

Cystic Fibrosis Research News

Title:

Concentration of Fractional Excretion of Nitric Oxide (FENO): A Potential Airway Biomarker of Restored CFTR Function

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What was your research question?

We thought that fractional excretion of nitric oxide (FENO) i.e. the amount of nitric oxide breathed out, which is typically low in CF patients, would demonstrate reproducibility (i.e. could be a precise reliable measurement to use repeatedly) during treatment independent of the cystic fibrosis transmembrane conductance regulator (CFTR), and increase during treatment targeting CFTR (ivacaftor treatment) in patients with CFTR gating mutations.

Why is this important?

Further investigation of FENO as an indicator that CFTR has been restored in the lower airways is warranted, particularly in CF patients before and after starting treatment to affect CFTR.

What did you do?

We examined the precision of the FENO measurement in children with CF admitted to the hospital for treatment of pulmonary exacerbations (flare ups of their disease), and over the three to six months after they had been discharged. Subsequently, we examined FENO, lung

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function, sweat chloride tests, and growth in five CF patients who had gating mutations and were candidates for ivacaftor treatment.

What did you find?

We found that the FENO values were quite stable over the periods of inpatient care and during outpatient follow up visits. As expected, lung function (FEV1 percent predicted) showed significant improvements during inpatient care, but FENO did not change. Most of the variability in FENO was between patients and not between readings, suggesting that it has good reproducibility for measurements that are performed in a particular person. We also found that after 28 days of ivacaftor treatment in patients with gating mutations, lung function, weight and FENO increased, while sweat chloride tests dropped by nearly 50 mM.

What does this mean and reasons for caution?

These results suggest that the increases in FENO that we saw in CF patients were a direct result of restored CFTR activity, and did not reflect other treatments that increase lung function (regardless of whether CFTR had been restored). The impact of ivacaftor on FENO was relatively strong; it was less than ivacaftor's impact on sweat chloride levels but more than its impact on lung function and weight. Together, the results suggest that measuring the change in FENO might serve as a rapid, simple, and portable test of restored CFTR function in CF patients treated with CFTR modulators.

What's next?

Further investigation of FENO as a measure of restored CFTR in the lower airways is warranted, particularly in CF patients before and after initiating CFTR modulator therapies.

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