

Letter to the Editor



Management of Severe Asthma During the COVID-19 Pandemic in Korea

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Since the coronavirus disease-19 (COVID-19) epidemic began in December 2019, more than 2.8 million confirmed cases have been reported worldwide, and the disease is still spreading. The World Health Organization declared the COVID-19 pandemic in March 2020, and several clinical guidelines have been recommended regarding strategies for COVID-19 in patients with various underlying diseases, including asthma. According to the reports so far, the prevalence and severity of the COVID-19 in asthmatic patients are not much different from those in the general population, suggesting that asthma may not be a risk factor for COVID-19, even though viral infection is the major triggering factor of asthma exacerbation (AE) in adult asthmatics.¹⁻⁴ This report is aimed to share our experience and provide valuable insight into management of adult patients with severe asthma during the COVID-19 pandemic.

MANAGEMENT OF STABLE ASTHMA DURING THE COVID-19 PANDEMIC

Asthmatic patients tended to avoid regular hospital visits and treatment for fear of contracting COVID-19, increasing the difficulty in asthma control. In particular, patients with severe asthma being treated with high-dose inhaled corticosteroids (ICSs), systemic corticosteroids (SCSs) or biologics⁵—which are often regarded as immunosuppressive or immunomodulators—there is concern whether pre-morbid use or continued administration increases the susceptibility to or the severity of COVID-19. However, experts recommend maintenance of ICSs and biologics to prevent AE, but minimal use of SCS.

There is no direct evidence that ICS use increases the risk of COVID-19.^{6,7} Furthermore, recent *in vitro* studies suggest that ciclesonide, an ICS, blocks severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ribonucleic acid replication and inhibits SARS-CoV-2 cytopathic activity, which may be of great relevance to reduction in the risk of COVID-19.^{8,9}

Although the effects of SCS on this infection are still controversial, it is advisable that clinicians maintain SCSs at the lowest possible dose and do not discontinue their administration to prevent AE in patients with severe asthma will may experience AE after sudden cessation of SCSs. In addition, there is no evidence that the biologics used in patients

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with severe asthma suppress immunity; therefore, biologics can also be continued. A new biologic treatment is initiated after the balance between therapeutic benefit and risk is assessed thoroughly explored.⁶

It is recommended that routine pulmonary function tests (PFTs), including spirometry be postponed and limited to inevitable tests for immediate treatment decision, because such tests can disseminate viral particles and staff and patients are exposed to risk of infection. If necessary, adequate infection control measures should be taken.⁶ Given the benefits of not doing routine PFTs in severe asthmatic patients, it seems appropriate to postpone the test only when COVID-19 peaks with community infection in each region. In several medical centers in this country, while COVID-19 incidence has peaked, spirometry has been postponed until patients with respiratory symptoms have negative results on reverse transcription polymerase chain reaction (RT-PCR) tests for COVID-19.

In addition, all asthmatic patients should be instructed to follow their personalized asthma action plans (AAPs). If an AE arises, an SCS can be used as specified in their AAP.⁶ In the regions with low use of AAP such as South Korea, it is not only necessary to establish a personalized AAP, but a specialized clinical plan should be designed to provide asthmatic patients with safe, immediate medical services. Thus, ICSs and biologics can be continued, while SCS use should be minimized.

MANAGEMENT OF AE DURING THE COVID-19 PANDEMIC

Among the patients with COVID-19 reported to the Centers for Disease Control and Prevention of the United States, higher percentages of patients with chronic lung diseases, including asthma and chronic obstructive pulmonary disease, were admitted to hospital or to an intensive care unit than those without.¹⁰ However, asthma does not seem to have a significant effect on COVID-19 deaths.^{4,11} These results are consistent with those from South Korea.¹² Moreover, COVID-19 does not appear to cause AEs, although there is no direct evidence on it. Data from 3 university hospitals including, 2 hospitals in Daegu, the epicenter of the outbreak in South Korea, show that 45 asthmatic patients with suspected AEs or pneumonia underwent COVID-19 RT-PCR tests, only 2 of whom were confirmed to have COVID-19. Both of these patients had pneumonia, but there were no obvious signs of AE. They had been well controlled with low- to medium-dose ICS treatment before being affected by COVID-19. During hospitalization for treatment of COVID-19 pneumonia, treatment with ICS and long-acting β_2 agonists successfully controlled their asthma symptoms. We infer carefully from our limited observations that COVID-19 does not have a significant impact on AE in asthmatic patients, particularly those with well-controlled non-severe asthma. It remains unclear whether SCS use to treat AEs caused by or combined with COVID-19 is beneficial or harmful in COVID-19. Clinical guidelines suggest careful use of SCSs for AE associated with COVID-19 in: (1) critically ill patients with COVID-19 pneumonia, (2) those with hypoxemia due to underlying disease or who regularly use SCSs for their disease, (3) those whose dosage should be low-to-moderate (≤ 0.5 -1 mg/kg/day methylprednisolone or equivalent), and (4) those whose duration is as short as ≤ 7 days.¹³

