

Cystic Fibrosis Research News

Title:

Insights into the variability of Nasal Potential Difference, a biomarker of CFTR activity

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What was your research question?

Nasal potential difference (NPD) is a test which evaluates the function of the defective protein in CF called CFTR by measuring the transport of sodium and chloride ('salt') in and out of cells in the nose. Our aim was to evaluate the variability of this test within the same subject (intrasubject variability), between different subjects (intersubject variability) and different centers (intercenter variability).

Why is this important?

The NPD test is used in proof of concept studies to evaluate the efficacy of novel drugs which aim to improve CFTR activity. However, employing NPD test in multicenter studies as a biomarker for CFTR activity requires knowledge of its reliability. Studies assessing the repeatability, the precision and the variability of this test are lacking. As a consequence, we needed to assess the above characteristics in order to avoid misleading interpretations.

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What did you do?

We reviewed NPD tracings of 116 patients with CF enrolled in the placebo arm (a substance that has no therapeutic effect, used as a control) of a multicenter study. Patients carried at least one nonsense mutation in the *CFTR* gene and underwent repeated NPD tests every 16 weeks. We investigated the intrasubject, intersubject and intercenter variability of NPD measurements among these patients. We also assessed the impact of different factors potentially influencing *CFTR* function including age, sex, genetic background and pulmonary exacerbation of the patients on the variability of the NPD measurements.

What did you find?

The NPD measurements related to sodium transport displayed the highest variability, mainly due to high intercenter and intrasubject variabilities. On the other hand, the measurements depicting the chloride transport demonstrated a large intrasubject variability but a smaller intersubject and intercenter variability. This variability was greater in patients reporting ongoing pulmonary exacerbations but was not influenced by the sex, age or genetic background of the subject. Finally, we could state that if a patient taking a *CFTR* modulator treatment presents a difference greater than 7.2 mV in absolute value between two NPD tests, this difference can be attributed, with a high degree of probability, to a treatment effect rather than to the variability inherent in the measurement.

What does this mean and reasons for caution?

The high variability of the NPD measurements related to sodium transport highlights the operator-dependent aspect of these measurements. Concerning the variability of the chloride transport related measurements. NPD should not be performed when a subject is experiencing a pulmonary exacerbation. The main limitation of the study is that we could not study the accuracy of the technic: e.g., the test being done at a few hour interval in the same patient by the same experimentator.

What's next?

Further standardization of the NPD test is needed in order to increase the precision and reliability of the test.

Original manuscript citation in PubMed

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Insights+into+the+variability+of+Nasal+Potential+Difference%2C+a+biomarker+of+CFTR+activity>



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