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Process and Outcome of Fecal Microbiota Transplants in Patients With Recurrent *Clostridium difficile* Infection

A Prospective Study

ABSTRACT

The incidence of *Clostridium difficile* infection is on the rise worldwide, causing high mortality rates and costing patients, hospitals, and insurance companies millions of dollars annually. Fecal microbiota transplants successfully treat recurrent *C. difficile* infections unresponsive to standard pharmacologic treatment such as flagyl, vancomycin, or rifaximin. Evidence in the literature provided the foundation for the development and refinement of this fecal microbiota transplant protocol. During the initial phase of the project, the protocol included patient selection criteria, donor screening/selection, infection control, fecal processing and delivery, and patient pre and postprocedure education. This article highlights the second phase of prospective testing of a nurse-driven protocol to implement fecal microbiota transplantation in patients with recurrent *C. difficile* infection. All stages of the protocol are explained as well as rationale for component parts to achieve successful patient outcomes when the protocol is carefully followed.

Clostridium difficile infection (CDI) is a significant healthcare-associated infection. Patients who receive antibiotic therapy are seven to ten times more likely to get CDI while receiving the antibiotics and for 1 month after antibiotics are stopped (Center for Disease Control and Prevention, 2015). In 2011, CDI was responsible for about 500,000 infections and about 29,000 deaths in the United States (U.S.) (Lessa et al., 2015).

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Background

The *C. difficile* organism is a gram–positive, spore-forming anaerobic bacillus that proliferates in the intestines when normal intestinal floras are destroyed by antibiotics (Gerding & Johnson, 2011). *C. difficile* toxin A and toxin B may cause formation of white-yellow plaques in the colonic mucosa. (See Figure 1, which illustrates the difference in normal intestinal mucosa and plaque formation called pseudomembranous colitis.) The distinct signs of CDI are a toxin-producing, foul-smelling diarrhea usually associated with fever, abdominal pain and/or tenderness, loss of appetite, and nausea. Mild cases of this infection are usually treated by discontinuing the antibiotic responsible for the diarrhea, if possible.

Typical first-line care for patients with CDI includes antibiotics such as metronidazole (Gerding & Johnson, 2011). Patients who do not respond to metronidazole or have a more severe infection receive oral vancomycin or fidaxomicin. Although these medications are available to treat CDI, not all patients respond successfully to this treatment. Patients being treated for CDI with pharmaceuticals alone have a 10%–25% chance of developing a relapse (Borody, Leis, Pang, & Wettstein, 2011).

Diarrhea associated with CDI can result in pseudomembranous colitis, toxic megacolon, and sepsis,

