

A web-based tool for improving adherence to sublingual immunotherapy

To the Editor,

Allergic rhinitis and asthma can be controlled by pharmacotherapy, but allergen-specific immunotherapy (AIT) is the only disease-modifying intervention (1). Sublingual immunotherapy (SLIT) is gaining attention due to lower risks of side effects compared with subcutaneous AIT, but requires regular administration for at least 3–4 yr to achieve a high immunologically active dose. However, poor compliance particularly with SLIT is an emerging problem in the treatment of allergic respiratory diseases (2). Recent real-life studies have shown that only about 50% of the allergic patients receiving SLIT continue the treatment in the 2nd year and even fewer in the 3rd year (3, 4). Therefore, improving adherence to SLIT is a priority to improve its efficiency. In the information era, parents and their children are making increasing use of the Internet, computers, and smart phones. Thanks to these technologies it is easier today to conceive programs which allow online communications between doctors and their patients (5).

To this purpose, a new online platform, Allergymonitor© (AM) (Technology Projects & Software Productions, Rome, Italy), was developed. AM consists of two main graphic interfaces: one accessed by the patient or the 'front end', and one accessed by the doctor or the 'back office', both allowed after personalized login. The front end includes several features such as a personalized treatment plan, including SLIT dosage, an online diary for daily or weekly registration of symptoms and eventually therapy-related adverse events, real-time graphic visualization of symptoms trend, and access to a chat messaging system which allows a direct, even if not in real time, interaction with the physician. All patients' data are encrypted in accordance with current Italian privacy and information laws. The back office permits doctors to assess all their patients' data, monitor allergic symptoms, adherence and side effects to medications and AIT, adjust patients' treatment plan, and remind patients of these adjustments in real time through the chat messaging system. Moreover, the back office provides validated graphic symptoms scores which can be matched to pollen count curves online and in real time (6). Doctors are then able to easily download every patient's recorded data in an Excel© format for any statistical analysis. Finally, AM permits the activation of automatic email and/or SMS alerts to patients when data registration is interrupted for more than two consecutive days, improving patients' management and adherence to the prescribed therapy.

Between April and December 2011, we conducted an observational pilot study on adherence to SLIT in 27 patients (age range, 6–20 yr) affected by allergic rhinitis, with or without intermittent or mild-persistent asthma, who were

recruited at the Pediatric Allergy Unit of the 'S. Pertini Hospital' in Rome and monitored with AM. The primary aim of the study was to determine whether the use of AM could improve patients' adherence to the prescribed SLIT. Due to the observational design of the study, the starting month of the SLIT was different among the 27 patients. Nevertheless, all participants were asked to register their symptoms with AM on a daily basis for the first 2 months of SLIT and thereafter once a week. Data on SLIT dropouts in the AM group at the end of the studied period were also compared with dropouts of a control retrospective group treated with the same SLIT brand in the previous year by the same allergist (S.T.). The retrospective group was extracted in a blinded manner by an informatics engineer from electronic clinical records and was age-, sex-, skin prick tests- (SPT), and allergic status-matched with the studied group but not monitored with AM. The number of dropouts in both groups was calculated on the basis of SLIT reorders to the producer at the beginning of the 2nd year of treatment, and these figures were kindly provided by the manufacturer as SLIT is patient named in Italy.

Patients underwent a full allergologic workup and were recruited after parents' informed consent. The SLIT (Stallergenes, Antony, France) was prescribed according to current guidelines and with a scheme of three times per week (7). Exclusion criteria were a history of severe chronic disease, previous courses of immunotherapy, and lack of an Internet-connected computer at home. Instructions on the use of AM were given to each patient and his/her parents at the recruitment and were also made available online and through a help desk. The study was embedded in a larger epidemiological study on pollen allergy approved by the ethic committee of the 'S. Pertini Hospital', Rome (8).

According to the ARIA classification, the 27 participants (17 males, 66.6%; mean age of all patients 11.1 ± 3.5 yr) were affected by a moderate-to-severe persistent allergic rhinitis (9). A total of 12 children (44%) had also intermittent or mild-persistent asthma. A total of 19 of the 27 children (70.4%) had clinically relevant positive SPT (weal reaction ≥ 3 mm) to pollens and 8/27 (29.6%) had positive SPT to *Dermatophagoides pteronyssinus* and *farinae*. Pollens' sensitization was as follows: 11/27 (40.8%) only to *Grass pollens*, 3/27 (11.1%) to *Grass pollens* and *Parietaria judaica*, 3/27 (11.1%) to *Grass pollens* and *Olea europea*, 1/27 (3.7%) only to *P. judaica*, 1/27 (3.7%) to *P. judaica* and *O. europea*. All these children were prescribed SLIT as follows: 11 for grasses, three for grasses and *Parietaria*, three for grasses and *Olea*, one for *Parietaria*, one for *Parietaria* and *Olea*, and eight for mites. The control retrospective group included 18 subjects (11 males, 61%; mean age of all patients 12.0 ± 2.8 yr; $p = \text{NS}$).

During the 9-month observation period, only one of 27 patients in the AM group (corresponding to 3.7% of the

Abbreviations:

AIT, allergen specific immunotherapy; AM, Allergymonitor©; SLIT, sublingual immunotherapy; SPT, skin prick tests.

