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Severe asthma and COVID-19: lessons from the first wave

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ABSTRACT

Objective: Severe asthma is considered a risk factor for SARS-Coronavirus 2 (SARS-CoV-2) infection but scientific evidences are lacking.

Methods: we performed a literature search and review based on PubMed database national, international recommendations as well as papers on severe asthmatic patients and their management during SARS-CoV-2 pandemic.

Results: the majority of international recommendations, expert panels and editorials provide indications about management of severe asthmatic patients. No published studies evaluated the effects of biologic agents on severe asthmatic patients during SARS-CoV-2 pandemic.

Conclusions: the relationship between SARS-CoV-2 and asthma is variable worldwide and severe asthmatic patients were seldom reported in published cohorts. International recommendations suggest maintaining asthma under control to limit exacerbations occurrence, by using all available treatment. The minimum steroid dosage effective to control symptoms should be maintained to avoid exacerbations; biologic agents administration should be regularly scheduled encouraging patient support programmes.

Abbreviations: COVID-19: Coronavirus disease 2019; GINA: Global Initiative for Asthma; ICS: inhaled corticosteroids; OCS: oral corticosteroids; SARS-CoV-2: SARS-Coronavirus 2

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Severe asthma during SARS-CoV-2 pandemic

Since January 2020, SARS-Coronavirus 2 (SARS-CoV-2) affected millions of individuals worldwide causing Coronavirus disease 2019 (COVID-19). Asthmatic patients, as well as patients with other chronic lung diseases, were included in high risk population for SARS-CoV-2 infection based more on common sense than on scientific evidences (1,2). It is generally accepted that virus infection can increase the risk of exacerbations of allergic diseases, such as asthma (3). The initial insult to the epithelium, followed by the cytokine responses, triggers the exacerbation of lower respiratory symptoms (4). Previous pandemic coronavirus (SARS-CoV and Middle East respiratory syndrome coronavirus) were not associated with asthma exacerbations, but annually other nonpandemic seasonal coronavirus appeared to cause asthma exacerbations (5,6). To date, there are only few studies investigating the prevalence of SARS-

CoV-2 infection in asthmatic patients and data are conflicting: Asiatic reports showed a low prevalence of asthma in adult population affected by COVID-19 (7,8); on the contrary, in United States the Center for Disease Control and Prevention reported an overall prevalence of 17% in patients with laboratory-confirmed diagnosis of COVID-19 (9). However, it is important to highlight that asthma is underdiagnosed and undertreated in China, where an asthma prevalence of 4.2% is reported (10), perhaps explaining this apparent discrepancy.

Results of the Belgian Severe Asthma Registry evidenced no deaths or cases of very severe COVID-19 in the cohort of adult severe asthmatic patients; their data support to continue to use biologics during the pandemic (11). In Italy, only a small part of severe asthmatic patients included in Severe Asthma Network in Italy (SANI) cohort experienced symptoms consistent with COVID-19, but this population had higher prevalence of diabetes and other comorbidities (12);

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concordant results were obtained in large Italian cohort of patients treated with biologic agents, with a prevalence of SARS-CoV-2 positivity at nasopharyngeal swab of 0.8% (13).

During the first wave of SARS-CoV-2 pandemic many authors, national and international scientific societies published their recommendations about the management of severe asthmatic patients and use of biologics.

Several published documents confirmed the indication to continue the ongoing treatment whether they inhaled drugs and/or biologic agents (14–19). Morais-Almeida et al. suggested to be careful in patients with eosinopenia due to preliminary results, even if not confirmed by more recent studies, of a possible relationship between eosinopenia and worse prognosis of SARS-CoV-2 infection (15).

Shaker et al. published an expert panel consensus providing suggestion for asthmatic patients' management, including biologic treatment administration, during SARS-CoV-2 pandemic (14). Finally, Levin et al. proposed a modified algorithm for the treatment of acute severe asthma: the flow-chart restricts the nebulized therapy to life-threatening cases, augments treatment according to a closer observation and a prompt initiation of systemic therapy, allows a more flexible passage from nebulized therapy to metered dose inhalers with spacer, and vice versa, on the basis of clinical trend (20).

Respiratory organization recommendations

Severe asthma management is challenging in everyday medical practice (21,22). Recent COVID-19 pandemic has turned light on these patients. On 25th March, Global Initiative for Asthma (GINA) published a document with answers to frequently asked question on asthma management: in this regard, experts suggest that in patients suffering from the most severe forms of asthma who might require long-term treatment with oral corticosteroids (OCS), this treatment should be continued at the lowest possible dosage to minimize the risk of severe attacks or exacerbations. In this respect and with this aim, biologic therapies should be maintained in order to limit the need for OCS (23).

