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CLINICAL EXPERIENCE ON SUBLINGUAL IMMUNOTHERAPY WITH MONOMERIC ALLERGOIDS EXTRACTS OF *DERMATOPHAGOIDES* IN CHILDHOOD WITH RESPIRATORY ALLERGY

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SUMMARY
We present preliminary results of a study involving a randomized open multicenter clinical trial in parallel groups of sublingual immunotherapy with monomeric extracts in comparison to conventional subcutaneous depot traditional extracts in asthmatic children allergic to Dermatophagoides and aged 4-16 years. The two treatment regimens showed a similar efficacy while the sublingual-treated group resulted to be better as regards to compliance.

Introduction

Specific immunotherapy has been the most utilized specific treatment of respiratory allergy.

In pediatric patients the general aim is to minimize the possible severe side effects due to the injectory route and for this reason increasing attention has been devoted to the so-called alternative routes of allergen-specific immunotherapy, such as the oral, sublingual, bronchial, and intranasal route.

Even if the results of clinical trials are encouraging, the underlying proposed mechanisms for alternative immunotherapy are different and not completely understood. Oral or sublingual administration, as well as nasal immunotherapy, have shown both clinical efficacy and the capacity to evoke a biologic response in some study (1, 2, 4), but their use is not generally accepted.

The aim of the present double blind multicenter parallel groups study was to evaluate the safety and the clinical efficacy of a new sublingual immunoterapy with monomeric allergoids in tablets of mites, in children with allergic bronchial asthma with or without rhinoconjunctivitis in comparison to conventional subcutaneous depot extracts.

Patients and methods

Study design

The present study is a randomized open multicenter clinical study in parallel groups of sublingual immunotherapy (SI), in comparison to conventional subcutaneous depot traditional extracts (SDT). For sublingual immunotherapy was used a monomeric allergoid extract (LAIS, Lofarma, Milano), and for conventional subcutaneous depot extract a conventional product of the same Company.

Patients

Asthmatic childrens allergic to Dermatophagoides and aged 4-16 years have been recruited and assigned in randomized way to sublingual (n. 30 patients) or traditional subcutaneous immunotherapy (n. 27 patients). The mean age of the two patients group was respectively 8 ±4 for SI and 9.5±3 for STD. The patients were recruited in five Italian cities (Catania, Florence, Naples, Milan and Pisa) and the baseline clinical conditions of the patients were assessed during the 1993. The treatment was administred from September 1994 till March 1996. Asthma with or without rhinoconjuntivitis was the main inclusion criterion. All the patients showed single sensitization to Dermatophagoides, assessed through clinical history, skin testing and specific IgE detection. None of the patients showed major anatomic defects of the upper airways, nor had any patient previously received immunotherapy.

Treatments

The SI was administred in tablets presented as monomeric allergoid. The treatment lasted 18 months and consisted in a first phase at increasing dosages and a second phase at constant dosage. The tablets administred at the more low dosage of 25 U.A. via sublingual in the morning at fast, was gradually increased to 100, 200, and 300 U.A in three weeks. After that, the maintenance dosage was reached: a dosage of 300 U.A. was administred for 18 months.

The STD was administred with a traditional extract of the same Company till reaching the maximum tolerated dosage

Symptoms

Parents were requested to keep a daily record of the presence and grade of symptoms (asthma, cough, rhinorrhea, nasal blocking, itching, conjunctivitis), following a zero to 3 scoring system (0 = absent, 1 = mild, 2 = moderate, 3 = severe), during the treatment. The daily intake of drugs during the study was recorded on the same diary card. Symptoms and medication scores have been recorded during the whole period. The patients also recorded each dose of SI assumed and the subsequent onset of possible side effects.
The statistical analysis was performed employing the Mann-Whitney test for intergroup comparison. Probability of < 0.05 was considered significant.

Specific Nasal Provocation test

The specific nasal provocation test (SNPT) was performed out of Dermatophagoides season (June-July 1994), after 6 months from the beginning of the therapy (March 95), and after 12 months from the beginning of the therapy (September 95).
All medications were withdrawn at least 10 days before the nasal challenge. Two ml lavages with lactate Ringer's solution at 37°C in each nostril were performed to obtain stable conditions. Then a series of challenges with increasing doses of allergen (Allerkin test, Lofarma, Milano, Italy) was performed at standard time intervals (15 minutes) until a clinical reaction was elicited. The clinical reaction was assessed as total symptoms score, according to an arbitrary rating scale from 0 to 3 (0 absent, 1 mild, 2 moderate, 3 severe) considering nasal itching, sneezing, rhinorrea, and nasal blocking. To define the allergen threshold dose, total symptoms score after challenge higher than 5 was considered a positive response. The threshold dose, fixed for each patient, was employed for the subsequent nasal challenges.

Results

We present the preliminary results of the first 18 months of observation.

The symptoms/medications score was considered as the sum of the monthly score, and its basal homogeneity was verified during the pre-treatment baseline period of observation during the 1993.
The comparison between pre-treatment and post-treatment score does not show a significant statistical difference between patients on SI respect to patients on SDT, even if patients on SI showed a less pronounced reduction of recorded scores. Both treatments were able to reduce the recorded symptoms and the drug consumptions.
The symptom scores after nasal challenge showed a significant reduction in both groups.
Nobody of the two groups showed any side effects, but six patients from the SDT dropped out because moved to another town or for poor compliance, while all patients of the SI group completed the trial.

Discussion

The purpose of the present study was to evaluate the safety and clinical efficacy of a sublingual immunotherapy with Dermatophagoides monomeric allergoids in tablets of mites in children with bronchial asthma with or without rhinitis.
As nobody of the studied children showed any side effect, we can conclude that, in our experience, this kind of treatment is safe and also could be self-administred by the parents with only periodical allergological controls. The SI could also lower the age in which the immunotherapy could be indicated. In this way the allergic inflammation, present even in very young patients, can be easier controlled.
The clinical efficacy of SI looks similar to the SDT therapy, even if we think that more comprehensive studies must be performed before their use will be generally accepted. Some recent studies have been published demonstrating the efficacy of SI in children (3, 5). The intimate mechanism unfortunatelly is not completely studied and understood. In our clinical experience, at the moment SI could be indicated in very young children, with symptoms clearly related to an allergic condition, or in children with families in which a traditional injective immunotherapy is not accepted.

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