

Efficacy of Injection Immunotherapy with Ragweed and Birch Pollen in Elderly Patients

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Key Words

Birch pollen · Elderly patients · Immunotherapy ·
Ragweed pollen · Respiratory allergy

Abstract

Background: The role of specific immunotherapy (SIT) in elderly allergic patients is still debated. **Objective:** The aim of this study was to assess whether SIT is associated with a better control of symptoms and a better quality of life also in older allergic patients. **Methods:** The effect of injection SIT was assessed in 39 patients [age >54 years, median 59; 29 patients (74%) with asthma, otherwise healthy] monosensitized to birch (n = 20) and ragweed (n = 19). Thirty-three younger subjects [age <50 years, median 35; 26 patients (79%) with asthma, otherwise healthy] monosensitized to birch (n = 10) and ragweed (n = 23), and 37 subjects >54 years old (25 males/12 females; age 55–79 years, median 59 years) monosensitized to birch (n = 18) and ragweed (n = 19) who refused to undergo SIT were enrolled as positive and negative controls, respectively. All groups had a disease duration <10 years; the disease was inadequately controlled with standard drug therapies in all cases. SIT was carried out using the same extracts and was administered using a

perennial schedule both in patients and controls. Seasonal therapies were the same in all groups and were not changed after SIT was started. After 1–5 years of SIT, patients and controls were asked to quantify symptom reduction on a visual analogue scale: reductions >50% were considered significant. Moreover, the use of cetirizine and/or salbutamol as an adjunct to standard therapies during the last pollen season was assessed as an objective measure of SIT outcome. **Results:** 37/39 (95%) patients versus 32/33 (97%) controls submitted to SIT reported a symptom reduction >50% after 1–5 years of SIT (nonsignificant). The median clinical efficacy of SIT was 80% in both groups (nonsignificant). 27/37 controls not submitted to SIT did not report any change in symptom severity at the follow-up visits, whereas 10/37 reported a more severe disease (4 subjects reported the appearance of seasonal asthma) ($p < 0.001$ vs. patients submitted to SIT). Patients used less frequently cetirizine ($p < 0.001$) and/or salbutamol ($p < 0.05$) than controls not submitted to SIT. **Conclusion:** Injection SIT can be considered an effective therapeutic option in otherwise healthy elderly patients with a short disease duration whose symptoms cannot be adequately controlled by drug therapies alone.

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Introduction

Allergic rhinitis and asthma are common disorders affecting 15–20% of the general population at any age. Injection allergen-specific immunotherapy (SIT) is an established means for the treatment of airborne allergies; its efficacy and long-term effect in reducing allergic symptoms have been shown by a number of studies [1–5]. However, whether SIT may be considered as a therapeutic option also in older patients is still debated. Position papers by the World Health Organization and the European Academy of Allergology and Clinical Immunology suggest that SIT should be started early in the disease process [1, 2] as the clinical response to the treatment in patients showing chronic, irreversible changes of the airways is poor [5, 6]. As a consequence, older patients with long-standing allergic disorders have been excluded from most studies of immunotherapy, and SIT is generally not considered a therapeutic option in these subjects. Clearly, otherwise healthy elderly allergic patients with short disease duration would be ideal to investigate the effects of SIT in the elderly.

During the last decades, the area of North of Milan was first colonized by birch [7, 8] and, more recently, by ragweed [9, 10]. The appearance of these two 'new' airborne allergens was followed by a striking, progressive increase in allergic sensitization to these pollens. Most newly sensitized patients did not show a family or personal history of allergic disorders, and their mean age was much older than that of subjects sensitized to other airborne allergens [11]. About 20% of these patients were older than 45 years at the onset of their allergic disorder, and in some cases allergy appeared in subjects >70 years old [11]. Due to the severity of allergic symptoms, many of these patients were unable to control adequately their disease with standard therapies and underwent injection SIT. The present study reports the effect of injection SIT in this particular subgroup of patients compared with younger patients also submitted to injection SIT and a group of age-matched controls not submitted to the treatment, all routinely followed up at this allergy center. The goal of the study was to assess whether SIT is associated with a better control of symptoms and better quality of life in older allergic patients.

Patients and Methods

Patients

Consecutive patients submitted to injection SIT fulfilling the following criteria were studied: (1) age >54 years at the beginning of SIT; no history of cigarette smoking, and otherwise healthy; (2) monosensitization to one airborne allergen, defined as the presence of a single positive skin prick test among grass, pellitory, ragweed, mugwort, plantain, birch, olive, cypress, house dust mite, *Alternaria*, *Aspergillus*, *Cladosporium*, *Candida*, dog dander, and cat dander (Allergopharma, Reinbek, Germany); (3) allergic symptoms (rhinoconjunctivitis with or without asthma) in keeping with the results of the skin prick test; (4) disease duration <10 years, and (5) inadequate control of symptoms and/or poor quality of life with standard therapies and frequent use of rescue therapy (anti-histamines and/or salbutamol).

