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Allergol Immunopathol (Madr). 2012;**40(3)**:135–137

Allergologia et immunopathologia

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EDITORIAL

Are we prescribing too much or too little immunotherapy for children with allergic rhinitis?

You are an experienced paediatric allergist. A mother and child of school age come into your office. In a few minutes you know that he has been suffering an offending allergic rhinitis for the last years. He has been only partially relieved with antihistamines. He is sensitised to common allergens in your region. You have some immunotherapy prescription pads on a shelf close to your hand. Are you going to take one of those pads at that moment? If you are working in Spain, there is 57% probability of doing so, according to a paper published in this issue of Allergologia et immunopathologia, reporting the paediatric results of a nationwide survey among Spanish allergists.[1] Is it too much? Is it too little?

Allergic rhinitis adversely affects the quality of life of as many as 10–20% of school age children in Spain, in an intermediate position in relation to other countries.[2] Natural history of this disorder shows a growing prevalence with age,[3] and increased risk of asthma in adult life.[4] Those most severely affected cannot do well without some kind of everyday drug therapy. Nasal steroids are effective and, although not proven, their effect on the growth of children is a cause of concern. In the paper by Ibero et al., fewer than half of children achieved good control of the disease with the use of symptomatic agents. In order to choose the best treatment for these children, we look for help from evidence-based medicine.

The efficacy of immunotherapy has long been under scrutiny and controversy. Several systematic reviews and meta-analysis have endorsed the ability of specific immunotherapy to improve the quality of life of patients suffering from several allergic diseases, including rhinitis and asthma.[5–7] Symptom relief can be fast, and similar or bigger than that obtained with pharmacotherapy.[8] More importantly, immunotherapy is able to change the natural course of the disease, extending its benefits beyond the completion of treatment.[9] Certainly, evidence in paediatric patients is scarcer (as in other fields of medicine).[10] However, as time goes by, better trials in children are reaffirming the efficacy of the vaccination with allergens in paediatric age.[11] Moreover, immunotherapy could be specially useful in children for some reasons. Firstly, the sooner the patient is treated, the fewer quality-adjusted life years (QALY) will be lost. Secondly, immunotherapy could perform more efficiently at the beginning of the disease, before remodelling makes it more resistant to treatment. Thirdly, the preventive effects of immunotherapy (for new sensitisations or for asthma) have been reported, although more studies are needed at this moment. Everything nice? Why are we not vaccinating everybody?

Upon looking closely over the trials on immunotherapy, some limitations arise. The evidence supporting the efficacy of immunotherapy for allergic rhinoconjunctivitis in children and adolescents has been questioned,[12] and the quality of systematic reviews and meta-analyses evaluating sublingual immunotherapy has been criticised.[13,14] Placebo effect has revealed as a huge obstacle for all treatments to demonstrate efficacy. Although immunotherapy has got through it, the margin for improvement is short and immunotherapy does not cover it all: you get better but not cured. Evidence supporting subcutaneous immunotherapy for rhinitis due to perennial allergens is not as complete as with seasonal rhinitis and is being analysed.[15,16] Choosing the allergens for immunotherapy in an individual patient can be more difficult than choosing a patient suitable for being vaccinated. Poly-sensitisation is a frequent problem and it is difficult to recognise if one allergen is responsible for the biggest part of the patient complaints (even though costly provocation tests are being used) or if several allergens are playing their part. The treatment is inconvenient due to the need to move to a sanitary facility for the shots, and the confidence in the adherence to treatment is the price to pay with the easier sublingual route.[17] Adverse effects are frequent and, although severe reactions are rare, mild and moderate reactions are not insignificant for many patients.

But evidence-based medicine (or practice) is not only composed of trials and papers. Two additional aspects play an important role in evidence-based decisions: individual clinical expertise and patient values and expectations. Experienced paediatric allergists (such as the one in our

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doi:10.1016/j.aller.2012.02.001

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vignette) are used to prescribe immunotherapy and to observe the problems and benefits that it produces in their young patients. As a matter of fact, a child should be referred to an allergist once the troubles produced by the rhinitis or the treatment required for its control are considered unacceptable. Some allergists will be prone to administer immunotherapy soon, provided the patient is expected not to improve any more that his current state. Some others may, as depicted by Ibero et al., adopt a ''wait-and-see'' approach, possibly with the idea of observing the course of the disease in their patients, sometimes fluctuating over time, to get the best from patient education, avoidance measures (when applicable) and drug therapy, before becoming convinced that immunotherapy is a good option for them. This implies that, beyond the first visit, more than that 57% will be prescribed allergen vaccines.

Last, but not least, the patient and, in paediatric age, the family has a lot to say. Each family is a little world, difficult to be understood in a brief interview. Patient and family priorities, perceived loss of quality of life and attitudes towards drugs are important factors to be considered before deciding to prescribe immunotherapy. Previous knowledge and expectations of a child, a teenager, a mother or other family members, about allergic diseases and their treatment with vaccines are not easy to perceive. As an example of the factors involved in those expectations, given the partially genetic nature of atopic diseases, more than a few parents of a child with allergic rhinitis will be suffering the same disease and, possibly, will have been treated with immunotherapy. Their own experience will be an important factor favouring or difficulting the prescription in their children. Costs are an important point for families and for society and, although few works have addressed this issue, they have found a favourable balance.[18,19] Form a societal point of view it should be important to know what we are obtaining (economic savings and quality of life) when we invest our money in vaccinating children with allergic rhinitis. But things can be different when we evaluate the cost-benefit ratio among different countries and even between different individuals in the same city. Again, family preferences and characteristics must be taken into account.

Another Spanish survey among paediatric allergists found a rate of prescription of immunotherapy for children with allergic rhinitis of 35%.[20] In the present survey, adults were prescribed immunotherapy a little less frequently (48%) than children.[21] Similar frequencies of immunotherapy prescription in patients attending allergy specialists were observed in France or Italy.[22,23] From a population point of view, 3% of newly diagnosed allergy rhinitis children in Florida were prescribed immunotherapy.[24] It is estimated that with regional variations, 1–5% of European children with allergic rhinitis are treated with specific immunotherapy.[10]

Concluding, is there an answer for the question entitling this editorial? Possibly not, we do not have enough data or a gold standard to measure it. So, what to do with our rhinitic child? Only face-to-face with the patient and the family can we choose the deemed best option for him. A complex algorithm incorporating all the mentioned aspects of evidence based practice is inside every paediatric allergist's brain: they are the most qualified to offer the best treatment for children suffering from moderate to severe allergic rhinitis.

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