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Perceived efficacy and satisfaction of patients with subcutaneous hypoallergenic high-dose house dust mite extract

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Key words

Allergoid; subcutaneous immunotherapy (SCIT); hypoallergenic; high-dose; effectiveness; perceived effectiveness

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Summary

The efficacy and safety of subcutaneous immunotherapy with modified, high-dose, major allergen house dust mite extract is widely supported by double-blind, placebo-controlled studies. However, little is known regarding patient-perceived efficacy and satisfaction.

An observational, retrospective, multicentre study in patients treated with Acaroid® was conducted to assess the efficacy and degree of satisfaction of the patients after the first six months of treatment with it. All the clinical study procedures were performed according to the routine clinical practice.

This study demonstrates that Acaroid® is effective and well tolerated. The patients' condition demonstrated a clear and marked improvement in the first 6 months after treatment initiation. Patients treated with Acaroid® were very satisfied, with a correlation to improvement in patient-perceived symptoms and the administration of treatment by a healthcare professional.

Introduction

The efficacy and safety of subcutaneously administered allergen-specific immunotherapy (AIT) is widely supported by numerous meta-analyses published on both the treatment of bronchial asthma (1-4) and IgE-mediated rhinitis (5). The preventive effect on the natural course of the allergy in patients with rhinitis should also be noted (6-8).

Patient compliance, appropriate patient selection for treatment with AIT and the most appropriate therapeutic extract are vital factors in achieving the desired therapeutic objectives in the event of prolonged treatment over time, as the recommended duration is no less than 3 years (8).

Therefore, given the increasingly active role of patients as health service users (9), it is important that both their perception of efficacy and their expectations, which are based on the information given by the prescriber, are taken into consideration to ensure that satisfaction with the various aspects of their treatment is as high as possible, thereby promoting appropriate adherence to treatment and compliance.

The optimum treatment to maximise patient adherence to treatment should involve the patient's knowledge and expectation regarding the time from treatment initiation to symptom relief, the degree of improvement to be achieved, rapid and evident efficacy, a treatment regimen that is as easy and short as possible and minimal side effects. Patient time and travel are

also two additional factors related to patient-initiated treatment discontinuation (10,11).
Reducing the allergenicity of allergen extracts through chemical modification with aldehydes without affecting their immunogenicity allows physicians to administer a maintenance dose of major allergens at the upper end of the WHO-recommended scale for the most effective results (9).
Double-blind, placebo-controlled studies have shown (12-14) that subcutaneous immunotherapy with modified, high-dose, major allergen house dust mite extract is safe and effective. However, no data is yet available on patient-perceived efficacy and satisfaction with the treatment. Therefore, the objective of this study was to evaluate these aspects in the first year of treatment in the context of the normal clinical practice of the researchers involved.

Methods

Allergen extract composition

Acaroid® (Allergopharma GmbH & Co. KG, Reinbek, Germany), the product tested, is an aluminium hydroxide-adsorbed depot allergoid preparation of standardised high concentrations of powdered diafiltered dust mite allergens modified with formaldehyde and glutaraldehyde. There are two different concentrations: strength A (1,000 TU/ml) and strength B (10,000 TU/ml). The manufacturer-recommended maintenance dose is 0.6 ml of strength B (6,000 TU). Allergens quantified in the final step prior to allergoidisation are 11.66 µg/ml Der p 1, and 10 µg/ml Der p 2 in the 100% *Dermatophagoides pteronyssinus* formulation, and 20 µg/ml Der f 1 and 15 µg/ml Der f 2 in the 100% *Dermatophagoides farinae* formulation.

Study design

An observational, retrospective, multicentre, nationwide study was conducted with 47 investigators from 8 autonomous regions. The study was approved by the ethics committees of the participating hospitals and the Spanish Agency of Medicines and Medical Devices (AEMPS) was notified.
During the observational period, investigators collected data from patients who met the following study inclusion criteria: 5-65 years of age with IgE-mediated rhinitis and/or bronchial asthma caused by house dust mites who had been considered for Acaroid® treatment as part of normal clinical practice and who were seen for follow-up within the first year of treatment for a minimum of 6 months.
To evaluate perceived efficacy, patients assessed their condition on a Visual Analogue Scale of 1 (worst) to 100 (best). Relevant clinical improvement was defined as an increase of at least 20 points compared to the self-assessed score before commencing treatment and at the time of the evaluation (1,15).
A questionnaire including a series of questions grouped into a number of variables was used to determine the degree of satisfaction of patients treated with Acaroid®. The variables included in the questionnaire were: the need for treatment to be administered subcutaneously and for this to be done by a healthcare professional, the impact having to go to the health centre had on subjects' daily routine, the level of improvement in symptoms with treatment and overall satisfaction with treatment. A Likert scale was used to objectively evaluate the questionnaire's variables, with 5 representing most satisfied (16).