39 patients (18 males/21 females, aged 55–72 years, median 59 years) monosensitized to birch ($n = 20$) and ragweed ($n = 19$), respectively, were finally studied. 29/39 (74%) patients had seasonal asthma. Therapies were not changed after the start of injection SIT. Patients were reevaluated in spring 2004 (ragweed) or in June 2004 (birch) after 1 ($n = 4$), 2 ($n = 12$), 3 ($n = 15$), 4 ($n = 7$) or 5 ($n = 1$) years of SIT.

Specific Immunotherapy

All patients underwent injection SIT with commercial depot aluminum-hydroxide-adsorbed birch or ragweed pollen extracts by different manufacturers: Allergopharma ($n = 28$), Pangramin (ALK-Abello, Lainate, Italy, $n = 5$), Stallergenes (Anthony, France, $n = 4$) and Lofarma (Milan, Italy, $n = 2$). SIT was administered following a perennial schedule: maintenance doses were reduced by half during the pollen season (from the end of February to mid-May for birch; from mid-August to the end of September for ragweed). Weekly doses were given during the 'build-up' (induction) phase in order to reach the planned maintenance dose which was 1.0 ml of the final vial in all cases. However, in practice this dose could not be achieved in all patients, and subjects were therefore maintained on the highest tolerated dose that did not elicit side effects. It has been proposed that this corresponds to the optimal dose for SIT [1]. Maintenance doses were given at 3-week intervals.

Controls

Two groups of controls were enrolled. Thirty-three subjects <50 years old (17 males/16 females; age 16–50 years, median 35 years) monosensitized to birch ($n = 10$) and ragweed ($n = 23$), fulfilling the same admission criteria as the patient group, represented the positive control group. 26/33 (79%) suffered from seasonal asthma. These patients underwent SIT with the same commercial extracts and following the same schedule as the older patients. Effectiveness of SIT was similarly assessed after 1 ($n = 6$), 2 ($n = 12$), 3 ($n = 11$), 4 ($n = 3$) or 5 ($n = 1$) years of treatment.

Thirty-seven subjects >54 years old (25 males/12 females; age 55–79 years, median 59 years) monosensitized to birch ($n = 18$) and ragweed ($n = 19$), fulfilling the same admission criteria as the patient group, who refused to undergo SIT were enrolled as negative control group (without SIT treatment). 14/37 (38%) suffered from seasonal asthma at the beginning of the follow-up period. These subjects were given the same therapies and were reevaluated 2 ($n = 21$) or 3 ($n = 16$) years after the first visit.

Table 1. Comparative analysis of patients and controls submitted to SIT

	Patients (n = 39)	Controls (n = 33)	p
Asthma	29 (74%)	24 (79%)	NS
Disease duration, years	2–10 (median 3)	2–10 (median 3)	NS
SIT duration, years	1–5 (median 3)	1–5 (median 2)	NS
Responders to SIT	37 (95%)	32 (97%)	NS
Median efficacy of SIT on VAS, %	80%	80%	NS

NS = Nonsignificant; VAS = visual analogue scale.

Table 2. Comparative analysis of cetirizine and salbutamol use in patients and controls

	A	B	C	A vs. B	A vs. C
Patients using anti-histamines, n/total	29/39 (74%)	27/33 (82%)	33/37 (89%)	NS	NS
Median time under anti-histamines, days (range)	4 (1–40)	4 (1–8)	17 (2–45)	NS	<0.001
Asthmatics that used salbutamol, n/total	10/29 (34%)	10/26 (38%)	13/14 (93%)	NS	<0.01
Median time under salbutamol, days (range)	2.5 (1–40)	2.5 (1–6)	7 (2–13)	NS	<0.05

A = Patients; B = controls submitted to SIT; C = controls not submitted to SIT; NS = nonsignificant.

Therapy

All patients and controls were given a standard therapy including nasal corticosteroids (fluticasone, mometasone or budesonide) once daily and cromolyn sodium eyedrops three times daily, plus oral anti-histamines (cetirizine 10 mg once a day) on demand throughout the pollen season (from the end of February to mid-May for those allergic to birch pollen, and from mid-August to the end of September for those allergic to ragweed); during the same periods patients with a history of asthma took inhaled long-acting β -agonists + steroids as dry powder 2 times daily, and were allowed to add short-acting β -agonists (salbutamol) on demand. Patients and controls were asked to record the use of rescue therapy (cetirizine and/or salbutamol) on a standardized calendar.

