Allergol Immunopathol (Madr). 2017;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

Predictivity of clinical efficacy of sublingual immunotherapy (SLIT) based on sensitisation pattern to molecular allergens in children with allergic rhinoconjunctivitis

A. di Coste[a,*], F. Occasi[a], G. De Castro[a], A.M. Zicari[a], R. Galandrini[b], A. Giuffrida[b], L. Indinnimeo[a], M. Duse[a]

[a] *Department of Pediatrics, Sapienza University of Rome, Italy*
[b] *Department of Experimental Medicine, Sapienza University of Rome, Italy*

Received 12 October 2016; accepted 24 January 2017

KEYWORDS
Allergic rhinoconjunctivitis;
Component resolved diagnosis;
Sublingual immunotherapy;
Average rhinoconjunctivitis total symptom score;
Average combined score

Abstract
Background: The diagnostic and therapeutic approach to grass pollen allergy is now possible by detecting specific IgE (sIgE) to its allergenic components.
Aim: To evaluate the correlation between the sensitisation to different molecular *Phleum pratense* (Phl p) allergens and clinical efficacy of SLIT.
Methods: The pilot study included 36 patients affected by allergic rhinoconjunctivitis, all treated with SLIT actively. We performed serum analysis of sIgE to Phl p 1, 2, 4, 5, 6, 7, 11 and 12. The Average Rhinoconjunctivitis Total Symptom Score (ARTSS) and the Average Combined Score (ACS) were evaluated before and after one year of immunotherapy.
Results: Three different groups of sensitisation were defined based on the range of IgE reactivity to *Phleum pratense* allergens at baseline: group I (sIgE reactive to 1–3 allergens); group II (sIgE reactive to 4–5 allergens); and group III (sIgE reactive to 6–8 allergens). At T0 ACS was 1.79 ± 0.18 in group I; 1.81 ± 0.23 in group II; and 1.95 ± 0.34 in group III. At T1 ACS was 0.85 ± 0.55 in group I; 1.01 ± 0.31 in group II; and 1.44 ± 0.39 in group III. At T1 there was a significant improvement of ARTSS and ACS for group I ($p = 0.001$).
Conclusions: Sublingual immunotherapy with a grass pollen is efficacious irrespective of the patients' baseline sensitisation to either single or multiple grass pollen molecular allergens. We found that patients with few sensitisations have a greater improvement in combined symptom and medication score. SLIT improves the clinical course of allergic patients although new sensitisations may appear.
Published by Elsevier España, S.L.U. on behalf of SEICAP.

* Corresponding author.
E-mail address: dicoste.annalisa@gmail.com (A. di Coste).

http://dx.doi.org/10.1016/j.aller.2017.01.001
0301-0546/Published by Elsevier España, S.L.U. on behalf of SEICAP.

Introduction

Allergic rhinoconjunctivitis induced by pollens is an increasingly prevalent condition affecting 8–25% of the general population,[1,2] limiting the social life, school learning and work productivity. Rhinitis often coexists with asthma and is regarded as one of its major risk factors. About 20 species from five subfamilies are considered to be the most frequent causes of grass pollen allergy. The most complete set of allergens has so far been isolated and cloned from *Phleum pratense* (timothy grass) pollen. Recombinant and purified allergens are currently available for determining specific IgE targeted to different allergenic components. Based on the prevalence of IgE antibody recognition among grass pollen-sensitised individuals, several allergens qualify as major, but members of two groups, groups 1 and 5, have been shown to dominate the immune response to grass pollen extract.[3]

The accurate dissection of the IgE repertoire offers new possibilities in the diagnosis, prophylaxis and treatment of paediatric allergic rhinoconjunctivitis and asthma. Different IgE molecular sensitisation profiles to an allergenic source can correspond to different clinical disease manifestations and severity. The molecular approach to the diagnosis of allergies, also called 'Component-Resolved Diagnosis' (CRD), is a diagnostic strategy that integrates the results of skin prick test (SPT) and/or sIgE with the results of IgE sensitisation detected at molecular component level. CRD can avoid the administration of irrelevant allergens in an SLIT preparation improving its clinical efficacy and cost-effectiveness.[4]

