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Research Article

Experience with Fecal Microbial Transplantation in Immunocompromised Patients: A Case Series of Five Patients

Tirumanisetty P[1], Syed T[1], Rander A[1], Sotelo JW[2] and Soota K[3]

[1]*Department of Internal Medicine, Unity Hospital, USA*

[2]*Department of Internal Medicine, Universidad Autonoma Metropolitana – Unidad Xochimilco, Mexico*

[3]*Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of Iowa, USA*

Abstract

Fecal microbial transplantation (FMT) has been increasingly used for the management of recurrent *Clostridium difficile* colitis. Despite its wide spread use, current guidelines do not have clear recommendations regarding the use of FMT for the management of *Clostridium difficile* colitis in immunocompromised patients. We performed FMT in 5 patients who were immunocompromised, with an 80% success rate, and no adverse effect profile. Our case series adds to the growing evidence of FMT use in immunocompromised patients.

Introduction

Clostridium difficile infection (CDI) being the most common cause of nosocomial infections that can cause diarrhea, is associated with health care costs estimated up to $800 million in the United States [1]. Immunocompromised (IC) patients are particularly at a higher risk for CDI [2].

Fecal Microbiota transplantation (FMT) has been used for recurrent CDI (RCDI) which is defined as a complete absence of diarrhea during the appropriate treatment period, followed by the reappearance of symptoms in a period of two to eight weeks after the treatment is stopped [3]. FMT has been proven to be effective in RCDI cases [3,4]. However, the use of FMT in RCDI in immunocompromised remains unclear in the current guidelines, despite some studies mentioning it to be safe, and well tolerated in a heterogeneous group of conditions [3,5]. Here, we describe a case series of five patients who were immunocompromised under different circumstances and received FMT for RCDI.

Methods

Five immunocompromised patients who had FMT were followed for 8 weeks from the day of FMT to assess for adverse events and clinical cure. There are no uniformly agreed definitions for clinical cure and treatment failure post FMT [6]. IDSA doesn't recommend using *Clostridium difficile* stool PCR post FMT to assess for clinical cure due to high rates of false positive tests in patients who are colonized [3]. However, stool PCR was used to assess clinical cure and treatment failure in a few studies [7-9]. Most other studies suggested to base these definitions on patient symptoms in the 8 week follow up period [10,11]. In our hospital the following definitions are used to define clinical cure and treatment failure. A Clinical cure is defined as <3 unformed stools/day during the 8-week follow up period. Treatment failure is defined as ≥ 3 unformed stools/day for 48 hours during the 8-week follow up, or positive stool *Clostridium difficile* toxin test, or a need for further medical or surgical management for CDI. Patient characteristics are mentioned in Table 1.

Results

The median age of our patients was 65 years. Patients had an average of 3.6 episodes of *Clostridium difficile* colitis. None of our patients were hospitalized secondary to *Clostridium difficile* colitis prior to index FMT. Four out of five patients (80%) who underwent large volume of 250cc-500cc FMT through colonoscopy had a clinical cure of their CDI (Table 1). One patient developed another episode of CDI in the 3rd week after FMT. There were no adverse events reported.

Discussion

Since its association in 1978 as the causative pathogen of the most cases of antibiotic-associated colitis, CDI has become one of the major infectious problems. Approximately half a million new cases of CDI occur per year in the United States as reported by the CDC [12]. Immunocompromised patients experience a higher incidence of CDI, ranging from 6% to 33% in the hematology-oncology patients, 9.2% in hematopoietic stem cell transplant recipients, 12.4% in solid organ transplant recipients, and 7.1%-8.3% among HIV-AIDS patients [13]. Treatment guidelines published in 2018 recommend using oral vancomycin or fidaxomicin for an initial episode of CDI [3]. Fecal microbiota transplantation (FMT) is effective for the treatment of RCDI [4,6].

