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BRIEF COMMUNICATION

Success of Self-Administered Home Fecal Transplantation for Chronic *Clostridium difficile* Infection

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BACKGROUND & AIMS: *Clostridium difficile* infection (CDI) can relapse in patients with significant comorbidities. A subset of these patients becomes dependent on oral vancomycin therapy for prolonged periods with only temporary clinical improvement. These patients incur significant morbidity from recurrent diarrhea and financial costs from chronic antibiotic therapy. **METHODS:** We sought to investigate whether self- or family-administered fecal transplantation by low volume enema could be used to definitively treat refractory CDI. **RESULTS:** We report a case series (n = 7) where 100% clinical success was achieved in treating these individuals with up to 14 months of follow-up. **CONCLUSIONS: Fecal transplantation by low volume enema is an effective and safe option for patients with chronic relapsing CDI, refractory to other therapies. Making this approach available in health care settings has the potential to dramatically increase the number of patients who could benefit from this therapy.**

Keywords: Clostridium difficile; Bacteriotherapy; Fecal Transplant.

Clostridium difficile infection (CDI) is a common cause of both community- and hospital-acquired diarrhea usually occurring after exposure to antibiotics. A common problem with CDI is the frequency of relapse with up to 40% of patients having at least one recurrence.[1] Multiple relapses can occur in some patients, making cure difficult. Reduced susceptibility to metronidazole has been increasingly recognized.[2] In cases with multiple recrudescences, prolonged tapering courses of vancomycin have been used with some success[3] but are very expensive, and some patients will continue to relapse despite this treatment.[3]

It is hypothesized that the fundamental factor responsible for the development of CDI is the disruption of the normal bowel flora, thus restoration of the normal flora may be an effective treatment option.[4,5] In 1958 Eiseman first used administration of human feces to cure these individuals where no other treatments had durable success.[6] This treatment referred to as "fecal transplant" or "fecal bacteriotherapy," has been slow to be accepted in North America, with greater utilization in Europe.[7–10] It has been given by nasogastric tube, high volume enemas, and by colonoscopy. Fecal bacteriotherapy has many advantages including low cost, absence of side effects, no drug resistance issues, and a high success rate in small case series.[2,3]

To enable safe home fecal transplantations, we have been advising patients and their families through the process and providing laboratory testing as required. We describe our experience.

Methods

Patient Selection

All patients (recipients) underwent a full history and physical examination.

Potential family member fecal donors were selected by the patients and were questioned for any of the following contraindications for donation: (1) any history of gastrointestinal illness including peptic ulcer disease, gastroesophageal reflux, irritable bowel syndrome, inflammatory bowel disease, or polyps; (2) any malignancy; and (3) antibiotic use or hospitalization within the past 3 months.

Laboratory Testing of Donors and Recipients

All donors underwent screening serology for human immunodeficiency virus (HIV), human T-lymphotropic virus I/II, syphilis enzyme immunoassay, hepatitis A immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, and *Helicobacter pylori* antibody.

Recipients had blood testing for: complete blood count, sequential multi-channel analysis with computer-20 (Chem-20), serum protein electrophoresis, serum immunoglobulins, HIV, and antigliadin antibodies.

Stools from both donors and recipients were obtained for culture and sensitivity, ova, and parasites (3 separate specimens), cryptosporidia, microspora and *Clostridium difficile* toxin (C. DIFFICILE TOX A/B II; Techlab, Blacksburg, VA).

Stool specimens were obtained from recipients prior to fecal transplantation and sent to the reference laboratory for culture and typing of *C difficile*.

Fecal Transplantation Protocol

Recipients were initiated on maintenance therapy with oral *Saccharomyces boulardii* (Florastor; Biocodex Inc, San Bruno, CA) 500 mg per os (PO) twice per day,[11–14] plus metronidazole

Abbreviations used in this paper: CDI, *Clostridium difficile* infection; HIV, human immunodeficiency virus; NAP, North American pulsotype; PO, per os.

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Table 1. Patient Demographics in This Case Series

Patient number	Age	Sex	Underlying illness in hospital	Duration of symptoms prior to transplant	Number of procedures	Who performed procedure	Duration of follow-up post procedure	Patient's relationship to donor
1	62	M	Subarachnoid hemorrhage	18 months	1	Son	6 months	Father
2	38	F	B cell lymphoma	12 months	1	Self	12 months	Sister
3	76	F	Congestive heart failure, Parkinson's disease	8 months	1	Daughter	14 months	Mother
4	30	M	Liver transplant	19 months	1	Wife	7 months	Husband
5[a]	72	F	Pneumonia	8 months	1	Self	10 months	Grandfather
6	87	M	Pneumonia	23 months	1	Self	7 months	Father
7	88	M	Pneumonia, multiple myeloma	6 months	1	Son	4 months	Father

[a]Stool cultured from this stool transplant recipient identified the NAP 1 strain.

500 mg PO 3 times per day or vancomycin 125 mg PO 4 times per day, to ensure they were asymptomatic until 24–48 hours prior to the procedure. All patients were asked to return to clinic for follow-up 2 weeks postprocedure.

Instructions to Recipients and Donors

Recipients and donors were given the following instructions.

