

Improvement of Clinical Symptoms and Gut Microbiome After Fecal Microbiota Transplantation: A Case Study of a 106-Year-Old Man with MODS

Jingyun Fang¹, Jiayu Yin², Qinghong Liu¹, Xiangyi Yang¹, Xuesong He², Shengzhou Wang³, Min Fan³, Mohammed Alnaggar³, Jingsu Wang³, Zhaoqun Deng^{4*}, Yuanfei Liu^{1*}

¹Ganzhou People's Hospital, Guangzhou, China

²GanzhouShanjian Bio-technology Co., Ltd., Ganzhou, China

³Jiangxi Shanxing Bio-technology Co., Ltd., Nanchang, China

⁴The Affiliated People's Hospital of Jiangsu University, Zhenjiang, China

*Corresponding authors: Zhaoqun Deng, zqdeng2002@163.com; Yuanfei Liu, l_yishi@163.com

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Abstract: Fecal microbiota transplantation (FMT) has been used in a wide variety of diseases. Many researchers hypothesize that the dysbiosis of intestinal microbiota plays an important role in the development of gut-derived infections; thus, FMT is a potential therapeutic target against multiple organ dysfunction syndrome (MODS). A 106-year-old male patient was initially diagnosed with cerebral infarction and pulmonary infection. During the course of hospitalization, the patient developed MODS. The patient received a single nasogastric infusion of sterile-filtered, pathogen-free feces from a healthy donor. Fecal samples were collected every two days post-infusion to monitor changes in the microbiota composition in response to treatment. After FMT, MODS and severe diarrhea were alleviated; the patient's fecal microbiome diversity resembled that of the healthy donor's fecal microbiome; moreover, his clinical symptoms improved remarkably with the changes in fecal microbiome. Additionally, no observable side effects were noted during FMT treatment. These findings warrant further investigation of FMT as a putative new therapy for treating microbiota-related diseases, such as MODS.

Keywords: MODS; Fecal microbiota transplantation; Therapeutic efficacy

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1. Introduction

Fecal microbiota transplantation (FMT) is a way to directly change the recipient's gut microbiota to normalize the composition, with the goal of curing diseases [1,2]. A growing body of evidence clearly showed that microbiota-host interactions have relationships with various disorders, such as *Clostridium difficile* infection (CDI), diabetes mellitus, inflammatory bowel disease, cancer, gut-brain disease, and so on [3,5]. It has been approved as a standard therapy for recurrent CDI by official guidelines [6]. Research has shown that gut microbiota may serve as a physical barrier that maintains mucosal integrity by preventing the penetration of the epithelial barrier by pathogens and by modulating immunological activity [7].

Multiple organ dysfunction syndrome (MODS) is defined as the development of potentially reversible physiologic derangement involving two or more organ systems that are not involved in the disorder, resulting in intensive care unit (ICU) admission, and arising in the wake of a potentially life-threatening physiologic insult [8]. MODS mostly occurs secondary to severe sepsis or septic shock, trauma, neoplastic diseases, and other causes of systemic inflammatory response syndrome (SIRS) [8,9]. The pathophysiology of MODS is still unclear. A growing number of evidence shows that translocation of microbes or components of microbes from the gastrointestinal tract have connection with immune system dysregulation [10]. We hypothesize that FMT might play a therapeutic role in the management of MODS following severe sepsis. Herein, we present a case of a 106-year-old patient who developed MODS and severe diarrhea following severe sepsis. 16S rRNA sequence analysis was performed to evaluate the microbiome diversity before and after FMT.

2. Case study

This is a case of a 106-year-old man, with a history of venous thrombosis, atrial fibrillation, osteoporosis, coronary heart disease, chronic obstructive pulmonary disease, and hypertension. In view of his advanced age, the patient was a chronic occupant in the Department of Geriatrics. Before he was transferred to ICU, he developed fever and had sudden loss of consciousness; computed tomography (CT) confirmed the presence of cerebral infarction near the right lateral ventricle and pulmonary infection. Consequently, the patient's fever persisted, and he progressed to MODS. Due to respiratory failure, the patient underwent tracheotomy and was supported by a ventilator. The patient was given a variety of antibiotics to control the infection. Thereafter, he developed progressive diarrhea on average six to eight times a day, with a total volume of 1,000 to 2,000 mL per day and stools of jam-like consistency. Then, the patient's fecal bacteria population was analyzed, and the results indicated severely perturbed intestinal microflora. Based on the above findings, it was agreed on that this patient was a good candidate for treatment with FMT.

3. Methods

3.1. Assessment of gut microbiome by 16S sequencing

Fecal samples were collected before and one week after FMT. A detailed description of donor stool sampling, 16S sequencing, and data processing were summarized. Sampling packages were distributed to the participant, and the fecal samples were collected and stored in sealed containers, which were then transported with frozen gel packs to provide a low temperature environment until delivered to the laboratory. The fecal samples were pre-treated, and 16S sequencing was used to characterize the gut microbiome. The variable V3V4 regions of the 16S rRNA genes were amplified by polymerase chain reaction (PCR) using universal primers (5'-GTACTCCTACGGGAGGCAGCA-3' and 5'-GTGGACTACHVGGGTWTCTAAT-3'). The original sequencing analysis was performed using QIIME2 for classification assignment [11,12].