The microarray technique allows to determine sIgE against multiple allergens simultaneously in the patient, with a minimum amount of serum. In addition, microarray technology will help explain cross-reactions, and will facilitate the evaluation of subjects in which skin tests cannot be performed.[5]

Allergen-specific immunotherapy is widely used and is recognised by the World Health Organisation as the only causal treatment for Type 1 allergy available today. The clinical efficacy of grass pollen SLIT has been established in large cohorts of patients but today there is not an established surrogate marker for SLIT efficacy. No clear correlation between antibody responses and clinical benefit has yet been established for individual treated patients. Furthermore, the efficacy of immunotherapy in patients exhibiting distinct patterns of IgE sensitisation (e.g. to major and/or minor allergens) remains debated, with the notion that natural extracts may not contain all needed allergens. Alternatively, IgE neo-sensitisation to allergens present in the vaccine may occur during specific immunotherapy, although in this regard, the risk appears higher with the subcutaneous route when compared with sublingual administration.[6]

Molecular diagnosis allows us to look forward to the availability of a personalised immunotherapy,[7–9] not based on undefined extracts anymore, but tailored to the single patient's sensitisation.

In the present study, we tried to assess the influence of different molecular profiles on clinical efficacy of SLIT over time in children monosensitised to grass pollen.

Material and methods

Study design

Thirty-six children monosensitised to grass pollen, affected by allergic rhinoconjunctivitis were included in the study. The main inclusion criteria were: age ≥6yr, clinical history of allergic rhinoconjunctivitis (at least two years), a positive skin prick test (SPT) responses to the relevant pollen extracts (wheal diameter 3 mm), sIgE for at least one major grass pollen allergen and never received immunotherapy previously.

After one year of observation, patients started grass pollen SLIT (T0). The study plan included two crucial visits, skin prick test and dosage of total and specific IgE (sIgE): at the start of treatment (T0) and after one year (T1). During the trial, patients recorded on diary cards the occurrence of daily symptoms of rhinitis and conjunctivitis, rescue medications and other complaints.

Written informed consent was provided by parents or tutors of all participants. The study design and procedures were approved by the ethics committee of our centre.

In vitro test

All sera contained timothy grass-pollen-specific IgE, as determined by the immunoenzymatic CAP method (Phadia, Uppsala, Sweden). Moreover, the sera were characterised in detail by determination of IgE antibodies to rPhl p 1, rPhl p 2, nPhl p 4, rPhl p 5, rPhl p6, rPhl p 7, rPhl p 11, rPhl p 12. sIgE levels were considered positive at the level of 0.35 kUA/l or higher (class 1).

Specific IT and pharmacological treatment:

The mix grass pollen SLIT Staloral 300 (Stallergenes Italia s.r.l., Saronno [VA], Italy) contains sodium chloride (0.059 g), glycerol (0.58 g), purified water, and 300 index of reactivity (IR) mix grass pollen in 1 mL, approximately 25 mg/mL of the group 5 major allergens. It was prepared as pressures (1 pressure = 60 IR) on the 300 IR/ml dispenser, administered as sublingual in the morning, after the patient had fasted. The patients were carefully instructed about the self-administration, and detailed written instructions were provided. The build-up phase, of about three days, involved the administration of the extract at progressively increasing concentrations (60, 120, 240IR). In the maintenance phase four pressures (240 IR) on the dispenser were daily given.

The SLIT was administered using a precoseasonal schedule. The following medications were allowed: oral antihistamines (loratadine or cetirizine 10 mg, 1 tablet/day), intranasal corticosteroid (beclomethasone dipropionate 1 puff b.i.d.) and oral corticosteroid (betamethasone 1 mg on demand).

Symptom and rescue medication scores

Average Rhinoconjunctivitis Total Symptom Score (ARTSS)[10]: ARTSS is the average of the daily RTSS throughout the pollen

Please cite this article in press as: di Coste A, et al. Predictivity of clinical efficacy of sublingual immunotherapy (SLIT) based on sensitisation pattern to molecular allergens in children with allergic rhinoconjunctivitis. Allergol Immunopathol (Madr). 2017. http://dx.doi.org/10.1016/j.aller.2017.01.001