

Children's compliance with allergen immunotherapy according to administration routes

To the Editor:

Allergen-specific immunotherapy is the only causal treatment for allergic subjects that is recognized to be effective¹ and to offer long-lasting results.² In children, immunotherapy has been shown to prevent new sensitizations.³

Subcutaneous immunotherapy (SCIT) has been long considered as the only way of giving this treatment, but more recently, other administration routes have been used, and today sublingual immunotherapy (SLIT) and local nasal immunotherapy (LNIT) represent other viable treatment options.^{4,5}

However, immunotherapy in any form requires commitment by the patient, which makes compliance issues particularly relevant. Nonetheless, thus far little attention has been paid to this aspect, with only a few compliance studies on SCIT^{6,7} and SLIT⁸ but no data on LNIT.

This study aims to prospectively investigate the compliance to treatment for these 3 methods of delivering immunotherapy by collecting data on the dropout rate among 2774 children aged 6 to 15 years who had allergic rhinitis, allergic asthma, or both for at least 1 year and were prescribed immunotherapy for only 1 allergen.

All the selected patients were divided into 3 groups according to the immunotherapy administration route used: group A consisted of 1886 patients who underwent SCIT, group B consisted of 806 patients who received SLIT, and group C consisted of 82 subjects who received LNIT.

The entire program of allergen immunotherapy in its different forms (and routes) was conducted in the period from 1998 through 2003 under controlled conditions,

either in a hospital setting (1234 patients) or in a private medical office setting (1540 patients).

All children were from Sicily and Calabria (South of Italy). The families of Calabrian children bore full cost of vaccines. Those of Sicilian children received a total reimbursement by the local government health service to buy the vaccines and for hospital treatments but not for private medical office treatments (allergy shots).

Immunotherapy was performed in the buildup phase according to the schedules suggested by the manufacturers and then, during the maintenance phase, at monthly intervals regarding SCIT and again according to the manufacturers regarding SLIT and LNIT (from 1 to 7 weekly administrations).

The extracts used for SCIT were from ALK-Abellø (Hørsholm, Denmark: Pangramin and Alutard SQ), from Stallergènes (Antony, France: Phostal), from Merck (Allergopharma, Joachim Ganzer-Hamburg, Germany), and from Lofarma (Milan, Italy). For SLIT, they were from Stallergènes (Staloral), from ALK-Abellø (Pangramin SLIT), from Lofarma (Lais), from Merck, and from Anallergo (Firenze, Italy). For LNIT, only Allerkin (Lofarma) was used.

A control visit was scheduled with a 4-month interval for the overall study duration (ie, 3 years for immunotherapy and up to 2 years after its discontinuation).

At each visit, the physician attending each patient collected the specifically designed charts filled in during the preceding months and registered the time of every interruption.

When SCIT was used, the date of stopping treatment was transcribed from the individual immunotherapy chart. Regarding SLIT and LNIT, when unclear data were discovered, the children's families were contacted to clarify the proceeding of the immunotherapy schedule. The major criterion for the definition of noncompliance

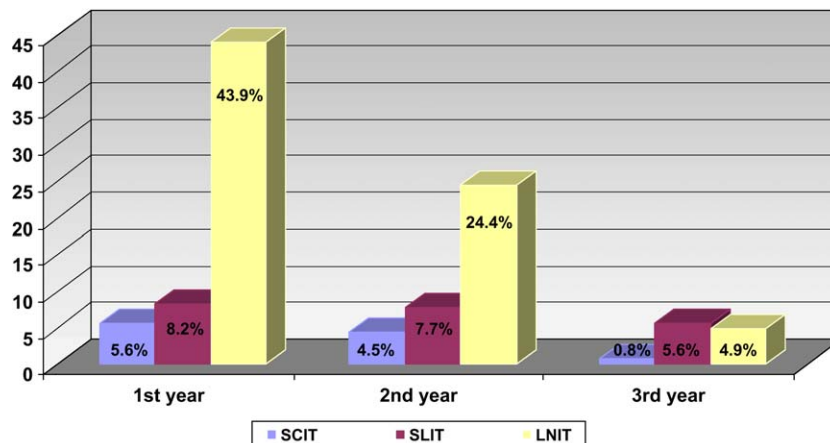


FIG 1. Percentages of patients who withdrew treatment during the first, second, and third year among those who underwent SCIT, SLIT, and LNIT.

TABLE I. Reasons for immunotherapy withdrawals in the 3 groups of subjects who underwent immunotherapy administration by means of SCIT, SLIT, or LNIT

	SCIT	SLIT	LNIT
Ineffective	13.0%	24.9%	18.3%
Expensive	39.6%	36.4%	13.3%
Unpleasant	8.7%	5.8%	56.6%
Time consuming	24.2%	17.9%	3.5%
Family problems	14.5%	15.0%	8.3%

was stopping immunotherapy without the authorization of the prescribing physician.

The patients who withdrew immunotherapy before the planned period of 3 years from the start of immunotherapy were considered noncompliant. In the whole study population, 440 (15.9%) of 2774 patients were considered noncompliant.

In terms of compliance, no significant differences were found between the patients followed in a hospital setting (87.2%) and those followed in a private medical office setting (81.7%).

The percentage of noncompliant individuals was significantly higher in group C (LNIT, 73.2%) with respect to both group B (SLIT, 21.5%; $\chi^2 = 10.28$, $P < .005$) and group A (SCIT, 10.9%; $\chi^2 = 25.92$, $P < .0005$). The percentage of noncompliant patients in group A was also significantly lower than in group B ($\chi^2 = 17.1$, $P < .0005$).

In groups A and B only 6.4% of patients withdrew immunotherapy very early (ie, during the first 12 months), whereas in group C the prevalence of patients who withdrew immunotherapy throughout the first 12 months was significantly higher (43.9% vs 6.4, $P < .0005$).

Times at treatment withdrawal in the 3 groups during the overall 3-year period are analytically illustrated in Fig 1. Reasons for immunotherapy withdrawal in the 3 groups, as determined from specific interviews with the patients' parents, are summarized in Table I.

The most common cause for treatment withdrawal both in groups A and B was the cost. For group B, another common reason for stopping immunotherapy was represented by an insufficient effectiveness. In Group C, the preponderant reason was represented by the discomfort for the repeated nasal reactions, which explains the very early interruption of immunotherapy in 43.9% of the patients belonging to this group. Therefore the nasal route of administration, even though scientifically demonstrated as effective, does not represent in practice an advisable option for immunotherapy.

In summary, SCIT, although expensive and time consuming, is considered to date the most suitable immunotherapy form and route of administration in children and adolescents. SLIT, however, is well accepted by more than three quarters of the patients.

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Plasma mannan-binding lectin levels and activity are increased in allergic patients

To the Editor:

The present report documents the presence of increased plasma levels of functionally active mannan-binding lectin (MBL) and their association with clinical markers in patients with respiratory allergic diseases. Respiratory allergic disorders, such as asthma and allergic rhinitis, result from a systemic inflammatory reaction triggered by allergens in genetically susceptible hosts. In addition to IgE- and T_H2-mediated events, a pathogenic role of complement pathways and their activation products C3a and C5a has been implicated in asthma and allergic inflammation.¹ Earlier studies showed the activation of