Fecal Microbiota Transplant: Could Your Stool Save a Life?

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ABSTRACT

The purpose of this article is to introduce health care providers to fecal microbiota transplant (FMT), a fairly new and promising option for the treatment of persistent *Clostridium difficile* infection (CDI). In this study we discuss CDI in general and the problems with the current treatments. We address the newly available FMT treatment approach, and describe its process, donor selection, costs, and overall advantages and disadvantages. It is important for providers to be aware of this treatment option for patients with persistent CDI.

Keywords: *Clostridium difficile*, cost, fecal, infection, insurance, prevalence, transplantation, treatment

WHAT IS *CLOSTRIDIUM DIFFICILE* INFECTION?

Clostridium difficile (*C difficile*) is a bacterium that forms spores that are able to live in the gut and on common surfaces such as toilet seats, counters, bed rails, etc.[1] Infection with the bacterium is usually preceded by treatment with broad-spectrum antibiotic agents, such as clindamycin. These antibiotics kill the normal fecal flora, allowing overgrowth of *C difficile* in the gut.[2] *C difficile* spores quickly outgrow normal flora, penetrate the mucosal layer, and produce toxins that cause inflammation and mucosal damage.[2]

C difficile infection (CDI) is a critical problem that is increasing in prevalence as current treatments fail to suppress the incidence, recurrence, and spread of infection. CDI is a major risk for hospitalized patients, with mortality reported to be 6% within 3 months of diagnosis.[3] The infection itself leads to multiple complications, ranging from simple diarrhea to death. Recurrent CDI greatly increases the risk of complications, some as severe as septic shock and possible perforation.[4] Many possibilities should be considered when a patient presents with diarrhea or abdominal discomfort. In every patient who presents with symptoms of diarrhea, fever, abdominal pain, or leukocytosis, it is important to consider risk factors for CDI, such as recent antibiotic use or close contact with an individual diagnosed with CDI. According to the United States Centers for Disease Control and Prevention (CDC), people with diagnoses needing extended use of antibiotics, and the elderly are at increased risk of acquiring this type of infection.[5] CDI also needs to be considered as a differential and potential cause for patients presenting with an acute abdominal complication, such as toxic megacolon and perforation, which could be life-threatening.[1] Having multiple episodes of diarrhea also puts patients at risk for electrolyte and fluid imbalances that can further lead to acute kidney injury.[6] Overlooking CDI treatment can lead to many acute and chronic problems that could potentially cause permanent harm to the patient.

The incidence of CDI is on the rise, which makes this critical care issue important for discussion. Between the years of 2005 and 2010 in nonmaternal hospitalized patients, the rate of CDI more than doubled to a rate of 11.6 per 1000 discharges.[1] To further aggravate the problem, there are now reports of new strains of the bacterium. The newly identified strains have been linked with a mortality rate almost triple that of previous strains, possible due to the capability of producing an increased toxin level.[6] The high recurrence rate highlights the importance of CDI prevention and management. The most commonly

affected people are those hospitalized as inpatients and older adults, and well as those with comorbidities, recently treated with antibiotics, history of gastrointestinal manipulation, or previous CDI.[6]

CURRENT CDI TREATMENT GUIDELINES

Current treatment practice suggests use of antibiotic therapy, initiating contact precautions, and close monitoring for complications.[7] The first-line treatment for CDI is with specific antibiotics, including metronidazole and vancomycin.[7] Another option being used for recurrent CDI, especially when patients cannot tolerate vancomycin, is fidaxomicin which is a macrolide.[7] This drug was approved by the FDA in 2011, but its cost far exceeds that of metronidazole and vancomycin, making its use less desirable.[8] The problem with these antibiotics is that, although they are able to kill CDI, they will continue to disrupt the normal flora of the gastrointestinal tract, which can lead to continued recurrence of CDI itself. After treatment with antibiotics, the normal flora is also suppressed and may not be able to prevent the proliferation of any residual *C difficile* bacteria.

Recurrence of CDI happens in 10%-20% of patients after initial antibiotic treatment and in 40%-65% of patients who have already had a recurrent episode.[9] CDI has become more severe and in many cases more difficult to treat with this standard regimen of antibiotics. Due to reports of decreased efficacy of metronidazole, Vancomycin has been emerging as the primary therapy.[10] The recurrence cycle leads to increased use of antibiotics and repeated admissions. Dodek et al. reported that there is a link between CDI acquired in the intensive care unit (ICU) and increased length of stay.[11] Of course, all this treatment comes at a price. According to Bakken, the cost to manage CDI in the US was estimated to be at least $1 billion per year.[10] It is clear that there is a need for a new, more effective treatment that can reduce the rate of recurrence of this infection.

WHAT IS FECAL MICROBIOTA TRANSPLANT?

Fecal microbiota transplant (FMT) has been recognized as a viable treatment alternative for cases of refractory CDI. FMT, also called fecal bacteriotherapy, involves instilling a saline stool suspension, obtained from a healthy and pre-screened donor, into the GI tract of the affected individual.[2] The first documented use of FMT dates back to 1958, in which 4 critical patients were given fecal enemas for treatment of pseudomembranous enterocolitis.[10] The process utilizes a donor to provide a stool that is administered into the GI tract of the CDI patient. FMT is effective in resolving the diarrhea and colitis that result from the overwhelming proliferation of *C. difficile* by restoring bacterial homeostasis in the GI tract of the host.[2] This approach is becoming more viable as the efficacy of antibiotics continues to decrease. Because antibiotics disrupt the normal gut flora, a vicious cycle is created, ultimately leading to recurrence. FMT works to restore the normal bacteria to not only help with the current infection but also guard against a relapse.

The process of FMT is rather simple once a suitable donor has been selected. The actual procedure consists of instilling a liquid suspension of the donated stool into the patient's GI tract by nasogastric, nasojejunal, upper tract endoscopy, colonoscopy, or retention enema.[4] All routes are acceptable and the route chosen is simply based on provider preference. Before FMT, most patients are instructed to discontinue use of antibiotics up to 4 days and many are given a polyethylene glycol bowel preparation before the procedure.[4] The preferred method is to use a fresh fecal sample within 6 hours of passage and the stool then mixed in a blender with either normal saline or 4% milk to prepare the solution for instillation.[10] The quantity of solution used for FMT depends on the route of administration with the smallest amounts being administered into the stomach and the largest amounts being administered into the cecum and ascending colon.[4] The volume of solution instilled rectally is estimated to be 1 L, although instillation through a nasogastric tube would only require 500 mL of solution.

Currently, use of FMT is very limited and employed only as a last option for refractory CDI. FMT for recurrent CDI may lack regulatory body approval, but with effective cure rates of $> 90\%$, it appears to be an increasingly attractive option when traditional management fails.[12,13]

FMT has been suggested for patients who have had at least 3 mild to moderate CDI occurrences that failed to respond to vancomycin therapy or for those