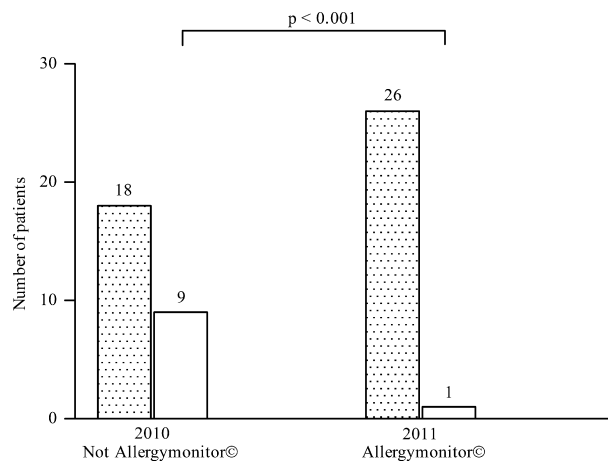


Figure 1 Comparison of sublingual immunotherapy dropouts after the 1st year of treatment between the studied population monitored with Allergymonitor© (AM) and a retrospective group of subjects related to the same allergist not monitored with AM. Dropouts correspond to white columns.

studied population, or 5.4% per year) discontinued SLIT, because of an unplanned move to a new city. A total of 11,710 doses were administered, with an average of 434 doses/patient, and 385 (3.3% per patient) SLIT-related adverse reactions were reported. There were no systemic SLIT-related adverse events such as asthma exacerbation or anaphylaxis and none of the patients required epinephrine administration. The most commonly reported adverse events were local, mild in severity and self-limiting reactions. A total of 10 of the 27 patients (37%) regularly registered their symptoms without interruption. Overall, 134 email alerts (8/patient) were sent to the remaining 17 patients because of interruption of registration. Notably, 16 of the 17 (94%) patients who interrupted registration of symptoms continued to compile the online diary immediately after they received the alert. Among the 26 patients who completed the study, the average of daily recording was 67 of 70 days (96%), whereas the weekly one was 8 of 11 wk (78%).

References

- Burks AW, Calderon MA, Casale T, et al. Update on allergy immunotherapy: American Academy of Allergy, Asthma & Immunology/European Academy of Allergy and Clinical Immunology/PRACTALL consensus report. *J Allergy Clin Immunol* 2013; **131**: 1288–96.
- Passalacqua G, Baiardini I, Senna G, Canonica GW. Adherence to pharmacological treatment and specific immunotherapy in allergic rhinitis. *Clin Exp Allergy* 2013; **43**: 22–8.
- Vita D, Caminiti L, Ruggeri P, Pajno GB. Sublingual immunotherapy: adherence based on timing and monitoring control visits. *Allergy* 2010; **65**: 668–9.
- Senna G, Lombardi C, Canonica GW, Passalacqua G. How adherent to sublingual immunotherapy prescriptions are patients? The manufacturers' viewpoint. *J Allergy Clin Immunol* 2010; **126**: 668–9.
- Klasnja P, Pratt W. Healthcare in the pocket: mapping the space of mobile-phone health interventions. *J Biomed Inform* 2012; **45**: 184–98.
- Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008; **86**: 8–160.
- Canonica GW, Bousquet J, Casale T, et al. Sub-lingual immunotherapy: World Allergy Organization Position Paper 2009. *Allergy* 2009; **64**: 1–59.
- Dondi A, Tripodi S, Panetta V, et al. Pollen-induced allergic rhinitis in 1360 Italian children: comorbidities and determinants of severity. *Pediatr Allergy Immunol* 2013; **24**: 742–51.
- Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol* 2010; **126**: 466–76.

In addition, SLIT dropouts in the retrospective group showed a very high significant difference ($p < 0.001$; Fig. 1). Although with limits of a retrospective comparison group, our findings in these subjects are in line with recent real-life studies showing a dropout of about 50% of allergic patients receiving SLIT after the 1st year of treatment (3, 4).

In summary, we demonstrated that AM is an innovative and useful tool to monitor the allergic status of patients in real time and to improve their adherence to SLIT. The added value of this new web-based tool is that it facilitates direct communications between doctors and patients through a chat messaging system. The possible limitations of AM could be the reliability of patients in understanding and recording the severity of their symptoms, which is a common limit of every symptoms recording tool. Moreover, physicians require basic knowledge of the use of computer software and a dedicated attention to the daily recorded data in order to assure a constant feedback to the patient. Finally, patients may have a low compliance to the daily registration of symptoms for long periods. Therefore, we suggest a daily registration for the first 2–4 months of SLIT followed by a weekly recording. A large-size, randomized, prospective, controlled study on the use of AM for improving adherence to SLIT is needed to confirm our findings.

Acknowledgments

We are grateful to Miss Jill Sutherland for editing the English version of the manuscript.

Conflict of interest

Salvatore Tripodi is a shareholder in TPS Production. All the other authors disclose no relevant conflicts of interest with the subject matter or materials discussed in this manuscript.

Salvatore Tripodi¹; Pasquale Comberiati² & Andrea Di Rienzo Businco¹
¹Pediatric Department and Pediatric Allergy Unit, "Sandro Pertini" Hospital, Rome, Italy; ²Department of Life and Reproduction Sciences, Pediatric Clinic, University of Verona, Verona, Italy
 E-mail: salvatore.tripodi@gmail.com
 DOI:10.1111/pai.12260