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The perception of allergen-specific immunotherapy among chest physicians: an Italian survey

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Summary

Background and Aim. This questionnaire-based study evaluated the overall level of knowledge about allergen-specific immunotherapy (SIT) among chest physicians, who are frequently involved in the management of respiratory allergies. This represents an interesting aspect, because chest physicians intercept many of the patients with allergic rhinitis w/wo asthma, in which SIT could be potentially indicated. **Methods.** A panel of experts prepared a questionnaire, involving 16 main points of interest/questions concerning the knowledge and use of SIT. Questionnaires were e-mailed (September-October, 2011) to randomly-selected specialists, and were returned anonymously. **Results.** 81 questionnaires from specialists using SIT were eligible. The respondent population had a mean age of 51 years (range 33-63 years, 74% male). The general knowledge on SIT is overall satisfactory among pulmonologists, and they are well aware that SIT is recommended in the available guidelines. Nevertheless, about 50% of physicians still believe that SIT has to be used as a last-choice adjunct when pharmacotherapy fails. Chest physicians are well aware that SIT has a disease-modifying effect, in addition to its short-term clinical efficacy. Finally, the majority of interviewed specialists agree on the need of getting more information and education on SIT. **Conclusions.** This survey about the perception of SIT among chest physicians in Italy highlighted a satisfactory overall knowledge of SIT and only few weak points. These results would allow to take appropriate educational actions and this questionnaire could be used to monitor the possible effects of divulgation and educational initiatives over time.

Introduction

Allergy still remains a major public health concern which has pandemic proportions, affecting more than 150 million people in Europe. Taking into account the epidemiological trends, it is hypothesized that within 15 years more than 50% of the European population will suffer from some type of allergy (1,2). Allergic patients suffer from a debilitating disease, with a major impact on their quality of life (QoL) and work/school performance, and constitute a significant burden on health economics, due to lost productivity and absenteeism (3). Given that allergy triggers such as urbanization, pollution and climate

change are not expected to change significantly, the only ways to afford this burden are strengthening and optimizing the preventive and treatment strategies. Nonetheless, it has been repeatedly shown that the available pharmacological treatments are neither capable to achieve a long-term effect once stopped, nor to induce significant immunological changes. On the contrary, allergen-specific immunotherapy (SIT), which is based on the subcutaneous (SCIT) or sublingual (SLIT) administration of high allergen doses, was proven able to reduce asthma/rhinitis symptoms and to achieve a long-lasting effect. However, SIT is currently used only as a second-line treatment, and often

suggested as a last-choice. Indeed, in the more recent guidelines and academic position statements, the use of SIT has been advocated for those patients with milder disease, also in order to prevent the progression of allergic respiratory diseases. In fact, the clinical value of SIT has been confirmed in multiple clinical trials and meta-analyses, also improving the patient reported outcomes, such as Quality of Life (QoL), long-term costs, burden of allergies, and effect on the course of the disease (4-6). Despite the aforementioned experimental evidence, SIT is still not receiving an adequate attention from Medical Institutions, as the general underuse of this treatment clearly demonstrates (7). In this context, the partnership and cooperation of different medical subjects (i.e. general practitioners, allergists, pediatricians, chest physicians) would be crucial. In a previous questionnaire-based study we observed that, at least among the Italian GPs, the perception of SIT as a valuable treatment was near to optimal (8). It is true that GPs are primarily responsible for education and information about respiratory allergy and its treatment, but it is also true that pulmonologists are often involved in the primary diagnosis and care of this disease (9). This survey was specifically designed for chest physicians, intended to assess their knowledge on SIT. This was done by a questionnaire-based survey.

