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Fecal Microbiota Transplantation Combined with Lifestyle Modification in the Management of Metabolic Dysfunction-Associated Fatty Liver Disease: Two Case Reports and Literature Review

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Abstract: Metabolic dysfunction-associated fatty liver disease (MAFLD) is highly prevalent condition, with gut microbiota dysbiosis playing a contributory role in its pathogenesis and progression. Fecal microbiota transplantation (FMT) has emerged as a potential therapeutic approach for MAFLD. This report describes two patients diagnosed with MAFLD who underwent FMT in combination with lifestyle intervention. Post treatment findings demonstrated notable improvements in body mass index (decreased by 20.7% and 3%, respectively), serum transaminases levels (decreased by 51% and 27.2%, respectively), lipid profiles, uric acid concentrations, and liver stiffness measurements (decreased by 22.2% and 24.2%, respectively). Additionally, microbiome analysis showed increased diversity, improved anti-inflammatory and colonization resistance capacity, reduced pathogens, and enriched probiotics. A review of seven Chinese and international randomized controlled trials (RCTs) investigating the application of FMT in MAFLD was conducted. Among these, four trials reported improvement in liver function post-treatment. Two trials reported reductions in small intestinal or gastric permeability, one trial demonstrated a decrease in homeostasis model assessment of insulin resistance (HOMA-IR), one trial noted a reduction in blood lipid levels, and one trial documented a decrease in fat attenuation index (FAI). Only one trial included histological evaluation of liver tissue before and after FMT, which did not demonstrate significant pathological improvement. The combination of FMT and lifestyle intervention has achieved quite satisfactory therapeutic effects in the treatment of MAFLD, providing new ideas and potential therapeutic targets for the management of MAFLD. This approach holds broad application prospects. However, further confirmation through large-scale RCTs is still needed.

Keywords: fecal microbiota transplantation, hepatic steatosis, lifestyle intervention, metabolic dysfunction-associated fatty liver disease, case report

Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) represents the most prevalent chronic liver disorder in developing countries. In 2020, the International Expert Consensus Panel proposed the terminology shift from nonalcoholic fatty liver disease (NAFLD) to MAFLD, which has sparked extensive discussions among experts, clinicians, and the scientific community. The pathogenesis of MAFLD remains unclear and involves a variety of factors, including genetics, diet, and environment. Patients with MAFLD are at increased risk of cardiovascular events, stroke, chronic kidney disease, sleep apnea syndrome, and malignancies. The mortality rates related to cancer, cardiovascular diseases, and overall mortality are also elevated. Compared with NAFLD, the nomenclature of MAFLD highlights the significant role of metabolic disturbances in the pathogenesis and progression of the disease, which is more in line with the

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characteristics of the condition. In its early stages, the condition presents as hepatic steatosis and may progress to cirrhosis or hepatocellular carcinoma in advanced stages. In addition to genetic predisposition, disruptions in lipid and bile acid homeostasis, as well as carbohydrate metabolism, play a role in its development. Gut microbiome dysbiosis has been identified as a significant contributor to the pathogenesis of MAFLD.[1] The condition is associated with alterations in the composition of gut microbiota and in microbial metabolites, including ethanol, choline, bile acids, and short-chain fatty acids.[2] Both animal experiments and clinical investigations have examined the therapeutic potential of gut microbiome- targeted therapies in the management of MAFLD. Although there have been clinical and animal experimental studies on the treatment of MAFLD based on gut microbiota modulation, including probiotics, prebiotics containing dietary fiber, and nonabsorbable oral antibiotics, these studies are limited by the use of single strains, insufficient bacterial quantities, small sample sizes, and inconclusive results.

