



Faecal Transplant

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Introduction

Fecal microbiota transplantation (FMT), or infusion of a fecal suspension from a healthy individual into the gastrointestinal (GI) tract of another person to cure a specific disease, is best known as a treatment for recurrent *Clostridium difficile* infection (RCDI); FMT, however, also has been used successfully for inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), idiopathic constipation and a variety of non-GI diseases. Recent studies have shown that the intestinal microbiota plays an important role in immunity and energy metabolism and that an imbalance in our commensal intestinal bacteria can predispose to disease development.[1] Re-establishment of the wide diversity of intestinal microbiota via infusion of donor feces into the colon is the proposed mechanism by which FMT results in clinical improvement in patients with RCDI.

Is it Novel?

FMT is by no means a new therapeutic modality, however, it did not receive public attention until recently, after several studies were published showing that stool is a biologically active, complex mixture of living organisms with great therapeutic

potential for *Clostridium difficile* infection (CDI)[2-4] and perhaps other GI[5-8] and non-GI disorders.[9,10] The revelations about the human microbiome being published by the Human Microbiome Project consortium is bringing the strength of science to clinical observation, thereby enhancing our understanding of the complexities of our intestine and stool.[11] The administration of human fecal suspension by mouth for patients with food poisoning or severe diarrhea was first reported in fourth century China by Ge Hong.[12] In the 17th century, FMT was used in veterinary medicine and later termed 'transfaunation'. [5] The first use of fecal enemas in humans for the treatment of pseudomembranous colitis was reported in 1958 by Eiseman et al.[13]

Route of Administration

Until 1989, retention enema was the most common technique for FMT,[14] however, alternate methods have been used subsequently, including nasogastric tube (1991),[15] colonoscopy (2000),[16] and self-administered enemas (2010).[17] To date, over 400 cases of FMT have been reported worldwide including approximately 75% by colonoscopy or retention enema,

and 25% by nasogastric or nasoduodenal tube, or by EGD. [18,19] Although there is no consensus, the colonoscopic approach is favored over fecal enema for RCDI because enemas only reach the splenic flexure,[16] whereas with colonoscopy, the entire colon and ileum can be inoculated and disease extent and severity can be elucidated.[18]

Donor Screening

In general, donors are excluded if they have taken antibiotics within the preceding 3 months; are on immunosuppressive or chemotherapeutic agents; have known or recent exposure to HIV; hepatitis B or C; have a current communicable disease; are morbidly obese; have IBD, IBS, atopy, chronic diarrhea or constipation; GI malignancy or polyposis; participate in high-risk sexual behaviors; use illicit drugs; have a history of recent incarceration or travel to areas with endemic diarrhea. Donor blood testing should be performed for HIV, hepatitis A, B and C; donor stool testing includes culture, *C. difficile* toxin, ova and parasites, *Giardia* antigen, *Cryptosporidium* antigen and *Helicobacter pylori* antigen if the oral route is to be used.[14]

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Uses for FMT

Clostridium difficile

Current literature on FMT for RCDI is predominantly comprised of single center case series and case reports,[30–41] a meta-analysis[42] and one systematic review.[20] In all, about 92% of patients were cured of their RCDI, with a range of 81–100%.[20,30–42] A multicenter long-term follow-up study of patients who underwent colonoscopic FMT for RCDI reported an astounding overall ultimate cure rate of 98%.[21] Patients in this study had symptoms for an average of 11 months before FMT and most (74%) reported resolution of diarrhea within 3 days. [21] Immediate symptom resolution and long disease-free intervals after FMT for RCDI also have been reported in other studies,[5,20,31,32] and may result from the durable effect of FMT on re-populating the colon with normal commensal organisms.[2,3]

A systematic review of FMT, including all methods of administration and comprising 317 patients from eight countries and 27 case series and reports, reported an overall cure rate for RCDI of 92%.[20] FMT via colonoscopy or enema has proved more successful for RCDI than the nasogastric route; the latter gives an overall resolution rate of 80%.[20]

Perhaps surprisingly, FMT has been found to be quite acceptable to patients. In the recent multicenter study, 97% of patients with RCDI reported willingness to undergo another FMT if they were to have a repeat CDI episode, and 53% stated that they would choose FMT as first-line therapy before antibiotics.[21] of three high-dose liquid anti-parasite drugs directly into the colon.

