Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

RESEARCH LETTER

OPEN ACCESS

Change of administration route of allergen immunotherapy: Rates and causes

Cristina Rivas-Juesas, Ana Delgado Vicente

Paediatrics Department, Sagunto Hospital, Port de Sagunt, Valencia, Spain

Received 8 August 2024; Accepted 21 November 2024
Available online: 1 March 2025

KEYWORDS
allergen immunotherapy;
administration route;
subcutaneous immunotherapy;
sublingual immunotherapy;
treatment adherence;
respiratory allergy

Abstract
Allergen immunotherapy (AIT) has shown efficacy in the short and the long term in the management of allergic respiratory diseases, and it's administered subcutaneously (subcutaneous immunotherapy, or SCIT) or sublingually (sublingual immunotherapy, or SLIT), being both effective and safe options.

Introduction

Allergen immunotherapy (AIT) has shown efficacy in the management of allergic respiratory diseases in the short and the long term, and it is administered subcutaneously (subcutaneous immunotherapy, or SCIT) or sublingually (sublingual immunotherapy, or SLIT). Both SLIT and SCIT are effective in managing allergic rhinitis in children, but SLIT offers advantages in terms of safety and convenience, which may make it a more suitable mode of treatment in pediatrics.[1]

To obtain the best results, treatment adherence for a minimum of 3 years is very important.[2,3] However, the adherence described across studies differs widely depending on the population under study, the allergen, patients' age, and the route of administration.[4,5]

The change in the route of administration requested by patients is not only because of personal preferences, but it may also improve treatment adherence, as patients request for this change to continue taking the medication. For this reason, this study analyzed the rates of change of the route of administration requested by pediatric patients, and its causes.

This is a retrospective, descriptive study in patients aged below 15 years with allergic rhinoconjunctivitis, with or without associated asthma, who started AIT between January 1, 2019, and December 31, 2021, in the Pediatric Service of Sagunto Hospital, Valencia, Spain. To

*Corresponding author: Cristina Rivas- Juesas, Paediatrics Department, Sagunto Hospital, Port de Sagunt, Valencia, Spain. *Email address*: crisrijue@gmail.com

https://doi.org/10.15586/aei.v53i2.1196

be included in the study, patients had to attend follow-up visits for at least 1 year. The study protocol was approved by the Research Ethics Committee of Sagunto Hospital. The requirement for informed consent was waived because of the retrospective nature of the study. All patients who reported a desire to change the route of administration were included in the analysis during the study period; no patients were excluded.

The hospital's electronic medical records were accessed to collect patient epidemiological and clinical data, AIT administration routes at the start and end of treatment, duration of treatment, and causes provided by patients for the change in the administration route of AIT. In the case of pollens, all treatments were administered perennially, except for grass pollens, where a pre-co-seasonal approach was used with a type of tablet. These causes were grouped into the following categories: patient perception of lack of efficacy, disagreement with the posology, psychological rejection of treatment administration, forgetfulness to take the medication, undesired adverse effects, cost of therapy, and others.

Quantitative variables were presented as the mean and standard deviation (SD), or the median and range. Qualitative variables were described as frequencies and percentages. All analyses were performed using the SPSS software, version 21.

A total of 807 patients who started treatment with AIT were included in the study. Patient baseline characteristics are summarized in Table 1. Mean (SD) age of these patients was 8.1 (2.6) years, they predominantly males, and most presented with asthma and rhinoconjunctivitis. Initially, about five out of six patients (83.3%) were prescribed SCIT, and the rest were prescribed SLIT (16.6%), mainly drops.

However, 35 (4.3%) patients requested for a change in the route of administration of the AIT initially prescribed to them, which corresponded to 6 SCITs and 29 SLITs (drops in almost all cases). Mean (SD) age was 9.8 (2.7) years, and they were mainly male patients. Most patients presented with rhinoconjunctivitis alone, and about half were polysensitized to different environmental allergens. Most AITs prescribed to these patients contained house dust mites (Table 1). It should also be noted that, in 23 (65.7%) cases, the change in the route of administration was requested by the patient's parents within a median (range) of 6 (3–24) months after the prescription of the AIT.