Fecal microbiota transplantation (FMT) is a technique that involves the transfer of a healthy individual's gut microbiota into the gastrointestinal tract of a patient to restore normal gut microbial function. Currently, there are few clinical studies applying FMT for the treatment of MAFLD, and its potential in this therapeutic area warrants further exploration. Lifestyle modification is the cornerstone of MAFLD management. A considerable number of patients with MAFLD can achieve significant improvement in their condition through lifestyle interventions such as dietary control, increased physical activity, and enhanced awareness. However, some patients still have poor outcomes despite conventional lifestyle modifications and pharmacological treatments. In these cases, FMT based on gut microbiota modulation, offers a new therapeutic target for MAFLD. Moreover, continuous lifestyle changes are also necessary to consolidate the therapeutic effects of FMT. Therefore, this paper reports on the therapeutic effects of FMT combined with lifestyle modification in two patients with MAFLD, providing a new approach for the treatment of MAFLD.

Case Data

Case 1

An 18-year-old male, with a 10-year history of MAFLD, presented to the gastroenterology outpatient clinic on February 6, 2024. At the time of evaluation, anthropometric measurements revealed a height of 182 cm, weight of 120 kg, and body mass index (BMI) of 36.2 kg/m^2. Comprehensive biochemical and imaging assessments were conducted. Laboratory findings included alanine aminotransferase (ALT) of 34.3 U/L [9–50U/L], aspartate aminotransferase (AST) of 24.1 U/L [15–40U/L], fasting plasma glucose of 6.4 mmol/L [3.9–6.1mmol/L], triglycerides (TG) of 3.51 mmol/L [0.4–1.82mmol/L], total cholesterol (TC) of 6.3 mmol/L [3.1–5.2mmol/L], low-density lipoprotein cholesterol (LDL) of 4.03 mmol/L [2.62–3.41mmol/L], high-density lipoprotein cholesterol (HDL) of 1.10 mmol/L [1.16–1.42 mmol/L], and uric acid (UA) of 616 μmol/L [208–428umol/L]. Abdominal ultrasonography confirmed fatty liver disease. Noninvasive liver fibrosis testing demonstrated a liver stiffness value of 8.1, corresponding to a Metavir stage of F2–F3.

Gut microbiome analysis indicated a gut microbiome health index of −0.78, intestinal anti-inflammatory capacity of 44, intestinal immunity of 35, gut microbiome species count of 962, gut microbiome diversity index of 7.26, gut microbiome colonization resistance (B/E) of 0.15, and a Firmicutes/Bacteroidetes (F/B) ratio of 1.19. Enterotype analysis classified the microbiome as type II with a predominance of *Prevotella* species. The most abundant pathogenic bacteria identified were *Salmonella* (1.89), *Streptococcus* (0.69), *Clostridium* (0.53), and *Mycobacterium* (0.2). The leading opportunistic pathogens were *Bacteroides* (8.04), *Escherichia* (3.1), *Veillonella* (0.96), and *Enterococcus* (0.74). The most abundant probiotics were *Faecalibacterium* (11.12), *Bacteroides* (8.04), *Rothia* (4.29), and *Blautia* (0.98).

Lifestyle interventions were initiated, consisting of cognitive education, dietary planning, and physical exercise. The intervention program included the following components:

(1) Cognitive education: The patient was informed about the risks associated with obesity and the importance of weight management, with emphasis on the complications associated with MAFLD. Educational sessions were conducted biweekly and included question-and-answer discussions, experience sharing, and practical training. (2) Dietary planning: A standardized nutritional program was designed by a clinical nutritionist. The program focused on caloric restriction, emphasizing the intake of high-quality proteins, and limiting carbohydrate consumption. Saturated fats and trans fatty acids were minimized, while the intake of vegetables and fruits was encouraged. Nutrient distribution consisted of > 20%

protein, < 40% carbohydrates, and < 30% fat. (3) Physical exercise: A combination of aerobic and resistance training was recommended. Moderate intensity aerobic activities such as rope skipping, jogging, or swimming were recommended for 60 minutes per session, which could be divided into two 30-minute sessions with a 10-minute rest interval, to be performed at least three times per week. Resistance training, including exercises such as push-ups, dumbbell workouts, and elastic band training, were recommended in sets of eight repetitions at least three times per week.

