Fecal Microbiota Transplantation: Patient and Physician Attitudes

Lawrence J. Brandt
Montefiore Medical Center, Bronx, New York

(See the Major Article by Zipursky et al, on pages 1652–8.)

Fecal microbiota transplantation (FMT) has been shown in numerous case series to be a rapidly acting (within hours to weeks), safe (no serious adverse effects definitely attributed to FMT), and highly effective (worldwide average success rate, 91%) therapy for recurrent Clostridium difficile infection (CDI), even when all other treatments have failed. At present, there remain only 2 impediments to its wide-scale acceptance into the anti-CDI armamentarium. The first is the lack of a randomized controlled trial to prove its effectiveness against a valid comparator. Two current studies will be of value in this regard. The first, the so-called FECAL (Fecal therapy to Eliminate Clostridium difficile Associated Long-standing diarrhoea) trial, has already been completed, and its results are eagerly awaited. In this 3-armed study by Van Nood and colleagues from Amsterdam [1], vancomycin alone (group 1) or with colon lavage (group 2) was compared with nasoduodenal tube administration of FMT after vancomycin and colon lavage (group 3). The second study, whose principal investigators are Colleen Kelly and myself, was recently approved by the National Institutes of Health. This study has a randomized, controlled, blinded design: FMT with either donor stool or patient (recipient) stool (placebo) is used to treat patients with ≥3 recurrences of CDI; failure to respond to treatment will enable the recipient to subsequently receive donor stool in an open fashion.

The second impediment to acceptance of FMT, which seems more common in physicians than in patients, is the “yuck” factor. In a prior questionnaire-type study, using data generated by 5 academic physician practices in disparate areas across the United States from patients who had undergone FMT for recurrent CDI and were followed up for ≥3 months, 2 major conclusions were reached. First, 91% of patients were cured by the first FMT, and 98% were either cured by a second FMT or responded to vancomycin, which they had not responded to before FMT. Second, 73% of patients said they would undergo FMT again, and 53% said they would opt to undergo FMT as initial therapy for a future CDI episode [2].

The present study by Zipursky and colleagues in this issue of Clinical Infectious Diseases confirms that patients are open to FMT as an alternative treatment for recurrent CDI and expands that observation [3]. Whereas Brandt et al questioned patients’ medical and CDI histories and their personal experience with FMT, Zipursky et al used a structured survey questionnaire that included 2 hypothetical scenarios to assess patients’ perceptions about the aesthetics of FMT and their willingness to consider it as a treatment option. The advantage and disadvantage of this clever design is its allowance for patients to respond to the hypothetical situation without the confounding influence of being personally affected or—as in many cases—ravaged by recurrent CDI. Participants were adult outpatients and accompanying relatives in a variety of medical and surgical clinics. Of the 2 clinical scenarios that were presented to each participant, the first asked patients to choose between another course of antibiotics alone or an unexplained therapy called “Floral Reconstitution (FR),” whereas the second presented the respondent with an identical clinical scenario and the same treatment options but explained the fecal nature of FR; there was no difference in the percentage of patients (81% of patients who knew the nature of FR vs 84% who did not) choosing FR. Of note, women and older respondents rated all aspects of FR more and less unappealing, respectively, but significantly more respondents chose FR if their physicians recommended it. Understandably, a patient’s need to handle stool during the
treatment was “unappealing enough to interfere with acceptability.”

In my FMT practice, which just recently exceeded 100 patients, however, none of these sex- or age-related issues, or concern with handling stool seem to matter, and most of my patients have knowingly sought me out in their search for an alternative treatment for recurrent CDI; many had researched the topic, the technique, and my practice. They had often read published abstracts or papers and watched my presentations on YouTube, and they came with specific questions. Long before they came for consultation, their inhibitions and hesitations about FMT had been exorcised, and they just wanted relief. A similar attitude, that living with the disease was far worse than the thought of undergoing FMT, was expressed by patients and parents of children with ulcerative colitis regarding the use of FMT as an adjunct to standard treatment regimens [4]. Patients with CDI and their accompanying family and friends who come to see me were highly knowledgeable and not “turned off” by the fecal nature of the fecal reconstitute; rather they were “turned on” by the possibility—indeed the likelihood—of cure. For many the major stumbling block has been the intransient negativism of their physicians, who told them, uninfluenced by any of the positive reported data, that FMT was “quackery,” “a joke,” “snake oil,” or other pithy labels that were discouraging but served only to delay, not dissuade, these perseverant individuals.

In a presentation on physicians’ attitudes toward FMT at the American College of Gastroenterology in 2010, Colleen Kelly showed that of 60 physicians who had heard of FMT, 40% were not willing to try it, pending further demonstration of its efficacy safety and perceived patient acceptance [5]. Zipursky et al addressed the patient acceptance issue [3]. In the 2 years since Kelly’s report and despite a worldwide, published, positive experience with almost 500 cases, physicians still hesitate to recommend FMT, absent randomized controlled trials to show effectiveness and safety.

I sense that change is on the way, however, because patients are a powerful evolutionary force. With CDI being an epidemic with a high recurrence rate, I predict that patients’ needs and wishes will soon trump the objections of their physicians. Of course, use of formulations that are more aesthetically pleasing than suspensions of stool would probably make decision making even easier for patients and physicians, and industry is already moving in this direction. I believe that the tsunami of knowledge that is now coming to publication through the efforts of the Human Microbiome Project and other studies on the intestinal microbiota will not only reveal how this community of living organisms maintains our health and causes disease but will also lead the way to a heretofore-unparalleled change in how we treat disease. We have come a long way since Hippocrates said “All disease begins in the gut”; today he might instead say “Our health is determined by the microbiota in our gut.” We are witnessing a paradigm shift in the way we understand health and treat disease, and our microbiota are at its center.

Note

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References