FMT Outcomes in Immunocompetent and Immunocompromised Patients: A Single Center Experience

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Background

- *Clostridium difficile* infection (CDI) is a major infectious disease focus, with a high incidence and inclination to recur in up to 20% of patients[1]
- Fecal microbiota transplantation (FMT) involves instillation of fecal microbiota from a healthy individual to a patient with CDI in order to restore the colonic microbiota and suppress *C. difficile*
- FMT is a promising treatment modality for CDI, with mean success rates of 87-90 % in immunocompetent patients[2]
- Current literature has shown the risk of infection with FMT is minimal in immunocompromised patients[3]; however, data is limited in terms of guidance on the role of FMT in immunocompromised patients
- In 2015, Infectious Diseases providers at Tampa General Hospital (TGH) developed a Pharmacy & Therapeutics Committee-approved protocol for use of FMT for recurrent CDI, including immunocompromised patients

Methods

- Retrospective IRB-approved study of patients with recurrent CDI who received FMT at Tampa General Hospital, a 1,011 bed level 1 trauma center serving as the primary teaching affiliate for the University of South Florida Morsani College of Medicine, from May 2014 - October 2015
- FMT was performed via naso-duodenal administration of universal banked frozen stool (OpenBiome; Medford, MA)

Primary Outcome:

- To evaluate outcomes after FMT for recurrent CDI in immunocompetent and immunocompromised patients

Secondary Outcome:

- To identify risk factors for failure of FMT in the solid organ transplant (SOT) population

Inclusion Criteria:

- Patients 18 years of age and older
- Laboratory confirmed diagnosis of recurrent CDI utilizing *C. difficile* PCR technology
- Absence of neutropenia (absolute neutrophil count < 500 cells/mcl)
- Absence of toxic megacolon requiring emergent surgical intervention

Exclusion Criteria:

- Receipt of FMT for indication other than recurrent CDI

Definitions

Recurrent CDI:

- Three (3) or more episodes of CDI (return of symptoms after completion of treatment)

CDI Treatment Success:

- Improvement of symptoms sustained post-FMT with no recurrence of CDI within 3 months

CDI Treatment Failure:

- Cases that did not meet criteria for treatment success, including new onset of abdominal pain in conjunction with diarrhea

FMT Protocol at TGH

- Appropriate FMT candidates were determined in conjunction with developed protocol and therapy directed at discretion of Infectious Diseases Consult Service
- Consent was obtained from each patient for administration of FMT via naso-duodenal tube
- Universal banked frozen stool obtained from OpenBiome was used for each case
- Pre-screening performed by company for transmissible infectious diseases prior to shipment of product
- FMT recipient preparation:
  - Bowel preparation completed the evening prior to FMT
  - Dose of proton pump inhibitor (PPI) (pantoprazole 40 mg) given evening prior and morning of FMT
  - Dose of loperamide 4 mg given 1 hour prior to FMT
  - All CDI-specific antimicrobials stopped at least 24 hours prior to FMT
  - All other systemic antimicrobials recommended to be stopped or limited prior to FMT (when possible)
- Naso-duodenal tube placement confirmed by radiology & removed after FMT
- FMT product volume = 30 mL, product prepared per company instructions and diluted in small volume of normal saline to aid in administration via naso-duodenal tube
- Normal saline used to flush all administered product via tube to complete FMT
- Patients monitored to assess for development of adverse events, abdominal pain and/or discomfort after FMT procedure was complete
- Regular diet resumed post-FMT if patient remains stable; no specific diet or dietary restrictions were recommended
- Patients were moved to a new room post-FMT to minimize risk for re-inoculation of *C. difficile* spores

Results

Table 2: Immunocompetent (IM) Patients

Patient	CDI Treatment Received	Receipt of Antimicrobials Post-FMT	FMT Outcome
1	PO vancomycin, PO metronidazole	No	SUCCESS
2	PO vancomycin, IV metronidazole	No	SUCCESS
3	PO vancomycin	No	SUCCESS
4 (Ventricular Assist Device)	PO vancomycin, fidaxomicin	No	SUCCESS
5 (Ventricular Assist Device)	PO vancomycin, fidaxomicin	Yes	SUCCESS
6 (Myasthenia Gravis)	PO vancomycin, rifaximin	No	SUCCESS

Table 3: Immunocompromised (IC) Patients

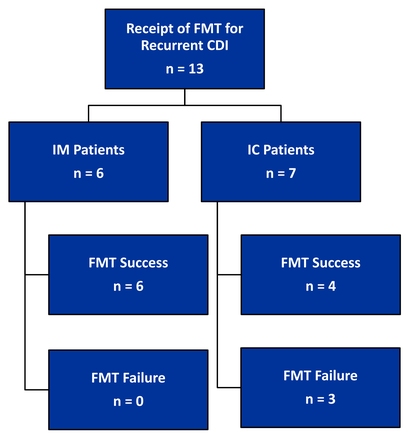
Patient	CDI Treatment Received	Timing of FMT Post-Transplant (years)	Receipt of Antimicrobials Post-FMT	FMT Outcome
1 (HIV)	PO vancomycin	N/A	Yes	SUCCESS
2 (Lung Transplant)	PO vancomycin, PO metronidazole, fidaxomicin	2	Yes	SUCCESS
3 (Kidney/Liver Transplant)	PO vancomycin, PO metronidazole	14	Yes	SUCCESS
4 (Kidney Transplant)	PO vancomycin	7	No	SUCCESS
5 (Kidney Transplant)	PO vancomycin, PO metronidazole, fidaxomicin	18	No	**FAILURE**
6 (Kidney Transplant)	PO vancomycin, IV metronidazole, fidaxomicin	26	No	**FAILURE**
7 (Kidney Transplant)	PO vancomycin, IV metronidazole	26	No	**FAILURE**

Study Population

Table 1: Patient Demographics

Baseline Characteristic	Immunocompetent (IM) N = 6	Immunocompromised (IC) N = 7
Age, mean ± SD	59.2 ± 22.3	63.4 ± 11.8
Male, n (%)	2 (33.3)	3 (42.9)
Diabetes, n (%)	13 (27.1)	47 (47.5)
Irritable Bowel Syndrome, n (%)	1 (16.7)	2 (28.6)
Number of CDI Episodes prior to Initial FMT, mean ± SD	3.7 ± 0.8	4.1 ± 0.7
Receipt of PPI Prior to FMT, n (%)	3 (50)	4 (57.1)
Receipt of Antimicrobials Prior to FMT, n (%)	1 (16.7)	6 (85.7)

Figure 1: Flowchart of Study Patients



Conclusions

- FMT was highly successful in immunocompetent patients with variable efficacy in immunocompromised patients
- FMT was shown to be safe and well tolerated across our study population
- Advanced age and prolonged duration of immunosuppression may contribute to single FMT failure in SOT patients
- Use of sequential FMT therapy in SOT patients may be considered to optimize restoration of intestinal microflora
- Further studies are needed to indicate the appropriate number of FMTs in the immunocompromised population

References

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