

# Cystic Fibrosis Research News

## Title:

Assessing the effect of adding chelating agent (Tris-CaEDTA) to nebulised tobramycin for improving bacterial killing and lung function in cystic fibrosis patients with *Pseudomonas aeruginosa* lung infection.

## Authors:

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## What was your research question?

We assessed whether Tris-CaEDTA inhaled with nebulised tobramycin would increase antibiotic effectiveness in treating *Pseudomonas aeruginosa* infection in people with cystic fibrosis (CF) by its ability to bind the excess iron found in CF airways, thereby preventing *Pseudomonas aeruginosa* from accessing this nutrient, essential for its survival.

## Why is this important?

In people with CF are at increased risk of lung infections with *Pseudomonas aeruginosa*. The iron-rich lung environment allows *Pseudomonas* to rapidly develop resistance mechanisms against antibiotic treatment, including the formation of biofilm, a protective gel layer around the organism which the antibiotic cannot penetrate. Cell culture and animal studies provide good evidence that chelating agents such as CaEDTA, by removing the iron from the environment, weakens these defense mechanisms and improves the ability of antibiotics to kill the *Pseudomonas* more effectively. Demonstrating that CaEDTA can improve treatment of antibiotic resistant bacteria will be a massive boost for people with CF.

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## What did you do?

We conducted a study in 25 people with CF from Sir Charles Gairdner and Princess Margaret Hospital, Perth, Australia where patients were randomly assigned to receive either Tris-CaEDTA or placebo nebulised in combination with tobramycin twice daily for six weeks with two additional doses of CaEDTA or placebo daily during first 2 weeks. This was followed with four-week safety follow-up. Patients had detailed clinical examination, blood tests, lung function, and sputum analysis prior to receiving the study drug and at 2 weeks, 6 weeks and 10 weeks follow up. Outcome measures included safety, tolerability, bacterial load of *Pseudomonas*, and lung function.

## What did you find?

In this pilot study in people with CF, adding Tris-CaEDTA to nebulised tobramycin was safe. In addition, the group of patients receiving CaEDTA added to their inhaled tobramycin showed an increased *Pseudomonas* killing in their sputum as well as a greater increase in their lung function measurements compared to patients treated with inhaled tobramycin alone.

## What does this mean and reasons for caution?

Our study supports the concept for improved bacterial killing and increased lung function measurements when Tris-CaEDTA and inhaled tobramycin are combined in treatment of *Pseudomonas* infections in people with CF. However, the differences of the effects between the treatment and placebo groups did not reach statistical significance, and with the small number of participants involved in the study, we were unable to draw any definitive conclusions. The two groups were also not well-matched as patients in the CaEDTA had lower lung function and larger amount of *Pseudomonas* growing in their sputum at admission and this has the potential to affect outcomes.

## What's next?

These results support further exploration of the potential of inhaled CaEDTA as an addition to antibiotic therapy in a larger clinical study where the groups are better matched.

## Original manuscript citation in PubMed

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