Following eight weeks of adherence to the lifestyle intervention program, including dietary modifications and regular exercise, the patient's weight decreased to 116 kg. However, imaging confirmed the persistence of severe fatty liver disease. Following a discussion regarding risks and benefits, and after obtaining informed consent, the patient underwent routine assessments to exclude contraindications for FMT. On April 20, 2024, the patient received 20 oral fecal microbial capsules (Treatgut Biotechnology Co., Ltd). No adverse reactions, such as abdominal pain, diarrhea, or fever, were reported following administration. Lifestyle interventions were continued throughout the post-FMT period.

At six months post-FMT, the patient's weight had decreased to 95 kg, with a BMI of 28.7 kg/m^2. Biochemical and imaging evaluations demonstrated marked improvements: ALT 16.8 U/L, AST 12.8 U/L, fasting plasma glucose 4.9 mmol/L, TG 1.23 mmol/L, TC 3.7 mmol/L, LDL 3.25 mmol/L, HDL 2.42 mmol/L, and UA 458 μmol/L. Liver stiffness measurement had decreased to 6.3 kPa, consistent with a Metavir fibrosis stage of F1–F2. Gut microbiome analysis demonstrated a gut microbiome health index of −0.24, intestinal anti-inflammatory ability of 58, intestinal immunity of 62, gut microbiome species count of 1027, gut microbiome diversity index of 8.21. The B/E ratio had improved to 0.57, and the F/B ratio had increased to 1.57. The microbiome remained classified as enterotype II, with a continued predominance of *Prevotella* species. The most frequently detected pathogenic bacteria were *Salmonella* (0.05), *Clostridium perfringens* (0.34), *Shigella* (0.21), and *Actinomyces* (0.15). The leading opportunistic pathogens included *Bacteroides* (8.04), *Veillonella* (2.52), *Klebsiella* (1.82), and *Enterococcus* (0.21). The most prevalent probiotics were *Prevotella* (9.25), *Phascolarctobacterium* (7.52), *Lactobacillus* (5.82), and *Faecalibacterium* (2.52).

Case 2

A 38-year-old male with a three-year history of MAFLD and a background of recurrent hyperlipidemic pancreatitis for more than one year, requiring multiple hospitalizations, was evaluated at the gastroenterology department on June 20, 2024. Anthropometric measurements showed a height of 183 cm, weight of 87.2 kg, and BMI of 26 kg/m^2. A follow-up examination was conducted at the gastroenterology outpatient clinic. Biochemical and ultrasound assessments demonstrated ALT of 30.8 U/L [9–50U/L], AST of 17.9 U/L [15–40U/L], fasting plasma glucose of 4.85 mmol/L [3.9–6.1mmol/L], TG of 8.64 mmol/L [0.4–1.82mmol/L], TC of 5.31 mmol/L [3.1–5.2mmol/L], LDL cholesterol of 5.84 mmol/L [2.62–3.41mmol/L], and HDL cholesterol of 2.27 mmol/L [1.16–1.42 mmol/L]. Abdominal ultrasonography confirmed fatty liver and pancreatic fatty infiltration. Liver stiffness measurement was 6.2 kPa, corresponding to a Metavir fibrosis stage of F1–F2.

Gut microbiome analysis demonstrated a gut microbiome health index of −0.69, intestinal anti-inflammatory capacity of 23, intestinal immunity of 52, gut microbiome species count of 372, gut microbiome diversity index of 1.53, B/E 0.14, and a F/B ratio of 0.08. Enterotype classification identified the microbiota as type I, with a predominance of Bacteroides species. The only pathogenic organism identified was *Streptococcus pneumoniae* (0.0025). Dominant opportunistic pathogens included *Bacteroides vulgatus* (12.37), *Sutterella* (1.61), *Collinsella* (1.44), and *Streptococcus* (0.64). The most abundant probiotics included *Bifidobacterium* (2.80), *Megamonas* (1.36), *Lachnospira* (0.59), and *Faecalibacterium* (0.5).

