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Cystic Fibrosis Research News

Title:

Analytical and Biological Variation in Repeated Sweat Chloride Concentrations in Clinical Trials for CFTR Modulator Therapy

Authors:

VA LeGrys [a], TC Moon [a], J Laux [b], MJ Rock [c], F Accurso [d]

Affiliations:

[a] Division of Clinical Laboratory Science, University of North Carolina School of Medicine Chapel Hill, NC
[b] The North Carolina Translational and Clinical Science Institute, University of North Carolina Chapel Hill, NC
[c] Department of Pediatrics, University of Wisconsin School of Medicine and Public Health Madison, WI
[d] Department of Pediatrics, University of Colorado Denver School of Medicine Breathing Institute Children's Hospital of Colorado Aurora, CO

What was your research question?

How much of the differences observed between repeated sweat chloride tests are due to normal biological fluctuations within a person and between various people? How much of the difference between repeated sweat chloride tests are due to measurement error in the laboratory instrument used for analysis?

Why is this important?

Decreases in sweat chloride concentration are used in drug trials to gauge the effectiveness of a study drug designed to repair the defective CF gene or protein. Currently, the amount of change in sweat chloride concentrations that reflects a positive response to an investigational drug is uncertain. Researchers conducting the drug trials need to know how much sweat chloride naturally fluctuate in untreated CF patients to determine the effectiveness of the study drug. If a treated patient's sweat chloride decreases more than the usual levels, then the change could be attributed to the drug intervention.

What did you do?

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We analyzed 979 repeated sweat chloride tests from 128 children and adults with CF who participated in the untreated (placebo) group for 2 different experimental drugs for CF treatment. We determined the difference in the repeated tests that was due to the laboratory analysis. We also determined the biological differences in repeated sweat chloride tests in the same patient as well as the differences between different patients.

What did you find?

We found that the measurement error was about 4%. Sweat chloride results could vary by about 5% within the same patient and the difference between patients was 8%. From these numbers we calculated the change values of 14% and 18% which is the medically or clinically significant change between two results for a sweat chloride test.

What does this mean and reasons for caution?

This means that given the results in the 2 clinical trials studied, if these placebo patients were to receive an investigational drug to repair the defective CF gene or protein, their sweat chloride would have to decrease by more than 14-18% from baseline to indicate a change beyond the usual sweat chloride analytical and biological variation. This change value is specific for the laboratory performing the sweat chloride test, and specific to these patients with their CF gene mutation.

What's next?

Future studies should incorporate more CF patients including infants, children, and individuals with different CF gene mutations so that a sweat chloride change value that would fit all circumstances can be determined for clinical drug trials.

Original manuscript in PubMed

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cfresearchnews@gmail.com