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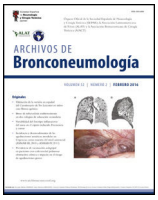

Editorial

Biologics in the Treatment of Asthma☆

Aproximación «biológica» al tratamiento del asma

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The rational examination of a disease begins by using clinical history and physical examination data to search for a cause. We then determine the underlying mechanisms, focus on the clinical manifestations, and finally decide on the most appropriate treatment to resolve these problems and to reestablish the patient's initial status.

Avoiding triggers is not always feasible in asthma. The symptoms reported by the patient rarely coincide with sensitization and the determination of one or more causative agents. Clinical data are the foundation of the patient-doctor relationship. The information reported by the patient and gleaned by the doctor from the interview constitute the groundwork for the diagnostic decision, and are, as such, important and necessary steps in the scientific approach to the pathological process. The treatment is the last stage of the journey. The success or failure of our actions and the ability of the ailing body to overcome the pathological assault are tested in this phase. In some diagnostic algorithms, therapeutic response is seen as an important factor in decision-making. But what about pathogenesis? The journey between the initial contact with the causative agent and the appearance of symptoms is long, and theoretical adjustments have become a necessity in the study and understanding of the process and modification of the disease course. In the case of the asthma, the progress of the antigen from the external environment to the host cell, contact with the Th0 lymphocyte and its transformation to Th2, the maturation of B cells and IgE synthesis, the binding of these molecules on the surface of the mast cells, the release of interleukins (IL), the long journey of IL-5, IL-4 and IL-13, encrypted messages to the bone marrow, synthesis, maturation, and the transfer of the eosinophils to the bronchial territory, etc., are factors that have greatly helped us understand inflammatory pathways and how to control them.[1]

The first successful biological treatment for asthma was omalizumab. This humanized monoclonal anti-IgE antibody, discovered in 1993[2] and approved by the FDA in 2003, has been administered to thousands of people around the world with excellent therapeutic outcomes. Indications have been expanded to both childhood asthma and chronic urticaria, and a new formulation simplifying administration has recently been approved.[3]

Since we embarked on this biological approach, the inflammatory mechanisms of the disease have become genuine therapeutic targets. New drugs (mepolizumab, reslizumab, benralizumab, dupilumab) have been introduced in recent years, mainly targeted at modulating the recruitment and action of eosinophils in the airways.[4] Scientific societies and expert groups state their position on the indications of each new drug[5,6] and leading editorials anticipate the position of the new therapeutic strategy in the framework of conventional treatment.[7,8] The *Institute for Clinical and Economic Review* has just published a review of the position of biologics in asthma.[9]

Although we continue to use escalating schedules based on the severity and control of asthma, the appearance of these new treatments, that are still reserved for more advanced or severe disease stages, has led us to ask what would happen if suitable patients were identified and these drugs were started at an earlier stage in the process. Any strategies that simplify patient management are always welcome, and an easy way of classifying asthmatics would be to categorize patients as mild-moderate and good responders to conventional treatment, or cases that are severe or poorly controlled with standard treatment, and in whom the new biologics may be biologically or clinically indicated.

The choice of therapy for the first group has already been assessed in depth, and variables such as shared decision-making with the patient, training in a simple inhalation procedure, drug tolerance, and patient age are well established. In the second group, the principal considerations are the biological features of the major mechanism causing asthmatic inflammation. In this respect, there is sufficient evidence for indicating omalizumab in patients in whom IgE plays a predominant role, whereas the other drugs already on the market should be reserved to neutralize the role of IL-5 as an inflammatory mediator. This division is merely for guidance, and overlaps will obviously occur.[10] These new drugs, which have a significant effect on eosinophil survival, also find a therapeutic application in patients who require a maintenance dose of oral steroids, or who frequently require oral corticosteroids for persistent eosinophil-related exacerbations. In this case, the recommendations of a recent review published by Professor Pavord[11] should be taken into account. According to some authors,

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eosinophil levels are the main variable to be controlled, although some controversy surrounds this claim.[12,13]

Economic considerations also merit consideration. The final report of the above-mentioned American Institute[9] draws attention to the high cost of these drugs and stresses the need to establish a precise indication and reserve these treatments for responders. In long-term treatment, omalizumab's positive QALY results, together with an accumulated experience of more than 15 years of follow-up, constitute an added value. The new biologics must demonstrate not only their effectiveness, but also their efficiency, and to achieve this, studies will be needed to compare their respective actions. Until comparative studies between the above-mentioned drugs are available, knowledge and caution should prevail. We will observe with interest the developments that help improve the lives of our patients, while maintaining the sustainability of a health system that is one of our most highly-prized assets.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.arbres.2019.03.024.

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