Lifestyle interventions were initiated, consisting of cognitive education, dietary planning, and exercise. The structured plan included:

(1) Cognitive education: The patient was educated about metabolic syndrome, fatty liver, and fatty pancreas, with emphasis on the risks of MAFLD and recurrent hyperlipidemic pancreatitis. Educational content was delivered through WeChat, Douyin, and patient education platforms. (2) Dietary planning: For management of metabolic syndrome and hypertriglyceridemia, a standardized dietary plan was developed by a nutritionist. The plan emphasized high-quality protein sources (such as soy, milk, fish, and eggs), complex carbohydrates (such as buckwheat, millet, and oats), and unsaturated fatty acids (such as olive oil, rapeseed oil, and walnut oil). Nutrient distribution consisted of > 30% protein, < 40% carbohydrates, and < 20% fat. (3)Physical exercise: Moderate-intensity aerobic exercise was prescribed, with sessions lasting 60 minutes, performed at least three times weekly.

The patient had previously undergone lifestyle intervention and treatment with fenofibrate and evolocumab, with limited effectiveness (Fenofibrate capsules 200 mg, oral administration, once daily, for continuous use over 6 months. Lipid control remained suboptimal. Subsequently, evolocumab 140 mg was added, administered via subcutaneous injection, every 2 weeks, for an additional 3 months. However, the therapeutic effect was still unsatisfactory). Following informed consent and the exclusion of contraindications, the patient received 20 oral fecal microbial capsules (Treatgut Biotechnology Co., Ltd.) on October 10, 2024. The procedure was well tolerated, with no adverse reactions, and lifestyle interventions were maintained.

At follow-up on March 28, 2025, laboratory investigations revealed improvement in biochemical markers: ALT was 22.4 U/L, AST 14.7 U/L, fasting plasma glucose 4.3 mmol/L, TG 2.23 mmol/L, TC 3.21 mmol/L, LDL 2.74 mmol/L, and HDL 2.58 mmol/L. Liver stiffness measurement had decreased to 4.7 kPa, consistent with a Metavir fibrosis stage of F1–F2. Gut microbiome analysis demonstrated notable changes, including a gut microbiome health index of 0.25, intestinal anti-inflammatory capacity of 58, intestinal immunity of 67, gut microbiome species count of 667, gut microbiome diversity index of 5.87. The B/E ratio had improved to 0.47, and the F/B ratio had increased to 2.89. Enterotype I was retained, with a predominance of *Bacteroides*. The most frequently identified pathogenic bacteria were *Salmonella* (0.85), *Proteus vulgaris* (0.68), *Campylobacter jejuni* (0.55), and *Streptococcus cholerae* (0.42). The leading opportunistic pathogens included *Bacteroides vulgatus* (3.21), *Megamonas* (2.52), *Lachnospira* (1.52), and *Coprococcus* (1.25). The most prevalent probiotics were *Prevotella* (2.75), *Rothia* (2.52), *Bacteroides* (2.25), and *Lactobacillus* (1.57).

The fecal material was obtained from a single donor as fresh yellow, formed soft stool weighing 2–20 grams. Fecal microbiota capsules were prepared and stored at –80°C for later use. Neither of the two patients underwent bowel preparation before FMT, and the transplantation was performed via oral administration.

This study was conducted with approval from the Ethics Committee of Hebei General Hospital (Approval Number: 2022–203), all participants had signed written informed consent for participation in this study and publication of any case details and/or images. We report this case report in line with the CARE guidelines.

