European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

MEASUREMENT OF FECAL ELASTASE IMPROVES PERFORMANCE OF NEWBORN SCREENING FOR CYSTIC FIBROSIS

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What was your research question?

We compared the performance of three different protocols used to diagnose cystic fibrosis (CF) in infants, who had a positive newborn screening result but in whom the first sweat test was unsuccessful: A) waiting several weeks to repeat the sweat test; B) extended genetic testing; C) measurement of fecal elastase in the stool.

Why is this important?

Newborn screening programmes for CF (CF-NBS) aim to detect children with classical CF. For these, early treatment improves outcome. Children with inconclusive CF diagnosis (CFSPID) should not be detected, because the potential harms of early detection (unnecessary treatments, distress and burden to the family) outweigh potential benefits. Sweat testing remains the gold standard in the diagnosis of CF. However sweat collection in small infants

is challenging, and has a high failure rate. Current NBS guidelines give no evidence-based advice about what to do when sweat tests fail.

What did you do?

In Switzerland, CF-NBS was introduced in 2011. All newborns get a heel prick test. Those with a suspicious result are then seen in a CF clinic for a sweat test, to confirm or rule out CF. We compared three different procedures for infants with unsuccessful sweat tests. In protocol A we repeated the sweat test after some weeks, until it was successful. In protocol B we performed extended genetic testing in all with failed sweat tests. In protocol C we measured fecal elastase: when it was low, we proceeded to genetic testing (as in B); when fecal elastase was normal we waited and repeated the sweat test (as in A). We compared CFSPID detection rate and time until a definite diagnosis between protocols.

What did you find?

Within four years, 339'685 babies were screened, and 368 referred to a CF centre. Of these, 103 were diagnosed with CF, 18 with CFSPID, 244 were healthy, and 3 had no follow up. The ratio CF:CFSPID differed significantly between the three protocols, and was 7:1 with protocol A, 2:1 with protocol B, and 14:1 with protocol C (see figure). The mean time to definite diagnosis was 42, 40, and 33 days for protocols A, B and C, and the proportion of families with more than 2 months waiting time until diagnosis was 17%, 15% and 7%, respectively.

What does this mean and reasons for caution?

This study suggests that measurement of fecal elastase in infants with an unsuccessful initial sweat test, followed by genetic testing in those with low fecal elastase performs best compared to the other protocols. It reduces the time parents have to wait for a definite diagnosis, while keeping the number of CFSPID children low. However, because fecal elastase can fluctuate in the first year of life, a normal level does not exclude CF and a repeated sweat chloride test is eventually needed for all children.

What's next?

Our results suggest to include fecal elastase after initial sweat test failure in the CF-NBS guidelines to keep the proportion of CFSPID low and the time until definite diagnosis short.

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Original manuscript citation in PubMed

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