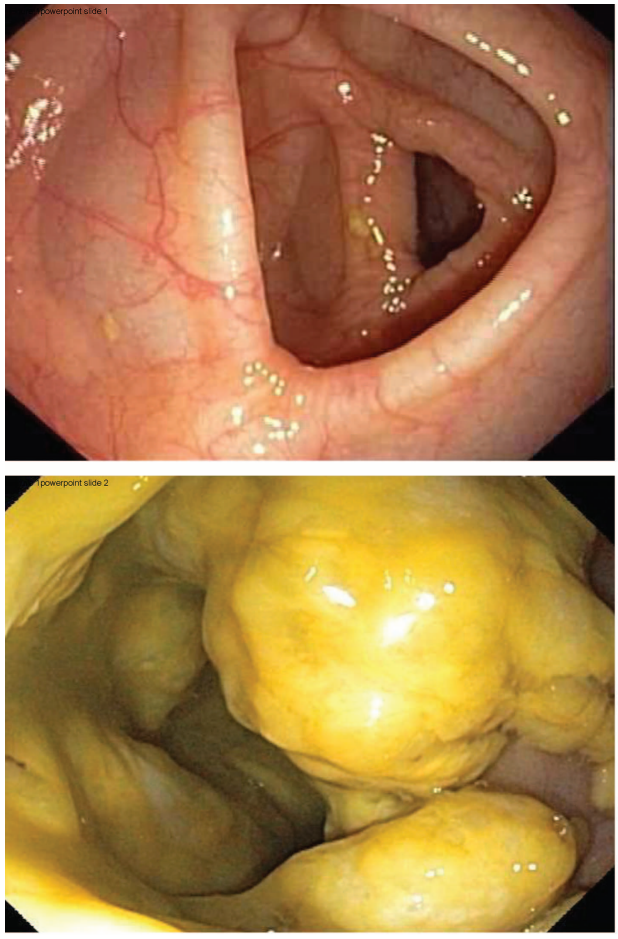

FIGURE 1. Normal intestinal mucosa versus pseudomembranous colitis.

which can all be life threatening (Myers, 2011). In 2009, 336,600 hospitalizations in the U.S. were associated with CDI (Lucado, Gould, & Elixhauser, 2012). The most common complication seen in these patients included dehydration and electrolyte disorders (81.2%), septicemia (26.7%), septic shock (8%), renal failure (23.6%), and prolonged ileus (4.7%). Some of these patients also suffered from toxic megacolon and intestinal perforation. Unsuccessfully treated CDI can cause severe patient debilitation. An alternative treatment for intractable CDI that is unresponsive to antibiotic first-line treatment is fecal microbiota transplantation (FMT), which restores normal bowel flora (Pant, Sferra, Deshpande, & Minocha, 2011; Rohlke, Surawicz, & Stollman, 2010; Weingarden et al., 2015). The evidence supporting FMT is discussed in the literature review section.

Literature Review

Researchers have studied the usefulness of fecal transplant in treating CDI since 1958 when Eiseman, Silen, and Bascom (1958) successfully treated four patients with pseudomembranous colitis caused by CDI by administering fecal transplants via enemas. With the advent of antibiotics to treat CDI and acknowledged aesthetic distaste some had with transplanting or receiving fecal material, fecal transplant fell out of practice. With misuse of antibiotics and resultant new resilient strains of the *C. difficile* organisms, in the early 2000s fecal transplantation was resurrected as an alternative treatment option (Floch, 2010; Van Nood et al., 2013). Recent research demonstrates that the bacterial flora composition in patients who receive FMT for recurrent CDI closely resembles the flora composition of the fecal donor (Weingarden et al., 2015) and metabolic components including bile salts and bile acids (Weingarden et al., 2014). The literature review focuses on treatment of recurrent CDI with FMT when first-line antibiotic therapy unsuccessfully treated CDI.

Retrospective studies and case reports indicate that recurrent CDI can be successfully treated with a donor fecal transplant. Rabe (2014) conducted a comprehensive review of six studies (Garborg, Waagsbo, Stallema, Matre, & Sundoy, 2010; Kassam, Hundal, Marshall, & Lee, 2012; Kelly, Leon, & Jasutdar, 2012; Rohlke et al., 2010; Silverman, Davis, & Pillai, 2010; Yoon & Brandt, 2010), which focused on fecal transplant as an intervention for recurrent CDI. These studies included six retrospective case reports/chart audits and two prospective studies with small sample sizes ($n = 7$ or $n = 26$). Regardless of retrospective or prospective data collection, 83%–100% of patients with recurrent CDI were cured. None of the 131 patients in these studies had any adverse events secondary to the fecal transplant.

Other researchers also demonstrated in retrospective studies that a fecal transplant creates clinical resolution of the CDI infection when the infection is unresponsive to several attempts to cure with typical antibiotic therapy (Drekonja et al., 2015; Kassam, Lee, Yuan, & Hunt, 2013; Postigo & Kim, 2012). Current evidence indicates that a variety of fecal delivery approaches are successful. In a meta-analysis, a lower FMT delivery approach had a higher rate of CDI clinical symptom resolution than use of an upper FMT delivery approach (Kassam et al., 2013). In an analysis of pooled data, no significant difference was found when comparing outcomes in patients who received an FMT via nasogastric tube versus colonoscopy (Postigo & Kim, 2012). Rabe (2014) reported FMT success regardless of the route of fecal instillation (enema, gastroscope, or colonoscope). Conflicting information therefore exists for determining the best fecal transplant delivery approach.

