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.

Commentary on Eosinophilic Inflammation, Coronavirus Disease 2019, and Asthma

Are inhaled corticosteroids the missing link?

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Thank you for allowing us the opportunity to reply to the recent correspondence of Ramakrishnan et al[1] regarding the study "Eosinophilic inflammation, COVID-19, and asthma—are inhaled corticosteroids the missing link?" We are grateful for the kind remarks and insightful comments.

The correspondence reinforces the importance of eosinophils in coronavirus disease 2019 (COVID-19), from playing a protective role against severe COVID-19 illness among patients with and without asthma to being a biological marker of recovery.[1,2] Moreover, the benefits of systemic corticosteroids in COVID-19 raise the question of whether previous inhaled corticosteroid (ICS) use has any role in COVID-19 outcomes in patients with asthma.[3,4] The authors noted that the magnitude of the protective effect of eosinophils at levels greater than or equal to 200 cells/μL was more significant ($P < .001$) in those with asthma than those without, speculating whether ICS use may be responsible for this difference in outcomes. However, data on ICS use before and during hospitalization was not available to us. There may be a complex interplay among viral infections, allergic or type 2 inflammation, and the immunologic response to viral infections and asthma beyond the effect of ICSs.[5] Nevertheless, ICS use has been found to reduce coronavirus replication and has an essential role in reducing viral exacerbations of chronic obstructive pulmonary disease.[6] The authors of OpenSAFELY (National Health Service, United Kingdom) attributed the very slight increase in mortality in those using high-dose ICSs in COVID-19 to unmeasured confounding factors.

In contrast, others have found that ICS use was not associated with worsened outcomes.[7] The role of ICSs in reducing the expression of 2 proteins, TMRSS2 and ACE2, involved in the viral entry of severe acute respiratory syndrome coronavirus 2 into host cells, provides a possible explanation for the protective effect of ICSs. However, it must be noted that our study found that improved outcomes were seen in patients without asthma with elevated eosinophil counts who would not be on ICSs, suggesting that ICS use was not the only possible explanation for improved outcomes in patients with eosinophilia.

We read with great interest and applaud the work of Ramakrishnan et al[8] on their phase 2 clinical trial describing the role of ICSs in outpatients with COVID-19. The study illustrates that ICS use can reduce the risk of clinical deterioration and prevent increased health care resource utilization. The potential for an inhaled, locally acting, and readily available medication such as an ICS to ameliorate the course of COVID-19 is very promising.

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