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EDITORIAL

Sublingual immunotherapy in children



Asthma and allergy are often found to be related. Indeed, up to 19–38% of all patients with allergic rhinitis present asthma, and 85–95% of all patients with asthma develop allergic rhinitis.¹ Both disorders represent an important health problem in the pediatric population, due to their high prevalence and associated impact upon the quality of life of the patients and their families, as well as the important healthcare costs they generate. The frequency of these two diseases has increased in recent decades, with great geographical variability. In this regard, the reported prevalence of asthma symptoms is 0.1–20.3%,¹ while that of allergic rhinitis is 2.2–45.1%.² Although these variations are conditioned by environmental and genetic factors, as well as by the characteristics of the healthcare systems in each region, the precise cause of such variability has not been fully clarified to date.

Since both asthma and rhinitis are often of an allergic nature, their management should include the avoidance of those allergens to which the patient is sensitized. However, due to the ubiquitous presence of certain allergens such as dust mites found in homes and public spaces, such a strategy may prove insufficient or ineffective.

In this context, specific allergen immunotherapy (AIT), administered both as subcutaneous immunotherapy (SCIT) and as sublingual immunotherapy (SLIT), constitutes first line treatment against allergic diseases. Since this treatment strategy is targeted to the underlying cause of the disease, it can modify the natural course of the latter, inducing long term immune tolerance and avoiding the development of new sensitizations, even after the end of treatment.^{3,4} The principal consequence of this management strategy is symptoms control, a lessened need for control and rescue medication, and improved patient quality of life. Furthermore, this kind of therapy is estimated to afford a 38% saving in the costs of the disease, in a way similar to the savings observed in adults.⁵

The use of AIT for the control and prevention of the symptoms of asthma and allergic rhinitis dates back to the early twentieth century. At present there is a large body of evidence warranting the efficacy of both SCIT and SLIT in children.⁶ Nevertheless, until recently there were no clear and consensus-based recommendations on the use of these therapies in the clinical practice guides on asthma and

allergic rhinitis.^{3,7–9} This lack of recommendations is conditioned by the great heterogeneity of the studies found in the literature, which makes direct comparisons difficult.¹⁰ Such heterogeneity in turn is due to the following factors, among others: the characteristics of the patients included in the studies (age, type of disease and duration, number and intensity of sensitizations); the characteristics of the extract used (native or allergoid, perennial or seasonal allergens, duration of AIT); the administration regimen and route (conventional or cluster, scaled or progressive, sublingual or subcutaneous); the study design (prospective, number of centers, type of blinding and comparator used); and the efficacy (symptoms, medication, lung function, immune response, controlled exposure tests) and safety criteria involved.

At present, a number of the most important clinical guides, such as the Global Initiative for Asthma (GINA) and the Allergic Rhinitis and its Impact on Asthma (ARIA) guide, recommend immunotherapy in different situations, for the treatment of both asthma and allergic rhinitis.^{8,9} These recommendations are based on the fact that both SCIT and SLIT have been shown to be effective and safe in treating asthma and allergic rhinitis in children.^{3,11} Although SCIT involves the traditional administration route, it poses a series of inconveniences, such as the need for frequent visits to the clinic for administration, or patient discomfort caused by the injections. In contrast, SLIT is a convenient and effective alternative that can be administered in the home and has almost no adverse effects. Its efficacy and safety in the treatment of asthma and allergic rhinitis in children has been extensively demonstrated by many randomized trials and meta-analyses.^{12–14} Nevertheless, further studies are needed to evaluate the long term efficacy of SLIT, and to define the treatment strategy with the most optimized doses of each allergen extract. Likewise, it seems advisable to analyze this treatment in Asian populations, with distinctive environmental and genetic conditions – since the results obtained may differ, as evidenced by other studies.¹⁵

In the present number of *Allergologia et Immunopathologia*, Tang et al. describe the efficacy and safety results of SLIT with *Dermatophagoides farinae* extracts in the treatment of allergic rhinitis among children between 2–13 years of age in the region of Beijing (China). After two years

of treatment, the symptoms of rhinitis (sneezing, rhinorrhea, nasal obstruction and pruritus) decreased significantly versus baseline, in the same way as the TNSS (Total Nasal Symptoms Score), VAS (visual analog scale) and TMS (Total Medication Score) values. The effects of SLIT were seen to be statistically significant from 6 months after the start of treatment, reaching a maximum effect after one year, and with no significant differences between one and two years after therapy. There were no statistically significant differences in efficacy between the patients aged 2–6 years and those aged 7–3 years. The treatment was very well tolerated, with no need for hospital admissions and no study dropouts due to adverse effects. These results are consistent with those of other studies in children in the same age range,^{16,17} which likewise recorded a significant decrease in asthma and allergic rhinitis symptoms after 6 months of treatment with SLIT – no differences being observed between one and two years after therapy.

The study of Tang et al. has a number of limitations that must be taken into account. In addition to the same limitations inherent to other regional studies when it comes to extrapolating the findings to other zones, the patient sensitization profile was not specified (i.e., polysensitized or monosensitized to dust mites), in the same way as the dust mite battery tested. This is of great importance in the region of Beijing, where *D. farinae* and *Dermatophagoides pteronyssinus*, among others, are the predominant dust mite species.¹⁸ On the other hand, the study was carried out during a period of only two years, without specifying the total duration of SLIT or the long term effects. Furthermore, the results indicate that from one year of treatment no further therapeutic benefits are obtained – this being in contradiction to the findings of other studies and consensus documents, where a minimum of three years is advised in order to obtain long term benefits.¹⁹

Despite its limitations, this study, in the same way as those previously published on the use of SLIT, demonstrate the adequate efficacy and safety profile of this treatment strategy, which offers a suitable alternative for the lessening of symptoms and the control of children with asthma and allergic rhinitis.

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