Although COVID-19 does not seem to cause AE, the longer the pandemic duration, the greater the cumulative frequency of AEs due to aggravating factors such as seasonal/perennial allergens and other respiratory infections during the pandemic.¹⁴ Guidelines recommend that

patients with AE not caused by COVID-19 should receive a short course of SCS prescription by their attending physicians to prevent serious consequences.⁶

As described above, many patients with asthma are reluctant to visit medical institutions in fear of exposure to COVID-19 and to discontinue medications, which can be significant risk factors of AE. Therefore, it is important to establish a specialized clinical plan to provide asthmatic patients with proper treatment to prevent serious AE during the COVID-19 pandemic.

PREVENTIVE STRATEGIES FOR COVID-19 IN PATIENTS WITH SEVERE ASTHMA

During the ongoing COVID-19 pandemic while maintaining a social distance of 2 m during daily activities has been proposed, many regular visits to medical centers and health care could be delayed or handled through telemedicine. However, patients with asthma, especially severe asthma, need to continue face-to-face visits to the medical institutions even during the COVID-19 pandemic to maintain control of their asthma. However, there is no consensus on how to prioritize medical services for patients. The government of South Korea has designated 'Public Relief Hospitals' during the period of the COVID-19 pandemic to guarantee general medical services and to prevent the virus from spreading. The purpose of this system is to separate areas for general patients from those for respiratory patients to prevent infection in hospital. Therefore, general patients without risk of COVID-19 or any suspicious symptom of COVID-19 could be permitted to visit medical institutions. Ironically, under the Public Relief Hospitals system, although patients with asthma, especially when they have AEs, should be prioritized for face-to-face care, optimal medical services cannot be provided until a negative result of the COVID-19 RT-PCR test is confirmed because they usually present respiratory symptoms such as cough, sputum, and dyspnea, which are difficult to distinguish from COVID-19. For appropriate management of patients with asthma, experts suggest specialized clinical plans based on updated clinical guidelines and state-of-the-art information on COVID-19.¹⁵ Such plans should include the following: (1) patients with well-controlled asthma or stable mild-to-moderate asthma in the past 6 to 12 months may postpone routine face-to-face visits, and use telemedicine or care by proxy to ensure continuity of care; (2) patients with severe asthma are encouraged to visit the medical institutions for face-to-face care and prescriptions; (3) asthmatics with AEs or in poor asthma control status need to follow COVID-19 screening protocols in order to determine their risk of COVID-19 infection and need for testing at a designated facility; and (4) in cases of severe asthma with COVID-19 risk, face-to-face treatment is carried out by medical staffs wearing personal protective equipment (PPE) in the negative pressure isolation ward while waiting for test results (**Figure**).

Specifically, the designated hospitals for the treatment of COVID-19 in Daegu, Korea's largest COVID-19 outbreak area, follow a specialized clinical plan for patients visiting the emergency department with suspicious symptoms of AE: (1) COVID-19 risk evaluation at the initial triage—major symptoms including fever, cough, and dyspnea—and epidemiological risk evaluation such as contact history with a confirmed or suspected case and travel history; (2) COVID-19 RT-PCR test and chest X-ray imaging in an isolated room under negative pressure by medical staff wearing PPE; (3) general management of AEs after release of quarantine for patients with negative COVID-19 testing—treating with systemic corticosteroids and short-acting bronchodilators using metered-dose inhalers with spacers instead of nebulizers, since