Methods

A panel of experts, based on guidelines and literature analysis prepared a questionnaire of 16 points of interest/questions specifically dedicated to chest physician specialists. The questionnaire (Y/N or multiple-choice answers) was subdivided into five main sections (clinical/general aspects, efficacy perception, pharmacoeconomic aspects, SLIT versus SCIT, awareness of guidelines) (see **table 1**). The study, since cross-sectional and observational, did not need an official approval by the Ethic Committee to whom it was simply notified to warrant the privacy of the recorded data. The questionnaires were emailed to 115 specialists in Respiratory Medicine, randomly selected from the databases of the Italian societies of respiratory medicine, and had to be returned anonymously. Only the returned questionnaires of those physicians currently using SIT were taken into consideration. The selection of the chest physicians also took into account the harmonic distribution across the Italian Country, in order to avoid any "bias" connected to different attitudes about SIT. Questionnaires were sent to pulmonologists from the beginning of September to the end of October 2011.

Table 1 - Number and % of responses to the items in the SIT - pulmonologist questionnaire.

ITEM	N	%
1. In subjects with respiratory allergies (rhinitis and asthma), do you believe that SIT allergenic extracts may be a valid therapeutic option?		
Yes	73	90
No	8	10
2. Do you give the SIT directly to your patients?		
Yes	53	65
No	16	20
I follow patients when SIT was initiated by another specialist (e.g. allergist)	12	15
3. If so, how many patients come in a year?		
More than 10 patients	36	44.5
Between 5 and 10 patients	20	24.5
Between 1 and 5 patients	25	31
4. In patients dealing with SIT, the decision was taken:		
Not answering	15	18.5
After consulting with allergist	16	20
In total autonomy	50	61.5
5. If using the SIT, which is its main indication?		
Asthma	10	12
Rhinitis plus asthma	50	61.5
Rhinitis	21	26.5

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ITEM	N	%
6. If administering the SIT, which allergenic extracts do you use?		
Perennial	20	24.5
Seasonal	17	21
Both in equal measure	44	54.5
7. Which schedule does the patient usually follow (pre-coseasonal, continuous, continuous for seasonal forms also)?		
Pre-coseasonal	25	31
Continuous	33	41
Continuous for seasonal forms also	23	28
8. In your opinion, SIT is:		
An alternative treatment with respect to pharmacologic therapy	2	2.5
A limited efficacy treatment	4	5
A treatment that can only be used in a small proportion of patients	10	12
The only treatment available	24	29.5
A complementary treatment to drug therapy	41	51
9. Which route of administration do you use primarily?		
Sublingual	50	62
Subcutaneous	11	13.5
Both	20	24.5
10. Which route of administration do you consider clinically superior?		
Effective in equal measure	29	36
Sublingual	21	26
Subcutaneous	31	38
11. How long do you continue the SIT treatment?		
5 or more years	16	20
3 years	60	74
1 year	5	6
12. Can SIT modify the natural history of the respiratory allergic disease?		
Yes	65	80
No	16	20
13. Which of the following statements do you believe is the most significant?		
SIT may reduce the risk of new sensitizations	8	10
SIT is effective in reducing the use of medications	16	20
SIT may reduce the risk of asthma	21	26
SIT is effective in reducing allergic symptoms	36	44
14. In a symptomatic asthmatic patient, do you continue to administer SIT?		
No	7	8.5
Yes	21	26
Only after having checked the symptoms with anti-asthma drugs	53	65.5
15. Would you like to receive more information about SIT (meetings/respiratory medicine journals)?		
Yes	74	91.5
No	7	8.5
16. Is SIT mentioned in asthma/rhinitis guidelines, as GINA and ARIA?		
Yes, in both	64	79
No	5	6
Only in ARIA guidelines	9	11
Only in GINA guidelines	3	4

Results

Among the 115 interviewed chest physicians, 90 (78%) responded as users of SIT, and 81 were fully analyzed (9 were inadequately completed). The respondent population had a mean age of 51 years (range 33-63, 74% male). The pneumologists were distributed as follows: 62 worked in hospital, 12 on the territory, 5 were private practitioners, and 2 worked into a University setting. The distribution on the national territory was the following: Northern Italy 29%, Central Italy 34%, and Southern Italy 37%.

