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Is bile acid malabsorption really a common feature of Crohn's disease or is it simply a consequence of ileal resection?

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A commentary on

Bile acid malabsorption in inflammatory bowel disease: assessment by serum markers
by Lenicek, M., Duricova, D., Komarek, V., Gabrysova, B., Lukas, M., Smerhovsky, Z., and Vitek, L. (2010). Inflamm. Bowel Dis. 17, 1322–1327.

To the Editor,

We have read with great interest the recently published article by Lenicek et al. (2010) on the importance of the determination of bile acid malabsorption (BAM) in inflammatory bowel diseases (IBD). The authors suggest that BAM may occur in over 40% of patients with Crohn's disease (CD) and that routine measurements of BAM should be incorporated in the diagnostic algorithm of CD. However, it is questionable whether BAM is really a CD-specific alteration or simply is a consequence of the ileal resection? If we further analyze the data of Lenicek et al. (2010) we can calculate that abnormal serum C4 level was observed in 67% (103 of 167) of the resected patients, whereas BAM developed in only 12% (13 of 109) of the non-resected CD patients. BAM occurred more frequently (87%) in case of more extensive resection. On the basis of these data, it might be concluded that the development of BAM rather depends on a condition caused by shorter small bowel than a CD-specific alteration. On the basis of the observation that BAM occurred in 11% of patients with colonic and in 14% of patients with non-resected ileal CD also confirm that the location of CD really does not matter in this context. Our opinion is that the theoretical association between the ileal inflammation and the impaired function of the ileal sodium/bile acid transporter (ASBT) does not work in the clinical routine. This is in accordance with the results of Holzer et al. (2008), who reported that diminished expression of ASBT mRNA in non-obese patients with gallstones is independent from ileal inflammation. Lenicek et al. (2010) also concluded that BAM can not be predicted based solely on clinical data. We agree with this observation, since the development of clinical symptoms is the consequence of a very complex mechanism. It is well known that the leading symptom of CD, namely watery diarrhea, is not only observed after small bowel resection, but it is also very common in patients who underwent cholecystectomy. Importantly, cholestyramine, a polymeric bile acid sequestrant, lowers the concentration of bile acids and ameliorates the diarrhea in these patients (Hofmann and Poley, 1972). These clinical data strongly suggest that bile acids are involved in the development of diarrhea in the case of BAM.

It is known that ion transporters are involved in the development of diarrhea in IBD. The impaired activities of ion transporters are usually characterized by increased Cl^- secretion and/or inhibited Cl^- and Na^+ absorption. Importantly, these transport mechanisms have been found to be influenced by bile salts in the gastrointestinal tract (Mauricio et al., 2000; Venglovecz et al., 2008; Goldman et al., 2010). In pancreatic (Venglovecz et al., 2008) and esophageal (Goldman et al., 2010) epithelial cells, bile acids, in millimolar concentration, inhibited Na^+/H^+ exchangers. In colonocytes, bile acids inhibited amiloride sensitive Na^+ (Hofmann and Poley, 1972) and water absorption, moreover, induced Cl^- (Mekjian et al., 1971; Hofmann and Poley, 1972) and water (Mekjian et al., 1971) secretion. All of these effects in the colon will enhance fecal water content and thus augment diarrhea. Therefore, BAM, which definitely occurs more frequently in resected ileal CD than in the non-resected ones, will aggravate the disease.

The incidence of gallstones is elevated by about twofold in CD (14.35/1000 person/year vs. 7.75 in matched controls; Parente et al., 2007). Should asymptomatic CD patients with BAM be treated in order to prevent gallstones? Probably yes, if BAM would be the unique factor which leads to increased gallstone morbidity. However, it seems that this process – as every other – is multifactorial: the localization and duration of CD, number of recurrences and previous hospitalizations, extensive resections and multiple total parenteral nutrition treatments also increase the risk of gallstone development without BAM.

Finally, should BAM be routinely measured? Nowadays, 61% of the responded experts had never used BAM measurements (neither did we). However, the publication of Lenicek et al. (2010) convinced us that the examination of BAM can indeed be useful in selected cases: CD patients with unexplainable diarrhea and in the case of relatively short small bowel resection.

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