Two randomized clinical trials focused on patients unsuccessfully treated for CDI with typical antibiotic regimens. Van Nood et al. (2013) found that vancomycin, followed by bowel lavage and FMT, was statistically superior to vancomycin alone or vancomycin plus

bowel lavage to treat CDI. Youngster et al. (2014a) processed healthy nonrelative donor stool, froze it as an inoculum for up to 156 days, and thawed it before FMT infusion. The frozen stool successfully treated the CDI and no significant difference existed in outcome based on fecal infusion via colonoscope or via nasogastric tube in treating CDI in these 2 groups. Both of these studies had small sample sizes so generalization of information is limited, but the results provide positive indicators of the effectiveness of FMT.

The selection process for fecal microbiota donors consistently requires careful health history assessment and laboratory work-up to determine the appropriate donor. Discrepancies exist regarding whether it is best for the donor to be unrelated to the receiving patient (anonymous donor) or a patient-selected relative of the person receiving the FMT (Bakken et al., 2011). Kassam et al. (2013) reported in a systematic review and meta-analysis of FMT that in 11 studies with a total of 273 patients, no significant clinical difference was detected when comparing patient-selected and anonymous donors. Paramsothy et al. (2015) demonstrated the challenges of recruiting long-term healthy donors to be maintained in a stool bank. Only 12 (10%) of the potential donor respondents met the eligibility criteria to be an anonymous donor.

Limited evidence exists to support the use of probiotics when treating recurrent CDI. A Cochrane analysis reported insufficient evidence to recommend probiotics as an adjunct to antibiotics to treat CDI diarrhea (McFarland, 2006, 2010). Practice guidelines for the diagnosis, treatment, and prevention of CDI also report that no strong evidence exists to support the use of probiotics to decrease recurrence of CDI (Surawicz et al., 2013). Additional trials with randomization in large samples are needed to clarify the role of probiotics and CDI.

Innovative approaches to treating CDI show promise in preliminary studies. Petrof et al. (2013) created synthetic stool made from intestinal bacterial cultures from a healthy donor. Two patients who failed three courses of antibiotic treatment for CDI received the synthetic stool via colonoscopy. Within 2–3 days, both patients had normal bowel patterns and remained symptom free at 6 months postinfusion. Post-treatment microbial changes in the subject's intestinal microbes were consistent with normal intestinal microbes. Jiang et al. (2014) freeze-dried fecal material and used it at a later time for successful FMT. Finally the use of oral capsules containing fecal microbiota also successfully treated CDI (Youngster et al., 2014a, 2014b).

Although ongoing progress is occurring in CDI treatment, many questions still exist regarding "BEST approach" to treat this potentially debilitating infection. Would fecal transplant be a less costly alternative treatment if one round of antibiotics is an unsuccessful treatment? A prospective study using a consistent protocol is a needed addition to the current science that supports fecal transplant to treat CDI.

Fecal Transplant Study: Development and Testing of the Protocol: Phases 1 and 2

The aim of the project was to develop all components of a fecal transplantation protocol to eliminate CDI in patients suffering from debilitation after months of diarrhea, weight loss, and anorexia and who were unresponsive to standard therapy. In order to achieve this aim, a two-phase process was used to develop, refine, and test the protocol. Phase 1 goals included conducting a literature review, forming a team of healthcare professionals who have expertise in gastroenterology and infection control, developing and implementing an evidence-based fecal transplant protocol which provides safe and effective care, revising the protocol as warranted, and finally, prospectively testing the protocol to establish a consistent fecal transplant protocol.

