Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Early experiences of SARS-CoV-2 infection in severe asthmatics receiving biologic therapy

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Clinical Implications

- We present an early experience with patients with severe asthma treated with different biologics and affected by severe acute respiratory syndrome coronavirus 2 infection.

Recently, most countries have been suffering from the spread of a highly contagious new coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes an infectious disease, referred to as "coronavirus disease 2019" (COVID-19) by the World Health Organization. The Chinese Center for Disease Control published the epidemiologic characteristics of the COVID-19 outbreak along with associated risk factors for death. So far, the most important identified risk factor was age, and chronic respiratory diseases have been also included in the list of potential morbidities at risk.[1] Around 334 million people have asthma worldwide, which makes it the most common chronic lung disease.[2] With the limited published evidence, allergic diseases and asthma do not seem to be risk factors for SARS-CoV-2 infection.[3] These results, however, have not been assessed in larger populations or in different countries.

Among 2226 adult patients admitted for SARS-CoV-2 infection at La Paz University Hospital, 5.5% had asthma, being a comorbidity for 3.5% of those patients who died.[4] Keeping in mind that approximately 5% to 10% of patients with asthma are affected by severe asthma and are on high-dose anti-inflammatory treatment,[5] and that a remarkable proportion of these patients requires mAbs aiming to achieve optimal asthma control, we investigated the impact of COVID-19 on such a vulnerable population, which may be at risk of potential complications.

A total of 71 patients with severe asthma in treatment with biologics (46 omalizumab, 14 mepolizumab, 6 benralizumab, and 5 reslizumab) were contacted by phone to check their clinical situation and proper administration of biologics. The study was approved by the Ethics Committee of our institution (PI-4201). All patients gave verbal informed consent, which was then registered in their electronic charts. Most patients were being treated with biologics at home on a self-administration program, with the exception of the 5 patients receiving reslizumab, 2 patients on treatment with omalizumab, and 1 with mepolizumab who were attending the day hospital for administration.

Because of the pandemic situation at that moment, specific questions were asked about symptoms suggestive of COVID-19 (hyposmia, ageusia, fever, sore throat, dyspnea, arthralgias, myalgias, asthenia, and diarrhea), close contacts with confirmed cases of COVID-19, asthma exacerbations, level of asthma control (based on GINA 2020 specific questions),[6] or open questions about any other situation that they considered could influence their asthma condition. Of these patients with severe asthma, 7 had been diagnosed with COVID-19: 4 of them with a confirmed diagnosis of COVID-19 respiratory infection and 3 subjects with a high suspicion of infection during the peak of the curve in Madrid (Spain) (last 2 weeks of March 2020). Patients' characteristics are described in Table I. There was only 1 patient with confirmed pneumonia who required a short hospitalization, the clinical pictures being much milder in the rest of the patients. No asthma exacerbations or worsening of asthma control was observed in these 7 patients during the COVID-19 infection.

Our findings suggest that the use of biologics in severe asthma does not have an impact on poorer clinical outcomes due to COVID-19 respiratory infection. However, our study has some limitations that should be noted. We have included only 7 patients who had symptoms suggestive of COVID-19 at the time of the phone interview, but we do not know the evolution of the patients who were asymptomatic at that time. No patients on treatment with biologics have died in this period. There was no confirmation of the infection in 3 patients, although they were highly suspicious of being infected, but unfortunately, in Spain massive testing has not been considered so far by our policymakers. However, the rate of infection in our patients (9.85%) was similar to the estimated rate of incidence among the population of Madrid (11.3%).[7] In addition, several studies have reported false-negative results of real-time RT-PCR, giving a supplementary role of chest X-ray or computed tomography features in cases of pneumonia[8] but not in milder clinical situations. In our infected patient population, we have not found associations with any comorbidity, and the clinical profile of infected patients was similar to that of the COVID-negative patients with severe asthma (mean age, 53.3 ± 13.74 years; 68.75% females; 40.84% had nasal polyps) followed in our severe asthma unit. Notwithstanding, 3 of the infected patients (42.8%) had a diagnosis of aspirin-exacerbated respiratory disease versus 25% in the COVID-negative patients ($P = .05$), but the potential existence of an association of this condition with COVID-19 will need further evaluation in larger cohorts. It has been described that the spike protein of SARS-CoV-2 binds with angiotensin-converting enzyme 2 to invade host cells and that smoking can upregulate angiotensin-converting enzyme 2 receptors.[9] From our results, however, we cannot conclude that smoking is a relevant factor for infection in these patients treated with biologics.

In conclusion, we report 7 patients with severe asthma treated with different biological therapies who have suffered and recovered from COVID-19. To our knowledge, there is no other published evidence regarding this important topic. However, more rigorous research to estimate the real impact of this infection in severe asthma is needed.

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TABLE I. Characteristics and treatment of the study patients

Sex	COVID-19 confirmed by PCR	Age (y)	Biologic	Clinical manifestations	COVID-19 treatment	Hospital admission	Smoking	Blood eosinophils (cells/μL)	Total IgE (kU/L)	Maintenance treatment
Male	Yes	50	Mepolizumab* (100 mg every 4 wk)	Fever/cough/dyspnea/ myalgias	Hydroxychloroquine	No	No	550	35	Salmeterol/fluticasone 25/250 μg twice a day Tiotropium 5 μg/24 h
Female	No	49	Omalizumab (300 mg every 4 wk)	Fever/cough	No	No	No	160	311	Formoterol/budesonide 9/320 μg twice a day Tiotropium 5 μg/24 h
Female	No	51	Omalizumab (450 mg every 4 wk)	Fever/dyspnea myalgias	Hydroxychloroquine/AZT	No (recommended, but stay home with medical supervision)	No	260	220	Formoterol/budesonide 9/320 μg twice a day Montelukast 10 mg/24 h
Female	Yes	63	Omalizumab (60 mg every 2 wk)	Fever/myalgias	No	No	Yes	190	1354	Formoterol/beclometasone 6/200 μg twice a day Tiotropium 5 μg/24 h
Female	No	32	Omalizumab (600 mg every 2 wk)	Myalgias	No	No	No	660	1400	Formoterol/budesonide 9/320 μg twice a day Tiotropium 5 μg/24 h Montelukast 10 mg/24 h
Male	Yes	47	Reslizumab (250 mg every 4 wk)	Pneumonia COVID	Hydroxychloroquine/AZT	Yes (2 d)	Ex-smoker	70	76	Formoterol/budesonide 9/320 μg twice a day Tiotropium 5 μg/24 h Montelukast 10 mg/24 h
Female	Yes	62	Omalizumab (225 mg every 4 wk)	Fever/cough	No	No	No	120	536	Symbicort 4.5/160 (2-0-2) + PRN Montelukast 10 mg/24 h

AZT, Azithromycin; *kU*: kilounit; *PRN*, as needed.
*5 mg prednisone/24 h.

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Conflicts of interest: J. Domínguez-Ortega has served as a consultant to LETI-Pharma, Mundipharma, AstraZeneca, Chiesi, Novartis, and GlaxoSmithKline (GSK) and has received lecture fees by Chiesi, GSK, Novartis, Leti, AstraZeneca, Sanofi, Stallergenes, and TEVA. D. Romero has participated in advisory boards and lectures for Mundipharma, AstraZeneca, Novartis, Bial, TEVA, and GSK. S. Quirce has served as a consultant and has received lecture fees by LETI-Pharma, Chiesi, GSK, Novartis, AstraZeneca, Sanofi, ALK, Boehringer Ingelheim, and TEVA. The rest of the authors declare that they have no relevant conflicts of interest.

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