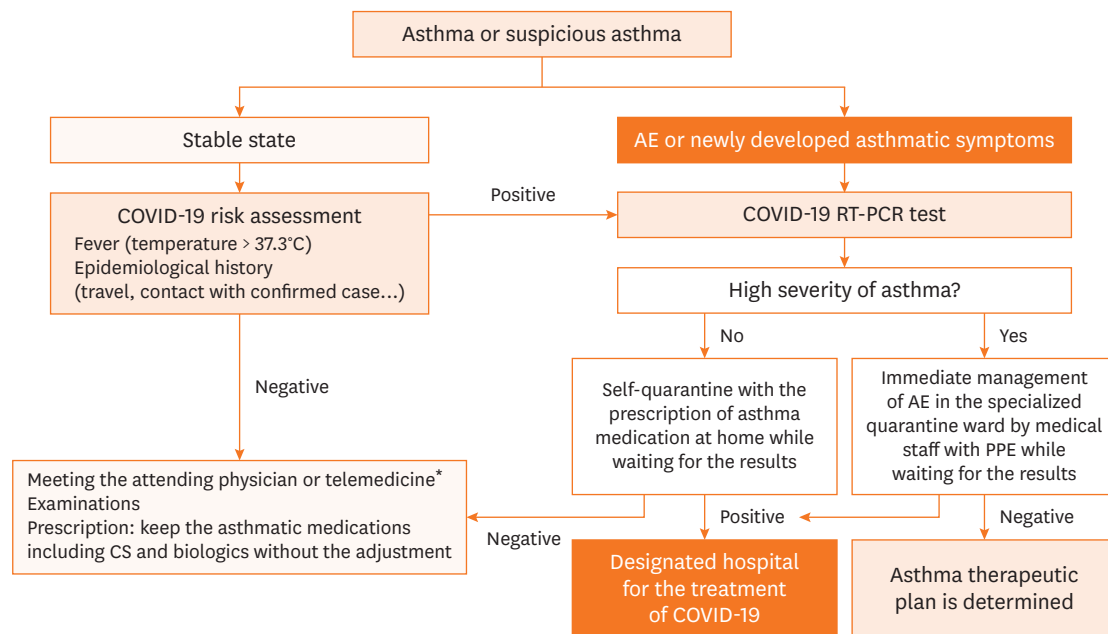


Figure. Specialized clinical plan for the management of asthmatic patients during the COVID-19 pandemic.

COVID-19, coronavirus disease-19; RT-PCR, reverse transcription polymerase chain reaction; CS, corticosteroids; AE, asthma exacerbation; PPE, personal protective equipment.

*In South Korea, telemedicine is temporarily allowed only during the COVID-19 pandemic.

the use of nebulizers inside healthcare facilities including the emergency department may increase the risk of aerosol spread of virus particles.⁶

In terms of personal quarantine, asthmatic patients are also advised to maintain general personal hygiene including wearing a face mask and to maintain a social distance of 2 m. In some patients with asthma, wearing a face mask can lead to further difficulty in breathing, but it is important to wear a mask when visiting medical facilities and enclosed public space such as locker rooms and elevators, or when new respiratory symptoms occur. However, it is better to choose a mask type that is easy to breathe, depending on the respiratory condition. Most of all, optimal asthma control is expected to be the best protective strategy for all asthmatic patients against AE caused by COVID-19 or other factors.

In conclusion, there have been few studies to demonstrate a specifically increased risk for COVID-19 in patients with asthma, and it cannot be ruled out that COVID-19 may cause AE. Thus, based on up-to-date information, we should prepare effective strategies for the prevention and treatment to protect patients with asthma. To maintain health, patients with severe asthma should maintain their controller medications including, ICSs, SCSs, and biologics, continue visits to medical facilities, and prepare an immediate clinical management plan for severe AE, including a COVID-19 RT-PCR test. Under physicians' supervision, SCSs can be used for the control of AEs. Importantly, the plans should also follow personal quarantine guidelines.

In human history, outbreaks of infectious diseases have repeatedly occurred. The process of overcoming COVID-19, a new infectious disease that can be fatal due to damage to the respiratory tract, can be an opportunity to learn more about asthma management.

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