According to the results (shown in **table 1**), it seems that the general knowledge on SIT is overall satisfactory among pulmonologists, and that they are well aware that SIT is recommended in the most diffused guidelines (item 16). Nevertheless, a relevant proportion of chest physicians (> 50%) still believe that SIT is an adjunct to pharmacotherapy, to be used only when drugs fail to control asthma. This may be the result of the statements reported in previous guidelines such as GINA. Also, chest physicians are well aware that SIT has a disease-modifying effect in addition to the short term clinical efficacy (item 12). The main differences between sublingual immunotherapy (SLIT) and subcutaneous immunotherapy (SCIT), especially concerning the efficacy aspects, are known as well. Importantly, the majority of Italian chest physicians herein involved agree on the need to improve the cooperation with other specialists, and auspicate to get more information and education on the specific aspect of SIT, for instance in scientific meetings (item 15). Due to the cross-sectional design of the study, no specific investigation on adherence, outcomes or functional approaches could be done.

Discussion

Among the treatments currently available for respiratory allergy (including allergen avoidance and pharmacotherapy) SIT is the only approach capable to act not only on the symptoms, but also on the immunologic aspects. In fact, more than 200 trials have confirmed its efficacy and safety (both for SCIT and SLIT) in allergic rhinitis and asthma (10). Current available data give solid evidence on the clinical efficacy of both SCIT and SLIT in allergic rhinitis and asthma. SIT is the only treatment that causally addresses IgE-mediated immunopathology and modulates the natural course of the disease (11-14). Furthermore, SIT has been shown to prevent the progression of the disease and the onset of new sensitizations and asthma long after it was discontinued.

The current burden of allergic diseases, estimated by both direct and indirect costs, is very relevant. In fact the cost estimation for rhinitis amounts globally to 4-10 billion dollars/year in the U.S. and to an average annual cost of 1089 euros per child/

adolescent and 1543 euros per adult in Europe. The estimated annual costs in Northern America for asthma amounted to 14 billion dollars. Consequently, preventive strategies aimed at reducing the clinical severity of allergy are potentially able to reduce its costs. Among them, SIT joins to the preventive capacity the carryover effect once treatment is discontinued. Several studies, conducted in different Countries confirmed a favorable cost-benefit balance (15-16).

In previous surveys among Italian GPs about the modality of use of SIT (17,18) we found that: a) physicians are overall familiar with SIT and most recommendations of the guidelines are observed; b) the majority of physicians perform SIT in a hospital environment; c) the availability of resuscitation facilities and/or drugs to treat possible severe reactions is still not optimal; d) a poor attention is paid to the education of the patients (17). It is true that GPs remain the primary responsible for education and information when SIT is prescribed, and their cooperation with specialists in managing allergies is auspicated; it is also true that chest physicians are often involved in the diagnostic process concerning asthma/rhinitis, since they intercept many patients suffering from respiratory allergy. Thus, we performed a specifically designed survey to assess the level of knowledge about SIT among chest physicians. This survey, designed to evaluate the perception of SIT among chest physicians, was established to assess their knowledge on SIT. Among the interviewed pulmonologists, 78% use SIT. According to the respondents' opinion, they are well aware that SIT is recommended in the most diffused guidelines. Nevertheless, a relevant proportion of pulmonologists believe that SIT should be an adjunct to pharmacotherapy to be used as a last choice. This may be the result of the statements reported in previous guidelines such as GINA (19). Also, chest physicians are overall aware that SIT has a disease-modifying effect in addition to the short-term clinical efficacy. The main differences between SLIT and SCIT, especially those concerning the efficacy aspects, are known as well. A special point of this survey is that, for the first time, SLIT was specifically investigated in a pneumological area of expertise.

Importantly, the majority of pulmonologists agree on the need to improve the cooperation with other specialists, and express the auspice to get more information and education on the specific aspect of SIT, for instance in scientific meetings. In conclusion, our survey about the perception of SIT among Italian chest physicians highlighted a satisfactory overall knowledge of SIT and only few weak points. These results would allow to take appropriate educational actions and this questionnaire could be used to monitor the possible effects of divulgation and educational initiatives over time.

