Cystic Fibrosis Research News

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What was your research question?

We wanted to evaluate whether the prevalence of meconium ileus (MI, a type of bowel obstruction at birth) in CF patients carrying the same cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations can be used to classify CFTR mutations by their severity. This is similar to the pancreatic insufficient prevalence (PIP) score.

Why is this important?

The relationship between CFTR gene mutation and disease severity in CF is not straight forward. Researchers have grouped CFTR mutations based on their anticipated effect on CFTR function into 6 classes, summarized as mild and severe. Using PIP as an example, patients with severe mutations are mostly pancreatic insufficient (high PIP score). Patients with at least one milder mutation were mostly pancreatic sufficient (low PIP score). The PIP score shows that known disease characteristics like pancreatic insufficiency can be used to classify the severity of CFTR mutations. We wanted to see if we could make similar scores using meconium ileus.

What did you do?

We looked at the prevalence of MI (how common MI is) for different mutations on the CF gene using data from four different countries: Canada, the United States, Germany, and Italy. We also looked at the association of MI with other markers of disease severity, like lung function and body mass index (BMI).

What did you find?

We found that counting the prevalence of meconium ileus (MIP score) in patients with the same CFTR gene mutations allowed us to sort CFTR mutations by their severity. Furthermore, the MIP score showed an overall association with lung function and BMI (weight), which are two clinical markers that show the severity of CF disease.

What does this mean and reasons for caution?

Using MIP and PIP scores is one way to assess the severity of the CFTR mutations. However, we have only looked at patients carrying at least one copy of F508del mutation, assigning the severity to the

other CFTR mutation. While the F508del mutation may result in a very diverse set of characteristics the MIP score was pretty consistent across all 4 databases.

On an individual patient basis, the PIP and MIP score may help to get a general idea of disease severity. We know that other modifying factors including other genes underlie diversity in CF disease.

What's next?

It will be interesting to investigate whether PIP and MIP scores are associated with response to CFTR-modifying drugs, once more patients with different CFTR mutations are on this treatment. It will also be interesting to see whether other characteristics can be used to develop additional scoring systems.