

Adherence issues related to sublingual immunotherapy as perceived by allergists

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Objectives: Sublingual immunotherapy (SLIT) is a viable alternative to subcutaneous immunotherapy to treat allergic rhinitis and asthma, and is widely used in clinical practice in many European countries. The clinical efficacy of SLIT has been established in a number of clinical trials and meta-analyses. However, because SLIT is self-administered by patients without medical supervision, the degree of patient adherence with treatment is still a concern. The objective of this study was to evaluate the perception by allergists of issues related to SLIT adherence.

Methods: We performed a questionnaire-based survey of 296 Italian allergists, based on the adherence issues known from previous studies. The perception of importance of each item was assessed by a VAS scale ranging from 0 to 10.

Results: Patient perception of clinical efficacy was considered the most important factor (ranked 1 by 54% of allergists), followed by the possibility of reimbursement (ranked 1 by 34%), and by the absence of side effects (ranked 1 by 21%). Patient education, regular follow-up, and ease of use of SLIT were ranked first by less than 20% of allergists.

Conclusion: These findings indicate that clinical efficacy, cost, and side effects are perceived as the major issues influencing patient adherence to SLIT, and that further improvement of adherence is likely to be achieved by improving the patient information provided by prescribers.

Keywords: adherence, sublingual immunotherapy, efficacy, cost, side effects

Background

Sublingual immunotherapy (SLIT) is currently accepted as a viable alternative to subcutaneous immunotherapy (SCIT) to treat allergic rhinitis and asthma,¹ and is widely used in clinical practice in many European countries. The clinical efficacy of SLIT has been established in a number of clinical trials and meta-analyses,² and its safety profile has been reported to be satisfactory in adults and children using high allergen doses.³ However, because SLIT is self-administered by patients without medical supervision, assessment of adherence to treatment is still a concern, although the advantage of home administration does remove one of the main causes for no adherence, ie, the need to go to a physician's office for treatment, which was previously the case with SCIT.⁴ The first studies of SCIT in the 1990s reported an adherence rate of about 50%, with better rates (up to 75%) subsequently found using less demanding injection schedules.⁴ With SLIT, higher adherence rates of up to 90% have been described.⁴

Adherence is commonly defined as the extent to which the patient's behavior matches the treatment recommendations from the prescriber⁵ and is essential for the success of any medical treatment, especially for chronic diseases, such as rhinitis and asthma. Medication intake can be assessed using several direct or indirect methods. Direct methods,

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which measure the concentration of a specific drug in blood or urine, cannot be used for assessment of SLIT adherence. Indirect methods require periodic counting of leftover doses or use of questionnaires in which patients report the amount and frequency of drug intake. Considering the recent literature, adherence to SLIT in clinical trials and postmarketing surveys would appear overall to be satisfactory, ranging from 75% to 90%,^{6–8} with inconvenience and cost of treatment being the main causes for nonadherence. All these studies focused on patients, but the role of physicians must not be overlooked, because their attitude towards a treatment influences the information they provide to patients when prescribing SLIT in their everyday clinical practice which, in turn, may influence patient adherence. For example, insufficient information on the common side effects of SLIT, such as local reactions in the mouth, may lead to unnecessary treatment modification and even to withdrawal.⁹ The present questionnaire-based survey sought the opinions of Italian allergists on SLIT adherence.

Methods

A multiple-choice questionnaire was administered to 325 Italian allergy specialists, randomly selected from a national list, who commonly recommend treatment with SLIT. The questionnaire comprised 10 questions concerning different factors which can favorably influence patient adherence with SLIT. These factors were perceived efficacy, tolerability, cost reimbursement, administration regimen (pre-coseasonal/continuous), ease of administration, regular contact with the patient, approval of the treatment by the general practitioner, patient education, and follow-up visits. The allergist's perception of the proportion of patients completing the recommended SLIT duration of three years was used to estimate the extent of follow-up.¹ Each question was to be answered using a 10cm visual analog scale (VAS) ranging from 1 ("extremely important") to 10 ("of no relevance"). The VAS is recognized as a very useful tool for detecting an individual's perception of a specific medical issue.¹⁰ The physicians were also asked to choose the most relevant factor that, in their opinion, impaired adherence.