Statistical analysis

The estimated sample size was calculated on the basis of the number of investigators involved. As this was an observational, retrospective study, which depended on the feasible number of patients for whom each investigator may consider administration of Acaroid® appropriate in their usual clinical practice, it was not possible for the optimal sample size to be calculated in advance.
A descriptive analysis of all the variables in the patient questionnaire was carried out for the entire sample. Mean and standard deviation (SD) in normally distributed variables were used as statistical descriptions of quantitative variables, and median and interquartile range if distribution was not normal. For the categorical variables, proportions were used. In the bivariate analyses, average-to-average for normally distributed continuous variables and nonparametric tests for non-normal distribution were used. A contingency analysis for categorical variables was carried out. The significance level of the statistics calculated was $p < 0.05$.

Results

Between September and November 2012, data was collected from patients diagnosed with dust mite IgE-mediated rhinitis and/or bronchial asthma who had commenced treatment with Acaroid®. A total of 435 patients were recruited, of whom 130 (29.9%) were paediatric. 420 patients (96.5%) had a diagnosis of rhinitis and 236 (54.2%) had bronchial asthma (**table 1**).

Patient-perceived efficacy

The patients' overall score increased by 33.8 points (from 42.6 to 76.4 points; $p < 0.001$, giving a perceived efficacy of 79.34%), an improvement of between 30 to 50 points for 50.5% of the overall population (220 patients), which was clinically significant (> 20 improvement points) in 362 patients (83.2%).
In the paediatric population, the overall improvement was 35.3

points (42.3 to 77.6 points, p < 0.001, giving a patient-perceived improvement of 83.45%), with an improvement of between 30 to 60 points for 54.61% of the population and over 20% (clinically significant) in 108 patients (83.07% of the total) (**figure 1** and **2**).

Table 1 *- Population demographics.*

	Overall population	**Paediatric**
No.	435 (100%)	130 (30%)
Age		
Range	5-65	5-16
Mean (SD)	24.6 (13)	10.9 (3)
Sex		
Male	204 (46.9%)	88 (67.7%)
Female	231 (53.1%)	42 (32.3%)
Diagnosis		
Rhinitis / rhinoconjunctivitis	420 (96.5%)	123 (94.6%)
Bronchial asthma	236 (54.2%)	77 (60.2%)
Acaroid® composition		
House dust mite mix	262 (60.2%)	87 (68%)
D. pteronyssinus	172 (39.6%)	41 (32%)
D. farinae	1 (0.2%)	

Interpreting the graph: the bars represent the individual improvement for each patient group and the two vertical lines represent the mean pre-treatment and post-treatment score (standard deviation), 42.6 and 76.4 respectively (p < 0.001).
Interpreting the graph: the bars represent the individual improvement reported by each patient group and the two vertical lines represent the mean pre-treatment and post-treatment score (standard deviation), 42.3 and 77.6 respectively (p < 0.001).

Satisfaction questionnaire

Overall patient-satisfaction with the treatment was 4 (out of a maximum of 5 points), with 224 patients being very satisfied (51.5% of the population). No differences were observed in the paediatric sub-population.
The need for treatment to be administered by a healthcare professional was well received by 95.1% (414 patients), which was consistent with the results obtained for the impact having to go to a medical centre for administration had on the subject's daily routine, which was not a drawback for 86.8% (375 subjects).
Although subcutaneous administration was not a significant drawback for 358 patients (82.3%), it was the variable with the lowest satisfaction score.
When study subjects were asked if the treatment had resulted in a potential improvement in their symptoms, 324 of them (75% of total population) reported a clear clinical improvement (**table 2**).
The treatment was well tolerated by 429 patients (98.63% of the population). Six patients overall suspended treatment due to adverse events (1.37%).

