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LETTER

Common concerns in managing bronchial asthma during the COVID-19 pandemic

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Dear Editor,

The use of corticosteroids and nebulised bronchodilators in bronchial asthma (BA) is a major concern during the COVID-19 pandemic. Inhaled corticosteroid (ICS) is the recommended treatment for all levels of BA severity, while oral corticosteroid (OCS) is used in severe asthma and acute exacerbation of BA (AEBA).[1] Because corticosteroid is an immunosuppressant, BA patients on corticosteroid treatment are theoretically at a higher risk of contracting COVID-19 and may suffer more severe disease. Nebulisation of bronchodilators is a frequent treatment modality for patients attending an emergency department for AEBA because of a common perception that it is more effective and faster in symptom relief. However, nebulisation may cause dispersion of SARS-CoV-2 into the surrounding environment, putting other patients and

healthcare workers at risk. There are several issues that need to be addressed. First, AEBA precipitated by COVID-19 is difficult to distinguish from other respiratory tract infections. Second, patients may have asymptomatic COVID-19 and their AEBA may be precipitated by other causes. Third, AEBA may be the only complaint of the COVID-19 patients, who lack symptoms such as fever, headache etc. In this Letter, we address some common concerns in managing BA during the COVID-19 pandemic.

First, are patients with BA more susceptible to SARS-CoV-2 infection? The prevalence of BA in COVID-19 patients in China is remarkably low (see Table). A recent study by Li et al. reported that only 0.9% of COVID-19 patients admitted to a hospital in Wuhan, China, had BA.[2] Two other studies specifically looked for BA among COVID-19 patients but did not report any cases.[3,4] BA was not included as a significant comorbidity reported by other studies conducted in China. In contrast, studies in the United States reported the prevalence of BA to be 17% among hospitalised COVID-19 patients and 9.1% among COVID-19 patients admitted to intensive care units, which is higher than the national average of 7.7%.[5,6] Based on these data, there is no consistent evidence to suggest patients with BA are more susceptible to COVID-19.

The second concern is whether BA patients suffer from severe COVID-19 if infected by SARS-CoV-2. Li et al. reported that BA is not associated with more severe disease or higher mortality in COVID-19.[2] To date, no other study has reported BA patients are at higher risk of poor outcomes or have more severe exacerbation if infected by SARS-CoV-2. Since SARS-CoV-2 utilises angiotensin-converting enzyme 2 (ACE-2) as a cellular entry receptor to infect the human host, one possible explanation for the reduced susceptibility of BA patients to SARS-CoV-2 infection and to severe COVID-19 is the reduced ACE-2 gene expression in nasal and bronchial epithelial cells in patients with allergic rhinitis and atopic asthma.[7]

Next, should regular ICS or OCS be withheld during the COVID-19 pandemic? The Global Initiative for Asthma and the National Institute for Health and Care Excellence has recommended continuation of ICS and OCS as clinically indicated during the COVID-19 pandemic.[1] Withdrawal of corticosteroids may lead to worsening of asthma control and severe AEBA. Seeking treatment at healthcare facilities for uncontrolled BA during the pandemic may predispose these patients to SARS-CoV-2 infection and further overwhelm the healthcare facility. Therefore, corticosteroids should be maintained during the pandemic to keep BA under control. There is also some evidence suggesting ICS may be beneficial in treating COVID-19. First, the combination of ICS with bronchodilator has been shown to supress coronavirus replication and cytokine production in vitro.[8] Second, inhaled ciclesonide, a corticosteroid

commonly used to treat allergic rhinitis and BA has been shown to successfully treat three cases of COVID-19 pneumonia.[9]

A fourth concern is the administration of bronchodilators by nebulisers to patients with moderate-to-severe AEBA during the pandemic. Current evidence indicates that COVID-19 is transmitted by droplets, direct contact and fomites. Airborne transmission of COVID-19 from person-to-person has not been reported. However, nebulisation may promote airborne transmission of respiratory viruses, including SARS-CoV-2. Viable SARS-CoV-2 is reported in aerosols generated by jet nebuliser for up to 3 hours.[10] The use of a jet nebuliser to deliver bronchodilators to a severe acute respiratory syndrome (SARS) patient was the cause of a major nosocomial SARS outbreak.[11] SARS-CoV-2 has a higher binding affinity to the ACE-2 receptor than the SARS coronavirus. Therefore, it is very likely nebulisation of bronchodilators can cause aerosol transmission of COVID-19. If possible, nebulisation should be avoided. Airborne precautions should be strictly adhered to if nebulisation is unavoidable, such as in patients with life-threatening AEBA.

The fifth concern is how to administer bronchodilators for moderate-to-severe AEBA during the COVID-19 pandemic. Randomised control trials (RCTs) have reported that delivery of bronchodilators using pressurised meter-dose inhalers (pMDIs) with a spacer is equally effective and safe as nebulisation in adults with non-life-threatening AEBA.[12] The 2005 joint report by the American College of Chest Physician and the American College of Asthma, Allergy and Immunology concluded that there is no significant difference in terms of efficacy and adverse outcomes among patients receiving pMDIs, dry powder inhalers (DPIs), or nebulisation for AEBA.[13] Therefore, either pMDI with spacer or DPI can be used to administer bronchodilators in AEBA. The former does not depend on the patient's inspiratory effort which is frequently reduced during AEBA, making it a better option than DPI. A meta-analysis of several RCTs concludes that patients with AEBA receiving a combination of inhaled short-acting ß$_2$-agonist (SABA) and short-acting muscarinic antagonist (SAMA) are more likely to have lung function improvement and less likely to be hospitalised compared to inhaled SABA alone.[14] Based on this evidence, pMDI of SABA and SAMA with a spacer is the most appropriate treatment for adults with moderate-to-severe AEBA.

Finally, the use of systemic corticosteroids to treat AEBA may raise safety concerns during the COVID-19 outbreak. Systemic corticosteroids significantly reduce hospitalisations and exacerbation relapse in adults with AEBA. To our knowledge, an adverse effect of systemic corticosteroids has only been reported in patients with severe SARS and Middle East Respiratory Syndrome (MERS), but not in patients with COVID-19. Guidelines by the WHO

do not recommend against the use of systemic corticosteroids in COVID-19 patients if the use is clinically indicated, such as for AEBA.[15] Therefore, short courses of systemic corticosteroids can be given to patients with AEBA during the COVID-19 pandemic.

In conclusion, other than avoiding nebuliser use, the management of BA during the COVID-19 pandemic is not different from the usual practice. However, more studies are needed to determine whether BA patients are more susceptible to COVID-19 or have more severe COVID-19.

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Table Prevalence and severity of BA in COVID-19 patients

		Prevalence		
		Chronic lung		BA and severe
	Patients	disease	BA	COVID-19
Study	*n*	*n* (%)	*n* (%)	*n* (%)
Li[2]	548	22 (4.0)	5 (0.9)	3 (0.5)

Guan[3]	1,590	24 (1.5)	0	NA
Zhang[4]	140	2 (1.4)	0	NA
Garg[5]	159	55 (34.6)	27 (17.0)	NA
Arentz[6]	21*	9 (42.8)	2 (9.1)	NA

*All patients were admitted to the intensive care unit.

BA = bronchial asthma.