

CLINICAL VIGNETTE

Fecal Transplantation in Recurrent *Clostridioides difficile*

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Case

A 75-year-old female presented to urgent care with one week of watery diarrhea. She did not have fever or significant abdominal pain. She denied sick contacts or recent travel but reported being on cefpodoxime for a urinary tract infection a month prior. She was empirically started on ciprofloxacin. Eleven days later, she presented to gastroenterology complaining of increased stool frequency, 10 to 12 times a day. Stool testing was positive for *C. difficile* PCR. Enteric pathogen panels for bacteria and parasites were negative. She was prescribed oral vancomycin for 10 days with diarrhea resolving on vancomycin.

However, a week after completion of vancomycin, she developed five episodes of watery diarrhea a day for several days. She represented to her gastroenterologist who prescribed pulse tapered vancomycin for six weeks. Approximately half-way into her vancomycin course, she was started on amoxicillin-clavulanate for bacterial sinusitis. After completing the vancomycin, the patient reported that while her stools were now formed, she was still having seven bowel movements a day.

A week later, the patient presented to the emergency room (ER) with severe lower abdominal cramping and up to twenty loose, non-bloody stools that day. Labs showed a normal white blood cell count and normal creatinine. CT scan of the abdomen and pelvis revealed thickening of the colon and rectum consistent with proctocolitis. Given clinical stability, she was discharged home with vancomycin, which her gastroenterologist then switched to a 10-day course of fidaxomicin.

One month later, she continued to experience up to five soft stools a day, fecal urgency, and mild abdominal cramping. *C. difficile* stool PCR was repeated and was positive. This time she was prescribed a six-week pulse tapered vancomycin followed by a 14-day course of rifaximin.

After completion of antibiotics, given she had three documented recurrences of *C. difficile*, she underwent fecal microbiota transplant (FMT) via colonoscopy. Four months later, she continues to be symptom-free.

Discussion

Clostridioides difficile is a spore-forming, toxin-producing, gram-positive anaerobic bacillus that colonizes the human gut after the normal gut flora has been altered by antibiotics. The

pathogenicity of *C. difficile* is mediated by Toxins A and B which lead to diarrhea and colitis. Risk factors for *C. difficile* infection (CDI) include recent antibiotics, age > 65 years, severe medical comorbidities, and recent hospitalization.

The first step of therapy, where possible, is cessation of the inciting antibiotic. Initial antibiotic treatment is with vancomycin 125 mg orally four times daily for 10 days or fidaxomicin 200 mg orally twice daily for 10 days. Fidaxomicin is similar in efficacy to vancomycin but more expensive.

Recurrent CDI (rCDI) is defined by the IDSA as resolution of symptoms while on therapy followed by reappearance of symptoms within two to eight weeks after treatment has been completed.¹ For the first recurrence, if vancomycin was used previously, then treatment is pulse-tapered oral vancomycin over 6 to 12 weeks (i.e., vancomycin 125 mg orally four times daily for 10 to 14 days, then 125 mg orally twice daily for 7 days, then 125 mg orally once daily for 7 days, then 125 mg orally every 2 to 3 days for 2 to 8 weeks), or oral fidaxomicin 200 mg orally twice daily for 10 days.

For the second recurrence, options are pulse-tapered oral vancomycin or oral fidaxomicin as outlined above, or vancomycin 125 mg orally four times daily for 10 days followed by rifaximin 400 mg orally three times daily for 20 days.

For the third or subsequent recurrence, fecal microbiota transplant (FMT) is recommended. In this procedure, healthy donor stool is instilled into the recipient's gastrointestinal tract in order to repopulate the patient's gut microbiome. The donor stool is provided by a stool bank which screens the donor's blood and stool for infectious diseases. Colonoscopy is the most common route of administration, however FMT may also be performed via oral capsules, nasoenteric tube, or retention enema. Antibiotics are stopped two days before FMT.

The cure rate of FMT for rCDI ranges between 70-95%.²⁻⁷ In a trial of patients with rCDI where patients were randomized to FMT via colonoscopy or nasojejunal tube following 4-10 days of vancomycin; 10 days of fidaxomicin alone; or 10 days of vancomycin alone, the clinical cure rates were 71%, 33%, and 19%, respectively.² In a meta-analysis of 13 clinical trials comprising over 600 patients with rCDI who underwent FMT, cure rates were lower in randomized trials than in open-label or

observational studies, with weighted pool rates of 68% vs 83% respectively.⁴ There does not appear to be a significant difference in effectiveness of fresh vs frozen stool preparation, with cure rates of 84% vs 85%.⁵

The chosen route of administration depends on patient preference, risks, availability, experience, and cost. FMT via oral capsules is not inferior to delivery by colonoscopy.^{4,6} In a randomized trial of 116 patients randomly assigned to FMT by oral capsule or by colonoscopy, both groups had a cure rate of 96% at 12 weeks.⁶ However, FMT via enema is associated with lower cure rates than colonoscopy, 67% vs 87%, respectively.⁴

More than one FMT may be needed to achieve cure. One open label study showed 70% clinical cure after one capsule-based FMT and 90% after a second treatment.⁷ In a randomized trial in which patients with rCDI were treated with FMT via enema, patients who did not respond after 4 days received an additional FMT, and those who did not respond to two FMT were offered another FMT or antibiotics; in this study, the efficacy increased from 50% to 75% to 90% for one, two, or three or more FMT.⁵

In an observational study of 137 patients who underwent FMT for rCDI, 82% had no recurrence of CDI at a median of 22 months follow-up.⁸ Those who experienced rCDI post-FMT had significantly more exposure to antibiotics than those who did not experience recurrence.⁸

The most common adverse events from FMT are abdominal discomfort, bloating, and gas. Physical complications such as upper gastrointestinal bleeding or aspiration pneumonia with nasoenteric tube insertion or perforation from colonoscopy are similar to when those procedures are performed for other indications. In a systematic review, the incidence of serious adverse events for upper and lower gastrointestinal routes was 2.0% and 6.1%, respectively.⁹ Such serious events included death (3.5%) infection (2.5%), and relapse of inflammatory bowel diseases (0.6%).⁹

The FDA recently issued a safety alert regarding two cases of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* infections following FMT from the same donor.¹⁰ Both patients were immunocompromised and one died. While the stool underwent a routine screening process, it had not been tested for those specific pathogens prior to use. The FDA reminds physicians that informed consent for FMT should include alerting patients to the potentially serious adverse reactions of this investigational procedure.¹⁰

Conclusion

FMT is an effective treatment option for patients with three or more recurrences of CDI. Various routes of administration are available, with oral capsules and colonoscopy being the most effective and commonly used. However, it is important to note that the procedure is not without risks, which may range from mild abdominal discomfort to potentially fatal infection.

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