# Urine bicarbonate test offers new, safe quantification of CFTR function in cystic fibrosis patients

November 1 2022

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A study of 50 adult patients with cystic fibrosis (CF) has found that challenged urine bicarbonate excretion may offer a new, simple, and

safe quantification of cystic fibrosis transmembrane conductance regulator (CFTR) function and the extent of its pharmacologic improvement. The study is published in *Annals of Internal Medicine.*

The management of cystic fibrosis has changed with the recent introduction of therapies that target the disease-causing mechanism. Cystic fibrosis transmembrane conductance regulator (CFTR) modulators, including elexacaftor, tezacaftor, and ivacaftor, are novel drugs that either potentiate or correct CFTR channel dysfunction. They can also partially restore CFTR function.

Measurement of sweat chloride concentration is the most used method to assess CFTR function in vivo. However, sweat chloride only associates marginally with clinical disease features, is time consuming, requires experienced staff, and has large intraindividual variation. Many other biomarkers for CFTR exist but have complicated approaches that limit their clinical use.

Renal dysfunction may be related to CF and may be measured through tests quantifying bicarbonate secretion in the kidney that occurs via pendrin. CFTR is fully necessary for the function and regulation of pendrin, which in CF leads to an impaired ability to excrete excess bicarbonate. These patients have a reduced ability to increase renal base excretion after oral sodium bicarbonate loading, making a challenge test a potential option for drug treatment monitoring.

Researchers from Aarhus University, Aarhus, Denmark, studied 50 adult patients with CF starting CFTR modulator therapy with elexacaftor/tezacaftor/ivacaftor to evaluate the association between challenged bicarbonate excretion and clinical characteristics at baseline, quantify the CFTR modulator drug–induced changes of challenged bicarbonate excretion after six months of treatment, and characterize the intraindividual variation in healthy adults.

The authors evaluated and quantified urine bicarbonate excretion after an acute oral sodium bicarbonate challenge before and six months after elexacaftor/tezacaftor/ivacaftor treatment. They found that challenged urine bicarbonate excretion was associated with CF disease characteristics. The use of elexacaftor/tezacaftor/ivacaftor increased bicarbonate excretion to about 70% of that seen in control participants.

According to the authors, their early-stage evaluation shows that that challenged urine bicarbonate excretion offers a new, simple, and safe functional assessment quantifying the biological consequences of reduced CFTR function and the extent of functional recovery after pharmacologic treatment.

**More information:** Peder Berg et al, Challenged Urine Bicarbonate Excretion as a Measure of Cystic Fibrosis Transmembrane Conductance Regulator Function in Cystic Fibrosis, *Annals of Internal Medicine* (2022). DOI: 10.7326/M22-1741

Provided by American College of Physicians