Gut microbiota modulation in cirrhosis: A new frontier in hepatology

Bajaj JS, Heuman DM, Hylemon PB, et al. Randomised clinical trial: Lactobacillus GG modulates gut microbiome, metabolome and endotoemia in patients with cirrhosis. Aliment Pharmacol Ther 2014 March 16. doi:10.1111/apt.12695 [Epub ahead of print]

Bajaj JS et al. (1) recently published a study in APT about gut microbiota modulation and consequences in cirrhotic patients. Cirrhotic patients with MHE patients were randomised 1:1 into LGG or placebo for 8 weeks. The aim was to determine gut microbiota composition and concomitant changes in function (metabolome) in cirrhotic patients with minimal hepatic encephalopathy (MHE). Serum, urine and stool samples were collected at baseline and study end. Safety was assessed at weeks 4 and 8. Endotoxin and systemic inflammation, microbiome using multi-tagged pyrosequencing, serum/urine metabolome were analysed between groups using correlation networks. Thirty MHE patients (14 LGG and 16 placebo) completed the study without any differences in serious adverse events. Only in the LGG-randomised group, endotoxemia and TNF-a decreased, microbiome changed (reduced Enterobacteriaceae and increased Clostridiales Incertae Sedis XIV and Lachnospiraceae relative abundance) with changes in metabolite/microbiome correlations pertaining to amino acid, vitamin and secondary BA metabolism.

This was a phase I study about Lactobacillus GG in cirrhotic patients. No adverse events were noted during and after the study. There were some benefits in improvement of dysbiosis and metabolic functions of the microbiome. Previous studies showed that with advancing cirrhosis, with and without alcoholic liver disease, there is expansion of Proteobacteria, the phylum containing gram-negative families such as Enterobacteriaceae (2,3). This was associated with a reduction in endotoxemia as would be expected with reduced gram-negative abundance but also a reduction in TNF-alfa levels. This is the first study showing that Lactobacillus GG as a drug-quality probiotic, is safe and able to improve gut microbiota composition (healing dysbiosis) and modulating the functional aspect of the microbiome. This study also showed that probiotic Lactobacillus GG decreases endotoxemia and decreasing systemic inflammatory response in cirrhotic patients. A recent study by the same authors indicated that progressive changes in the gut microbiome accompany cirrhosis and become more severe in the setting of decompensation (4). They found a cirrhosis dysbiosis ratio (CDR) and this ratio might be a useful quantitative index to describe microbiome alterations accompanying cirrhosis progression. In the longitudinal matched-cohort, microbiota was significantly different between infected/uninfected cirrhotics at baseline and a low CDR was associated with death and organ failures within 30 days (4).

Gut microbiota changes (quantitative and/or qualitative) and therapeutic modulation of microbiota are having potential value in the future for management of cirrhotic patients. This might be probiotics with specific ability to improve liver functions or testing microbiota for prediction of morbidity/mortality. Until then, we need large cohort studies in specific populations such as Bajaj and colleagues' excellent trial.

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