

Intestinal Microbiota Transplantation for Recurrent *Clostridium Difficile* Infection

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Diarrhea is one of the most complications associated with antibiotic Therapy and colitis is one of the most serious. Attack rate vary depending on the antimicrobial agent used, microbial agent used, the epidemiologic setting and the host. Overall, attack rates for antibiotic-associated diarrhea in hospital range from 3.2% to 29%. Almost 15% of hospitalized patient receiving B-lactam antibiotics develop diarrhea, and rates for those receiving clindamycin range from 10% to 25%. (1) predisposing host factor and circumstances affecting the frequency and severity of disease include advanced age, underlying illness, recent surgery and administration of drug that affect bowel motility.¹

Clostridium difficile infection (CDI) is a gastrointestinal disease believed to be causally related to perturbations to the intestinal microbiota. The term *microbiota* refers to the community of microorganisms that inhabit a particular region of the body (2). In the human gut, there are ~300-500 species of microorganisms (intestinal microbiota), with roughly 10^{12} bacterial cells per gram stool. These organisms aid in several functions, including digestion of complex carbohydrates, energy storage, immune functions, and protection against invasion by pathogens (3). Existing evidence shows that certain classes of antimicrobials have profound effects on the intestinal microbiota (4). The widely accepted model for *C. difficile* pathogen is that the use of broad spectrum antimicrobials alters the balance of the intestinal microbiota, allowing pathogenic strains of *C. difficile* to infect the intestine (3). Primary episodes of CDI are treated with metronidazole or vancomycin after cessation of the antibiotic believed to be related to the infection (4), and up to 35% of patient treated experience a recurrence of symptoms after initial improvement (5). Up to 65% of these patients develop a chronic recurrent pattern of disease (recurrent CDI) (5). Recurrent CDI is typically treated using a tapered (31% recurrence rate) or pulsed (14% recurrence rate) regimen of metronidazole or vancomycin (4, 5). Given the poor treatment outcomes for CDI, especially recurrent CDI, it is not surprising that investigation of treatment alternatives has continued over several decades (2, 4). One potential alternative to standard therapy is the use of indigenous intestinal microorganism from a healthy donor (via infusion of a liquid suspension of stool) to restore the intestinal microbiota of a diseased individual. Fecal bacteriotherapy, also called intestinal microbiota transplantation (IMT), may be a useful treatment for CDI through restoration of the intestinal microbiota (5). IMT has not been widely adopted as a therapeutic tool probably due to concerns regarding safety and acceptability. Despite these concerns, the procedure has been performed in a growing number of patients throughout the world. In addition to treating CDI, IMT has also been used to treat pseudomembranous colitis (PMS), believed to be caused by

C. difficile toxins, inflammatory bowel disease and irritable bowel syndrome (IBS), a disease also believed to be causally related to the intestinal microbiota (6). IMT protocols vary with regard to the quantity of donor stool used, preparation of recipients, methods for infusion of donor stool, and measurement of outcomes.

In a study done by Ethan Gough and et al, they analyzed a systematic review of IMT treatment for recurrent CDI and pseudomembranous colitis. In 317 patient treated across 27 case series and reports IMT was highly effective, showing disease resolution in 92% of cases. Effectiveness varied by route of instillation, relationship to donor stool, volume of IMT given, and treatment before infusion. Death and adverse events were uncommon. These findings can guide physicians interested in implementing the procedure until better designed studies conducted to confirm best practices. (7)

In Iran most patient with *C. diff* colitis received treatment on preparation with Metronidazole or oral Vancomycin. Patients who experience relapse usually respond to a repeated course of either Metronidazole or Vancomycin, but the treatment of patient with multiple relapse remain problematic. Four week administration of saccharomyces boulardii in addition to standard antimicrobial therapy yielded significantly fewer treatment failure in recurrent but not initial *C. difficile* disease. Antimicrobial long term administration of oral Vancomycin with tapering and then intermittent low dose of oral Vancomycin over 6 week in is another option. Useful IVIG, Fidaxomicin, Tolevamer, Rifaximin and vaccine has been used. Unfortunately administration of fecal suspension to establish the clonic biota has not tried in Iran yet. Despite the simplicity of the procedure, cooperation with gastrointestinal could guide physicians interested in implementing the procedure to confirm best practices.

References

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