Literature Review

Search Process

To evaluate the efficacy of FMT in the management of MAFLD, a systematic search was conducted across multiple databases, including PubMed, EMBASE, the Cochrane Library, Web of Science, CNKI, VIP, and Wanfang. The search strategy employed combinations of the following keywords: “non-alcoholic fatty liver disease”, “nonalcoholic fatty liver disease”, “nonalcoholic fatty liver”, “fatty liver”, “NAFLD”, “non-alcoholic steatohepatitis”, “nonalcoholic steatohepatitis”, “NASH”, “metabolic dysfunction-associated fatty liver disease”, “MAFLD”, “metabolic dysfunction-associated steatotic liver disease”, and “MASLD”. Terms related to FMT included: “fecal microbiota transplantation”, “fecal microbiome transplantation”, “fecal microbiota transplant”, “fecal microbiota transfusion”, “fecal microbiota transfer”, “donor feces infusion”, “FMT”, “stool microbiota transplantation”, “stool microbiota transfusion”, “bacteriotherapy”, “fecal therapy”, “fecal bacteriotherapy”, “intestinal microbiota transplantation”, “intestinal microbiota transfer”, “intestinal microbiome transplantation”, “intestinal microbiota transplant”, “intestinal microbiome transplant”, “fecal transplant”, “fecal transfusion”, “fecal implantation”, “fecal implant”, “fecal instillation”, and “fecal reconstitution”.

Eligibility criteria were defined using the PICOS framework (Population, Intervention, Comparator, Outcomes, Study design). Studies were included if they met the following criteria: (1) randomized controlled trial (RCT) design; (2) diagnosis of MAFLD confirmed by liver histology or noninvasive imaging modalities (such as abdominal ultrasound, CT and MRI); and (3) reporting of at least two of the following outcomes: serum levels of TC, TG, ALT, AST, gamma-glutamyl transpeptidase (GGT), LDL cholesterol, HDL cholesterol, homeostasis model assessment of insulin resistance (HOMA-IR), BMI, or histological changes evaluated by liver biopsy, magnetic resonance imaging (MRI), or ultrasound elastography. Histological outcomes included the NAFLD activity score (NAS), steatosis, activity, and fibrosis (SAF) score, necro-inflammatory score, fibrosis score, or steatosis score. MRI-based outcomes included estimated fibrosis staging, while elastography outcomes evaluated parameters such as fat attenuation and fibrosis stage.

Exclusion criteria were as follows: (1) studies involving participants under 18 years of age; (2) studies including individuals with severe comorbidities unrelated to MAFLD, including but not limited to severe heart disease, respiratory failure, liver and kidney failure, malignant tumors, severe infections, blood system diseases, autoimmune diseases, mental disorders, etc.; (3) patients who are currently taking hormones, antibiotics, gastrointestinal motility drugs, traditional Chinese medicines or microecological preparations and (4) studies with incomplete data. A total of 1918 references were initially retrieved, and following a detailed review, seven RCTs met the inclusion criteria and were included in the final analysis.[3–9]

Study Characteristics

A total of seven RCTs were included in the analysis, comprising three double-blind trials, one single-blind trial, and three open-label trials, with a combined total of 288 participants. Six studies reported including both male and female participants, while one study did not provide demographic data regarding participant sex. Geographically, four studies were conducted in China, one in Canada, one in the Netherlands, and one did not specify its study location or participant demographics. FMT administration routines varied across studies: colonoscopy was used in three trials, gastroscopy in two, a combination of gastroscopy and duodenal tube in one, and a gastric tube in one. Microbial preparations were derived from fresh feces in two studies and frozen feces in one, while four studies did not describe stool characteristics. The fecal microbiota sample size ranged from 2 to 100 g. Pre-transplantation bowel preparation was reported in three studies. Among these, one study employed proton pump inhibitors with flushing, while three studies did not specify whether bowel preparation was performed. Four studies reported using multiple donors, three studies did not specify whether donors were single or multiple, and two studies specifically employed related donors. Donor screening criteria were described in four studies, although only one provided detailed information about donor profiles (see Table 1).

