Clinical Practice Assessment

Fecal transplantation for recurrent Clostridium difficile infection

Question:
In patients with recurrent Clostridium difficile infection is fecal transplantation effective therapy?

Bottom line:
Yes, fecal transplantation is associated with a high cure rate. One small 10 week controlled open-labeled randomized study shows an 81% cure with one infusion and in the nonresponders a 94% cure rate with a second infusion.\(^5\)

Synopsis:
The most common healthcare associated infection is Clostridium difficile. It causes at least 25% of all cases of antibiotic-associated diarrhea in hospitalized patients. It is becoming more frequent and severe, more refractory to standard therapy and more likely to relapse. Standard treatment includes discontinuation of the offending/inducing antibiotics and Clostridium difficile targeted antibiotic therapy with metronidazole or oral vancomycin. Although generally effective in the majority (more than 90%) of patients in achieving clinical improvements, this therapy does not restore intestinal microbiota. There is a high recurrence rate (20-60%) and the emergence of new hypervirulent strains. Risk factors for recurrent disease include inadequate antitoxin antibody response, persistent disruption of the colonic microbiota, gastric acid suppressive therapy, nasogastric feeding, immunosuppressive therapy, residence in a long-term care facility, advanced age, prolonged hospital stay, and long-term dialysis. Optimal management of recurrent/relapsing disease remains challenging.

Fecal transplantation has been used sporadically since the 1950’s with a trend toward increased interest based on an increase in the volume of published clinical studies since 2005.

An open-labeled randomized, controlled trial assigned 43 patients with a relapse of C difficile after at least one course of adequate antibiotic therapy with a positive stool test and symptoms of diarrhea to one of three treatments. The primary end point was cure without relapse within 10 weeks after initiation of therapy. A second infusion could be given. Cure was defined as an absence of diarrhea or persistent diarrhea with 3 consecutive negative stools tests for C. difficile toxin.

Of the 16 patients in the fecal transplantation infusion group 81% were cured after the first infusion. The 3 remaining patients received a second infusion from a different donor and 2 were cured for a total of 94% cure. In the two control groups cure occurred in 31% and 23% P<0.01.
with recurrence occurring at a median of 23 and 25 days. There were no significant adverse events. In the fecal transplantation group there was a significant increase in fecal microbiota matching the donor.

Exclusion criteria were prolonged compromised immunity due to chemotherapy, HIV with CD4 counts of less than 240 or prolonged use of prednisolone at a dose of at least 60mg a day, pregnancy, use of antibiotics other than for treatment of C. difficile infection at baseline, admission to an ICU or need for vasopressor medication.

Treatment consisted of initial vancomycin 500mg po qid for 4-5 days followed by bowel lavage with 4 liters of macrogol solution (Klean-prep) on the last day of antibiotic treatment and subsequent infusion of a solution of donor feces through a nasoduodenal tube. The donors were < 60 years of age and volunteers screened for potentially transmissible disease. Feces was collected by the donor the day of infusion, diluted with 500ml of sterile saline, stirred, the supernatant strained and poured in a sterile bottle. Within 6 hours after stool collection the solution was infused through a nasoduodenal tube (2-3 min per 50ml).

Seven full-text case series and many more reports have been published (1, 2, and 4). Five of the full-text studies were retrospective. Follow-up was generally short. In none of the studies were all five criteria for quality of the study met, thus all had a quality rating of poor. 124 patients were included in the 7 studies ranging from 7 to 40 patients per case series. The mean age was over 65 years in 6 of 7 studies. All patients had recurrent/refractory disease after standard care with oral metronidazole or vancomycin. Most donors were family members or relatives and were screened for blood and stool pathogens. Fecal suspensions were infused via NG tubes, gastroscopy, colonoscopy or retention enema. Prior to fecal transplantation all patients were treated with metronidazole or vancomycin which was discontinued 12 hours to 3 days before the procedure. Volumes of fecal suspension delivered varied and most received only a single procedure.

In the studies reporting, no adverse events were observed. Follow-up varied but was most often limited to about 3 months. Most patients (83%) experienced resolution of diarrhea following the first procedure within 1-7 days and remained diarrhea free during the follow-up period. The small number of patients in the studies did not allow for a clear relationship to be defined between delivery methods, volumes or frequency of transplantation procedures and effectiveness.

In conclusion, fecal transplantation has been shown in a level one study to cure a high percent of patients with relapsed C difficile infection with one or two infusion.

The Dean Gastroenterology Department adds that fecal transplantation would only be a consideration for recurrent disease. The single small open-labeled randomized controlled study observational studies indicate a high response rate, an apparent low incidence of relapse and good safety. Their suggested protocol for treatment of Clostridium difficile would be:

- First treatment: metronidazole or vancomycin for two weeks
- Second treatment: vancomycin for two weeks
- Third recurrence: several week tapering course of vancomycin
- Fourth recurrence: fecal transplant or fidaxomicin (Dificid)

References: