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Cystic Fibrosis Research News

Title:

Alpha-1 Antitrypsin for Cystic Fibrosis Complicated by Severe Cytokinemic COVID-19

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What was your research question? Coronavirus disease 2019 (COVID-19) results from a SARS-CoV-2 (coronavirus) infection and is a global threat to health. We tested the use of alpha-1 antitrypsin (AAT). AAT is a naturally produced protein with anti-inflammatory properties. We tested AAT as a salvage therapy in a critically unwell person with CF (PWCF) who developed COVID-19 while awaiting lung transplantation.

Why is this important? Although public health initiatives such as regular hand-washing, social distancing, cocooning, mask-wearing and cough etiquette may reduce the exposure of PWCF to the coronavirus, they may still become infected and develop COVID-19. Unfortunately, treatment options for severe COVID-19 are limited, as are effective anti-inflammatory therapies for severe infective exacerbations of CF.

This study was also important regarding the allocation of resources such as ventilators and intensive care unit (ICU) beds during a pandemic. As allocation discussions included prioritizing people without progressive lung disease, PWCF became at risk of being overlooked because of their genetic diagnosis and the assumption that their likelihood of recovery may not be worth the use of limited resources required of ventilating.

What did you do? The patient, in this case, deteriorated rapidly and progressed to acute respiratory distress syndrome (ARDS), a type of lung injury that is associated with a very poor prognosis in COVID-19. We analysed blood and airway samples from the patient after she was admitted to the ICU. These samples demonstrated increases in pro-inflammatory proteins. After attempts to improve her clinical condition using conventional ARDS treatment strategies failed, we explored the possibility of using AAT as a patient-tailored salvage therapy. We gave high-dose AAT

(120mg/kg) intravenously (directly into the blood) because the high levels of inflammation were observed in the patient's blood, not just her lungs.

What did you find?

Almost immediately after her first dose, the levels of inflammation in the patient's blood and lungs decreased, and she improved clinically. However, as the effects of the drug wore off, her inflammation went up again, and she declined once more. A repeat dose – given one week after her first infusion – was followed by fresh reductions in levels of these inflammatory markers. Further doses, given at weekly intervals, were matched by additional clinical and biochemical improvements. By one month, the patient's inflammation levels had returned to their baseline, and she was well enough to leave the ICU.

What does this mean and reasons for caution?

The results may inform future efforts to provide personalized care for PWCF, may prompt consideration of AAT as an anti-inflammatory therapy for use in severe infective exacerbations of CF and, potentially, as a treatment for those with COVID-19. However, not all patients with COVID-19 display the same clinical and biochemical features as this patient, and therefore the results may not be generalizable to COVID-19 patients who do not have CF.

What's next?

The patient has since been successfully discharged from the intensive care unit and has been re-accepted back onto the active transplant list. She had been de-listed following her diagnosis of COVID-19 and subsequent rapid deterioration. A clinical trial of AAT for non-CF patients with severe COVID-19 is now underway.

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