

Cystic Fibrosis Research News

Title:

Oxidative Stress and Abnormal Bioactive Lipids in Early Cystic Fibrosis Lung Disease.

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What was your research question?

Lung inflammation and structural changes are evident in the lungs of children with cystic fibrosis (CF), even before the onset of long-term bacterial infections. This underlines the importance of early intervention to prevent lung damage. We aim to understand how early CF lung disease develops, so that we can improve treatment.

Why is this important?

Current treatment of CF is only partially effective, and progressive lung disease remains the most important issue. The complex molecular processes involved in lung disease are still poorly understood. Identifying and measuring the molecules involved in the abnormal communication between cells in the lungs of an infant with CF would help us to show any effect of early treatment and may also reveal new opportunities for therapy.

What did you do?

In a program initiated by the Australian CF community (AREST-CF), children with CF are comprehensively monitored at the ages of one, three and five years old. We have analyzed

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lung fluid obtained during bronchoscopy from children with lung disease, with and without CF. We used a method that allows us to measure a large number of molecules at the same time, called mass spectrometry. We compared the results of the lung fluid analyses from children with and without CF. We also investigated the relationship between the molecules in the fluid and the severity of the CF lung disease.

What did you find?

We focused on lipid molecules which we know are linked to lung inflammation and tissue damage. We saw differences between children with CF and other children with lung disease. Furthermore, we found that the amount of specific molecules correlated with the severity of lung disease in children with CF.

What does this mean and reasons for caution?

The study was performed in a relatively small group of children, because the protocol is complicated and invasive. The results suggest that cells in the lungs of children with CF produce specific lipid molecules that point to, and may even actively boost, levels of inflammation. In further studies, effective treatment of early CF lung disease is expected to show a reduction in these specific molecules in lung fluids. Therefore, an assessment of these specific molecules in lung fluids might be useful as markers to show how children with CF are responding to current and future clinical treatment. Although the study by itself does not explain exactly what the relationship between the lipids and the lung disease is, our results are prompting us to investigate how we can reduce the biological activity of these lipid molecules to reduce or even prevent the progression of lung disease in children with CF.

What's next?

The current study will be continued in children with CF that are monitored several times from the first to the fifth year of life, to establish if the lipid molecules can help us to monitor and predict the progression in time of early lung disease. This information can be used to adapt treatment to the individual patient, and to establish the effect of new and established treatment on the progression of early CF lung disease. In cell culture models of CF we will try to establish the active role that the lipids we identified play in causing lung inflammation and structural changes, and test the effect of experimental medicines that reduce this activity. Eventually we can test such medicines in the CF patients, using the same monitoring system.



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