Phase 1

Initial protocol development and refinement of the fecal transplantation protocol occurred between 2009 and 2012. During this phase, an interdisciplinary team, including nursing, medicine, and infectious disease, formed to address all components of protocol development. Gastroenterology nurses led this team in conducting the literature review and developing/refining the protocol. Other team members contributed input regarding the process. As the process was implemented, modifications in the protocol occurred. A retrospective chart audit on the patients receiving an FMT during protocol refinement demonstrated an 87% success rate in treating recurrent CDI unresponsive to typical antibiotic therapy. During Phase 1, several of the patients were extremely debilitated from prolonged diarrhea and yet had symptom relief within 1 day of the fecal transplant.

Lessons learned from Phase 1 informed the final protocol. These lessons included more closely assessing the normal bowel routine and pattern of the donor to increase the likelihood that the donor be able to produce fecal material the day of the scheduled transplant. In addition, we learned that the minimum amount of fecal donation was 50 g of stool. More is better, but 50 g is the minimum needed to process the stool and have sufficient quantity for transplant. Fecal transplant successfully served as a palliative treatment to control CDI even in terminally ill patients to eradicate diarrhea and abdominal cramping pain. Finally, it was more cost-effective to use a new disposable,

dedicated household blender ($18.00 cost, disposed of after each transplant) to prepare the fecal material than sending nondisposable equipment to central processing to be gassed between use ($70.00). Details of the final protocol appear in the following discussion of Phase Two.

Phase 2

The goals of Phase 2 (2012–2014) were to implement all components of the protocol consistently with all patients, and secondly, to prospectively study the outcomes of fecal transplantation in patients with recurrent CDI based on consistent protocol implementation. The major protocol components include patient referral and intake, fecal donor selection and testing, patient preparation, the procedure, and post-procedure care and follow-up outcomes. Specific information on each of these components is explained.

Patient Referral and Intake

One of the fecal transplant nurse coordinators manages all phases of the protocol once a gastroenterologist refers a patient for a fecal transplant. The coordinator sets up a consultation with the patient, family, caretaker, and the potential donor to explain the process and procedure. The nurse coordinator takes the patient's health history and explains the procedure and specific criteria the donor must meet. If the donor is known at that point, the nurse completes a donor health history and arranges for donor laboratory screening. During this initial consultation, the nurse educates the patient and family about contact isolation precautions and the need for terminal cleaning of the patient's home environment with hypochlorite solution before returning to it after the procedure (Cohen et al., 2010). The nurse coordinator reviews the consult report with the referring gastroenterologist; the type of endoscopy and patient preparation is determined and ordered based on this assessment.

Fecal Donor Selection and Testing

Because of the potential risk of contagious disease transmission from donor to recipient, a diligent screening process is used. In a multisociety letter written by presidents of national gastroenterology and infectious disease societies, clear fecal donor guidelines exist based on the current state of knowledge (Relman, Rustgi, Bousvaros, Vender, & Wang, 2013). Stool donor selection focuses on two factors: the donor health history and negative blood/fecal laboratory results. Typically a healthy adult with normal bowel habits and limited, if any, co-morbidities is considered the ideal candidate for fecal donation. No requirement exists that the donor is a relative because genetics play no role in the selection process. It is preferred that the donor is not the patient's primary caretaker and does not live in the same household as the patient to decrease the chance of cross-contamination and positive donor laboratory results.

Blood:
- Hepatitis A, B and C
- Rapid Plasma Reagin (Treponema Pallidum)
- HIV

Stool:
- C. Difficile toxin EIA
- Culture for bacterial pathogens
- Ova and Parasites

(Borody, Leis, Pant and Wettstein, 2011)

FIGURE 2. Screening tests for fecal donor.

In our facility, the patient is given the choice of providing a fecal donor or the patient may choose to use a fecal donor who serves as a universal donor for our laboratory. The universal donor is tested and interviewed every 90 days to remain on the universal donor list. Donors are excluded if they have undergone antimicrobial therapy for any reason in the past 6 months (as this can alter the intestinal microflora), are immunocompromised, or have a history of gastrointestinal (GI) disorders or multiple comorbidities (Relman et al., 2013). The donor must have normal bowel habits and successfully pass the required donor testing to rule out blood and fecal-borne infections (Figure 2).

