

Patient Knowledge and Attitudes About Fecal Microbiota Therapy for *Clostridium difficile* Infection

Colin Goodman, MD; Nicholas O'Rourke, PharmD; Carla Amundson, MA; and Dimitri Drekonja, MD, MS

In a survey of patients with *Clostridium difficile* infection, physician recommendation seemed to be the largest factor affecting the likelihood of patients considering future fecal microbial therapy.

C*lostridium difficile* (*C difficile*) infection (CDI) is a leading cause of infectious diarrhea among hospitalized patients and, increasingly, in ambulatory patients.^{1,2} The high prevalence of CDI and the high recurrence rates (15%-30%) led the CDC to categorize *C difficile* as an "urgent" threat (the highest category) in its 2013 Antimicrobial Resistance Threat Report.³⁻⁵ The Infectious Diseases Society of America guideline recommended treatment for CDI is vancomycin or metronidazole; more recent studies also support fidaxomicin use.^{4,6,7}

Patients experiencing recurrent CDI are at risk for further recurrences, such that after the third CDI episode, the risk of subsequent recurrences exceeds 50%.⁸ This recurrence rate has stimulated research into other treatments, including fecal microbiota transplantation (FMT). A recent systematic

review of FMT reports that 85% of patients have resolution of symptoms without recurrence after FMT, although this is based on data from case series and 2 small randomized clinical trials.⁹

A commonly cited barrier to FMT is patient acceptance. In response to this concern, a previous survey demonstrated that 81% of respondents would opt for FMT to treat a hypothetical case of recurrent CDI.¹⁰ However, the surveyed population did not have CDI, and the 48% response rate is concerning, since those with a favorable opinion of FMT might be more willing to complete a survey than would other patients. Accordingly, the authors systematically surveyed hospitalized veterans with active CDI to assess their knowledge, attitudes, and opinions about FMT as a treatment for CDI.

METHODS

In-person patient interviews were conducted by one of the study authors at the Minneapolis VA Health Care System (MVAHCS), consisting of 13 to 18 questions. Questions addressed any prior CDI episodes and knowledge of the following: CDI, recurrence risk, and FMT; preferred

route and location of FMT administration; concerns regarding FMT; likelihood of agreeing to undergo FMT (if available); and likelihood of enrollment in a hypothetical study comparing FMT to standard antibiotic treatment. The survey was developed internally and was not validated. Questions used the Likert-scale (Survey).

Patients with CDI were identified by monitoring for positive *C difficile* polymerase chain reaction (PCR) stool tests and then screened for inclusion by medical record review. Inclusion criteria were (1) MVAHCS hospitalization; and (2) written informed consent. Exclusion criteria were the inability to communicate or participate in an interview. Patient responses regarding their likelihood of agreeing to FMT for CDI treatment under different circumstances were compared using Wilcoxon rank sum test. These circumstances included FMT for their current episode of CDI, FMT for a subsequent episode, and FMT if recommended by their physician. Possible concerns regarding FMT also were solicited, including infection risk, effectiveness, and procedural aesthetics. The MVAHCS institutional review board approved the study.

Dr. O'Rourke is a pharmacist at the Mayo Clinic Hospital Rochester. **Ms. Amundson** is a medical researcher, and **Dr. Drekonja** is a staff physician, infectious diseases, at the Minneapolis VA Health Care System, all in Minnesota. **Dr. Goodman** is a first-year resident in internal medicine at the University of Illinois in Chicago. **Dr. Drekonja** is an associate professor of medicine at the University of Minnesota Medical School in Minneapolis.

SURVEY. Patient Knowledge and Attitudes Regarding Fecal Microbiota Therapy for *Clostridium difficile* Infection

At any time patients may ask questions. These questions will be recorded in writing and compiled to determine which questions are most common. No elements of protected health information will be recorded as part of this interview.

Hello, my name is (interviewer's name), and I am part of a research project that assesses patient attitudes about a particular treatment for *Clostridium difficile* (*C difficile*) infection of the intestines for which you are being treated. We learned about your infection from the Microbiology Laboratory/your treating team.

The research project involves asking patients who have this infection about 12 to 17 questions on a potential new treatment and whether they would be interested in the treatment if it were available.

Would you be willing to spend 10 to 20 minutes answering these questions about *C difficile* and this treatment that we will tell you about? Your responses will help determine whether it is feasible to study this treatment in this or in other VA facilities. There is no benefit to you for participating in this study.

1. Are you willing to continue with this study?

Yes—Continue.

No—Thank you. If you change your mind and want to participate, please call this telephone number.

C difficile infection is a bacterial infection of the intestines that leads to diarrhea and occasionally more severe symptoms. *C difficile* is typically triggered by antibiotic treatment, which can destroy the normal bacteria that live in healthy intestines. This disruption of the normal bacteria allows *C difficile* bacteria to multiply and cause infection.