In order to obtain a detailed patient monitoring, and to avoid as much as possible admissions to Outpatient Clinics, the British Thoracic Society statement underlines the importance of an asthma action plan where patients register everyday asthma symptoms and treatment compliance and receive indications on how to manage asthma flares at home. Moreover, it should be emphasized to ensure a

sufficient supply of inhalers and to avoid sharing spacers with family members or friends (24).

The consensus-based expert panel of allergy/immunology specialists from United States and Canada provides several indications to clinicians for patients treated with biologic agents for severe asthma (14). The Authors proposed a guide for service reduction and prioritization in case of asthma and other immunologic conditions. First, the role of corticosteroids during COVID-19 as medication for the management of chronic diseases is addressed. The low prevalence of asthma in COVID-19 observational studies suggests that asthmatic patients may not be at increased risk of more severe disease, even in case of ICS regular use. It is more likely that asthmatics exacerbate for other causes (i.e. seasonal allergen exposure, other respiratory viruses) when controllers are discontinued. Experts state that asthma management should follow current guidelines and recommendations until studies conducted on asthmatics with SARS-CoV-2 show opposite evidence (14). Second, the administration of biologic agents in severe asthmatic patients is of crucial importance: Shaker et al. concluded that there is no evidence that suggests an impairment of immune response to SARS-CoV-2 in patients treated with anti-IL-5, anti-IL-5R, anti-IL-4/IL-13 and anti-IgE drugs. In particular, the first administration of biologics should be performed at home during visits of health care services; if this management is not feasible, a maximum of 2 visits to the hospital should be allowed for in-office initiation, Authors stated that the administration of biologic agents during COVID-19 pandemic should be continued followed by self-administration (14). In Europe, omalizumab home administration is approved after the first four administrations in clinic, whereas this is not the case in other countries. For other biologics, the switching to prefilled syringe encourages the transition to self-administration at home, given that the patient or the caregiver have been trained in the correct sub-cutaneous injection technique and the recognition of the early signs and symptoms of serious allergic reactions. This would avoid the potential risk of missing doses.

In line with this, the recently published NICE (National Health Institute for Health and Care Excellence) rapid guidelines on severe asthma management during COVID-19 confirmed the possibility to start a monoclonal antibody only after the consideration of all the possible risks and benefits. Besides, patients with severe asthma should maintain OCS at their prescribed dose because stopping them can be harmful (25).

The Canadian Thoracic Society confirmed the indication to maintain an exacerbation management according to national and international asthma treatment guidelines, expecting to minimize the risk of SARS-CoV-2 exacerbation. They suggest using prednisone to treat severe asthma exacerbations whether or not triggered by SARS-CoV-2. Finally, biologic should be continued, eventually self-administered, and, when temporally interrupted, implementing other controller therapies (26).

Up to now, during the second pandemic wave no position papers were published neither international guidelines updated their indications for the management of severe asthmatic patients. We actually must record the use of steroids in patients with SARS-CoV-2 pulmonary infection, as demonstrated in RECOVERY trial: in this trial the use of dexamethasone led to a reduction of 28-day mortality among those who received either invasive mechanical ventilation or oxygen alone (27).

Conclusions

In conclusion, the interactions between SARS-CoV-2 and asthma are still nebulous, requiring further investigations; up to now, the relationship between COVID-19 and asthma is variable worldwide due to different methodologic approaches of published studies. From the first pandemic wave, we have learned some important lessons: it is fundamental to maintain asthma under control in order to limit the possibility of serious exacerbations occurrence, with all available treatment and those that are currently in place. Experts consensus and recommendations suggest maintaining the minimum steroid dosage effective to control symptoms and to avoid exacerbations, whereas biologic agent administration should be regularly scheduled, possibly at home, encouraging patient support programmes (28). It would be desirable an update of guidelines and recommendations for the second wave of the pandemic, in order to give to clinicians most recent information and indications for the management of severe asthmatic patients.

Authors' contributions

Patrucco Filippo: Conceptualization, Methodology, Writing original draft, Writing review & editing; Benfante Alida: Conceptualization, Methodology, Writing original draft, Writing review & editing; Villa Elisa: Conceptualization, Methodology, Writing original draft; Principe Stefania: Writing original draft, Writing review & editing; Scichilone Nicola: Conceptualization, Methodology, Supervision, Writing review & editing; Solidoro Paolo: Conceptualization, Methodology, Supervision, Writing

review & editing. All authors read and approved the final version of the manuscript.

Declaration of interest

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