Fecal donor screening tests for a donor chosen by the patient occur within 7 days before the planned fecal transplant to diminish the possibility of donor exposure to a communicable disease. Laboratory result turnaround time is typically 72 hours and costs approximately $350.00 out-of-pocket expense with no insurance reimbursement. The patient and donor must therefore determine in advance how the screening costs will be covered. The nurse coordinator ensures that there are no reimbursement concerns, the donor fecal/blood tests are normal, and the physician performing the GI procedure is aware of these results. If the patient chooses to use a universal donor identified by our laboratory, donor testing and screening occurs every 90 days, which costs less for the patient. To aid in adequate fecal transplant quantity, all donors are instructed to eat healthy foods, increase fiber, and (if needed) to take a stool softener the night before the donation. Donors come to the endoscopy laboratory the morning of the procedure to provide the fecal transplant specimen.

The nurse coordinator also discusses the costs associated with the fecal transplant, which is approximately $2,300.00. Some insurance companies pay a minimal amount (about $200.00) of the transplant costs. Financial implications and arrangements are discussed with the patient at this time.

Patient Preparation

Patient preparation depends on the fecal delivery approach. If a patient is getting the transplanted material via colonoscopy, the patient does a bowel preparation starting at 3 p.m. the day before the procedure to clear stool from the colon before the procedure. The patient remains non per os (NPO, i.e. nothing by mouth) after midnight. Each patient brings an extra set of uncontaminated clothes to wear home following the fecal transplant.

On the day of the procedure, the patient signs the consent for fecal transplantation. The consent form used is consistent with the Department of Health and Human Services (2013) requirements that all FMT recipients are aware that FMT is an investigational procedure to treat CDI which did not respond to standard antibiotic therapy. In addition, the consent includes risks including postprocedure symptoms such as transient cramping (1–3 days), bloating, gaseousness, potential altered bowel habits (constipation), and low-grade fewer for no more than 12–24 hours. Other potential risks mentioned on the consent form include possible reaction to anesthetics, transmission of infectious organisms contained in the donated stool, missed polyp or other lesion (infusion of stool interferes with visualization of the GI mucosa), allergic reactions to antigens in the donor stool, and other procedural complications such as perforation of the mucosa.

After a discussion and signature of the informed consent, the staff assesses the success of the preprocedure bowel preparation. The staff, patient, and family members maintain contact isolation from the patient's arrival time to the time of discharge (Cohen et al., 2010). The patient puts on a patient gown, and the clothes the patient wore into the unit are placed in a sealed bag to be taken home for laundering.

Based on the fecal coordinator assessment report, the gastroenterologist determines the route for fecal transfusion, either upper enteroscopy (deposits the fecal donation into small bowel) or via colonoscopy (deposits the fecal material into the terminal ileum). The anesthesia provider determines premedication requirements for each patient based on patient comorbidities and route of fecal transplant delivery. Anesthesia providers typically use propofol to achieve conscious sedation during the procedure. Patient preparation per anesthesia for the upper endoscopy approach is NPO after midnight and premeds including famotidine 10 mg, and metoclopramide 10 mg the morning of the procedure. In addition to these medications, patients having a colonoscopic approach also receive diphenoxylate 2.5 mg to reduce intestinal motility and promote better retention of transplanted material. Metoclopramide promotes upper GI motility to control postoperative nausea that may occur secondary to propofol, and it also promotes forward movement of the fecal transplanted material and decreases emesis potential.

Fecal Donation, Specimen Preparation, and Fecal Administration

On the day of the transplant, the donor uses a nonsterile stool collection container (fecal hat) to preserve a fresh stool specimen of at least 50 g of fecal material. Tongue blades are used to move the stool from the stool collection container into the blender. The fecal transplant is instilled within 6 hours of the donor producing the stool. All personnel in the room wear protective equipment including mask, face shield, gown, and gloves during the procedure. All supplies needed for stool processing appear in Figure 3.