SIT Outcome Measure

Subjective Measure. At the follow-up visits, both patients and controls were asked to compare symptom severity to baseline (considered as 100%) as worse/unchanged, or better; in this case patients were asked to quantify symptom reduction on a visual analogue scale: only reductions equal or better than 50% were considered significant. In their evaluation, patients were asked to consider frequency, duration, and severity of the following symptoms: (1) nose: blockage; sneezing or runny nose [12]; (2) eye: itch, watery eye or swollen [12], and (3) asthma: shortness of breath or chest constraint.

Objective Measures. The frequency of use of cetirizine and/or salbutamol during the last pollen season was recorded by patients and controls and served as a measure of disease control.

Statistical Methods

Due to the skewed distribution, disease duration and efficacy of SIT were compared by non-parametric means using the Mann-Whitney U test. Proportions were compared by two-tailed χ^2 test with Yates' correction.

Results

The clinical data of patients and controls submitted to SIT are compared in table 1. Apart from age, the two populations did not show any significant baseline difference. After 1–5 years of injection SIT, 37/39 (95%) patients and 32/33 (97%) controls reported a symptom reduction >50% (nonsignificant). The median clinical efficacy of SIT was 80% in both groups (nonsignificant). Neither a difference in baseline features nor in outcome was observed between patients allergic to birch or ragweed pollen (data not shown). Clinical efficacy of injection SIT was already apparent after only 1 year of treatment, and the only 2 non-responder patients had undergone SIT for 3 years.

Patients and controls not submitted to SIT did not show baseline differences apart from the prevalence of asthma that was higher in patients [29/39 (74%) vs. 14/37 (38%); $p < 0.01$]. At the follow-up visits, symptom severity had not changed in 27/37 control subjects, and had worsened in 10/37 cases (4 subjects reported the appearance of seasonal asthma); no control subjects reported a spontaneous reduction in the severity of respiratory symptoms ($p < 0.001$ by comparison with patients submitted to SIT).

The use of cetirizine and/or salbutamol by patients and controls is shown in table 2. Patients and controls submitted to SIT did not differ in the use of both drugs during

the last pollen season. A similar proportion of patients and controls not submitted to SIT used cetirizine during the pollen season, but the former used the drug much less frequently (median 4 vs. 17 days, respectively; $p < 0.001$). Only 10/29 (34%) asthmatic patients versus 13/14 (93%) asthmatic controls not submitted to SIT had to take salbutamol to gain a better control of their disease ($p < 0.01$); moreover, patients used the drug less frequently than controls (median 2.5 vs. 7 days, respectively, $p < 0.05$).

Discussion

Very few studies specifically addressing the efficacy of SIT in the elderly can be found in the medical literature. This is probably due to the fact that the majority of allergic patients diagnosed and followed up at the various allergy centers are young, and that in most cases older patients have long-lasting diseases that are unlikely to respond to desensitizing treatment [5, 6]. Nonetheless, in a study carried out in Florida, otherwise healthy patients >60 years and controls <60 years showed a similar, favorable response to SIT, suggesting that age alone should not be a decision factor in the initiation of SIT in the elderly [13]; unfortunately, in that study disease duration was not reported. The de novo sensitization of a number of otherwise healthy, elderly subjects without a history of allergy that occurred in this geographical area following the appearance of birch and ragweed pollen [11] represented an ideal situation to evaluate the role of injection SIT in elderly patients. This open study clearly shows that in these patients SIT is equally effective as in younger ones.

A double-blind, placebo-controlled study would have probably been a stronger argument in favor of SIT in elderly patients. However, this analysis was carried out within the normal practice of this allergy center; in view of the well-established effectiveness of SIT, the inclusion of an age-matched group of severely allergic controls given injection placebo treatment would have raised a number of ethical problems, and would not have been easily accepted by the patients, too. To overcome these problems, age-matched subjects not willing to undergo SIT served as controls. Most of these subjects did not observe any change in the severity of their respiratory allergy during the follow-up period, and several of them reported a worsening of their clinical condition. On the contrary, patients submitted to SIT reported a much better quality of life and an improved symptom control by standard therapy, as shown by the reduced use of cetirizine and salbutamol, and by the fact that most of them reported the disappearance of asthma. On the basis of these findings, injection SIT should be considered as a therapeutic option in elderly patients, given that they are otherwise healthy and show a reasonably short disease duration. Further studies will be needed to investigate whether immunologic changes induced by SIT in elderly patients are identical to those observed in younger subjects.

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