Figure 1 summarizes the reasons why these 35 patients chose to change the route of administration of the AIT. In the case of patients initially prescribed with SCIT, the main cause was the occurrence of adverse effects (especially pain) after administration, followed by fear or phobia of needles. In the case of patients initially prescribed with SLIT, the main reason for requesting a change in the route of administration was the excessive number of times they forgot to take the medication, followed by undesired adverse reactions in the oral cavity. Only one patient wanted to change SLIT to SCIT because of the higher price of the former.

Several and varied retrospective studies were performed to assess AIT adherence and persistence because of the variability in the design, geographical location, and studied populations. For this reason, tools have been developed to measure adherence in retrospective studies, in an attempt to increase their validity.[6] However, in our study, the measurement of the effect was the change of administration route, not the discontinuation of treatment. The change in the route of administration was directly associated with lack of adherence in the case of the sublingual route because the need to take SLIT daily was the main reason for patients requesting for the change.

Table 1 Baseline characteristics of all study patients and those who asked for a change in the route of administration (RA) of allergen immunotherapy (AIT).

	All patients (N=807)	Patients changing AIT RA (N=35)
Demographic characteristics		
Age (years), *mean (SD)*	8.1 (2.6)	9.8 (2.7)
Sex (women), *N (%)*	363 (45.0)	11 (31.4)
Clinical characteristics, *N (%)*		
Allergy symptoms		
Asthma	86 (10.7)	2 (5.7)
Rhinoconjunctivitis	135 (16.7)	19 (54.3)
Asthma and rhinoconjunctivitis	586 (72.6)	14 (40.0)
Type of allergy sensitization		
Monosensitized	323 (40.0)	19 (54.3)
Polysensitized	484 (60.0)	16 (45.7)
AIT at baseline		
Composition		
House dust mites	524 (64.9)	29 (82.9)
Pollens	160 (19.8)	6 (17.1)
Olive	70 (8.7)	3 (8.6)
Parietaria	28 (3.5)	2 (5.7)
Grass	28 (3.5)	1 (2.9)
RA and dosage form		
SCIT	676 (83.8)	6 (17.1)
SLIT	131 (16.2)	29 (83.0)
Drops	79 (9.8)	27 (77.1)
Tablets	52 (6.4)	2 (5.7)

SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

Regarding the sublingual route, most changes requested in our study corresponded to the prescription of drops, suggesting that sublingual tablets may offer better tolerance and adherence.

With respect to the population, the patients requesting a change were mainly adolescents or pre-adolescents, which is consistent with the reviewed literature that indicates better compliance among younger children as they are supervised by their parents or caregivers.[7]

On the other hand, price is a major deterrent in the continuing of AIT.[8] This is not the case in our study, as most patients had full or partial funding for AIT.

In summary, our results indicate that, in a pediatric population, there was less adherence for SLIT than SCIT, mainly because of the forgetfulness to take the medication on a daily basis but also due to local reactions. However, changes associated with sublingual tablets were much fewer in relation to sublingual drops.

