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Cystic Fibrosis Research News

Title:

Rapid chloride and bicarbonate determination by capillary electrophoresis for confirmatory testing of cystic fibrosis infants with volume-limited sweat specimens

Lay Title:

A rapid sweat test for chloride and bicarbonate to confirm the diagnosis of infants with cystic fibrosis

Authors:

Stellena Mathiaparanam,[1] Adriana Nori de Macedo,[2] Biban Gill,[1] Katherine Keenan,[3] Tanja Gonska,[4] Linda Pedder,[5] Stephen Hill,[6] Philip Britz-McKibbin[7]

Affiliations:

1 Department of Chemistry and Chemical Biology, McMaster University, Canada.
2 Department of Chemistry and Chemical Biology, McMaster University, Canada; Department of Chemistry, Federal University of Minas Gerais, Belo Horizonte, Brazil.
3 Program in Translational Medicine, The Hospital for Sick Children, Canada.
4 Program in Translational Medicine, The Hospital for Sick Children, Canada; Department of Pediatrics, University of Toronto, Canada.
5 Department of Pediatrics, McMaster University, Canada.
6 Department of Pathology and Molecular Medicine, McMaster University, Canada.
7 Department of Chemistry and Chemical Biology, McMaster University, Canada; Department of Pathology and Molecular Medicine, McMaster University, Canada.

What was your research question?

Our study aimed to address two main questions: 1. Does the level of bicarbonate in sweat improve diagnostic testing for cystic fibrosis? and 2. Can much smaller amounts of sweat be analyzed for chloride levels from infants using capillary electrophoresis - a microseparation technique that separates ions in an electric field according to their size and charge.

Why is this important?

The current methods of diagnosing cystic fibrosis relies on coulometric titration (is a method used to measure the amount of chloride based on its reaction with silver ion released from electrolysis of silver electrodes) that only measures chloride levels in sweat and needs at least 10 microliters of sweat. However, this approach may result in inconclusive diagnostic test results and premature and low birth weight infants may not be diagnosed with cystic fibrosis

late because it is difficult to collect adequate sweat volume. As a result, there can be a delay in obtaining a reliable cystic fibrosis diagnosis due to the need for repeat testing, which also contributes to prolonged anxiety for parents with an inconclusive test result.

What did you do?

We tested a new diagnostic test for cystic fibrosis in infants which is based on capillary electrophoresis. This allows for the simultaneous analysis of chloride and bicarbonate levels in as little as 1.0 microliter of sweat. We compared sweat chloride levels measured by capillary electrophoresis with those measured using coulometric titration (as the gold standard). We also tested how easy it would be to use capillary electrophoresis to reliably measure bicarbonate levels, which are not routinely measured in sweat despite its role in cystic fibrosis disease in other organ secretions. We tested our method of measuring sweat chloride and bicarbonate levels to see if we could differentiate cystic fibrosis from non-cystic fibrosis in 53 infants who tested positive for cystic fibrosis in a screening test (i.e., presumptive screen-positive infants).

What did you find?

Our study confirmed that we can use capillary electrophoresis to reliably measure sweat chloride with results that are consistent with coulometric titration in infants who have tested positive following newborn screening. As expected, sweat chloride was able to differentiate infants with confirmed cystic fibrosis disease from nonaffected carriers or infants who had a false-positive screening result. However, we did not find that measuring sweat bicarbonate was clinically useful in confirming a diagnosis of cystic fibrosis.

What does this mean and reasons for caution?

Compared with the standard method for diagnosing cystic fibrosis, capillary electrophoresis may reduce the rates of inconclusive tests in premature and low birthweight infants since it needs much lower amounts of sweat Therefore, it could be used to support universal newborn screening since a large fraction of presumptive screen-positive infants may not actually have cystic fibrosis. This would allow for cystic fibrosis to be detected early in vulnerable infants who benefit from prompt treatment leading to better long-term clinical outcomes. Capillary electrophoresis may also be useful to measure bicarbonate levels in other biological fluids relevant to cystic fibrosis. For example, analysis of bicarbonate from pancreatic and lung fluid secretions using this method may provide new insights into how cystic fibrosis disease progresses and responds to therapy.

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What's next?

In the future, we aim to identify novel biomarkers in sweat specimens from a subset of infants who have an inconclusive sweat chloride test result to better understand how late-onset cystic fibrosis is likely to progress. This remains an important diagnostic dilemma in newborn screening programs for cystic fibrosis.

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