Figure 1 *- Overall population satisfaction, mean score pre IT / post IT (SD).*

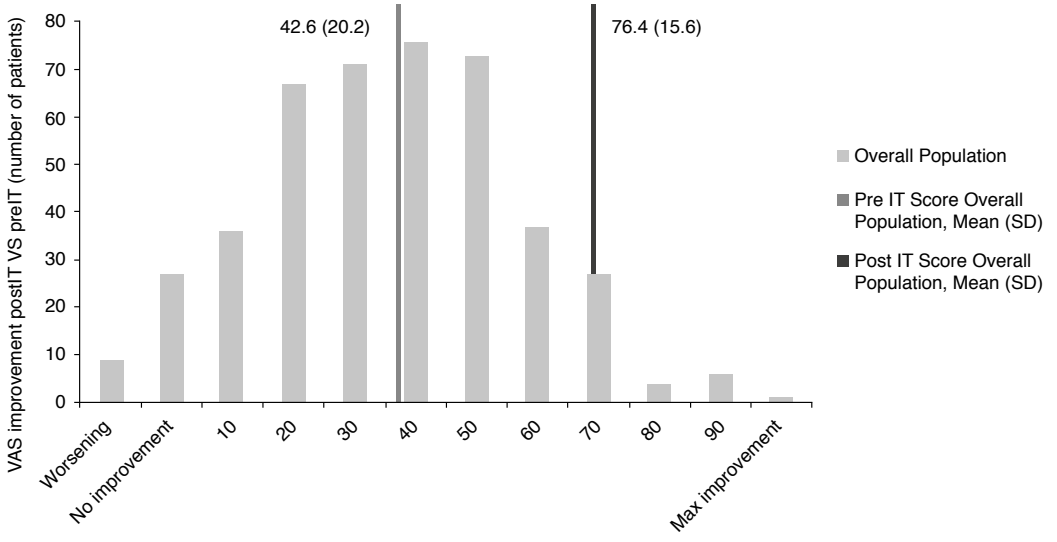

Figure 2 *- Paediatric population satisfaction, mean score pre IT / post IT (SD).*

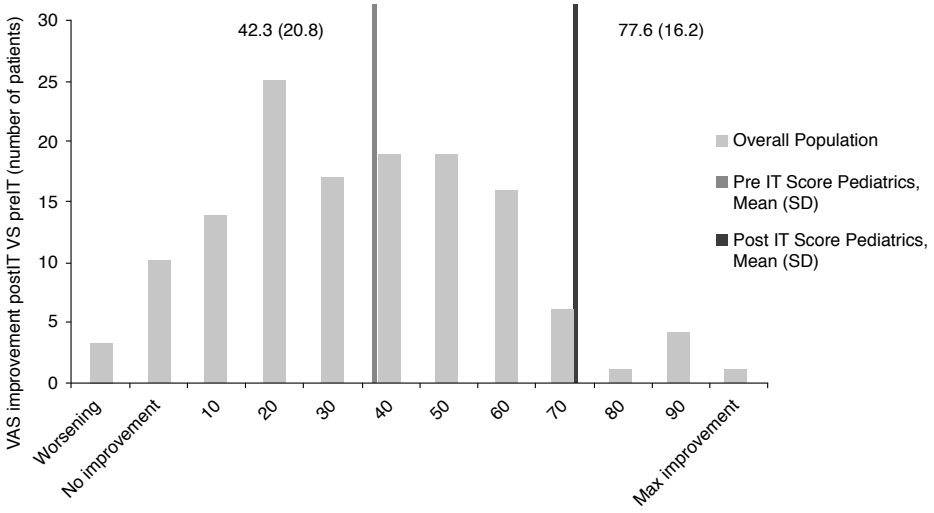

Table 2 *- Patient satisfaction survey results, rating various treatment aspects (scale from 0 to 5).*

	Overall population[1] Mean (SD)	**Paediatrics[1] Mean (SD)**
Healthcare professional administering treatment	4.4 (0.9)	4.5 (0.7)
Improvement in symptoms	4 (0.9)	4 (0.9)
Frequency (the number of visits for treatment to be administered)	3.7 (1.2)	4 (1.1)
Disruption (impact on daily routine)	3.7 (1.2)	4 (1.2)
Subcutaneous administration	3.6 (1.3)	3.6 (1.4)
Physical discomfort following injection	3.4 (1.2)	3.6 (1.2)
Degree of overall satisfaction with treatment	4 (0.9)	4.2 (0.9)

[1]Satisfaction scale from 0 (dissatisfied) to 5 (very satisfied).

Discussion

The objective of this study was to collect data on patient-perceived efficacy, satisfaction with and tolerance to Acaroid® treatment in routine clinical practice in Spain.

This is the first study to be carried out in routine clinical practice in Spain using satisfaction questionnaires and evaluating perceived improvement with treatment of a large sample of adult and paediatric patients diagnosed with rhinoconjunctivitis and/or IgE-mediated bronchial asthma caused by dust mite allergy and treated with allergen-specific immunotherapy using a modified, standardized, high-dose extract of the major *Dermatophagoides* allergens.