Current therapy for *C difficile* involves using antibiotics to kill the *C difficile*, which then allows the normal bacteria grow back. First-line treatment is with 10 to 14 days of an antibiotic called metronidazole or a different antibiotic called vancomycin. For recurrent episodes, longer courses of metronidazole, vancomycin, or other antibiotics are used.

2. Have you ever had *C difficile* in the past? (Yes—Continue; No—Go to question 7.)

3. How many episodes of *C difficile* have you had?

4. Have you ever had a *C difficile* infection severe enough to require intensive care stay?

5. On a scale of 1 to 10, if 1 represents no limitation whatsoever and 10 represents severe limitation in your quality of life, how would you say your *C difficile* infections have affected your quality of life?

6. What treatments for *C difficile* have you received in the past? If you do not know, would you permit us to review your chart to determine which treatments you have had?

7. After a first episode of *C difficile*, assuming proper treatment, what percentage of patients do you think would be expected to have a second (or recurrent) episode? (Record answer.)

After the first *C difficile* infection, we actually expect 20% to 30% of patients to have a second episode.

8. If a person gets a second episode of *C difficile* and is treated properly, what percentage would be expected to have a third episode (or a second recurrence)? (Record answer.)

After the third episode of *C difficile*, up to 50% of patients may have recurrence.

9. Have you heard of fecal microbiota treatment, more commonly known as a stool transplant? (Yes—Go on.

No—Go to text after question 10.)

10. If so, where did you hear about it? (Record answer.)

Fecal microbiota treatment uses stool from a donor patient to create a mixture that can be delivered to the recipient's intestines in different ways, including a tube placed through the nose into the small intestine, a colonoscope into the colon (large intestine), or a rectal enema. The procedures allow rapid restoration of the normal intestinal bacteria and have a reported cure rate of 90% in cases of recurrent *C difficile*.

11. How likely is it that you would agree to undergo fecal microbiota treatment for your current *C difficile* episode? (1—Not at all likely; 10—I would certainly agree to fecal microbiota treatment if it were available.)**12. If you had another episode of *C difficile* after this current episode, how likely would you be to consider fecal microbiota treatment then?** (1 to 10 rating)

The following questions are about ways to administer fecal microbiota therapy.

13. Assuming all methods of administering fecal microbiota treatment work equally well, which method would you prefer if you had this treatment?

- a. tube from the nose into the small intestine
- b. colonoscopy
- c. enema
- d. none of the above
- e. no preference

14. Would you prefer that this procedure be performed in the hospital or would you rather give yourself an enema at home, following a set of instructions?**15. Would you prefer that the donor stool be provided by a family member (if available) or as a standardized frozen sample provided at the hospital by an anonymous donor?** (In either case, the samples would be tested for communicable pathogens such as hepatitis virus, HIV, and others.)**16. How much concern do you have about the following issues regarding fecal microbiota therapy?**

- a. risk of infection (1 = not at all concerned; 2 = mild concern; 3 = moderate concern; 4 = large amount of concern; 5 = overwhelming concern (would not undergo this procedure because of my concerns))
- b. the aesthetics, or “yuck factor” involved with this procedure (1 = not at all concerned; 2 = mild concern; 3 = moderate concern; 4 = large amount of concern; 5 = overwhelming concern (would not undergo this procedure because of my concerns))
- c. concerns about effectiveness (1 = not at all concerned; 2 = mild concern; 3 = moderate concern; 4 = large amount of concern; 5 = overwhelming concern (would not undergo this procedure because of my concerns))

17. If a study were to be conducted here at the Minneapolis VA comparing the effectiveness of fecal microbiota therapy vs standard treatment, eg, 10 to 14 days of oral vancomycin, how likely is it that you would enroll?

(1 = almost certainly would not enroll; 2 = probably would not enroll; 3 = equally likely to enroll or not enroll; 4 = probably would enroll; 5 = almost certainly would enroll).

Those are all the questions. Thank you for participating in this study.

RESULTS

Stool PCR tests for CDI were monitored for 158 days from 2013 to 2014 (based on availability of study staff), yielding 106 positive results. Of those, 31 (29%) were from outpatients and not addressed further. Of the 75 positive CDI tests from 66 hospitalized patients (9 patients had duplicate tests), 18 of 66 (27%) were not able to provide consent and were excluded, leaving 48 eligible patients. Six (13%) were missed for logistic reasons (patient at a test or procedure, discharged before approached, etc), leaving 42 patients who were approached for participation. Among these, 34 (81%) consented to participate in the survey. Two subjects (6%) found the topic so unappealing that they terminated the interview.

