Correspondence: Antibiotic-Associated Disruption of Microbiota Composition and Function in Cirrhosis is Restored by Fecal Transplant

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To the Editor:

The study from Bajaj and colleagues – evaluating gut microbiome-metabonome changes in cirrhotic patients receiving fecal microbiota transplant (FMT)[1] – merits further discussion of its conclusions.

In this study, cirrhotic patients with hepatic encephalopathy (HE) taking standard of care (SOC) therapy were randomised to either continue with SOC alone, or to also receive five days of antibiotics prior to a single FMT enema. The investigators demonstrate partial recovery of microbiota, bile acid, and short-chain fatty acid (SCFA) profiles for patients in the FMT arm, and conclude that FMT directly restores gut microbiome-metabonome interactions in antibiotic-treated cirrhotics[1]. However, there was no arm in this study where patients received antibiotics but no FMT; therefore, it is impossible to distinguish whether any changes observed were directly caused by FMT as claimed, or at least partly represent purely gut microbiota recovery after completion of antibiotics.

There are certainly grounds for questioning the efficacy of the FMT. Specifically, despite selecting a stool donor with high relative abundance of *Lachnospiraceae* and *Ruminococcaceae,* FMT recipients actually demonstrate a significantly reduced relative abundance of these bacterial families post-FMT (day 20) compared to baseline values (day 0) (Figure 2[1]). Furthermore, it is well-established that human gut microbiota structure recovers to a profile comparable to that found pre-antibiotics within a short period following completion of an antibiotic course[2]. Additionally, whilst poorly-explored in cirrhosis, SCFA[3] and bile acid profiles[4] reconstitute over a time course of days to weeks after antibiotic cessation in healthy rodents without any specific intervention.

If FMT directly treated HE through modulation of gut microbiota-metabonome interactions, then it would be expected that at least some of these variables would exceed baseline values post-FMT, rather than only match baseline levels at best, as shown. Adverse events associated with FMT are uncommon, but serious adverse events are described – including bacteraemia – in the non-cirrhotic population[5]; such concerns are clearly amplified in decompensated cirrhotics, given this group's propensity to and outcomes from sepsis. Until the safety profile of FMT within cirrhotic patients has been further evaluated – and a potential mechanistic link between FMT and improvement in HE defined - then FMT remains at too early a stage to consider more widely as HE treatment.

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List of abbreviations:

FMT fecal microbiota transplant

HE hepatic encephalopathy

SOC standard of care

SCFA short chain fatty acids

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