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Cystic Fibrosis Research News

Title:

Gamma-glutamyl transpeptidase-to-platelet ratio as a biomarker of liver disease and hepatic fibrosis severity in paediatric cystic fibrosis

Lay Title: A simple blood test to detect how severe liver disease is in children with CF.

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What was your research question?

Can we detect the development of liver disease and its progression to liver damage or scarring (fibrosis and cirrhosis) in children with cystic fibrosis (CF) by using a simple, readily available biochemical measurement from routine blood tests called the gamma-glutamyl

transpeptidase-to-platelet ratio (GPR)? GPR can be measured to assess liver function when the child is at the CF clinic.

Why is this important?

CF can damage the liver due to thickened bile secretions that slow down bile moving from the liver into the intestine. Ill health, infections, CF treatments and abnormal nutrition can commonly cause liver blood tests to be slightly abnormal. However, around 10% of children will go on to develop advanced CF-associated liver disease (CFLD) which may be severe enough to harm health and life expectancy. Existing methods of detecting advancing CFLD can be inaccurate and it is difficult to monitor how liver damage is progressing without an invasive liver biopsy. Therefore, we need a non-invasive, readily accessible blood test that can be repeated at regular visits to the CF clinic to both detect developing CFLD and to monitor how damage is progressing.

What did you do?

This study enrolled 237 children with CF between 1991 and 2016. 76 children had CFLD (as measured using standard clinical, blood and ultrasound tests) and of these, 54 children had liver biopsies performed to work out how severe their liver disease was. 161 children had CF but no evidence of liver disease. We calculated GPR from liver functions tests obtained through routine blood collection when the children enrolled in the study. We then assessed GPR as a tool to distinguish those children with CFLD and to stage the severity of liver disease including those with portal hypertension (enlarged spleen with or without enlarged oesophageal veins to indicate advanced liver disease).

What did you find?

GPR was a lot higher in children with CFLD compared to those children with CF who did not have liver disease. It was accurate at diagnosing CFLD at a cut-off value of 0.2. In children with CFLD, a GPR above 0.32 could distinguish those with moderate-to-severe liver damage from those with mild CFLD. In addition, a GPR above 0.61 was able to detect those children with advanced/severe liver disease. Finally, this study showed that a GPR above 0.84 detected children with CF who had portal hypertension.

What does this mean and reasons for caution?

GPR provides a cheap, reliable, non-invasive blood test to diagnose liver disease and determine liver disease severity in children with CF. Importantly, GPR can be used regularly to monitor progression of CFLD without needing to perform an invasive liver biopsy. This will

greatly assist in better managing the clinical needs of children with CF. It is very interesting that this blood test can easily be calculated from measurements obtained via routine liver function tests in all pathology laboratories. However, GPR results for detection and progression of disease severity should be used together with other clinical observations and laboratory results by clinicians with expertise in treating children with CF.

What's next?

This single centre study needs confirmation by other researchers in larger groups of children with CF to confirm GPR cut-off values for both detecting and monitoring liver disease severity. GPR, along with other recently investigated non-invasive blood tests and ultrasound-based technologies, could be useful to assess the management of liver disease if novel therapeutic interventions become available in the future.

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