Cystic Fibrosis Research News

Title:

Abnormal Pro-Gly-Pro pathway and airway neutrophilia in pediatric cystic fibrosis.

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What was your research question?

An important problem in cystic fibrosis (CF) is excessive airway inflammation. Inflammation is one way the body fights infection, and usually, when infection is cleared, inflammation subsides. Persistent inflammation can cause harm. We questioned whether an imbalance between pro-inflammatory (switching on) and anti-inflammatory (switching off) processes in the body is related to excessive inflammation in CF.

Why is this important?

Airway inflammation in CF is characterised by large numbers of inflammatory cells called neutrophils. Neutrophils release enzymes that fight bacteria, but these enzymes can also damage airway tissue. As a result of airway damage, a substance called PGP is generated; PGP makes inflammation worse unless it is broken down. In healthy people, there is a balance

between enzymes that generate PGP (pro-inflammatory) and those that break down PGP (anti-inflammatory), so that the body can deal with inflammation appropriately.
In CF, excessive inflammation contributes to lung damage and declining lung health. Understanding pathways that stimulate and limit inflammation in CF is important to identify treatments and minimize lung damage.

What did you do?

We examined samples of airway fluid from children with and without CF. The samples were collected during tests as part of routine medical care and consent was given for research use. In this fluid we measured the concentration of PGP, and the concentrations and activity of enzymes that generate and degrade PGP. We also measured the number of neutrophils and other inflammatory cells in each sample.
We compared these measurements between three groups of children: those without CF; those with CF diagnosed during the newborn period but without any symptoms; and older children with CF who had symptoms.

What did you find?

We found that most children without CF had no detectable PGP in their airway fluid. In contrast, most older children with CF who were displaying symptoms had raised levels of PGP and high numbers of neutrophils. Most newborn infants with CF had no detectable PGP, similar to the group without CF. Overall children with the highest levels of PGP had the highest number of neutrophils in airway fluid. In older children with CF and symptoms, the enzymes that generate PGP were raised, and the enzymes that degrade PGP were abnormally reduced.

What does this mean and reasons for caution?

Our study suggests that the accumulation of PGP may play a part in excessive inflammation in the airways of people with CF. This PGP accumulation appears to be related to an imbalance between the enzymes that generate PGP and those that degrade it. Interestingly, high levels of PGP were not found in newborn babies with CF, suggesting that the PGP may build up as disease progresses, perhaps after exposure to infection.
However, we should be cautious about these results because the study was small and we collected samples opportunistically. This means that we could not be sure that symptoms that the children were experiencing at the time of tests did not impact on our results.

What's next?

Ideally, future studies would measure PGP in the same children at different times, so that changes in PGP could be tracked with inflammation and infection. This would help us to understand whether PGP is an accurate predictor of inflammation and disease prognosis and could potentially be targeted with treatments.

Original manuscript citation in PubMed
https://www.ncbi.nlm.nih.gov/pubmed/?term=Abnormal+Pro-Gly-Pro+pathway+and+airway+neutrophilia+in+pediatric+cystic+fibrosis.