Table 1 Clinical Parameters and Outcomes of Seven RCTs on FMT in MAFLD

Author/Year	Main Outcome Measures	Clinical Efficacy Outcomes
Lanfeng et al, 2022[3]	Liver function, lipid profile, liver fat failure values	No statistically significant differences were detected in liver function or lipid levels. Liver fat failure values decreased in the FMT group, with greater reductions observed in individuals with lean NAFLD compared to those with obesity.
Qiu et al, 2021[4]	Liver function, lipid profile, glucose metabolism, insulin resistance	ALT, AST, LDL-C, TG, TC levels decreased; HDL-C increased. Greater reductions in LDL-C, TG, TC, TNF-α, FPG, FINS, and HOMA-IR observed in the FMT group compared to the control group.
Witjes et al, 2020[5]	Liver biopsy, fasting glucose, liver enzymes, lipid profiles	No significant differences in NAS, steatosis, or fibrosis. Necro-inflammatory scores showed improvement in the allogeneic FMT group. GGT levels decreased in the allogeneic FMT group, and ALT levels declined more substantially in the allogeneic FMT group compared with the autologous FMT group. No statistically significant differences in glucose or lipid levels were identified between the two groups.
Craven et al, 2020[6]	Lipid profile, fasting glucose, HOMA-IR, hepatic PDFF, small intestinal permeability	No statistically significant differences were observed in HOMA-IR or proton density fat fraction (PDFF). Among allogeneic FMT recipients, small intestinal permeability initially increased in all seven individuals but subsequently decreased following transplantation, with two returning to normal levels. In the autologous FMT group, intestinal permeability decreased to normal in one recipient, while another exceeded normal levels. Free fatty acid levels decreased in the allogeneic FMT group, along with TC/HDL-C ratios, whereas other lipid parameters and fasting plasma glucose levels remained unchanged.

(*Continued*)

Table 1 (Continued).

Author/Year	Main Outcome Measures	Clinical Efficacy Outcomes
Ye et al, 2019[7]	Liver function	GGT, AST, and ALT levels in the FMT group were significantly lower both compared with pre-treatment values and with the control group, with statistically significant differences.
Ye et al, 2019[8]	Liver function, lipid profile	At four weeks post-treatment, ALT, AST, and TG levels in the FMT group were lower compared with the control group. At three months post-treatment, ALT, AST, GGT, and LDL-C levels were lower in the FMT group than in the control group. At six months post-treatment, ALT, AST, GGT, and TG levels remained lower in the FMT group, with all differences reaching statistical significance.
Parvathy et al, 2018[9]	Small intestinal (SIP) and gastric permeability (GP), HOMA-IR	After six weeks, the small intestinal permeability (SIP) improvement rate was 73% in the allogeneic FMT group and 33% in the autologous FMT group. Regarding gastric permeability (GP), all three patients with elevated GP demonstrated a decrease. For HOMA-IR, 82% of patients in the allogeneic FMT group showed improvement; however, the difference did not reach statistical significance.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transpeptidase; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; FIN, fasting insulin; HOME-IR, insulin resistance index; TNF-α, tumor necrosis factor-α; PDFF, liver proton density fat fraction; SIP, small intestinal permeability; GP, gastric permeability.

Discussion

Growing evidence indicates that individuals with MAFLD present with gut microbiome dysbiosis. A recent meta-analysis reported reduced α and β diversity in the gut microbiota of individuals with MAFLD, accompanied by decreased levels of anti-inflammatory bacteria such as *Ruminococcus* and *Coprococcus*, and increased levels of pro-inflammatory bacteria including *Fusobacterium* and *Escherichia*.[10] These alterations are thought to influence the production of pro-inflammatory bacterial components and metabolites, thereby contributing to increased intestinal permeability. Individuals with MAFLD also exhibit elevated levels of endogenous ethanol, circulating endotoxins, and abnormalities in bile acid metabolism. Translocation of these factors via the portal circulation to hepatocytes may promote insulin resistance, hepatic lipid accumulation, inflammation, and fibrosis, ultimately exacerbating liver injury.[11] Consequently, therapeutic strategies aimed at restoring and supplementing gut microbial balance may provide clinical benefits for individuals with MAFLD. While various interventions, including probiotics, prebiotics, synthetic probiotics, and antibiotics, have been investigated for their capacity to modulate the gut microbiota, current evidence suggests that probiotic supplementation alone does not significantly improve clinical outcomes of MAFLD.[12] This limited efficacy may be attributed to constraints in microbial diversity, low bacterial load, and limited colonization capability.

