



Bronchoscopy in severe asthmatics: Is it a safe procedure?

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RESPUESTA A REVISORES

Comentarios al editor.

Queremos agradecer a los revisores el excelente trabajo realizado que, sin duda, ha mejorado mucho la proyección del manuscrito.

Hemos aceptado las propuestas del editor y adaptado el texto según las mismas.

Agradeciendo toda su asistencia y buen hacer en el proceso editorial, reciba un cordial saludo.

Borja G Cosío

Editorial

Asthma is a heterogenous disease that is characterized by airway inflammation resulting in airway hyperresponsiveness [1]. Currently, a percentage of asthma patients fail to achieve an adequate control of the disease with standard asthma medications and require oral corticosteroids to control their symptoms. In the last years, we are moving towards a precise phenotyping using imaging and different biomarkers aiming at personalization of asthma therapy with some provocative results [2]. In this context, the use of tissue biomarkers such as induced sputum or bronchoscopy samples have been proposed as useful tools in the work-up of severe asthma. Notably, the lack of access to induced sputum in most centers and the perception that bronchoscopy could be unsafe in patients with severe asthma are bottlenecks in the progression towards a more precise phenotyping. In our experience using both techniques, we would like to justify the usefulness and safety of bronchoscopy in the work-up of severe asthma patients.

~~Asthma is a heterogenous disease that is characterized by airway inflammation resulting in airway hyperresponsiveness. A percentage of asthma patients fail to respond to standard asthma medications (mainly inhaled corticosteroids (ICS) with / without second controller bronchodilators) and require oral corticosteroids to control their symptoms which is defined as severe asthma. [1] In the last years, we are moving towards a precise phenotyping using biomarkers aiming at personalization of asthma therapy, especially T2 inflammation which is targeted by new advanced therapies. [2] However, current biomarkers are still imprecise, and the use of tissue biomarkers such as induced sputum or bronchoscopy are proposed as useful tools in the work up of severe asthma. Nevertheless, the lack of access to induced sputum in most centers and the perception that bronchoscopy could be unsafe in patients with severe asthma are~~

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~~bottlenecks in the progression towards a more precise phenotyping. In our experience using both techniques, we would like to justify the usefulness and safety of bronchoscopy in the work-up of severe asthma patients.~~

Bronchoscopy is a minimally invasive technique that was firstly used in 1907 to study an asthma case with favorable results.[3] After the appearance of flexible bronchoscopy, it was extensively used in the 1980s and 1990s as a research tool to study airway physiology, airway inflammation and pathological changes in adults with asthma.[4] Few studies reported the safety of bronchoscopy in asthma patients [5] with a debate in its use in those with FEV₁ less than 60%. Elston et al [6] and Moore et al [7] performed bronchoscopy to severe asthma cases with FEV₁ 55% predicted and they found that the procedure including bronchoalveolar lavage (BAL) and endobronchial biopsy were well tolerated and safe among this subpopulation of asthma. Earlier, Van Vyve et al [5] performed bronchoscopy without premedication with bronchodilators for asthma population where some of them had a FEV₁ of 37% and the researchers found no significant fall in spirometric parameters after the procedure; the associated decrease in arterial oxygen saturation was not correlated with disease severity. Thus, Van Vyve et al [5] concluded that bronchoscopy is well tolerated and safe in patients with asthma. Similarly, Humbert et al [8] found that bronchoscopy and bronchial biopsy were well tolerated in asthmatic patients with similar fall in PEFr in both asthmatics and non-asthmatics; however, they reported bronchospasm in relation to BAL, but no delayed effect on asthma control was detected after 2 weeks of follow up.

~~In the last decade, Good et al [9] studied 58 refractory asthma patients to identify the causes of lack of control which could help in the personalization of therapy.~~

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Severe uncontrolled asthma patients have also been explored with bronchoscopic sampling. Good et al [9] ~~After bronchoscopy they~~ identified 5 different subgroups of asthma: subacute bacterial infection, tissue eosinophilia, gastroesophageal reflux disease, combination and nonspecific phenotypes. More recently, Cosio et al [10] studied 100 consecutive asthma patients with severe uncontrolled disease whom underwent bronchoscopy with bronchial biopsy as a part of their evaluation. They identified 3 different clinical clusters: upper airway, infection and nonspecific. 50% of the later cluster had submucosal eosinophilia while submucosal eosinophilia was less frequently found in the infection phenotype. Interestingly, both Good et al [9] and Cosio et al [10] found 43% and 27% of their asthma population respectively had bacterial infection in their samples. Further, both researchers' groups reported that bronchoscopy is a safe procedure in the asthma population. The analysis of the implications of these microbiological findings on asthma control would deserve a detailed analysis, but it serves to comment on the safety of the procedure in both studies with severe asthma.

Bronchial thermoplasty (BT) studies for asthma also provide data on the safety of the procedure. ~~Bronchial thermoplasty (BT)~~ is an endoscopic treatment for severe and uncontrolled asthma patients despite adequate medical treatment. Gordon et al [11] developed a histopathological score of structural not inflammatory bronchial changes in bronchial biopsy for the evaluation of persistent severe asthma patient prior to BT. They found that BT significantly reduced the airway smooth muscle prominence. Similarly, Pretolani et al [12] found that BT effectively reduce the airway smooth muscle in refractory asthma as assessed by bronchial biopsy. Ichikawa et al [13] found also that BT reduce the airway smooth muscle prominence but not reducing airway inflammation or affecting the endobronchial vasculature. None of the

authors reported complications in relation to bronchoscopy and bronchial biopsy. Muñoz-Fernandez et al also described the safety of a modified protocol of BT [14].

Currently, possible implications for the selection of treatments can be glimpsed. In the era of biological therapy, ~~In the era of biological therapy,~~ blood eosinophilia, IgE and FeNO are the biomarkers commonly used as a biomarker for T2 inflammation and direct the use of biological therapy. However, Cosio et al [15] found that 5.4% patients with blood eosinophilia had no tissue eosinophilia in submitted bronchial biopsies and on the contrary others (37.5%) had tissue eosinophilia but not in blood. Moreover, Cosio et al [15] validated a standardized pathological score (modified from Gordon et al [11]) in the systematic assessment of the bronchial biopsy as a part of the evaluation of severe asthma. The authors reported only one case had moderate bleeding during the procedure that was well controlled locally.

During the last 100 years, bronchoscopy has been used to study ~~in~~-asthma with all types of severity. The majority of studies reported the safety of the procedure among this population with mild and well-tolerated side effects. Further, bronchoscopy adds information that could be a cornerstone in directing future therapy of asthma and, in our opinion, it should be performed in the work-up of severe asthma patients due to its usefulness and safety.

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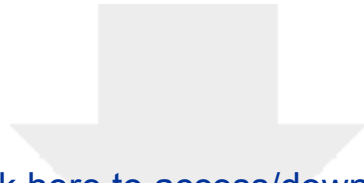
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Ethical disclosure

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