- Equipment needed: (1) bottle of normal saline (200 mL); (2) standard 2 quart enema bag kit available at a drug store (Life Brand Hot Water Bottle and Syringe kit; Shoppers Drug Mart, Toronto, ON, Canada); and (3) standard kitchen blender (1 L capacity) with markings for volume on side, available at any department store.
- Stop vancomycin/metronidazole 24–48 hours before procedure.
- Continue *S boulardii* during transplant and for 60 days afterwards.
- Add 50 mL of stool (volume occupied by solid stool) from donor obtained immediately prior to administration (less than 30 minutes) to 200 mL normal saline in the blender.
- Mix in the blender until liquefied to "milkshake" consistency.
- Pour mixture (approximately 250 mL) into the enema bag.
- Administer enema to patient using instructions provided with enema bag kit. Patient should hold the infusate as long as possible and lie still as long as possible on his or her left side so that the urge to defecate is prevented. Ideally perform the procedure after the first bowel movement of the day (usually in the morning).
- If diarrhea recurs within 1 hour, the procedure may be immediately repeated.

Ethics

Detailed information regarding the potential risks and benefits of the procedure including its experimental nature were provided to the patients and donors. Full informed consent was obtained. Pre- and post-test counseling was provided for HIV testing.

Results

All patients developed CDI in hospital, and then developed multiple recurrences at home. All patients were living at home at the time of transplant, and had recurrent CDI, confirmed by fecal toxin. Six of 7 (patient numbers 1 through 5 and 7) had relapses post treatment with at least 2 courses of oral metronidazole 500 mg PO 3 times per day for 14 days. One patient (patient number 6) developed peripheral neuropathy while using metronidazole and so was not retreated with this agent.

All patients became asymptomatic on multiple courses of oral vancomycin but relapsed whenever vancomycin was discontinued. All patients had been previously treated with vancomycin 125 mg PO 4 times per day for 14 days, then 500 mg PO 4 times per day for 14 days, then vancomycin with a tapering protocol with *S boulardii* being administered at the same time and continued after the taper was concluded and yet still relapsed post treatment.

Seven patients underwent the procedure (Table 1). All procedures were carried out at home, and were self-administered or administered by a family member. No patient had recurrent CDI post procedure. No adverse effects were identified. One patient (number 2) developed post infectious irritable bowel symptoms post transplant (intermittent constipation and diarrhea but consistently negative *C difficile* toxin testing, and no recurrence of chronic diarrhea. Repeat colonoscopy showed no evidence of colitis). Two patients were treated with antibiotics for urinary tract infections post transplant (patient numbers 1 [cotrimoxazole] and 5 [ampicillin/gentamicin intravenous and then oral ciprofloxacin]). One patient (number 6) received intravenous cefazolin for perioperative prophylaxis of a hip replacement post transplant. None of these 3 patients relapsed with CDI despite the antibiotic therapy.

In 1 patient, *C difficile* was successfully cultured from the recipient (patient number 5; Table 1). Pulsed field gel electrophoresis demonstrated that it was the North American pulsotype (NAP) 1 strain and was positive for the binary toxin (*cdt*) gene. Susceptibility testing showed that it was susceptible to metronidazole, had a minimum inhibitory concentration = 0.5 μg/mL for vancomycin (no interpretive breakpoints exist for this drug), and was resistant to moxifloxacin.[15,16]

Discussion

In this case series fecal transplantation was both well tolerated and efficacious in a group of highly motivated outpatients. No patient required a repeat procedure, and there were no treatment failures despite 3 patients receiving antibiotics in the post transplant period.

In many studies, large volume enemas or administration by nasogastric tube or colonoscopy have been used, but were felt to

be too invasive and impractical to be widely accepted. These approaches were felt to be necessary to enable recolonization of the ascending and transverse colon with normal flora. The success of our low volume enemas, would suggest that repopulation of the rectum with normal flora is rapidly followed by colonization of the rest of the colon. Further study (eg, with radiotracer dyes) would be required to confirm this hypothesis.

Potential Limitations

This was not a controlled study, and patient and investigator blinding to fecal transplantation was not possible. Nevertheless, the very long duration of symptoms prior to transplantation makes spontaneous remission unlikely. Similarly, although oral *S boulardii* was included in the transplant protocol, all patients had failed previous courses of vancomycin with *S boulardii* and so we do not think that the *S boulardii* was an active agent in the regimen. Furthermore, recent systematic reviews have concluded that there is insufficient evidence to support *S boulardii* therapy in CDI.[13,14] As this was not a comparative study, we cannot say that our regimen was more or less efficacious than other approaches for fecal transplant. Nevertheless the fact that patients or their family members were able to successfully self administer the treatment suggests that our regimen is very practical and simple. The low volume used enabled patients to tolerate the enema without back flow, despite the absence of a retention balloon. The 100% efficacy in this group of 7 highly refractory patients, suggests that this protocol is very promising. Nevertheless, a larger study would be required to more accurately determine efficacy.

This population involved highly motivated and self-selected people who were willing to self-administer the transplant. Our data may not be generalizable to a less motivated population.

The hypervirulent NAP 1 strain[17,18] was identified in 1 patient and raises the question whether these hard-to-treat cases are more common with this strain and could benefit from fecal transplantation. NAP 1 is the predominant outbreak strain in Ontario (our unpublished data). Culture was attempted but not successful in other patients in this series likely because they were using oral vancomycin at the time. More systematic surveillance of strain type and antibiotic susceptibility patterns is required for these cases.

Conclusions

Fecal transplantation by low volume enema is an effective and safe option for patients with chronic relapsing CDI, refractory to other therapies. Making this approach available in health care settings has the potential to dramatically increase the number of patients who could benefit from this therapy. Further study of this approach is warranted.

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Reprint requests

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Conflict of interest

The authors disclose no conflicts.