Serum bile acid profiling for inflammatory bowel disease characterization

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Based on serum bank material, BA profiling was applied in IBD patients and healthy controls which showed that most but not all BA species were decreased to a different extent in CD and UC. BA decreases were highly pronounced in CD patients with surgical interventions in the gut.

On the other hand, UC patients with additional liver and gallbladder diseases showed clearly increased levels of those BAs that are synthesized directly in the liver (primary BAs), or subsequently modified by intestinal bacteria (secondary BAs). Furthermore, a marked decrease in the toxic BA lithocholic acid (LCA) was found together with a marked increase in its physiological detoxification product, hyodeoxycholic acid (HDCA), irrespective of the IBD phenotype or clinical manifestation, which showed accelerated detoxification activity in IBD patients. Thus, serum BA profiling might serve as an additional diagnostic tool for IBD characterization and differentiation. In combination with expression profiles of nuclear pregnane X receptor (PXR)-regulated genes, it might allow us to estimate the BA detoxification potential of IBD patients.

Besides their digestive functions for lipid uptake in the intestine, BAs have been found recently to play an important regulatory role in numerous metabolic processes, e.g., energy and lipid balance and elimination of harmful substances. They are mediated by binding appropriate transcription factors in the cell, i.e., farnesoid X receptor (FXR) and PXR, depending on the chemical structure of individual Bas, which can be differentiated by means of LC-MS/MS.

In a research article to be published on July 7,2009 in the World Journal of Gastroenterology, Professor Gerd Schmitz from the Institute of Clinical Chemistry, Laboratory and Transfusion Medicine at the University Hospital , which yielded characteristic profiles of amino-acid-bound (conjugated), as well as free Bas, which reflect medical conditions in IBD far better than just measuring total BA levels or individual abundant BAs.

By this means, they could show that decreased serum BA levels were not restricted to CD alone, as previously reported, but were also found in UC if a defined set of specific BAs were considered, even if most serum BA levels in UC patients are not decreased as much as in CD patients. However, perhaps for the first time, they reported on invariably increased HDCA and decreased LCA in IBD compared to control sera, irrespective of the clinical findings, which reflected accelerated LCA detoxification processes in the liver and intestine. Moreover, the influence of extraintestinal manifestations (EMs) of the liver and biliary tract (e.g. hepatitis, bile duct inflammation, and gallstone disease) on serum BA levels in IBD was clearly demonstrated in UC patients. They showed a significant increase in primary and secondary BAs compared to EM-free patients, which indicated a high susceptibility of the physiological BA circulation between the liver and gut in IBD to additional EMs of the liver and biliary tract. Finally, they found that CD patients with partial small intestine resection showed significantly decreased conjugated BAs but increased free primary Bas, compared to patients without surgical interventions. This might be explained by an increased compensatory synthesis of primary BAs in IBD associated with an enhanced bacterial dissociation of the respective amino acid conjugates in the remaining intestinal sections.

According to the authors, these findings could further elucidate the intestinal contribution to the physiological BA balance and detoxification and expand our knowledge about the role of BA metabolism in IBD. They assume that serum BA profiling in IBD for diagnostic and prognostic purposes might be easily conceivable.

More information: Gnewuch C, Liebisch G,

Langmann T, Dieplinger B, Mueller T, Haltmayer M, Dieplinger H, Zahn A, Stremmel W, Rogler G, Schmitz G. Serum bile acid profiling reflects enterohepatic detoxification state and intestinal barrier function in inflammatory bowel disease. World J Gastroenterol 2009; 15(25):3134-3141, www.wjgnet.com/1007-9327/15/3134.asp

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