European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

PILOT STUDY TO TEST INHALED NITRIC OXIDE IN CYSTIC FIBROSIS PATIENTS WITH REFRACTORY MYCOBACTERIUM ABSCESSUS LUNG INFECTION

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What was your research question?

In this pilot clinical study, we assessed whether intermittent exposure to high concentrations of inhaled nitric oxide gas is safe in people with cystic fibrosis (CF) and chronic *Mycobacterium abscessus* lung infection. The secondary objective of his study was to assess the effects of inhaled nitric oxide on lung function and the amount of bacteria.

Why is this important?

M. abscessus is the most aggressive form of non-tuberculous mycobacteria (NTM). *M. abscessus* lung infection rates are on the rise globally, especially in patients with underlying lung disorders such as CF. Current standard-of-care is long-term therapy with cocktails of antibiotics that often prove to be ineffective and cause severe side effects. Nitric oxide is produced in our body and plays a crucial role in widening of blood vessels as well as defence against bacteria including Mycobacterium. Airways of people with CF commonly produce less nitric oxide, which may contribute to impaired lung function and defence mechanisms.

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What did you do?

We are investigating whether administration of inhaled nitric oxide is safe and if it can reverse the effects of low airway nitric oxide levels to improve clinical outcome in patients with chronic *M. abscessus* lung infection. Nine patients with CF and *M. abscessus* infection participated. Inhaled nitric oxide was administered five times per day (30-min each) for the first two weeks followed by three times per day for another week. Patients' vital signs, blood markers, Lung function, endurance, and amount of bacteria were assessed during nitric oxide treatment and at 7- and 11-week follow-up after the last treatment.

What did you find?

Inhaled nitric oxide was safe, and no drug-related serious adverse events were reported during the study. Blood tests did not reveal any significant systemic effect caused by nitric oxide therapy. Mild gains in patients' lung function and endurance were observed during nitric oxide treatment. Gains in endurance were sustained in follow-up period. Reductions in the amount of *M. abscessus* in the lungs were observed during NO treatment and the follow-up period, but *M. abscessus* did not disappear completely.

What does this mean and reasons for caution?

We find that treatment with high concentrations of inhaled nitric oxide is safe and well-tolerated in people with CF. Initial findings suggest the administration of nitric oxide may reverse the adverse effects of low airway nitric oxide in these patients and lead to improvements in lung function and endurance, and reductions in amount of bacteria in the lungs . However, the main limitation of our study is the small number of patients and therefore the results should be interpreted with caution.

What's next?

Plans are underway to confirm these findings in a new study by including larger number of patients with chronic *M. abscessus* lung infection. The new study will also examine the effects of longer term inhaled nitric oxide therapy (>3 weeks) to achieve full disappearance of lung infection with *M. abscessus* in these patients.

Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=PILOT+STUDY+TO+TEST+INHALED+NITRIC+OXIDE+IN+CYSTIC+FIBROSIS+PATIENTS+WITH+REFRACTORY+MYCOBACTERIUM+ABSCESSUS+LUNG+INFECTION

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