The majority of enrolled subjects were men (32/34, 94%), with a mean age of 65.3 years (range, 31-89). Eleven subjects (32%) reported a prior CDI episode, with 10 reporting 1 such episode, and the other 2 episodes. Those with prior CDI reported the effect of CDI on their overall quality of life as 5.1 (1 = no limitation, 10 = severe limitation). Respondents were fairly accurate regarding the risk of recurrence after an initial episode of CDI, with the average expected recurrence rate estimated at 33%. In contrast, their estimation of the risk of recurrence after a second CDI episode was lower (28%), although the risk of recurrent episodes increases with each CDI recurrence.

Regarding FMT, 5 subjects indicated awareness of the procedure: 2 learning of it from a news source, 1 from family, 1 from a health care provider, and 1 was unsure of the source. After subjects received a description of FMT, their opinions re-

garding the procedure were elicited. When asked which route of delivery they would prefer if they were to undergo FMT, the 33 subjects who provided a response indicated a strong preference for either enema (15, 45%) or colonoscopy (10, 30%), compared with just 4 (12%) indicating no preference, 2 (6%) choosing nasogastric tube administration, and 2 (6%) indicating that they would not undergo FMT by any route ($P < .001$).

Regarding the location of FMT administration (hospital setting vs self-administered at home), 31 of 33 respondents (94%) indicated they would prefer FMT to occur in the hospital vs 2 (6%) preferring self-administration at home ($P < .001$). The preferred source of donor stool was more evenly distributed, with 14 of 32 respondents (44%) indicating a preference for an anonymous donor, 11 preferring a family member (34%), and 7 (21%) with no preference ($P = .21$).

Subjects were asked about concerns regarding FMT, and asked to rate each on a 5-point Likert scale (1 = not at all concerning; 5 = overwhelming concern). Concerns regarding risk of infection and effectiveness received an average score of 2.74 and 2.72, respectively, whereas concern regarding the aesthetics, or “yuck factor” was slightly lower (2.1: $P = NS$ for all comparisons). Subjects also were asked to rate the likelihood of undergoing FMT, if it were available, for their current episode of CDI, a subsequent episode of CDI, or if their physician recommended undergoing FMT (10 point scale: 1 = not at all likely; 10 = certainly agree to FMT). The mean scores (SD) for agreeing to FMT for the current or a subsequent episode were 4.8 (SD 2.7) and 5.6 (SD 3.0); $P = .12$, but increased to 7.1 (SD 3.23) if FMT were recommended by their physi-

cian ($P < .001$ for FMT if physician recommended vs FMT for current episode; $P = .001$ for FMT if physician recommended vs FMT for a subsequent episode). Finally, subjects were asked about the likelihood of enrolling in a study comparing FMT to standard antimicrobial treatment, with answers ranging from 1 (almost certainly would not enroll) to 5 (almost certainly would enroll). Among the 32 respondents to this question, 17 (53%) answered either “probably would enroll” or “almost certainly would enroll,” with a mean score of 3.2.

DISCUSSION

Overall, VA patients with a current episode of CDI were not aware of FMT, with just 15% knowing about the procedure. However, after learning about FMT, patients expressed clear opinions regarding the route and setting of FMT administration, with enema or colonoscopy being the preferred routes, and a hospital the preferred setting. In contrast, subjects expressed ambivalence with regard to the source of donor stool, with no clear preference for stool from an anonymous donor vs from a family member.

When asked about concerns regarding FMT, none of the presented options (risk of infection, uncertain effectiveness, or procedural aesthetics) emerged as significantly more important than did others, although the oft-cited concern regarding FMT aesthetics engendered the lowest overall level of concern. In terms of FMT acceptance, 4 subjects (12%) were opposed to the procedure, indicating that they were not at all likely to agree to FMT for all scenarios (defined as a score of 1 or 2 on the 10-point Likert scale) or by terminating the survey because of the questions. However, 15 (44%)

indicated that they would certainly agree to FMT (defined as a score of 9 or 10 on the 10-point Likert scale) if their physician recommended it. Physician recommendation for FMT resulted in the highest overall likelihood of agreeing to FMT, a finding in agreement with a previous survey of FMT for CDI.¹⁰ Most subjects indicated likely enrollment in a potential study comparing FMT with standard antimicrobial therapy.

Strengths/Limitations

Study strengths included surveying patients with current CDI, such that patients had personal experience with the disease in question. Use of in-person interviews also resulted in a robust response rate of 81% and allowed subjects to clarify any unclear questions with study personnel. Weaknesses included a relatively small sample size, underrepresentation of women, and lack of detail regarding respondent characteristics. Additionally, capsule delivery of FMT was not assessed since this method of delivery had not been published at the time of survey administration.

CONCLUSION

This survey of VA patients with CDI suggests that aesthetic concerns

are not a critical deterrent for this population, and interest in FMT for the treatment of recurrent CDI exists. Physician recommendation to undergo FMT seems to be the most influential factor affecting the likelihood of agreeing to undergo FMT. These results support the feasibility of conducting clinical trials of FMT in the VA system. ●

Author disclosures

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