The stool is weighed and approximately 50 ml of nonbacteriostatic saline is added to every 30 g of stool, depending on the stool consistency. If the stool specimen is extremely dry, additional saline may be needed to create the appropriate viscosity. The mixture is homogenized in a blender starting on low speed and advancing to liquefy for 2–3 minutes. The fecal mixture is then filtered twice through a wire strainer to strain out particles. The desired consistency resembles a milkshake or smoothie, not so thick as to make mechanical movement difficult through the biopsy channel of the scope with a 60-ml syringe, but consistent enough to thoroughly coat the colon walls when introduced (Brandt, Borody, & Campbell, 2011; Myers, 2011; Rohlke et al., 2010). After the stool is homogenized and strained, it is transferred and stored in a sealed suction canister until it is time to transplant the fecal mixture.

While the nurse prepares the fecal material for transplant, the gastroenterologist advances the endo scope to the terminal ileum if colonoscopy is the delivery route or to the duodenum if fecal delivery is via upper endoscopy. As the scope is removed during the colonscopy approach, fecal material is injected into the ascending and transverse colon. The nurse infuses the prepared mixture via a 60-ml catheter tip syringe that fits into the biopsy port of the scope. All disposable equipment, including the blender and strainer, is discarded after each procedure.

Postfecal Transplant Procedure

The postprocedure protocol focuses on five important elements: routine postanesthesia recovery, promotion of intestinal dwell time of transplanted material for maximum effect, prevention of patient exposure to *C. Difficile* after the procedure, education for patient follow-up care, and evaluation of patient outcomes based on postprocedure symptoms and stool pattern. Routine vital signs and patient assessment are carried out to ensure safe anesthetic recovery occurs with each patient. Postprocedure care focuses on routine endoscopy sedation recovery with frequent vital sign monitoring. In addition, extended recovery time promotes increased

