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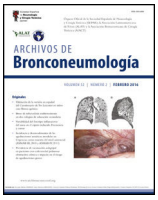

Editorial

Thermoplasty in the Spotlight☆

La termoplastia en el punto de mira

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The management of asthma recommended in guidelines is based on an escalating regimen, determined by severity.[1] In severe asthma, high doses of inhaled corticosteroids are combined with long-acting ß2-agonists (LABA). If control is not achieved, long-acting anticholinergics (LAMA), anti-leukotrienes, or other drugs, such as theophylline or macrolides, are added on a more individualized basis.

Fortunately, in recent years, biologics[2] and bronchial thermoplasty (BT)[3] have been included in the therapeutic arsenal for cases in which the initial options do not offer adequate control.

BT is a procedure in which heat generated by radiofrequency is applied to the bronchial wall through a catheter that is inserted into the bronchial tree with a bronchoscope.[3] The mechanism of action consists primarily of reducing the smooth muscle layer. Reduced basal membrane thickness has also been described, and it has even been postulated that this technique can reduce the inflammatory cascade, although indirect data suggest that it does not decrease eosinophilic inflammation.[4]

The procedure was approved by the FDA in 2010 on the basis of clinical effectiveness demonstrated in clinical trials[5–7] (improved symptoms and health-related quality of life [HRQOL] and fewer exacerbations). Since then, however, its implementation has been variable. Real-world data, with the exception of the PAS 2 study,[8] comprise very small patient numbers, and the largest series reports on only 24 cases.[9] Effectiveness in reducing exacerbations is maintained for at least 5 years.[10–12]

This, then, begs the question: if thermoplasty has been available for almost 10 years, why is it not yet a mainstream procedure?

The 2 main reasons for this are probably limitations in the clinical trials supporting the indication of this technique and the discovery of the highly effective biologics.

Only 1 of the 3 clinical trials on BT used a sham procedure as placebo,[7] and in that study, 64% of patients in the control group improved. In a series of 12 cases, Likura et al.[4] found that the proportion of patients with improved HRQOL after BT was the same as in the control group of the AIR2 trial,[7] so the possibility of a placebo effect with BT in clinical practice is very difficult to rule out.

Other relevant methodological limitations include the heterogeneity of the patients included in the studies, in terms of asthma severity, the various definitions of control, and previously administered maintenance treatment. In this respect, none of the patients included in BT clinical trials had undergone treatment escalation with LAMA or azithromycin, as currently recommended in the therapeutic guidelines.

Notwithstanding, one consequence of the significant breakthrough of biologics in the treatment of severe uncontrolled asthma (SUCA) is that the controversy over the residual role of BT has been rekindled.

Airway inflammation in asthma can be eosinophilic, neutrophilic, mixed granulocytic, or paucigranulocytic. With regard to inflammatory mechanisms and biopathological traits, the current classification of asthma is divided into T2 inflammation (includes allergic and/or eosinophilic asthma) and non-T2 inflammation (basically neutrophilic or paucigranulocytic).

Several biologics are available for T2-type SUCA, targeting either IgE (omalizumab) or cytokines IL-5/IL-5R, IL-4 and IL-13 (mepolizumab, reslizumab, benralizumab, and dupilumab).

It is unthinkable today to send a patient for BT without previously performing phenotyping to identify subgroups who might benefit from treatment with biologics. However, BT trials[5–7] fail to specify the IgE, FENO, and eosinophil values required for phenotyping. Furthermore, despite "presence of allergy" being mentioned in between 54% and 67% of patients, and "elevated eosinophils" in another study,[9] only 1.1% of patients in the AIR study[7] and 15.8% in PAS 2[8] had received biological therapy with omalizumab.

It is still difficult to identify patients who respond to BT. Given that treatment options for severe non-T2 asthma (neutrophilic or paucigranulocytic) are much more limited, and that this phenotype usually occurs in association with fixed airflow obstruction and/or airway hyperreactivity, these patients might be potential candidates for treatments that specifically target smooth muscle.[13] Similarly, a recent consensus proposes that patients with neutrophilic asthma could be candidates for BT after azithromycin has failed.[14]

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Yet another drawback is the long list of contraindications.[3,5–8] Special mention should be made of the technical discrepancies, particularly with regard to the number and location of activations.[9] Likura et al.[4] reported that the number of BT procedures in their study was 1.28-fold that of the AIR2 study. Muñoz-Fernández et al.,[15] in a small sample of 9 patients, modified the technique by increasing the number of activations, accessing peripheral bronchial subsegments, and including a wider bronchial area. It is unknown whether this modification will increase benefits without increasing long-term adverse effects.

In short, BT remains in the spotlight because of the plethora of unanswered questions, such as: Do the number of activations and extension of the treated area influence response? What is the most suitable phenotype for BT? Will biologics completely replace this technique? What are the long-term side effects?

Meanwhile, BT is coming up against highly effective competitors, such as monoclonal antibodies, which are gradually encroaching on the indications for BT. Our current knowledge suggests that BT is an option limited to a very small group of patients with SUCA and chronic airflow obstruction and phenotypes ineligible for biologics, or in patients in whom biologics have failed.

We appear to be at the beginning of a new era that perhaps heralds the end of the old one.

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