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Commentary: Effect of fecal microbiota transplantation on non-alcoholic fatty liver disease: A randomized clinical trial

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A Commentary on

Effect of fecal microbiota transplantation on non-alcoholic fatty liver disease: A randomized clinical trial

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Introduction

A study entitled “Effect of Fecal Microbiota Transplantation on Non-Alcoholic Fatty Liver Disease: A Randomized Clinical Trial” was recently published in *Frontiers in Cellular and Infection Microbiology* by (Xue et al., 2022). According to the summary of the respective article, fecal microbiota transplantation (FMT) can reduce hepatic fat accumulation by improving gut microbiota dysbiosis. Based on the participant’s preferences, individuals with non-alcoholic fatty liver disease (NAFLD) were included in the study and randomly assigned to either of the two groups: FMT or traditional treatment. The feces needed for the FMT group’s therapy as well as the healthy group’s feces were provided by healthy volunteers from Guangdong Pharmaceutical University. When L. Xue et al. examined the gut microbiota’s features and alterations, they discovered that patients with NAFLD before to FMT had lower Chaol indices [prior to FMT (pri-FMT) vs. healthy group, $p < 0.05$] than healthy people, indicating a reduced

abundance of the gut microbiota in NAFLD patients. In this case, there is no baseline data comparison between the healthy group and the pri-FMT group.

NAFLD is currently thought to be the hepatic manifestation of the metabolic syndrome and is frequently linked to metabolic risk factors such as obesity, dyslipidemia, hypertension, and diabetes (Buzzetti et al., 2016). However, not all NAFLD patients have the same disease drivers; for instance, some people may have disease that is primarily brought on by lipid dysregulation, while others may have disease that is brought on by increased inflammation or insulin resistance, or by a combination of host genetics, the microbiome, or other determinants (Loomba et al., 2021). Numerous studies have shown that the gut microbiota is crucial in the pathogenesis of NAFLD. (Boursier et al., 2016; Leung et al., 2016; Canfora et al., 2019; Aron-Wisnewsky et al., 2020; Tilg et al., 2020). Age, diet, exercise can also change gut microbiota, and all above can cause favorable changes in the structure and functions of the gut microbiota (Hasan and Yang, 2019; Gubert et al., 2020; Liu et al., 2020; Mohr et al., 2020). Thus, changing age, different diet and exercise habits were all involved in modulating gut microbiota. With age, there is a broad shift in the types of gut microbiota. For example, the Firmicutes phylum have the opposite tendency from those of the Bacteroidetes phylum, which tend to dominate numerically in youth but drastically fall in numbers as they age (Conlon and Bird, 2014). Obviously, there was a significant age difference between pri-FMT group and healthy group. For undergraduate students in the healthy group are fairly young, but the average age of pri-FMT group patients at around 57 years (Table 1), which greatly affected Chaol indexes of the gut microbiota. In addition, the usual lifestyle habits, including exercise and diet, also affect the

abundance of gut microbiota, which need to be given in the baseline information comparison table between pri-FMT group and healthy group.

Second, exercise variables (type/frequency/intensity/duration) were not all specified in the research design. It has been reported in the researches that different exercise lead to significantly differentiated abundances of the gut microbiota (Morita et al., 2019; Ticinesi et al., 2019), liver function and biochemical parameters in NAFLD patients (Golabi et al., 2016; Hashida et al., 2017; Zhou et al., 2021). In this study, only more than 40 minutes of exercise per day were recommended; the intensity and type of exercise were not specified. In practice, patient comprehension biases and varying exercise preferences may have an impact on the accuracy of the results. Therefore, the study should clarify both the type and intensity of exercise.

Third, despite the fact that there are numerous potential pathways into gut microbiota modification in NAFLD patients, this study did not evaluate the long-term efficacy of FMT, which is required for assessing the treatment potential for NAFLD. FMT treatment may be an effective supplement to NAFLD management, but more research is needed to identify its maximum validity.

Scientific knowledge regarding diversity and richness of gut microbiota in Patients with NAFLD is still being explored. Rapid progress in this field will be dependent on the falsifiability of hypotheses based on rigorous scientific evidence. We believe that the findings reported by L. Xue and colleagues will help to achieve this goal, either directly or indirectly; however, this report needs to be more rigorous in designing experimental protocols, to clarify that NAFLD is an independent factor contributing to gut microbiota disorders, and to determine the precise, long-term efficacy of FMT in treating NAFLD.

TABLE 1 Baseline comparison between FMT group and non-FMT group.

Characteristic	FMT group (n=47)		Non-FMT group (n=28)		P value
	Before treatment	After treatment	Before treatment	After treatment	
Gender (male)	25 (53.2%)		14 (50%)		>0.05
Age	57.3 ± 13.4		60.2 ± 8.5		>0.05
Hypertension	23 (48.9%)		12 (42.8%)		>0.05
Type 2 diabetes	15 (31.9%)		8 (28.5%)		>0.05
BMI (kg/m ²)	27.7 ± 4.5	27.4 ± 4.4	28.0 ± 5.2	28.4 ± 5.2	>0.05
PLT (10 ⁹)	231.8 ± 66.7	229.8 ± 60.1	221.4 ± 73.7	223.9 ± 75.6	>0.05
Hb (g/L)	137.9 ± 13.6	139.5 ± 14.4	134.6 ± 16.5	137.6 ± 12.8	>0.05
Fasting blood glucose (mmol/L)	5.3 ± 1.2	5.3 ± 1.3	5.6 ± 1.6	5.8 ± 1.9	>0.05
Fasting insulin (mU)	15.1 ± 8.9	13.4 ± 6.7	12.6 ± 6.0	15.8 ± 8.9	>0.05
HOMA IR	3.8 ± 2.9	3.4 ± 2.2	3.2 ± 1.7	4.5 ± 3.3	>0.05
Uric acid (umol/L)	366.5 ± 84.1	370.8 ± 81.3	419.5 ± 93.1	399.8 ± 81.3	>0.05

FMT, fecal microbiota transplantation; BMI, body mass index; PLT, platelets; Hb, hemoglobin; HOMA IR, homeostasis model assessment of insulin resistance. P, baseline FMT vs baseline non-FMT.

Author contributions

JW and JC wrote the manuscript with the support from MC. The original idea was conceived by MC. All authors contributed to the article and approved the submitted version.

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