References

1. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, Williams H. ISAAC Phase Three Study Group. World-wide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet*. 2006;368(9537):733-43.
2. Bousquet J, Khaltaev N, Cruz AA, et al; World Health Organization; GA(2)LEN; AllerGen. Allergic Rhinitis and its Impact on Asthma (ARIA). 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008;63Suppl86:8-160.
3. Pawankar R, Canonica GW, Holgate ST, Lockey RF. World Allergy Organization White Book on Allergy. 2011.
4. Passalacqua G. Specific immunotherapy: beyond the clinical scores. *Ann Allergy Asthma Immunol*. 2011;107:401-6.
5. Durham SR, Emminger W, Kapp A, de Monchy JG, Rak S, Scadding GK et al. SQ-standardized sublingual grass immunotherapy: confirmation of disease modification 2 years after 3 years of treatment in a randomized trial. *J Allergy Clin Immunol*. 2012;129:717-725.
6. Marogna M, Spadolini I, Massolo A, Canonica GW, Passalacqua G. Long-lasting effects of sublingual immunotherapy according to its duration: a 15-year prospective study. *J Allergy Clin Immunol*. 2010;126:969-75.
7. Canonica GW, Baena-Cagnani CE, Compalati E, Bohle B, Bonini S, Bousquet J et al. 100 Years of Immunotherapy: The Monaco Charter. Under the High Patronage of His Serene Highness Prince Albert II of Monaco. *Int Arch Allergy Immunol*. 2012;160:346-9.
8. Calderon M, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S. Allergen injection immunotherapy for seasonal allergic rhinitis. *Cochrane Database Syst Rev*. 2007;(1):CD001936.
9. Canonica GW, Bousquet J, Casale T, et al. Sub-lingual immunotherapy: World Allergy Organization Position Paper *Allergy*. 2009Dec;64 Suppl91:1-59.
10. Passalacqua G, Durham SR; Global Allergy and Asthma European Network: Allergic rhinitis and its impact on asthma update: allergen immunotherapy. *J Allergy Clin Immunol*. 2007;119(4):881-891.
11. Di Rienzo V, Canonica GW, Passalacqua G. Long-lasting effect of sublingual immunotherapy in children with asthma due to house dust mite: a 10 year prospective study. *Clin Exp Allergy*. 2003;33:206-10.
12. Jacobsen L, Niggemann B, Dreborg S and the PAT Investigator Group. Specific immunotherapy has long-term preventive effect on seasonal and perennial asthma: 10-year follow-up on the PAT study. *Allergy*. 2007;62:943-8.
13. Novembre E, Galli E, Landi F, Caffarelli C, Pifferi M, De Marco E, Burastero SE, Calori G, Benetti L, Bonazza P, Puccinelli P, Parmiani S, Bernardini R, Vierucci A. Coseasonal sublingual immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis. *J Allergy Clin Immunol*. 2004;114(4):851-7.
14. Tripodi S, Di Rienzo Businco A, Benincori N, Scala G, Pingitore G. Safety and tolerability of ultra-rush induction, less than one hour, of sublingual immunotherapy in children. *Int Arch Allergy Immunol*. 2005;139(2):149-52.
15. Berto P, Passalacqua G, Crimi N, Frati F, Ortolani C, Senna G, Canonica GW. Economic evaluation of sublingual immunotherapy vs symptomatic treatment in adults with pollen-induced respiratory allergy: the Sublingual Immunotherapy Pollen Allergy Italy (SPAI) study. *Ann Allergy Asthma Immunol*. 2006;97:615-21.
16. Berto P, Frati F, Incorvaia C. Economic studies of immunotherapy: a review. *Curr Opin Allergy Clin Immunol*. 2008;8:585-9.
17. Lombardi C, Bettoncelli G, Passalacqua G, Canonica GW. The perception of allergen-specific immunotherapy among general practitioners. *Eur Ann Allergy Clin Immunol*, in press.
18. Lombardi C, Passalacqua G. Specific Immunotherapy among Italian specialists. *Allergy*. 2006;61:898-9.
19. Global Initiative for Asthma. GINA Guidelines, last accessed Dec 2012. www.ginasthma.org