2014

Comparing Fecal Microbiota Transplant (FMT) to Vancomycin: in Treatment of Recurrent Clostridium difficile Infections (CDI)

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Abstract

- Clostridium difficile infection (CDI) is the main cause of antibiotic-associated pseudomembranous colitis.
- CDI has tripled over the last ten years due to the increased use of broad spectrum antibiotics. CDI has become increasingly difficult to manage with traditional therapies such as metronidazole and vancomycin due to mutations in the pathogen, resulting in resistant organisms.
- The purpose of this review was to determine if fecal microbiota transplantation (FMT) is more effective in treating and curing CDIs than traditional vancomycin therapy.
- The hypothesis was that FMT will have better treatment outcomes than traditional vancomycin therapy.
- The findings indicated that FMT is a more cost effective, safer, and overall better treatment option for CDI than traditional therapies such as vancomycin.

Introduction

- The purpose of this review is to determine if fecal microbiota transplantation (FMT) is more effective in treating and curing Clostridium difficile infections (CDIs) than traditional vancomycin therapy.
- The literature will examine research comparing treatment outcomes of FMT to vancomycin treatment in individuals with resistant CDI.
- This information will enable one to compare treatment outcomes between the two therapies, as well as the best delivery method for FMT.

Statement of the Problem

- CDI has become increasingly difficult to manage with traditional therapies such as metronidazole and vancomycin due to mutations in the pathogen resulting in resistant organisms.
- These drug resistant pathogens have caused death, longer hospital stays, and increased nosocomial infections due to the highly infectious nature of the spore forming CDI pathogen.

Research Questions

1. ***In people with recurrent CDI, does FMT have better treatment outcomes and less recurrence of CDI episodes than traditional vancomycin therapy?***
2. ***Do people who undergo FMT have better success rates with nasogastric or colonic administration of FMT?***

Literature Review

Pathophysiology

•Bakken, 2009; Normal gut flora comprised of strict anaerobes such as: Peptostreptococcus, Prevotella, Ruminococcus, Bacteroides, Bifidobacterium, Eubacterium, and Lactobacillus.

•Grehan et al., 2010; Individuals with C. difficile, aerobic and facultative anaerobic bacteria dominate the gut flora.

•Borody et al., 2004; C. difficile not problematic until the beneficial gastrointestinal microbiota is depleted

•Bakken, 2009; C. difficile has a spore-coat protecting the organism, it is relatively resistant to broad spectrum antibiotics, while the majority of the gut's other beneficial microbiota is not.

•Gough et al., 2011; CDIs recur in 35% of the patient population after treatment with antibiotic therapy, and 65% of these patients develop chronic re-manifestations of CDI.

•Agito et al., 2013; Subsequent CDI rates double after two or more infections.

FMT versus Vancomycin in treating recurrent CDI

•Van Nood et al., 2013; First randomized clinical trial to pit FMT against vancomycin in the treatment of recurrent CDI

•Gough et al., 2011; FMT was found to be safe and effective. 27 case series with 317 patients were examined where vancomycin treatment had failed. Disease resolution in 92% of cases after FMT.

•Kassam et al., 2012; performed a systematic review and meta-analysis which examined eleven studies with a total of 273 patients with recurrent CDI treated with FMT that had failed prior treatment with vancomycin. Researchers found CDI resolution in 89.7% of patients involved in the study.

Nasogastric tube (NGT) or Colonic administration of FMT

Table 2, Postigo & Kim (2012): Outcomes of patients who underwent FMT via either NGT or colonoscopy for recurrent CDI treatment

	NGT group, n=34	Colonoscopy group, n=148	P-value
Resolution after FMT (%)	29 (85.3)	138 (93.2)	0.162
No resolution after FMT (%)	5 (14.7)	10 (6.8)	
Relapse after FMT (%)	2 (5.9)	8 (5.4)	1.000
No relapse after FMT (%)	32 (94.1)	140 (94.6)	
Death due to CDI after FMT (%)	0 (0.0)	4 (2.7)	1.000

Discussion

- van Nood et al. (2013) randomized clinical trial comparing vancomycin and FMT effectiveness in the treatment of recurrent CDI.

