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POINT OF VIEW

Grass pollen sublingual immunotherapy and paediatric allergic rhinitis: A patient-oriented decision

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Abstract Guidelines and systematic review report that allergen immunotherapy (AIT) is, in general, effective in the treatment of allergic rhinitis. However, experts suggest not generalising the results of different clinical studies: for example, it would not be advisable to translate the results found in an adult population to a paediatric population or the results on the efficacy of AIT against a specific allergen to the AIT against a different allergen. Moreover, according to Evidence Based Medicine (EBM), clinical decisions are individualised and should derive from the ''integration of best research evidence with clinical expertise and patient values''. Taking into account the high specificity of the AIT and EBM principles, we tried to answer the question on how advisable it is to prescribe the AIT for the management of grass allergic rhinitis in children. To do this, we revised the scientific literature in order to solve a specific case scenario.

Introduction

The aim of our study was to evaluate the usefulness of a grass pollen immunotherapy for paediatric grass pollen rhinitis. To do this we chose a particular case scenario and we kept in mind the needs of a particular child and his family. We also considered that, as suggested by the experts, the allergen immunotherapy (AIT) has its own specificity: for example, it is not advisable to compare different brands of AIT, or transfer the results of adult patients to the paediatric population.

We described a decision path, as could happen to any doctor. We started from a guideline and then, when necessary, we continued our search until the primary studies.

Case scenario

We met GS, a nine-year-old boy, in September 2013. In the last three years, during the spring (April–June), he presented sneezing, watery rhinorrhoea, itching and nasal obstruction. Sometimes he had cough and breathlessness during physical activity. At the moment of the visit, we found mild pale oedema of the nasal mucosa and mild pulmonary

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wheezing. Skin prick test with the most common aeroallergens showed a single positivity against grasses. We suggested the daily use of mometasone furoate nasal spray from the end of March to the end of June, and the management of eventual acute asthmatic symptoms with salbutamol spray. A spirometry testing (at rest, after exercise and after salbutamol) performed one month after the first visit was normal.

GS carried out two more visits at the end of April 2014 and in August 2014; on this latter occasion, he told us that he needed the salbutamol spray to control asthma symptoms for a total of 15 days in 11 months (all the episodes were due to physical exercise); he had also used the steroid nasal spray as prescribed (one puff for each nostril in the morning and, sometimes, one more puff in the afternoon) with an almost complete prevention of rhinitis symptoms. He went to the seaside in July and he had no symptoms even without administering any drug. What GS would like to know now is if there is something more to do; we hinted at the possibility of using the grass pollen AIT, which is presented as a possible option in two authoritative position papers on rhinitis.[1,2] His father, affected by allergic rhinitis, tried AIT for five years without advantage but he trusts us and backs our decision.

The patient values

Evidence Based Medicine (EBM) suggests to take clinical decisions taking into account: ''(1) integration of best research evidence with (2) clinical expertise and (3) patient values''.[3] However, the third point is often unfulfilled because patients do not express a real preference but they just want the doctors to suggest what would be the best for them. So we identified some issues of interest:

- Will GS heal from his rhinitis through the AIT?
- Will the AIT prevent a worsening of his allergic symptoms, for example of the asthma?
- Will the AIT reduce the rhinitis symptoms? If yes, more or less than the steroid spray?
- Does the AIT have adverse effects? If yes, more or less than the steroid spray?
- Is the AIT administration more or less disturbing than the steroid spray?
- Is the AIT more expensive than the steroid spray?

It is important to know that today (May 2015) in Italy, both the AIT and the steroid nasal spray are charged to the patient if symptoms are controlled by drugs as it is in the case of GS.

The clinical expertise

This is the second pillar of the EBM, consisting in the ability of doctors to shift the best scientific evidence available to the single patient with his specificities. Going back to our patient:

- Like all the children of his age, GS does not want an injective therapy. That is why we cannot consider for him the subcutaneous AIT and so the sublingual AIT (SLIT) is our only option.
- His father is a teacher and his mother is a housewife, there are four people in his family and they cannot afford the tablet SLIT, which is too expensive; only the drop SLIT is left.
- GS is a child, affected by rhinitis, with a monosensitisation to grass pollen; this is the population we have to refer to (not others like children with asthma and sensitisation to mites or adults with grass pollen allergic rhinitis).
- In the last spring, GS administered daily steroid nasal spray with good results; he has already found a solution to his symptoms. An eventual different therapy should have clear and methodologically well-demonstrated advantages (deriving, for example, from double-blinded randomised controlled trials, DB RCT).

We have to take into account advantages and disadvantages in terms of efficacy, adverse effects and economic costs.

The best research evidence

Since, as said above, we are oriented to the drop SLIT, the World Allergy Organization (WAO) position paper (PP) on this topic[4] may be an important source of basic scientific information. This PP reports as follows: ''The literature suggests that, overall, SLIT is clinically effective in rhinoconjunctivitis and asthma, although differences exist among allergens... The relative change versus placebo, when reported, ranged between 20% and more than 35%''. The WAO PP[4] refers to the systematic review (SR) with meta-analysis (MA) of Radulovic et al.[5]. They compared SLIT vs. placebo, finding that the standardised mean difference (SMD) for symptoms was −0.42 while the SMD for the use of symptomatic drugs was −0.43. However, according the WAO PP,[4] the reliability of these results is limited by the great heterogeneity of the trials considered in the review. Anyways, thanks to the increasing number of available trials, it is now possible to do more specific SR with MA, thus reducing the statistic heterogeneity of resulting data. An example of these SR is the one published by Di Bona et al.[6] (also reported in the WAO PP), regarding the efficacy of SLIT in grass allergic rhinitis.

The specificity of the SLIT efficacy

In their SR, Radulovic et al.,[5] consider different parameters on specific SLIT efficacy, taking into account, for example, the culprit allergen or the age of the patient. Through this SR[5] we learned that the SLIT is significantly more effective than placebo in reducing symptoms (both in adults and in children) and that grass pollen SLIT itself is effective (even if, unfortunately, this last result is presented without distinction between adults and children). The importance of the concept of specificity in this particular field is stressed by Bachert et al.[7] who replied to the De Bot et al.'s paper[8] entitled ''Sublingual immunotherapy not effective in house dust mite-allergic children in primary care'' saying that ''The title suggests that sublingual immunotherapy for house dust mite (HDM) 'in general' is not effective, but should clearly state that SLIT for HDM with a specific product is not effective... We therefore suggest to specify the SLIT product