Clinical trial: Repurposed drug improves outcomes for patients with severe COVID-19 pneumonia

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A drug commonly used to treat cystic fibrosis improved outcomes for
patients with severe COVID-19 pneumonia and could be used to treat other respiratory infections, according to clinical trial results from researchers at UCL, UCLH and the Francis Crick Institute.

The study, published in *eLife*, found that the drug dornase alfa reduced hyper-inflammation in COVID-19 pneumonia patients, which occurs when the body's immune system reacts too strongly and can lead to tissue damage and death.

The next step will be to conduct larger clinical trials, with the ultimate goal of approving dornase alfa for wider use. As well as COVID-19, dornase alfa has the potential to treat other respiratory infections such as those caused by influenza or bacterial pneumonia, and even other lung diseases such as pulmonary fibrosis.

Since the beginning of the COVID-19 pandemic, the proportion of SARS-CoV-2 infections that result in death has fallen from a high of almost 1,400 deaths on 19 January 2021 to 143 deaths on 21 June 2024. This is partly down to increased immunity from prior infection or vaccination, as well as improved treatments for those who become seriously ill such as dexamethasone, a steroid that helps to tackle the hyper-inflammation that was a key factor in many COVID-19 deaths. But this treatment isn't suitable for some patients and is not always successful in severe cases.

In this study, researchers from UCL, UCLH and the Francis Crick Institute set out to assess whether dornase alfa could be used to improve outcomes for patients admitted to hospital with severe COVID-19 pneumonia who required oxygen.

Out of a total of 39 participants, 30 were randomized to receive twice-daily treatment with nebulized dornase alfa in addition to best available care (BAC) which included dexamethasone, with nine patients
randomized to BAC only.

Patients treated with dornase alfa had a 33% reduction in systemic inflammation on top of the reduction provided by dexamethasone, as measured by C-reactive protein (CRP) levels in the blood over seven days or until they were discharged from hospital.

Dr. Venizelos Papayannopoulos, senior author of the study from the Francis Crick Institute, said, "Dexamethasone has been highly successful in treating patients with severe COVID-19 pneumonia and is now standard care in the UK. But it isn't suitable for some patients, such as those with diabetes, those that do not require oxygen, and in very severe cases it may not be enough. Dornase alfa can be used to treat a wider variety of patients and gets right to the heart of the inflammatory response. Based on these results, we think it will be a valuable tool for tackling severe COVID-19 illness."

Patients treated with dornase alfa were also more likely to need less oxygen and be discharged sooner compared to patients who received BAC. These additional benefits could help to free up beds and resources in the UK's busy hospitals.

The next step will be to conduct larger clinical trials to ensure dornase alfa is safe and effective for treating severe COVID-19 pneumonia. There is also potential for the drug to be trialed for other respiratory infections and conditions, such as acute exacerbations of pulmonary fibrosis, where inflammation of already scarred lung tissue affects how well oxygen can be absorbed.

Professor Joanna Porter, first author of the study from UCL Medicine and UCLH, said, "Given that we observed a significant further reduction in C-reactive protein in patients who were already receiving dexamethasone, which also reduces inflammation, this trial is proof-of
concept that dornase alfa can be used to treat severe COVID-19 pneumonia. If we can help patients recover more quickly and get home sooner, this would be great for them and also help to reduce pressure on the NHS.

"I'm optimistic that dornase alfa will have applications for treating other respiratory infections, and acute exacerbations of other chronic lung diseases, such as pulmonary fibrosis, that may share mechanisms with severe COVID-19."

Catriona Crombie, Associate Director of Technology Transfer and Philanthropic Fund at LifeArc, said, "We were delighted to support this study that has demonstrated how repurposing of a treatment commonly used for cystic fibrosis can be effective in improving outcomes for patients with severe COVID-19. LifeArc is committed to helping take scientific ideas out of the lab and into medical breakthroughs for patients, especially where there is an unmet medical need. To date, we have provided more than £27 million to fund the search for new medicines and diagnostics to address COVID-19."


Provided by University College London
