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Q/ How effective and safe is fecal microbial transplant in preventing *C difficile* recurrence?

EVIDENCE-BASED ANSWER

A/ **FECAL MICROBIAL TRANSPLANT (FMT) IS REASONABLY SAFE** and effective. In patients who have had multiple *Clostridium difficile* infections (CDIs), fecal microbial transplant (FMT) results in a 65% to 80% cure rate with one treatment and 90% to 95% cure rate with repeated treatments compared with a 25% to 27% cure rate for antibiotics (strength of recommendation [SOR]: **B**, small open-label randomized controlled trials [RCTs]).

Fresh and frozen donor feces, administered by either nasogastric tube or colonoscope, produce equal results (SOR **B,** RCTs).

FMT has an overall adverse event rate of 30%, primarily involving abdominal discomfort, but also, rarely, severe infections (0.7%) and death (0.1%) (SOR: **B,** systematic review not limited to RCTs).

Evidence summary

An open-label RCT enrolled 41 immunocompetent older adults who had relapsed CDI after at least one course of antibiotic therapy.[1] Investigators randomized patients to 3 treatment groups:

- vancomycin therapy, bowel lavage (with 4 L nasogastric polyethylene glycol solution), and nasogastric-infused fresh donor feces;
- vancomycin with nasogastric bowel lavage without donor feces; or
- vancomycin alone.

Researchers defined cure as the absence of diarrhea or 3 negative stool samples (if patients continued to have persistent diarrhea) at 10 weeks without relapse.

Thirteen of 16 patients (81%) in the donor feces infusion group were cured with the first infusion. Two of the 3 remaining patients were cured after a second donor transplant. FMT produced higher total cure rates than those of vancomycin (94% vs 27%; $P<.001$; number needed to treat [NNT]=2). Bowel lavage had no effect on outcome.

FMT cures more patients than vancomycin alone

An open-label RCT of 39 patients compared healthy-donor, fresh FMT given via colonoscopy with vancomycin alone for recurrent CDIs.[2] Researchers recruited immunocompetent adults who had recurrent CDIs after at least one course of vancomycin or metronidazole.

Patients in the treatment group received a short course of vancomycin, followed by bowel cleansing and fecal transplant via colonoscopy. Clinicians repeated the fecal transplant every 3 days until resolution for patients with pseudomembranous colitis. Patients in the control group were treated with vancomycin for at least 3 weeks. Researchers defined cure as the absence of diarrhea or 2 negative stool samples (if patients continued to have diarrhea) at 10 weeks without relapse.

Thirteen of 20 patients in the FMT group (65%) achieved cure after the first fecal infusion. The 7 remaining patients received multiple infusions; 5 were cured. Overall, FMT cured more patients than vancomy-

cin alone (90% vs 26%; odds ratio=25.2; 99.9% confidence interval [CI], 1.26-502; NNT=2).

Fresh and frozen stool are equally effective

A randomized, double-blind noninferiority trial compared the effectiveness of frozen and thawed FMT with that of fresh FMT in 219 patients ≥18 years of age with recurrent or refractory CDIs.[3] Researchers prescribed suppressive antibiotics, which were discontinued within 24 to 48 hours of FMT, and then administered 50 mL of either fresh or frozen stool by enema. They repeated the FMT with the same donor stool if symptoms didn't improve within 4 days. Any patient still unresponsive was offered repeat FMT or antibiotic therapy.

Researchers defined a 15% difference in outcome as a clinically important effect. Intention-to-treat analysis yielded no significant difference in clinical resolution between groups (75% frozen vs 70.3% fresh; *P*=.01 for noninferiority).

Nasogastric delivery works as well as colonoscopy

An open-label RCT (not included in the reviews described previously) evaluated the effectiveness of colonoscopically administered FMT compared with that of nasogastric administration in 20 patients with recurrent or refractory CDIs.[4] Patients had experienced either a minimum of 3 episodes of mild-to-moderate CDI with a failed 6- to 8-week taper of vancomycin or 2 episodes of severe CDI resulting in hospitalization. Researchers offered patients from both groups a second FMT if symptoms didn't improve with the initial administration.

Eight patients in the colonoscopy group and 6 in the nasogastric group were cured (all symptoms resolved) after the first FMT. One patient in the nasogastric group refused subsequent administration. All 5 remaining participants chose to have subsequent nasogastric administration (80% cure rate). Both methods of administering FMT produced comparable cure rates (80% in the initial nasogastric group vs 100% in the initial colonoscopy group; *P*=.53).

A third of patients suffer adverse effects, but serious harms are rare

A systematic review analyzed 50 trials (16 case series, 9 case reports, 4 RCTs, 21 unreported type; 1089 FMT-treated patients) for adverse effects of FMT.[5] Most patients (831) had CDIs, 235 had inflammatory bowel disease, and 106 had both conditions. Donor screening tests for FMT included viral screenings (hepatitis A, B, and C; Epstein-Barr virus; human immunodeficiency virus; *Treponema pallidum*; and cytomegalovirus), stool tests for *C difficile* toxin, and routine bacterial culture for enteric pathogens (*Escherichia coli, Salmonella, Shigella, Yersinia, Campylobacter*), ova, and parasites.

Overall, 28.5% of patients receiving FMT experienced adverse events. Upper gastrointestinal (GI) administration resulted in more total adverse events than did lower GI delivery (43.6% vs 20.6%; *P* value not given), mostly abdominal discomfort. However, upper GI delivery was associated with fewer serious adverse events than was lower GI delivery (2% vs 6%; *P* value not given). FMT possibly or probably produced serious infections in 0.7% of patients, and there was one colonoscopy-associated death caused by aspiration (0.1% mortality).

Recommendations

Guidelines published by the American College of Gastroenterology in 2013 listed FMT as a treatment option for patients who have had 3 episodes of CDI and vancomycin therapy (based on moderate quality evidence).[6] JFP

Fecal microbial transplant cures 65% to 80% of recurrent *C difficile* infections with one treatment compared with a 25% to 27% cure rate for antibiotics.

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