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Letter to the Editor

The use of dornase alfa in patients with COVID-19

We compliment Carr et al. [1] for performing and reporting their global cohort study which investigated the impact of coronavirus disease 2019 (COVID-19) in patients with cystic fibrosis. In the present study, a multivariable analysis was performed to determine the risk factors for severe course of COVID-19 among patients with cystic fibrosis. It was observed that the pre-diagnosis use of cystic fibrosis transmembrane conductance regulator (CFTR) modulators was significantly associated with a reduced risk of severe course of COVID-19 in this population of patients (adjusted odds ratio = 0.43; 95% confidence interval 0.31 to 0.60; $P < 0.001$).

Nevertheless, we believe it is a waste of opportunity for not investigating the effect of pre-diagnosis use of dornase alfa on the risk of severe course of COVID-19 in this large global cohort of patients ($n = 1452$) with cystic fibrosis. Previously, a smaller prospective cohort study [2] ($n = 236$) which investigated the clinical course and risk factors for severe course of COVID-19 among patients with cystic fibrosis reported that the pre-diagnosis use of dornase alfa was significantly associated with a reduced risk of severe course of COVID-19 (adjusted odds ratio = 0.34; 95% confidence interval 0.13 to 0.88; $P = 0.026$).

The finding where pre-diagnosis use of dornase alfa was associated with reduced severity of COVID-19 suggest its value to be repurposed for the treatment of COVID-19. As a matter of fact, there are pharmacological rationales where dornase alfa could be beneficial for patients with COVID-19, especially in those with severe course of illness. The extensive research on COVID-19 since the beginning of the pandemic has led to our growing understanding on its pathophysiology, where it has come to the researchers' knowledge that neutrophil extracellular trap (NET) formation is implicated in the development of severe course of COVID-19. NETs and other by-products of NETosis can act as direct amplifiers of inflammation to promote multiorgan failure and thrombosis in patients with COVID-19 [3]. Indeed, it has been reported that in patients with COVID-19, persistent elevations in NETs post-disease diagnosis were detected in patients who developed severe illness but not in their counterparts with asymptomatic infection [4]. Moreover, NETs were detected in many organs of adult patients who died from COVID-19 related complications [4]. Patients with COVID-19 also displayed impaired NET degradation, which leads to the persistence of symptoms [4].

As a recombinant human deoxyribonuclease I, dornase alfa degrades extracellular DNA fragments. Since the double-stranded DNA constitutes the backbone of NETs, dornase alfa could promote the clearance of NETs in patients with COVID-19 to prevent further organ damage and thrombosis. Indeed, an observational study [5] has reported the positive effects of dornase alfa in patients with COVID-19 who developed acute respiratory distress syndrome, where improvement in oxygenation and reduction in ventilatory support were observed upon administration of aerosolized dornase alfa. The use of NET degraders such as dornase alfa may be more useful than NETosis inhibitors especially in patients with severe course of COVID-19, where extensive NETosis has developed, and there is impaired NET degradation. Therefore, we believe if the present study [1] with large global cohort of patients with cystic fibrosis could investigate the effect of the pre-diagnosis use of dornase alfa on the prognosis of COVID-19, it could lead to better understanding on the role of dornase alfa in the treatment of COVID-19. We also urge for the performance of clinical trials which investigate the use of dornase alfa in patients with COVID-19 if positive observational evidence is reported.

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Declaration of Competing Interest

All authors declare that they have no potential conflicts of interest that might be relevant to the contents of this article.

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