During this study, no serological tests were performed or specific medication or symptom scores collected, as both the efficacy and safety of Acaroid® for rhinitis and/or IgE-mediated bronchial asthma caused by hypersensitivity to house dust mites had already been demonstrated previously in double-blind placebo-controlled studies (12-14).

We are aware of the limitations of the retrospective, observational design. However, we would also like to point out that as our intention is to evaluate patient opinion in routine clinical practice, we believe that the study design is conducive to the aforementioned objective.

In this sense, given the importance that patient-perceived efficacy and treatment satisfaction have in achieving adequate patient compliance, we believe that good data on efficacy may provide clinicians with a useful tool for achieving patient compliance in their daily practice. It may be useful not only in terms of short-term efficacy, but also for the ultimate objective of achieving sustained, long-term efficacy and changing the natural course of the allergy.

Reisacher *et al.* reviewed the literature on patient adherence to allergen-specific immunotherapy for allergic disease. They concluded that effective communication between the patient and

the physician, and the simplicity of the regimen were frequently noted to be of primary importance (17).

There is a need to further investigate potential barriers and measures to enhance persistence and compliance in order to increase desired clinical benefits from immunotherapy and reduce overall costs associated with discontinuation (17,18).

One of the drawbacks most commonly associated with subcutaneously-administered specific allergen immunotherapy is having to periodically visit a healthcare professional for administration, and the subsequent impact this has on the patient's daily routine (10). The results obtained lead us to believe that this should not create a barrier to treatment but that the contrary is in fact true: knowing that each visit to the healthcare professional for administration allows them to control the course of their treatment and their health in terms of their allergy could encourage compliance and treatment-adherence, due to the safety and peace of mind it gives each patient. On top of this, delivery and treatment costs could be positioned as barriers for treatment adherence. However, results from a recent study do not appear to detect significant differences in adherence according to delivery route. Further research is required to enable any firm conclusions (11). As for treatment costs, the financial burden of SCIT is an important factor in patients discontinuing treatment (19).

These results are consistent with those presented by Pajno *et al.* (20) in a 3-year follow-up of a group of 2,692 patients, of whom 1,886 received subcutaneous immunotherapy and the rest, sublingual. It was seen that treatment-adherence was greater when administering subcutaneously versus sublingually.

Although the worst aspect for patients, as is to be expected, is the fact that treatment is administered subcutaneously, the results demonstrate that when patients' expectations in terms of efficacy and tolerability are met, this route of administration does not negatively affect target treatment compliance.

The high degree of tolerance obtained by the treatment, observed in 98.63% of patients, confirms the safety data demonstrated in earlier studies using this same therapeutic extract (12-14,21).

Although the study objective was not to compare data on perceived efficacy and satisfaction in adult and paediatric patients, we consider that a paediatric sub-population of 29.9% of the total population (130 patients) merited particular reference to the results of this subpopulation.

The degree of satisfaction is positively correlated to improvement in patient-perceived symptoms and the administration of treatment by a healthcare professional.

Matricardi *et al.* (22) recently published a comparative review of several meta-analyses in which they included at least 5 randomised, double-blind, placebo-controlled studies with the aim of evaluating the short-term efficacy of both symptomatic and allergen-specific medication. They concluded that, in the first pollen-season following commencement of immunotherapy, based on the nasal symptom score, allergen-specific immunotherapy was at least as effective as the symptomatic treatment available for patients with allergic rhinitis.

Conclusion & future perspective

In long-lasting treatments, two key factors for a successful outcome are patient compliance, and in relation, good patient satisfaction and patient-perceived effectiveness in the early stages of the treatment.

The results obtained in this study demonstrate how subcutaneous immunotherapy with high-dose modified house dust mite allergens is effective and well tolerated in an allergist's daily practice. The patients' condition demonstrated a clear and marked improvement in the first 6 months following commencement of treatment. Overall, patient satisfaction with Acaroid® treatment is in the range of very satisfied. The patients' overall perceived efficacy score increased by 33.8 points and 35.3 for the overall and paediatric population respectively.

The results shown here indicate a very good perspective in terms of efficacy and patient perception in the treatment of allergies. It is really remarkable that after 6 months of treatment the patient perceives an improvement of symptoms, which promotes greater adherence to treatment, with better prospects for treatment and preventing relapse. Further studies with a special focus on patient adherence and therapeutic compliance, with a longer follow-up, and linking the perceived short-term efficacy in routine clinical practice are needed.

Conflict of interest

Merck's Medical Affairs Department, represented by N. Cancelliere and J. Álvarez Nieto, has been actively involved in the elaboration of the manuscript. However, this collaboration has not influenced at any point the data presented in the study.

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