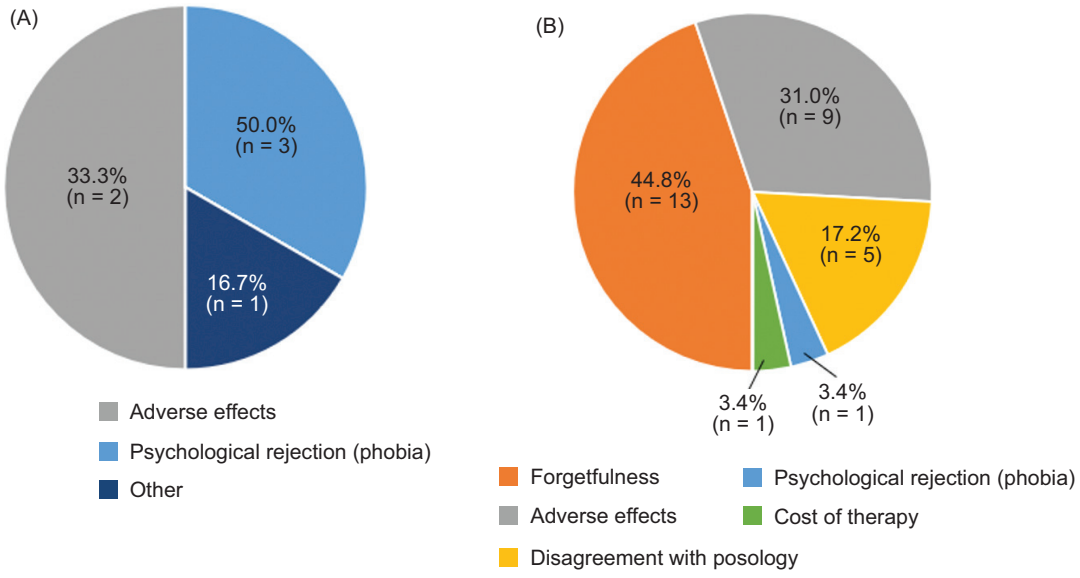

Figure 1 Causes of change of administration route of subcutaneous (A) and sublingual (B) immunotherapies.

Authors Contribution

Cristina Rivas Juesas: design, data collection, and article writing. Ana Delgado Vicente: data collection and article review.

Conflicts of Interest

Cristina Rivas Juesas declares the following conflicts of interest:

- Has been part of a pediatric advisory board for ALK.
- Has participated in symposiums organized by ALK, Allergopharma, and Allergy Therapeutics.
- Has been a paid speaker at educational courses or meetings organized by LETI Pharma, Diater, ALK, Merck, and Novartis.

Ana Delgado Vicente declares no conflicts of interest.

Funding

This work was awarded by the BEC-AT/SEICAP2023 program promoted by Allergy Therapeutics Iberica SL, Barcelona, Spain, for medical writing assistance provided by the i2e3 team (Alba Rebollo, PhD).

References

1. Yang J and Lei S. Efficacy and safety of sublingual versus subcutaneous immunotherapy in children with allergic rhinitis: A systematic review and meta-analysis. Front. Immunol. 2023 Dec 15;14:1274241. https://doi.org/10.3389/fimmu.2023.1274241
2. Muraro A, Roberts G, Halken S, Agache I, Angier E, Fernandez-Rivas M, et al. EAACI guidelines on allergen immunotherapy: Executive statement. Allergy [Internet]. 2018 Apr 1 [cited 2024 Mar 11];73(4):739-43. https://doi.org/10.1111/all.13420
3. Gehrt F, Xu Q, Baiardini I, Canonica GW, Pfaar O. Adherence in allergen immunotherapy: Current situation and future implications. Allergol. Sel. [Internet]. 2022 Dec 1 [cited 2024 Mar 11];6(12):876-84. Available from: https://doi.org/10.5414/ALX02318E
4. Senna G, Caminati M, Lockey RF. Allergen immunotherapy adherence in the real world: How bad is it and how can it be improved? Curr. Treat. Options Allergy [Internet]. 2015 Mar 1 [cited 2024 Mar 11];2(1):39-53. https://doi.org/10.1007/s40521-014-0037-6
5. Baiardini I, Novakova S, Mihaicuta S, Oguzulgen IK, Canonica GW. Adherence to treatment in allergic respiratory diseases. Expert Rev. Respir. Med. [Internet]. 2019 Jan 2 [cited 2024 Mar 11];13(1):53-62. https://doi.org/10.1080/17476348.2019.1554438
6. Pfaar O, Devillier P, Schmitt J, Demoly P, Hilberg O, DuBuske L, et al. Adherence and persistence in allergen immunotherapy (APAIT): A reporting checklist for retrospective studies. Allergy [Internet]. 2023 Aug 1 [cited 2024 Mar 11];78(8):2277-89. https://doi.org/10.1111/all.15723
7. Vogelberg C, Brüggenjürgen B, Richter H, Jutel M. Real-world adherence and evidence of subcutaneous and sublingual immunotherapy in grass and tree pollen-induced allergic rhinitis and asthma. Patient Prefer Adherence [Internet]. 2020 [cited 2024 Mar 11];14:817-27. https://doi.org/10.2147/PPA.S242957
8. Liu W, Zeng Q, He C, Chen R, Tang Y, Yan S, et al. Compliance, efficacy, and safety of subcutaneous and sublingual immunotherapy in children with allergic rhinitis. Pediatr. Allergy Immunol. [Internet]. 2021 Jan 1 [cited 2024 Mar 11];32(1):86-91. https://doi.org/10.1111/pai.13332