FMT, a novel therapeutic modality, is designed to restore the intestinal microbial ecosystem through the transfer of a complete microbial community from healthy donors, has been proposed as a potentially more effective intervention. Clinical investigations have begun to explore its potential role in the management of MAFLD.

Evaluation of clinical efficacy across the included studies primarily focused on post-FMT changes in biochemical parameters, imaging outcomes, intestinal permeability, and liver histology. Commonly assessed indicators included liver function tests, serum lipid profiles, fasting plasma glucose, HOMA-IR, hepatic fat content (as assessed by imaging), intestinal permeability, and histopathological findings. Among these, five studies reported liver function outcomes, with four documenting improvements after transplantation. Blood lipid alterations were evaluated in five studies, with three indicating reductions in lipid levels. Two studies assessed fasting plasma glucose and HOMA-IR, with no significant changes identified. Imaging-based assessments of hepatic fat content were described in two studies. In the study by Lanfeng et al, a reduction in fat attenuation index (FAI) was observed among individuals with MAFLD without obesity, compared to those with obesity. In contrast, the study conducted by Craven et al did not demonstrate statistically significant differences in hepatic proton density and fat fraction. Liver histology was evaluated in only one study, which

revealed no significant differences in NAS, steatosis grade, or fibrosis score before and after transplantation. However, necro-inflammatory scores exhibited a trend toward improvement in the allogeneic FMT group.

Two studies evaluated changes in small intestinal permeability using the urinary lactulose/mannitol ratio. In the study by Craven et al, all seven individuals in the allogeneic FMT group with baseline permeability abnormalities demonstrated reductions, with normalization observed in two cases. Within the autologous FMT group, one individual exhibited decreased permeability, while another demonstrated increased permeability. In the study by Parvathy, the allogeneic FMT group demonstrated a higher rate of improvement in small intestinal permeability compared to the autologous group, with all three individuals demonstrating decreases in gastric permeability. Overall, FMT was associated with modest improvements in biochemical markers, imaging findings, and intestinal permeability relative to pre-treatment values, although these effects did not reach statistical significance. No substantial changes in liver histology were observed, indicating a potential negative trend. These findings may have been influenced by small sample sizes and heterogeneity in FMT protocols.

In the present study, two patients with MAFLD who demonstrated inadequate responses to conventional lifestyle interventions underwent FMT. These two interventions are complementary. Lifestyle modification serves as the cornerstone of MAFLD treatment. Building on this foundation, FMT can enhance its therapeutic effects and help maintain the efficacy of FMT. Post-treatment assessments indicated significant improvements in lipid profiles, along with notable reductions in fatty liver severity and liver stiffness. Follow-up microbial analysis demonstrated increased gut microbiome diversity, enhanced proliferation of probiotics, and improved gut microbiome colonization resistance. No adverse reactions were observed, supporting the safety and potential efficacy of FMT in the management of MAFLD.

This study utilized a personalized oral capsule formulation prepared by a microbiota transplantation provider. This delivery method streamlined the transplantation process, improved patient compliance, and facilitated ongoing monitoring. Nevertheless, capsule-based delivery presents certain limitations, including challenges in dosage control and bacterial strain specificity. The relative therapeutic efficacy of upper versus lower gastrointestinal administration routes remains uncertain. Although a single FMT administration has been effective in most cases of recurrent *Clostridium difficile* infection (CDI), emerging evidence suggests that its effects in chronic metabolic disorders may be transient.[13] In this study, a single high-dose FMT was administered, and follow-up over six months demonstrated sustained clinical improvement; however, the durability of these effects requires further evaluation.

