



Cystic Fibrosis Research News

Title:

Primary Sclerosing Cholangitis is associated with abnormalities in CFTR

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What was your research question?

We asked whether there is a relationship between the liver disease, primary sclerosing cholangitis (PSC), and variants in CFTR. PSC, like cystic fibrosis liver disease (CFLD) is a chronic idiopathic biliary tract disorder that may slowly progress to cirrhosis and end stage liver disease.

Why is this important?

Cystic fibrosis related disorders are becoming increasingly recognized. These diseases are potentially related to mutations in the defective gene in CF patients, the chloride channel called CFTR. Under the microscope the livers in patients with PSC and CFLD look very similar. Most patients (70%) with PSC have either ulcerative colitis or Crohn's disease, which are inflammatory bowel diseases. Besides IBD there are more than 20 other known causes of sclerosing cholangitis. Some but not all studies found that many patients with PSC have CFTR

Cystic Fibrosis Research News

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Cystic Fibrosis Research News

mutations. The causes of these 2 liver diseases are not well understood. Neither PSC nor CFLD have effective therapies other than liver transplant.

What did you do?

We evaluated 32 adult Israeli PSC patients with genetic sequencing for CFTR mutations, nasal potential difference measurements (NPD) and sweat tests. The latter two tests help us to understand whether CFTR is working normally or is defective.

What did you find?

Four of our 32 patients with PSC had abnormal NPD, six had abnormal sweat tests and 15 had intermediate sweat tests. Thus, 66% had electrophysiological abnormalities in sweat tests or nasal potential difference, indicating some extent of CFTR dysfunction. Six patients had known CFTR mutations and 19 had CFTR variations which were higher than in a control Israeli population. In the 28 patients with normal NPD, 16 had sweat tests, in whom 3 were abnormal, 11 were intermediate and two were normal. Therefore, abnormal chloride channel function was present in 21/32 (66%) of our patients, which is higher than found in previous studies. The patients with abnormal sweat tests were referred to CF centers for evaluation and care. Sixteen of our 32 patients had either ulcerative colitis or Crohn's disease. All were adults between 23-62 years of age.

What does this mean and reasons for caution?

Our findings suggest that in some patients PSC may be a CFTR-related disorder or that having a CFTR mutation may predispose at risk patients (with UC/Crohns) to PSC. However, this study examined a small number of patients and was conducted in only one country.

What's next?

Studies enrolling more patients from many countries are needed to confirm these findings.

Original manuscript in PubMed

<https://www.ncbi.nlm.nih.gov/pubmed/29807875>