Cystic Fibrosis Research News

Title:
A Product of Immunoreactive Trypsinogen and Pancreatitis-Associated Protein as Second Tier Strategy in Cystic Fibrosis Newborn Screening

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What was your research question?
To improve newborn screening tests for cystic fibrosis (CF), we asked if combining the amounts of two proteins found in the blood better predicts the CF status of a newborn. We also assessed how the result of the screening test is affected by (1) different methods which are used to measure protein levels and (2) the age of the newborn.

Why is this important?
People with CF do better if they are diagnosed early. However, CF is a rare disease, and many newborns need to be screened to identify a single newborn with CF. Therefore, it is important that the tests used for this screening do not miss any newborn with CF (sensitivity) and that they do not incorrectly identify a newborn with CF (specificity). Measuring the levels of two proteins called ‘immunoreactive trypsinogen’ (IRT) and ‘pancreatitis-associated protein’ (PAP) in the blood also means that costly genetic testing does not need to be carried out in all newborns. However, sensitivity and specificity of screening strategies based on IRT and PAP levels could be improved.

What did you do?
We analyzed newborn screening data on more than 400,000 newborns from two laboratories, including 78 newborns with classical CF (generally the most severe form). The level of IRT in the blood was measured in all newborns. If IRT levels were found to be higher than normal, then PAP levels were also measured. Our study specifically assessed the best way to proceed with diagnostics if IRT levels were elevated. This involved comparing the standard strategy (looking at PAP levels only) to a new strategy (multiplying together IRT and PAP levels). We also compared two commonly used methods that measure PAP levels in the blood (known as fluorometry and photometry). Furthermore, we analyzed how PAP levels change over time after birth.

What did you find?
Our findings support that the new strategy is potentially better than the standard strategy to decide whether a newborn needs further testing for CF. We found that PAP levels vary depending on whether they are measured with the fluorometric method compared to the photometric method. Additionally, results show that older newborns have higher PAP levels in their blood, suggesting that they might have CF even if they do not.
What does this mean and reasons for caution?
The new strategy could be used in screening laboratories to better detect CF. However, our observations should be confirmed by the work of other researchers. When laboratories measure PAP levels in the blood, they should take into account which method they are using. Finally, blood samples should be taken at the right time after birth for the CF screening test to work well, because PAP levels change with time and this makes it more difficult to identify newborns with CF.

What’s next?
We hope that other laboratories can confirm the value of our new screening strategy. CF screening guidelines using IRT and PAP should be aware of how the specific measurement method and the time of blood collection might affect the result.

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