Results

Of the 325 allergy specialists contacted, 296 (91%) returned a valid questionnaire with all questions answered. The mean age of the allergists was 51 years; 40.5% were female, and 5% were in private practice, 60% in hospital practice, and 35% worked in a territorial health care setting.

The patient's perception of clinical efficacy was considered to be the most important factor influencing adherence,

and was ranked 1 ("extremely important") by 54% of allergists; this finding was further confirmed by considering the sum of the first three ranks (Tables 1 and 2), with 78.1% of allergists considering this to be the most important factor. The second important factor influencing adherence was considered to be the possibility of cost reimbursement by the National Health Service, with 34% of allergists ranking this first (Table 3). The absence of treatment side effects was considered to be the third important factor influencing adherence, ranked first by 21.3% of allergists (Table 4).

The remaining factors ranked first in less than 20% of the answers. Patient education, acceptance by the general practitioner, and regular follow-up visits were not considered particularly relevant to maintenance of adherence. Also, the ease of administration of SLIT received low consideration by allergists. Considering the main causes of treatment discontinuation, the cost of SLIT was reported by 98% of physicians, followed by side effects (48%), and lack of perceived clinical efficacy (42%).

When asked to define a method to increase patient adherence, the majority (57.8%) of allergists chose telephone contact as a more useful tool than frequent follow-up visits. Finally, most allergists (57.8%) thought that a three-year course of SLIT would have an adherence of 50%–80%, while 29.4% estimated adherence to be over 80%, and only 7.1% estimated adherence to be lower than 50% (Table 5).

Discussion

Adherence to the recommended therapeutic regimen is crucial in all aspects of medicine,^{11–13} especially in chronic diseases, such as rhinitis and asthma. This is particularly true with SLIT which is self-administered by patients at home and involves prolonged treatment without medical supervision, and the potential therefore exists for arbitrary modification of the dosing regimen, which can lead to a progressive

Table 1 Percentage of allergists who ranked questionnaire issues influencing adherence to SLIT at 1–3

	n	%
Perceived efficacy of treatment by patients	231	78.1
Tolerability	196	66.2
Cost reimbursement	171	57.8
Patient education	117	39.4
Ease of use	106	35.7
Regular physician-patient contact	95	32.1
Regular follow-up visits	90	30.4
Administration regimen (pre-co seasonal)	72	24.3
Administration regimen (continuous)	65	21.9
Approval from general practitioner	49	16.6

Abbreviation: SLIT, sublingual immunotherapy.

Table 2 Allergists' ranking of perception of efficacy as the most important factor in adherence to SLIT

Ranking	n	%	CI 95%	
			Lower	Upper
1	161	54.4	48.7	60.1
2	49	16.6	12.3	20.8
3	21	7.1	4.2	10.0
4	7	2.4	0.6	4.1
5	15	5.1	2.6	7.6
6	5	1.7	0.2	3.2
7	7	2.4	0.6	4.1
8	13	4.4	2.1	6.7
9	6	2.0	0.4	3.6
10	8	2.7	0.9	4.6
ND	4	1.4	0.0	2.7
Total	296			

Abbreviations: SLIT, sublingual immunotherapy; CI, confidence interval; ND, not defined.

reduction of clinical efficacy and finally, discontinuation of treatment. A treatment duration of 3–5 years has been shown to be optimal for modifying the natural history of both house dust mite^{14,15} and pollen¹⁶ allergy. Patients embarking on SLIT should therefore aim for this treatment duration.

