Editorial: Diagnosing bile acid diarrhoea with blood tests.

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<th>Journal:</th>
<th>Alimentary Pharmacology &amp; Therapeutics</th>
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<td>Manuscript ID</td>
<td>Draft</td>
</tr>
<tr>
<td>Wiley - Manuscript type:</td>
<td>Invited Editorial</td>
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<tr>
<td>Date Submitted by the Author:</td>
<td>n/a</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>Walters, Julian; Hammersmith Hospital, Gastroenterology</td>
</tr>
<tr>
<td>Keywords:</td>
<td>Diarrhoea &lt; Topics, Diagnostic tests &lt; Topics, Functional GI diseases &lt; Disease-based, Irritable bowel syndrome &lt; Disease-based</td>
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Editorial: Diagnosing bile acid diarrhoea with blood tests.

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Making the diagnosis of bile acid diarrhoea (BAD) depends first on the awareness of clinicians of this disorder in patients with functional gastrointestinal disorders such as IBS-D, and secondly, on the availability of simple and reliable tests.\textsuperscript{1,2} The recent paper by Vijayvargiya et al. \textsuperscript{3} provides important information on performance characteristics of potential diagnostic blood tests.

Excess colonic bile acids result in secretion, increased motility, and symptoms of loose stools, frequency and urgency, which patients report adversely impact on quality of life.\textsuperscript{4} Raised colonic bile acids can be secondary to malabsorption, as in ileal Crohn’s disease, or result from impaired regulation of synthesis and overproduction of hepatic bile acids in primary BAD.\textsuperscript{5} When bile acids are absorbed in the ileum, they stimulate transcription of fibroblast growth factor 19 (FGF19) via a process dependent on the farnesoid X receptor. FGF19 enters the portal venous system, and inhibits new bile acid synthesis,\textsuperscript{6} which can be quantified by measuring the precursor 7α-hydroxy-4-cholesten-3-one (C4) in blood by HPLC or tandem mass spectrophotometry.

Previous work showed that median levels of fasting FGF19 in patients with primary BAD were lower, about half that of controls.\textsuperscript{5,7} Fasting C4 is raised in BAD, and is negatively correlated with FGF19.\textsuperscript{7,8} A recent review compared the proportions of patients with functional bowel disorders who had abnormal tests for FGF19, C4, the nuclear medicine tauroselcholate (SeHCAT) test, or faecal bile acid measurements, and found that 17-30% of patients were positive.\textsuperscript{9}

Blood biomarkers would have potential advantages compared with collection of faeces for bile acid quantification, or the SeHCAT test, which involves a small exposure to radiation and is not licensed or marketed in many countries including the U.S.A. The performance of serum FGF19 has been compared with SeHCAT as gold standard. This had specificity around 80% at different SeHCAT cut-offs, and a negative predictive value for mild BAD (SeHCAT <15%) of 68%, which improved to 75% when C4 and age/BMI corrections were included, and was 86% for a SeHCAT <10%.\textsuperscript{7}

In the report of their series of patients, Vijayvargiya et al. add to these findings by reporting measures of consistency of replicate FGF19 and C4 (70% and 78% concordance respectively). They determined specificity of abnormal blood measurements for raised 48h faecal bile acids, finding 78% for FGF19 and 83% for C4. The negative predictive values for each are 78-79%.

The conclusions of these two studies, one looking at SeHCAT and one at faecal bile acids, are remarkably similar. Normal values of C4 and FGF19 make it reasonably unlikely that the symptoms are due to BAD. Abnormal C4 or FGF19 values should lead to further testing, depending on availability, or a therapeutic trial of bile acid sequestrants.
More work is needed to understand causes of variability in C4 and FGF19, and it may be that a stimulation test of FGF19, as recently reported, will be advantageous. Simpler, validated methodology is needed. Hopefully this will then lead to better recognition and treatment of patients with BAD.

ACKNOWLEDGEMENTS

Declaration of personal interests: Julian Walters has served as a speaker, advisory board member or consultant for Albireo, GE Healthcare, Intercept Pharmaceuticals, NGM Biopharmaceuticals, and Novartis.

References