Inflammatory Bowel Disease

FMT for refractory ulcerative colitis has been described in four publications, comprising nine patients, [6–8,46] all of whom had severe, active longstanding ulcerative colitis (mean, 8.6 years) refractory to treatment with corticosteroids, 5-aminosalicylates and azathioprine.[5] FMT was administered as retention enemas and resulted in the complete resolution of all symptoms

with cessation of ulcerative colitis medications within 6 weeks without relapse.[5] Remission was maintained for up to 13 years and follow-up colonoscopy in eight of the nine patients showed no evidence of ulcerative colitis (n = 6) or only mild chronic inflammation (n = 2).[6–8] Only one case report has been published on FMT for Crohn's disease, a patient who was refractory to prednisone and salazopyrin and responded to FMT within three days allowing discontinuation of medications;[6] disease relapsed within 18 months.[5]

Use of colonoscopic FMT followed by self-administered fecal enemas in a tapered fashion and as maintenance therapy for ulcerative colitis has been described in an additional eight patients (Brandt and Aroniadis, ACG annual meeting, 2012). After FMT, seven of these eight (88%) patients reported improvement in stool frequency and abdominal pain, however, the degree of benefit varied widely and was maximal in those with concomitant CDI (n = 3), or newly diagnosed ulcerative colitis in the setting of antibiotic use (n = 1) and those who were able to effectively retain the enemas.

Irritable Bowel Disease

Postinfectious IBS has been reported in up to 30% of patients with acute gastroenteritis, suggesting that the pathogenesis of IBS may be intimately linked to an altered intestinal microbiota.[47–49] The composition of the intestinal microbiota in patients with IBS has not been extensively studied, however, patients with constipation-predominant IBS have been shown to increase population of sulphate-reducing bacteria compared with healthy controls.[50] Probiotics can restore the intestinal microbiota in patients with IBS[49,51] and result in improvement of postinfectious IBS in animal models;[11] FMT, however, may prove more beneficial, as donated feces, in a sense, are the ultimate human probiotic.

In a case series of 55 patients with IBS and IBD treated with FMT, cure

was reported in 20 (36%), decreased

FMGT in Non Gastrointestinal disease

Studies in germ-free animals suggest that intestinal microbiota may contribute to pathogenesis of non-GI diseases. Significant responses have been reported in the following diseases: ITP Multiple Sclerosis, Autism, Rheumatoid Arthritis, SLE, Obesity, Type 2 DM and depression.

Conclusion

FMT re-establishes a balanced intestinal microbiota and results in impressive cure rates in patients with recurrent CDI. Standardization of FMT protocols and a randomized controlled trial are ongoing. The complexity of the fecal microbiota is actively being defined and recent studies have shown that the pathogenesis of many diseases, both GI and non-GI, result from microbiota-related dysregulation. FMT is likely to achieve widespread therapeutic benefit for a variety of diseases in the future.

symptoms in nine (16%) and no response in 26 (47%) patients.[6] In another series, 45 patients with chronic constipation were treated with colonoscopic FMT and subsequent fecal enema infusions, 89% of whom (40 of 45 patients) reported relief in defecation, bloating and abdominal pain immediately after the procedure. [52] Normal defecation, without laxative use, persisted in 18 of 30 patients (60%) contacted 9–19 months later.[52]



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The next wave of anti-obesity therapy looks set to involve changing the gut micro biome with faecal microbial transplant.

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