Patient	Age (y)	Sex	Immunocompromised state	Drug	Number of CDI before FMT	FMT delivery route	Volume of fecal filtrate per transplant	Outcome	Adverse events
1	65	F	Rheumatoid arthritis	Etanercept	4	Colonoscopy	200 cc Terminal ileum and 50 cc Cecum	Clinical cure	No
2	71	F	Ulcerative colitis	Prednisone (20 mg/day for >3 months) and Azathioprine	5	Colonoscopy	200 cc Terminal ileum and 50 cc Cecum	Clinical cure	No
3	65	F	Myasthenia gravis	Prednisone (30 mg day for 45 days) and Methotrexate	3	Colonoscopy	500 CC cecum	Clinical cure	No
4	65	F	Rheumatoid arthritis	Methotrexate	3	Colonoscopy	125 CC terminal Ileum and 50 cc cecum	Clinical cure	No
5	30	M	Ulcerative colitis	Vedolizumab	3	Colonoscopy	125 CC terminal Ileum and 50 cc cecum	Treatment failure	No

Table 1: Patient characteristics and outcomes of fecal microbial transplantation.

Alrabaa et al. reported a 57% success rate of FMT, in a study of 13 patients, of which 7 were immunocompromised due to chemotherapy for solid organ transplantation [14]. In another study from Battipaglia et al., 10 patients who were on immunosuppressive treatment post stem cell transplantation underwent FMT for RCDI and reported a 70% success rate [15]. Both of these studies did not experience any adverse events. A multicenter retrospective study by Kelly et al. demonstrated a 78% success rate after the first attempt of FMT in immunocompromised patients including 75 adults and 5 pediatric patients. Case series of 5 solid organ transplant patients by Lin et al., mentioned 80% success rate after one session of FMT [16]. Mandalia et al., reported an overall success rate of 94.6% patients in their retrospective review of 35 immunocompromised patients who received FMT for RCDI through either colonoscopy or esophagogastroduodenoscopy [2]. The most common adverse events reported in the above studies were cramping and constipation. Constipation is likely due to the anti-diarrheal medications like loperamide or diphenoxylate that were given post FMT to delay the defecation for a while so that the new microbiome in the fecal filtrate will have a chance to establish in the recipient's colon.

A recent systematic review by Shogbesan et al., reported an 87% success rate after the first attempt of FMT and 93% after multiple treatments in a pooled analysis of 303 immunocompromised patients [17]. The main route of FMT in 77% of these patients was colonoscopy and the rest were through either esophagogastroduodenoscopy or nasogastric tube. Two deaths were identified in these 303 patients which were reported in a retrospective review of 80 patients by Kelly et al., but they did not clarify whether those deaths were related to FMT or not [5]. In a study of 77 patients by Brandt et al., four patients developed new diseases like Sjogren's disease, rheumatoid arthritis, idiopathic thrombocytopenic purpura and peripheral neuropathy [18]. It is not clear whether these new medical problems are related to FMT or preexisting conditions that came into light post FMT. Rebello et al., reported cure of alopecia in 2 patients post FMT [19]. This can suggest that fecal microbiota that were transplanted through FMT can not only cure CDI but can also influence other conditions that are likely related to the gut microbiome.

Conclusions

Data has been emerging on the efficacy of FMT for recurrent CDI in immunocompromised patients, with studies claiming different success rates varying from 57.15% to 94.6% after the first attempt of FMT [2,5,14-16]. Current literature weighs in favor of FMT in immunocompromised patients, with an acceptable adverse effect profile and minimal risk of infectious adverse events. However, large scale studies and randomized controlled trials to validate the utility of FMT in immunocompromised patients are yet to be performed [20].

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***Corresponding author:** Pratyusha Tirumanisetty Department of Internal Medicine, Unity Hospital of Rochester, 1555Long Pond Road, Rochester, 14626 New York, USA; Tel: 5623147098, Email: tirumanisettypratyusha@gmail.com

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