
Effectiveness of Biologics in Patients With Severe Asthma and Psychiatric Comorbidities

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To the Editor:

Asthma is a chronic inflammatory disease that affects up to 5% of Spanish adults; around 10% of patients have severe uncontrolled disease [1]. Biologics are currently a favorable option for managing severe asthma [1]. The prevalence of mental disorders in Spain is around 27.4%, with anxiety being the most frequent [2]. A significant percentage of patients with severe asthma have a concomitant psychiatric condition, which often interferes with asthma control and classification of severity and complicates assessment of the effectiveness of biologics [3]. Chronic psychological distress may cause a proinflammatory condition and be associated with increased superoxide and cytokine production [4]. Hurtado-Ruzza et al [4] found higher Beck's Depression Inventory scores in patients with asthma than in nonasthmatic controls and a direct correlation between the severity of depressive symptoms and that of asthma.

The incidence of anxiety is also higher in patients with asthma than in the general population [5]. The exact correlation between asthma and anxiety/depression remains unclear. Regarding anxiety in asthma, patients may experience continuous distress and fear of an attack, even when the disease is controlled. Since asthma symptoms can mimic anxiety attacks, and vice versa, affected patients, and sometimes even their treating physicians, confuse the two, especially those described by Patella et al [5] as “hyper-perceptors”, who sometimes perceive their usual asthma symptoms as very severe [5]. Moreover, depression or alexithymia are often associated with hypoperception of asthma symptoms, placing

patients at risk of a near-fatal outcome owing to delayed consultation with an asthma physician [4].

Therefore, it is necessary to have objective parameters to establish rigorous control of asthma, particularly in patients with psychiatric comorbidity, and especially when biological treatment is being considered for severe uncontrolled asthma.

The aim of our study was to analyze the efficacy of biologics in patients with severe asthma and psychiatric comorbidities. The patients gave their permission for their case data to be published.

We performed a single-center retrospective and descriptive study of patients followed up at the Severe Asthma Unit of Hospital Clinic, Barcelona within the last 5 years. We included all the patients with severe asthma treated with biologics who had at least 1 significant comorbidity diagnosed by a psychiatrist (anxiety, depression, major depression with suicide attempts, and/or schizophrenia) and who had received a biologic for at least 6 months. Clinical data were collected from the medical records.

We included 46 patients (37 women, 9 men) treated with 1 of the following biologics: omalizumab, mepolizumab, reslizumab, dupilumab, and benralizumab. The mean duration of biologic treatment was 48 months. Efficacy was assessed according to the recommendations of current Spanish guidelines, based on the reduction in annual exacerbations, the improvement in forced expiratory volume in 1 second (FEV₁), the reduction in systemic corticosteroids (SCS), and the degree of asthma control as measured using the Asthma Control Test (ACT). T2 biomarkers (fractional exhaled nitric oxide [FeNO], blood eosinophils, and total IgE) were also compared before and after treatment.

The 46 patients represented 37% of all the patients with severe asthma receiving biologics at the time of the analysis. The most prevalent psychiatric comorbidity was anxiety in 18 patients (39.1%), anxiety and depression in 15 (32.6%), depression in 6 (13%), anxiety-depression and attempted suicide in 4 (8.7%), depression with a suicide attempt in 2 (4.4%), and schizophrenia in 1 (2.2%).

When assessing the efficacy of biologics (Supplementary Table 1), we found a mean reduction in the annual number of exacerbations from 3.3 to 0.9. Mean FEV₁ improved from 1780 mL to 2000 mL (+220 mL), and FEV₁ (%) improved from 70% to 81% (+15.71%). The mean annual cumulative dose of SCS (calculated in milligrams of prednisone equivalent) decreased by 64.41%. The ACT score improved from 12 to 21 points. In addition, all T2 biomarker values decreased, although the difference was not statistically significant (Supplementary Table 1).

The criteria proposed by the 2022 Consensus of the Spanish Society of Pulmonology and Thoracic Surgery were used to assess the efficacy of biologic treatments. This consensus classifies the response as no response, partial response, control, and complete response, based on the 4 items we measured,

namely, exacerbations, ACT, FEV₁, and SCS. According to this score (the EXACTO score), a very good response was achieved in 66% of the patients (complete response in 52% and control in 14%), a partial response in 27%, and no response in 7% [1,6].

There is limited evidence on treatment of asthma with biologics in patients with psychiatric comorbidities. Patella et al [5] reported a significant improvement in disease management, perceived stress, and symptoms of anxiety and depression after a 16-week course of biologics (irrespective of the drug prescribed) for severe asthma during the COVID-19 pandemic [5].

In our series, we observed a good response to biologics in patients with severe asthma and serious psychiatric comorbidities in a real-world setting. Asthma was controlled, exacerbations were reduced, and lung function improved.

An Italian study found that anxiety, in particular lifetime anxiety disorders, represented the only psychiatric condition significantly associated with asthma, with a possible bidirectional, anxiety–asthma relationship [7]. Various scales can be used to measure anxiety and depression during an asthma evaluation in clinical practice, although these are mainly administered in the initial evaluation, not during follow-up. The Hospital Anxiety and Depression Scale, a self-administered questionnaire aimed at identifying anxiety and depression in patients with organ diseases [8], is a useful tool, although it has yet to be used as part of daily clinical practice in most severe asthma units.

As physicians who treat asthma, our objective is to clearly identify those patients with poorly controlled asthma using objective, standardized, and clearly defined measures, independent of patient perceptions and self-reported symptoms [9,10].

Our study has several limitations, namely, its retrospective design, the lack of a control group, the small sample size, the limited range of psychiatric conditions, and the fact that it does not account for other potential confounding factors that could affect asthma control and psychiatric status, such as lifestyle, socioeconomic level, and concurrent medications. Nonetheless, our real-world evidence shows that prescribing biologics when indicated in patients with comorbid psychiatric conditions is significantly beneficial and easily objectifiable in terms of asthma control based on the widely available and well-known parameters currently recommended by guidelines [6].

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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