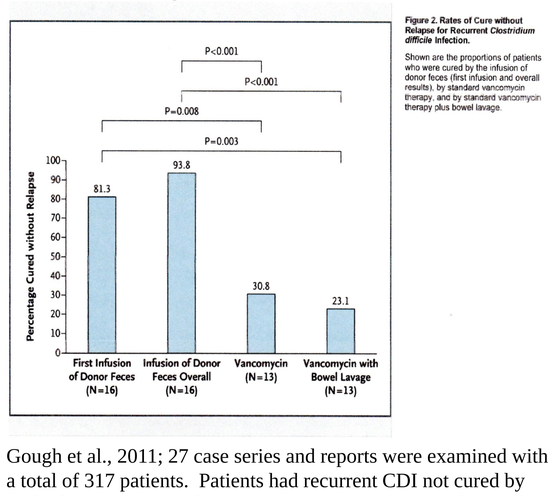

Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.

Shown are the proportions of patients who were cured by the infusion of donor feces (first infusion and overall results), by standard vancomycin therapy, and by standard vancomycin therapy plus bowel lavage.

- Gough et al., 2011; 27 case series and reports were examined with a total of 317 patients. Patients had recurrent CDI not cured by multiple treatments with vancomycin. 89% cure rate of CDI after a single FMT treatment and 92% after a second treatment. Only 5% of patients had CDI relapse.
- Postigo and Kim, 2012; No statistical difference in the treatment efficacy between NG tube and colonoscopy guided FMT. All studies examined commented that FMT was a safe treatment option with relatively few adverse side effects.
- Borody & Campbell, 2012; other possible clinical uses for FMT: crohns , ulcerative colitis, IBS, non-genetic autism, celiac . . . .

Case 1

A 21-year-old patient with a 10-year history of severe UC, uncontrolled with anti-inflammatory agents, steroids, antibiotics, and finally anti–tumor necrosis factor therapy underwent FMT. Pre-FMT symptoms included severe diarrhea with marked urgency and presence of blood and mucus. The patient underwent colonoscopy where the first FMT was administered. After this, daily rectal infusions were performed for 7 days followed by 26 weekly rectal infusions. The patient experienced an immediate reduction in symptoms, passing 2 formed stools daily without blood, urgency, or mucus. Follow-up colonoscopy at 12 months revealed virtually nil inflammation or edema and she remains clinically well at 12 months on no medication.

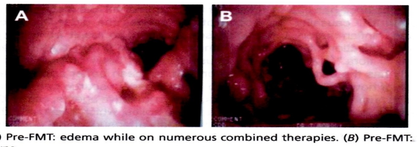

Fig. 1. *(A)* Pre-FMT: edema while on numerous combined therapies. *(B)* Pre-FMT: extensive pseudopolyps.

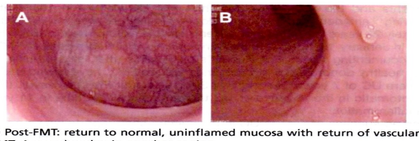

Fig. 2. *(A)* Post-FMT: return to normal, uninflamed mucosa with return of vascular pattern. *(B)* Post-FMT: 1 pseudopolyp in another region.

Applicability to Clinical Practice

- After reviewing the outcomes of FMT in the literature and examining CDI recurrence rates with currently suggested treatment protocols, I believe we are not using the best first-line treatment option for CDI cases. FMT should be used as a first-line treatment and not a last ditch effort. Outcomes for FMT are better than vancomycin, as well as more durable.
- Although more research is needed in these areas, FMT was also successfully utilized in the treatment of ulcerative colitis, IBS, and crohns. Implications for FMT were directed at the treatment of celiac and other colonic infections and disturbances. The primary obstacle keeping FMT from branching out as a treatment option in the afore mentioned areas is public acceptance of the therapy.
- FMT has been partially accepted as a therapy for CDI only because the medical field is running out of good options to treat recurrent CDI. The rising number of cases of vancomycin resistant enterococci (VRE) is forcing FMT to the front lines as a primary treatment option in these cases.
- The medical field uses other bodily fluids on a daily basis for their beneficial attributes. Fecal matter is no different. Let's not waste a valuable resource by flushing it away. Save it for FMT!

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Thanks . . .

The author would like to thank Dr. Susan Kuntz, Travis Schulz, and fellow students who helped contribute to this research project through editing help and location of articles. Special thanks to my wife for her continued support and interest in this project as well as her portion in the editing process.