, positivity to Phleum skin prick tests (+ + +) and specific IgE (3.5 kU/L). Prick tests were performed with extracts from Stallergenes; serum specific IgE for Phleum and rPhlp1, rPhlp2, rPhlp5, rPhlp6, rPhlp7, and rPhlp12 were determined through the Unicap system 100 IgE FEIA (Phadia Usala, Sweden). Wilkoxon and Fischer method were performed. Rast inhibition rPhlp1/rPhlp1, rPhlp1/rPhlp2 and rPhlp1/rPhlp4 were evaluated.

Results: IgE for rPhlp7 and rPhlp12 present only in some patients did not show significant modifications. Most patients treated with SIT for 2 years and all those showing improvement in symptoms, showed a less evident increase of specific IgE for rPhlp1 and rPhlp5 if compared with that of minor allergens, ie, rPhlp2, rPhlp4, rPhlp6. This difference was absent in control patients and in patients not showing clinical improvement. In patients showing clinical improvement the IgE ratio rPhlp5/rPhlp2 was significantly decreased (P = 0.02). A RAST inhibition study showed no cross-reactivity between rPhlp1/rPhlp2 and rPhlp1/rPhlp4.

Conclusions: After 1 and 2 years of SLIT, the data show the following results:
- a significant increase of specific IgE for minor allergens and a less evident increase of specific IgE for major allergens in patients showing a clinical response to SLIT
- a drastic decrease in IgE ratio for rPhlp5/rPhlp2. These results suggest that SLIT not only induces a TH2-TH1 isotypic switch, but also can act with a mechanism of immunological replacement. In fact, the production of specific IgE for minor allergens (rPhlp2, rPhlp4, rPhlp6) tends to replace the production of specific IgE for major allergens (rPhlp1, rPhlp5).

IMMUNOTHERAPY TRAINING

490 Immunotherapy (IT) Training in Canada: Perspectives of Fellows-in-training on the First Immunotherapy Training Manual

Teresa Pun, HBSc, MD, FRCP,1 Monika Kastner, PhD,2 Harold Leeyonge Kim, MD, FRCP,3 D. William Moote, MD, FRCP,4 and Susan Waserman, MD, FRCP5

1. Adult Allergy and Clinical Immunology, Health Sciences