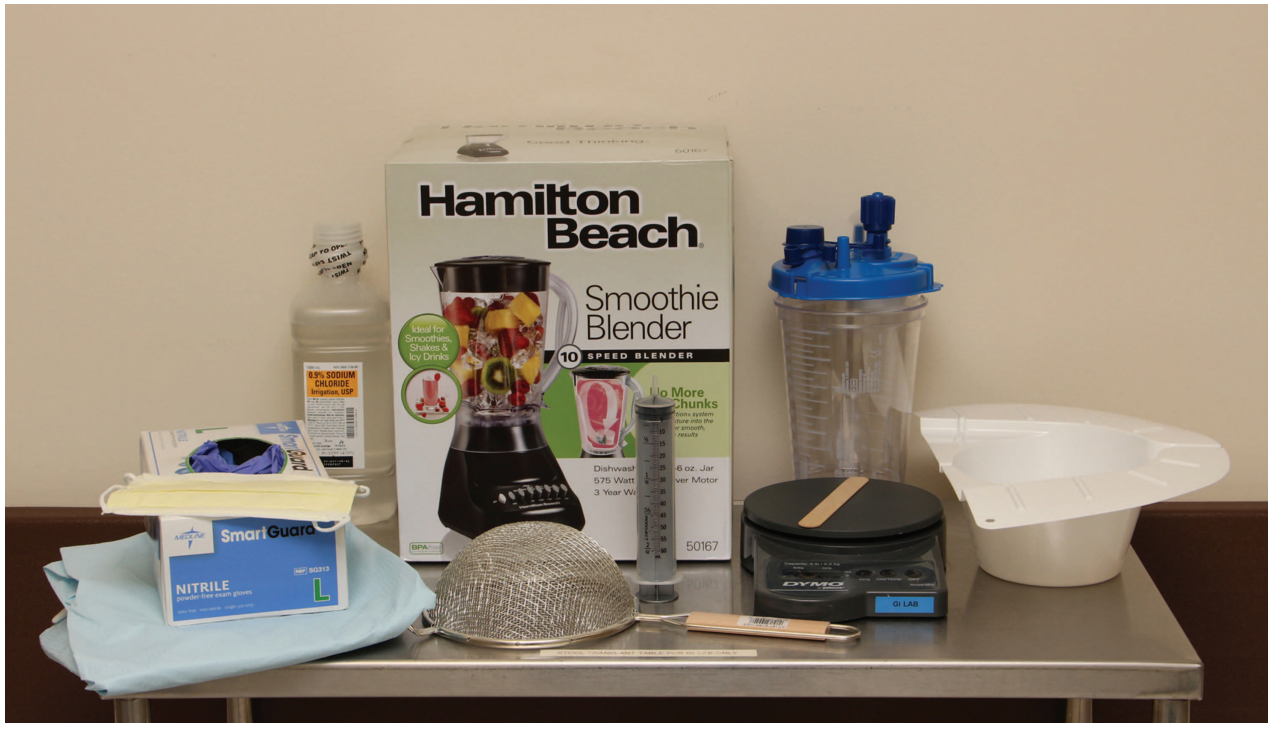

FIGURE 3. Supplies needed for fecal transplant preparation.

fecal dwell time. After colonoscopy fecal deposits, the patient lies flat for 2–3 hours, and after an upper endoscopy, the patient is maintained in a head of bed 45° posture for 4 hours and NPO for 3–4 hours. These positional interventions are to increase dwell time of transplanted fecal material based on understanding of the anatomy and physiology of the GI tract and gravity. No clear research exists regarding positional interventions.

To prevent recontamination after the procedure, the patient's recovery occurs in a clean area while maintaining contact isolation. When the patient is ready for discharge, the patient puts on clean clothes. If the patient is returning to an extended care facility, terminal cleaning of the unit with chlorine-based solutions is needed for the entire room. If a patient goes home, the toilet facilities must be cleaned with chlorine solution to kill *C. Difficile* spores (Cohen et al., 2010). All bed linens are changed before use when the patient returns to home. These interventions remove traces of *C. difficile* from the home environment to prevent re-infection. All parties are instructed to maintain isolation contact precautions until the patient has formed stool. The patient continues probiotics, if taking them prior to the transplant procedure, and discontinues vancomycin or any other antibiotic therapy.

Patient education includes discussion of the risks related to future antibiotic use. If the patient needs antibiotics within 2 months of the transplant, they are instructed to call their GI physician who may order a probiotic, Florastor, to be taken with the antibiotic to prevent CDI relapse. Florastor is a yeast-based probiotic that decreases the flora killed by the antibiotic. Data on the benefits of using probiotics to prevent CDI relapse due to antibiotics after transplant are weak. Patients follow their regular diet without restrictions from a GI perspective. The RN fecal transplant coordinator makes a follow-up phone call to each patient 2 days postprocedure to evaluate current bowel function and GI symptoms and to answer patient questions.

Data Collection

Data collected for the Phase 2 prospective study included patient age, gender, previous treatment received for CDI, transplant performed by enteroscopy or colonoscopy, amount of stool collected from the donor, relationship of the donor to the patient, living arrangement of the patient, patient comorbidities, the process used to mix the stool for instillation, and patient pre- and posteducation. Data were analyzed using the SPSS data analysis package.

The Phase 2 protocol analysis included 36 patients positive for CDI who were all unresponsive to typical pharmacologic therapy to eradicate the infection. The average age of the sample was 70 years, with an age range of 30–86 years. The sample differed in gender with 15 (41.7%) being male and 21 (58.3%) being female. The sample did not significantly differ on

TABLE 1. Ineffective Pharmacologic Treatment Used in Sample Before Fecal Transplant

Drug Regimen	*n* (%)
Vancomycin only	6 (16.7%)
Metronidazole only	1 (2.8%)
Vancomycin and metronidazole	24 (66.7%)
Vancomycin, metronidazole, and fidaxomicin	1 (2.8%)
Vancomycin, metronidazole, and rifaximin	4 (11.1%)
Total	36

relationship to stool donor, living arrangement of the patient, or patient comorbidities. All patients in the sample previously received pharmacologic treatment that was ineffective to resolve the CDI. Table 1 demonstrates the type of pharmacologic regimen used to try to unsuccessfully resolve the infection.