The present study investigated how specialists perceive SLIT adherence issues using a questionnaire canvassing factors that are commonly believed to affect compliance. As expected, the patients' perceived clinical efficacy was the most relevant issue, and was even more important than the presence of side effects. It is worthy of note that perceived clinical efficacy may also have a negative effect, because the patient might feel that once the symptoms are controlled the treatment is no longer needed, which leads to premature cessation of treatment.¹⁶ This misconception could be addressed by patient education, as recommended in

Table 3 Ranking of cost reimbursement in adherence to SLIT

Ranking	n	%	CI 95%	
			Lower	Upper
1	102	34.5	29.0	39.9
2	32	10.8	7.3	14.3
3	37	12.5	8.7	16.3
4	26	8.8	5.6	12.0
5	19	6.4	3.6	9.2
6	12	4.1	1.8	6.3
7	16	5.4	2.8	8.0
8	20	6.8	3.9	9.6
9	11	3.7	1.6	5.9
10	16	5.4	2.8	8.0
ND	5	1.7	0.2	3.2
Total	296			

Abbreviations: SLIT, sublingual immunotherapy; CI, confidence interval; ND, not defined.

Table 4 Ranking of treatment tolerability in adherence to SLIT

Ranking	n	%	95% CI	
			Lower	Upper
1	63	21.3	16.6	25.9
2	82	27.7	22.6	32.8
3	51	17.2	12.9	21.5
4	19	6.4	3.6	9.2
5	19	6.4	3.6	9.2
6	15	5.1	2.6	7.6
7	11	3.7	1.6	5.9
8	15	5.1	2.6	7.6
9	12	4.1	1.8	6.3
10	6	2.0	0.4	3.6
ND	3	1.0	-0.1	2.2
Total	296			

Abbreviations: SLIT, sublingual immunotherapy; CI, confidence interval; ND, not defined.

consensus documents for any level of severity of allergy.¹⁷ By contrast, perhaps surprisingly, patient education (and parental education, when SLIT is administered children) and ease of administration were not judged by the allergists to be relevant issues. An accepted definition of patient education is “the process by which health professionals and others impart information to patients that will alter their health behaviours or improve their health status”.¹⁸ It was recently demonstrated that patients receiving an educational programme on SLIT showed better compliance than patients receiving standard verbal instructions.¹⁹

Because adherence is considered to be a dynamic process, patient perception of treatment efficacy should be regularly evaluated by the attending allergist. Moreover, before beginning SLIT, physicians should give correct instructions and explanations to patients, especially concerning the treatment duration needed before assessing symptomatic relief, to avoid unrealistic expectations. The other two issues judged by the allergists to be important in compliance were tolerability and treatment cost. It is known that SLIT has a good safety profile, with local reactions in the mouth or gastrointestinal tract being the most common side effects,²⁰ but generally these reactions are quite easy to manage and do not require

Table 5 Three-year SLIT adherence as perceived by allergists

Adherence	N	%	95% CI	
			Lower	Upper
>80%	87	29.4	24.2	34.6
80%–50%	171	57.8	49.3	66.3
<50%	21	7.1	1.2	13.0
NA	17	5.7	0.0	12.5
Total	296			

Abbreviations: SLIT, sublingual immunotherapy; CI, confidence interval; NA, not available.

interruption of treatment.⁹ In this regard, patient education is likely to be a crucial factor in adherence.

It has been clearly demonstrated that SLIT is cost-effective in terms of reducing the use of symptomatic drugs, and becomes even more cost-effective when SLIT can be stopped after an adequate treatment duration and continues to be effective in controlling allergic symptoms.²¹ However, it is understandable that patients absorbing the cost of SLIT may not be convinced on this issue, even after adequate information is given.

In conclusion, the results of this survey suggest that there is still room for improving the extent of patient adherence with SLIT, and that patient understanding of the specialists' perception, beliefs, and attitudes might be a fruitful advance. In particular, the perception of some aspects of treatment appears to some extent to be unrelated to the current scientific knowledge about SLIT, and may be improved by more complete information being provided. Moreover, the allergists' preference for telephone contact is another factor potentially able to improve adherence to treatment, as has been demonstrated in diabetic patients.²²

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