For safety considerations, a single donor preparation was selected. Current donor screening typically emphasizes clinical phenotypes associated with beneficial microbiomes. Although donor selection does not appear to significantly influence outcomes in recurrent CDI, its role may be more significant in conditions such as inflammatory bowel disease and metabolic syndrome. In these contexts, donor microbiota enriched with butyrate-producing taxa may provide greater benefits.[14,15]

Furthermore, a meta-analysis by Levast et al indicated that multi-donor preparations were associated with higher clinical remission rates in individuals with ulcerative colitis compared with single-donor preparations.[16] Multi-donor strategies also offer advantages in standardization, reduction of inter-batch variability, and enhancement of microbial diversity, advantages that may not consistently achievable with single-donor formulations. However, the applicability of this approach to MAFLD and its potential impact on adverse reaction rates warrant further investigation.

Although FMT has produced favorable clinical outcomes in recurrent CDI and certain forms of inflammatory bowel disease, its therapeutic value in metabolic disorders, including MAFLD, remains under investigation. Current evidence is largely limited to case reports, with more than ten registered clinical trials underway. Large-scale, standardized clinical studies are essential to establish the efficacy of FMT in this population. Additionally, both cases reported in this paper were male. Therefore, caution should be exercised when extrapolating the results to the female MAFLD population. Future studies with rigorous designs and the ability to conduct gender subgroup analyses are needed to further validate the efficacy of FMT.

Conclusion

The clinical and gut microbiome profiles of two patients with MAFLD treated with FMT in combination with lifestyle intervention demonstrated significant post-treatment improvements. These included reductions in BMI, transaminase levels, serum lipid profiles, uric acid concentrations, and liver stiffness measurements. Gut microbiome analysis further indicated increased microbial diversity, enhanced intestinal anti-inflammatory capacity, improved colonization resistance,

decreased abundance of pathogenic and opportunistic taxa, and an increased abundance of probiotic microorganisms. However, these promising findings must be interpreted with caution due to the inherent limitations of a case-report design, including the small sample size and lack of a control group.

A review of relevant Chinese and international literature indicates that FMT in combination with lifestyle modification, is generally associated with improvements in biochemical parameters, imaging parameters, and intestinal permeability in individuals with MAFLD. These findings highlight the therapeutic potential of microbiome-based interventions in the clinical management of MAFLD. However, further data from large-scale, randomized controlled trials are needed to confirm the efficacy, durability, and long-term safety of this therapeutic approach. Future studies should also focus on establishing standardized FMT protocols and comparing the efficacy of different delivery methods.

Abbreviations

MAFLD, Metabolic associated fatty liver disease; NAFLD, Nonalcoholic fatty liver disease; FMT, Fecal microbiota transplantation; FAI, Fat attenuation index; BMI, Body mass index; NAS, NAFLD Activity Score; SAF, Steatosis Activity Fibrosis; CDI, clostridium difficile infection; ALT, Alanine aminotransferase; AST, Aspartate transaminase; ALP, Alkaline phosphatase; GGT, Gamma-glutamyl transpeptidase; ALB, Albumin; TG, Triglyceride; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; UA, Uric acid; HOME-IR, Homeostasis model assessment for insulin resistance; Cr, Creatin; F/B, Firmicutes/Bacteroidetes; B/E, Bacteroidetes/Eukaryotes; FPG, Fasting plasma glucose; FIN, Fasting serum insulin; TNF-α, Tumor necrosis factor-α; PDFF, Proton density fat fraction; SIP, Small intestinal permeability; GP, Gastric permeability.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of Hebei General Hospital (Approval Number: 2022-203). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for Publication

All participants signed a document of informed consent for publication of any case details and/or images.

Author Contributions

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All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflict of interests.

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