3.2. FMT procedure

The infusion of donor feces was carried out on day 0, and the patient underwent a total of four times of FMT, at a frequency of once every five days. An 11-year-old male, who was willing to participate in this study, was chosen to donate fecal microbiota. Before the study, he tested negative for both blood-borne diseases and common stool pathogens, including but not limited to hepatitis A (HAV-IgM), hepatitis B (HBsAg), hepatitis C (HCV-IgG), hepatitis D (HDV-Ab), hepatitis E (HEV-IgM), human immunodeficiency virus (HIV), cytomegalovirus (CMV), syphilis, roundworm, pinworm, hookworm, amoeba, and duovirus, among others in his fecal samples.

3.3. Statistical analysis

The correlation between two variables was tested by linear regression analysis using Pearson test. The relative intensity of each band was calculated and expressed as a percentage of the sum of all fragments in the same lane of the gel. A P value < 0.05 was considered statistically significant.

4. Results

4.1. Changes in intestinal microflora following FMT

The abundance of nonpathogenic microbiota in the healthy donor's fecal samples was higher than that of pathogenic microbiota. Notably, the gut microbiota composition of the patient exhibited a trend toward the microbiota composition of the healthy donor's feces. After the patient was treated with FMT, it was found that the diversity of his intestinal flora improved, the proportion of beneficial bacteria increased, while the proportion of harmful bacteria decreased, the overall intestinal flora balance greatly improved, with intestinal metabolism and absorption ameliorating. The abundance of nonpathogenic microbiota (*Bacteroides fragilis*, *Bifidobacterium*, and so on) increased greatly; however, the abundance of harmful bacteria (*Escherichia coli*, *Shigella*, and so on) decreased significantly (**Figure 1**).

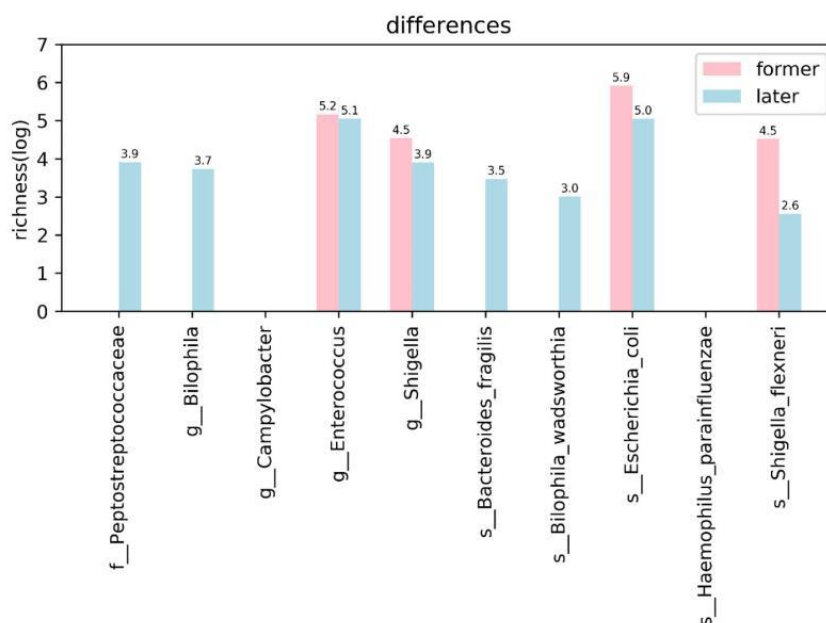


Figure 1. The differences between the former and later of FMT.

4.2. Clinical outcomes

Based on the evidence of disturbed microbiota, FMT was used to treat MODS and severe diarrhea. As expected, the response to FMT was satisfactory in the patient. On day 1 post-FMT, the patient's body temperature decreased from 39.6°C prior to infusion to 37.1°C after infusion, with heart rate and frequency of diarrhea reducing. After the fourth FMT, the patient's brain natriuretic peptide (BNP) declined dramatically; in addition, the patient was able to breathe spontaneously without ventilator. Unfortunately, due to his advanced age, the patient eventually died after five months of treatment with FMT.

5. Discussion

Inside the human intestine, there are approximately 40 trillion bacteria residing, indicating that there are at least as many cells of microbial origin as those of human origin [13]. A large body of evidence now suggests

that microbiome plays a critical role in maintaining host homeostasis. Microbiome can be altered in many disease states, such as cancer, inflammatory bowel disease, heart disease, and so on [14-16].

MODS is a life-threatening and complex condition with multiple etiological factors. It has long been hypothesized that the gut is “the motor” of multiple organ dysfunction syndrome (MODS). In recent years, many studies have reported that the application of FMT has shown to be effective in patients with MODS. In this research, the patient is a 106-year-old man, who is considered to be of advanced age. With FMT, there was disease remission, and the patient could even breathe without ventilator, which was really a miracle. Unfortunately, due to his advanced age, the patient eventually died after five months of treatment with FMT.

In this study, the intestinal microbiota before and after FMT were compared. The significant alterations in the intestinal microbiota post-FMT were identified via 16S rRNA analysis. It was found that the proportion of dominant bacteria in the intestine increased significantly. The study on the involved mechanisms of gut microbiota will be further pursued.

6. Conclusion

In summary, FMT can effectively maintain microecological homeostasis and antagonize pathogenic microorganisms, so this therapy seems to be a promising treatment for intestinal failure regardless of the causative factors.

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Disclosure statement

The authors declare that there is no conflict of interest.

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