European Cystic Fibrosis Society

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Cystic Fibrosis Research News

Title:

Effect of Ivacaftor Therapy on Exhaled Nitric Oxide in Patients with Cystic Fibrosis

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What was your research question?

We were interested in the question of whether treating people with cystic fibrosis with ivacaftor would result in changes of the levels of nitric oxide in the airways.

Why is this important?

Nitric oxide (NO) is a molecule that is important for regulating functions of the lungs, including narrowing of airways and defence against certain bacteria such as Pseudomonas. Previous studies have shown that cystic fibrosis (CF) airways contain a lower amount of NO, and low airway NO in people with CF was associated with poor pulmonary function as well as increased rates of infections with Pseudomonas aeruginosa. The reasons for the low airway NO in CF are not completely understood but may be linked to the genetic defect in CFTR, the chloride channel that causes CF when mutated.

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What did you do?

Ivacaftor is the first approved drug that improves CFTR function in people with CF and certain, so called gating mutations. We closely followed children and adults with CF who were started on ivacaftor treatment in Toronto, Canada. In 15 individuals with CF pulmonary function tests, NO in exhaled breath and sweat tests were measured before and 4 weeks after starting ivacaftor treatment in this study. The effect of ivacaftor on NO was compared to other established treatments i.e. inhaled dornase alfa (15 participants) and hypertonic saline (16 participants) for 4 weeks, respectively.

What did you find?

A total of 15 people treated with ivacaftor were studied. As expected, pulmonary function improved. Interestingly, mean airway NO concentrations doubled with treatment. The effect on NO was more pronounced in children compared to adults. There was no clear relation between changes in NO, pulmonary function or sweat chloride concentration. Neither inhaled dornase alfa (15 participants) or hypertonic saline (16 participants) resulted in a change in airway NO.

What does this mean and reasons for caution?

In summary, treatment with ivacaftor results in an increase in airway NO concentrations. The lack of relation between changes in NO, pulmonary function and sweat chloride concentrations suggests that this previously unrecognized effect of ivacaftor on airway NO could be independent of its effect on CFTR function. The observation of an increase in airway NO in the context of improved pulmonary function may warrant further clinical studies aiming to increase airway NO formation in people with CF.

What's next?

Further studies will be needed to understand the mechanisms that result in increased airway NO with ivacaftor treatment.

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