EDITORIAL

IS IMMUNOTHERAPY JUSTIFIED IN THE TREATMENT OF RESPIRATORY ALLERGY?

In view of its frequency, prolonged clinical course and severity, asthma is the allergic disease requiring most attention on the part of the clinician and the health authorities, due to the economical burden it poses.

Although allergic rhinitis is the only respiratory disorder in many people, it often precedes the manifestations of asthma.[1] In fact, almost all asthmatics also suffer allergic rhinitis as an expression of the functional unity of the respiratory mucosa. The same situation is observed in eosinophilic bronchitis, where the absence of bronchial hyperresponsiveness explains the absence of episodes of bronchospasm.

Sensitization to aeroallergens in predisposed atopic individuals is the etiological basis of these diseases, the course of which may depend upon the number of allergens implicated, and which can increase over time. Inflammation and bronchial remodeling are a consequence of the repetition of symptoms. Logically, therapy should attempt to combat both conditions: allergic sensitization (etiological treatment) and inflammation (pathogenic treatment). Early and suitable treatment are essential for exerting a positive influence upon the course of the disease: progression from rhinitis to asthma, with the initiation and persistence of inflammation.

The need to reduce bronchial inflammation is the key to improvement of respiratory function and the reduction of symptoms which affect these patients with more or less intensity and frequency. Inhaled corticosteroids and/or anti-leukotrienes are the usual medications recommended by the most widely accepted management Guides (GINA[2], BGMA[3]), which also indicate how to combat the acute episodes and symptoms that may arise in the intervals between crises. Treatment is therefore approached from a pathogenic and symptomatic perspective. Nevertheless, as with any other disease, treatment targeted to the cause of the process (etiological treatment) is the most effective option for avoiding (as far as possible) chronification and increased severity of the clinical condition.

Measures designed to reduce environmental allergens are able to reduce both acute and occasional symptoms. However, the most indicated approach is to achieve desensitization of the causal allergens and avoid further sensitizations. This can be achieved provided adequate treatment is started as soon as possible, in the form of immunotherapy

– the efficacy of which has been warranted by many studies. Moreover, this is the only treatment that remains valid after its introduction almost a century ago.[4] Nevertheless, the Guides reflect a certain skepticism and caution in the use of immunotherapy. The use of such treatment is recommended when neither the environmental measures nor anti-inflammatory drugs are able to control the symptoms, and placing preference on the treatment of rhinitis rather than asthma.[5] These recommendations run counter to the demonstrated efficacy of treatment when started early, that is, as soon as sensitization to a given allergen has been confirmed and is related to the clinical process.[6]

There are two ways to investigate the usefulness of immunotherapy: one based on the clinical evolution and the other on the changes in immune response. The reduction in the frequency and intensity of the acute episodes, of the symptoms between crises or the symptoms of rhinitis, together with a lessened need for rescue medication or antiinflammatory drugs, is the usual approach for assessing the efficacy of immunotherapy. This habitual approach is generally based on subjective patient perception, which can be influenced by mood states. Abramson et al have compiled the double-blind studies made to assess these data, and have concluded that the treatment is effective.[7] With the same criterion, Calderon et al[8] confirmed the usefulness of immunotherapy in the management of allergic rhinitis, and likewise were able to achieve another objective: avoidance of the development of asthma in susceptible patients (Passalaqua et al).[9]

A more objective approach is to assess not only the clinical picture but also respiratory function. This has been demonstrated by a number of studies, including the work of Nagaya et al in asthmatic children, or of Grembiale et al, evidencing simultaneous improvement in bronchial hyperresponsiveness in patients that only suffer rhinitis.[10,11] Equally objective is the observation that most patients treated in this manner not developed further sensitizations over time, or did so to a lesser degree than patients who did not receive immunotherapy.[12-14]

While clinical assessment may imply such subjective interpretation, knowledge of the changes taking place in immune response as a result of immunotherapy defines the latter as decisive, by demonstrating its capacity to modify the anomalous response of patients with atopia to elements (aeroallergens) that are well tolerated by individuals who are not susceptible, as well as prevent sensitization to other allergens.[15] The reduction in Th2 lymphocyte activity in favor of Th1, by the intervention of T-regulatory cells (Treg), limiting the production of specific IgE against allergens and the activity of the eosinophils while favoring specific IgG4 production as possible blocking antibody, essentially represent the way in which immunotherapy exerts its beneficial effects.

In contrast to these positive aspects, the guides consider that "the role of specific immunotherapy in adult asthma is limited", and "in view of the relatively modest effect of

allergen-specific immunotherapy compared to other treatment options, these benefits must be weighed against the risk of adverse effects and the inconvenience of the prolonged course of injection therapy..." (GINA[2]). "There are as yet no properly controlled studies making direct comparisons between conventional asthma pharmacotherapy and allergen immunotherapy. Immunotherapy may reduce asthma symptoms and use of asthma medication, but the size of benefit compared to other therapies is not known" (BGMA[3]). "Immunotherapy should only be used in seasonal allergic rhinitis (pollen rhinitis) unresponsive to antiallergic drugs. Patients with asthma should not receive desensitizing vaccines, since they are more vulnerable to severe adverse reactions" (Spanish Therapeutic Prescription Guide[16], reproduced from BNF[5]). In contrast, the Canadian guide CACG[17] accepts immunotherapy in children with the usual recommendations, though in adults (from adolescence onwards) it maintains the negative criterion established in its 1999 edition: "Immunotherapy is generally not recommended in the treatment of asthma".

To the above considerations on the benefit of immunotherapy we must add that the adverse reactions cited in the guides are not frequent; most are of only minimal magnitude and do not require treatment interruption. Moreover, such reactions are often attributable to administration error, and are easy to resolve.[18] More serious and even fatal reactions are exceptional, and their frequency may be compared to the other drugs.

In view of all the above, is immunotherapy justified as basic and etiological treatment of allergic respiratory disease? A positive reply to this question is supported by many studies, based on extensive experience, with clinical and evolutionary controls, showing the efficacy and protection against new sensitizations by correcting host immune response.[19,20-22] The earliness of treatment introduction[23-25] and adhesion to the recent recommendations, based on those of the WHO, are the best guarantee for ensuring optimum results.[26]

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