The prospective data collection verified that all components of the protocol were followed using the same approach to donor testing, specimen preparation, patient preparation, and patient education. Fecal donors in this study included one relative who lived with the patient (2.8%); 15 (41.7%) donors who were relatives, not living with the patient; and 20 (66%) donors who were nonrelatives, not living with the patient. The median amount of nonbacterial normal saline mixed with the donated stool was 150 ml. Fecal blending time ranged from 2 to 3 minutes followed by straining the mixture to remove particulate matter in all cases. The amount of fecal mixture instilled ranged from 130 to 450 ml, with a median amount of 250 ml. Colonoscopy was the fecal mixture delivery mechanism for 29 (80.6%) patients, gastroscopy was used in five (13.9%) patients, and the remaining two patients (5.6%) had both colonoscopy and gastroscopy approaches.

Of the 36 patients treated with fecal transplant in Phase 2, 35 (97.2%) reported relief from all symptoms and return of formed stool without diarrhea, abdominal cramping, or other symptoms. Because of insufficient amount of fecal material during an initial transplant, the remaining one patient required a repeat fecal transplant to eradicate the CDI. Two of the 35 patients who were successfully treated required the use of antibiotics to treat a urinary tract infection in one and pneumonia in the other. Both of these patients experienced a CDI relapse and required a second fecal transplant after antibiotic use that successfully treated the recurrent CDI.

Discussion

The success of fecal transplantation in this Phase 2 study is consistent with the positive results of other researchers. The 36 patients treated during the Phase 2 prospective study did not have severe debilitating GI symptoms as compared to the 51 transplants (87% success rate) in the Phase 1 retrospective study. In addition, the patients in the Phase 2 study were referred earlier for fecal transplant and had less severe debilitating disease than the patients in the Phase 1 retrospective study. Earlier patient referral for fecal transplant occurred due to the success and availability of FMT to treat CDI in our facility.

The protocol outlined is currently followed consistently with all patients except for one change. In our current practice, patients may still locate a donor for testing, but our GI laboratory now has a routine stool donor who provides a fecal specimen as needed. With a routine donor, the laboratory work-up is done once a month instead of before each transplant, which cuts down on the cost of screening donors.

Recommendations

Additional research with higher levels of evidence is needed to answer the following questions: Is there a "best approach" for instillation of fecal material (enema, upper endoscopy, lower endoscopy)? Where is the ideal location for the transplanted materials to be instilled? Is there a best time frame for spacing antibiotic use in patients who have had CDI in the past to prevent reinfection? Should probiotics be taken when a CDI is diagnosed and if so, how long should the probiotics be continued? How much time should a patient who has been successfully treated for CDI avoid antibiotic use if needed? Does patient positioning to increase transplant dwell time after the FMT assist in the success of the procedure or does it really make a difference? What are the characteristics of the "BEST" donor for FMT? How much research-based evidence is needed to convince insurance companies to pay for FMT to treat patients with recurrent CDI who have been unresponsive to typical antibiotic treatment? Research is needed on larger sample sizes and with more stringent research designs to answer all of these questions.

Conclusions

Consistent use of a fecal transplant protocol increases the likelihood of successful treatment of recurrent CDI. Healthcare providers need to be knowledgeable about the effectiveness of this approach to decrease complications associated with uncontrolled CDI. Earlier referral and treatment will result in early relief of diarrhea and other symptoms in these patients. The physiologic benefit of microbiota transplant in persons with recurrent CDI is known, but many questions remain about many components of this treatment. ✪

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