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ORIGINAL ARTICLE

Safety and Efficacy of Fecal Microbiota Transplant for Recurrent *Clostridium difficile* Infection in Patients With Cancer Treated With Cytotoxic Chemotherapy: A Single-Institution Retrospective Case Series

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Abstract

Objective: To study the safety and efficacy of fecal microbiota transplant (FMT) for *Clostridium difficile* infection (CDI) in patients with cancer treated with cytotoxic chemotherapy in a single-institution retrospective case series.

Patients and Methods: Twenty-three consecutive patients with underlying hematologic (n=13) or solid (n=10) malignancies who underwent FMT for recurrent CDI from August 1, 2012, through June 30, 2016, were studied.

Results: All the patients had received cytotoxic chemotherapy a median of 12 months (range, 1-340 months) before FMT. Patients had experienced a median of 4 (range, 2-9) CDI episodes and had been treated with a median of 106 days (range, 42-495 days) of vancomycin, metronidazole, or fidaxomicin before FMT. Twelve patients (52%) had severe/severe-complicated CDI at some stage. Eight patients (35%) had active cancer and 5 (22%) had received chemotherapy within 12 weeks of FMT. Diarrhea resolved without recurrence within 60 days of FMT in all but 3 patients (13%) (all had negative *C difficile* results). Of the 22 patients who were alive 60 days or more after FMT, 11 (48%) underwent further chemotherapy and 10 (43%) received more antibiotics. Two patients (9%) developed recurrent CDI 14 and 22 months after FMT. One death occurred 5 days after FMT as a result of cardiac arrest unrelated to FMT. There were no other severe adverse events and no infectious complications directly attributable to FMT.

Conclusion: This series demonstrates that FMT is a highly effective and safe therapeutic option for multiply recurrent CDI in patients with cancer treated with cytotoxic chemotherapy.

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Clostridium difficile infection (CDI) is the most common health care–associated infection[1] and is recognized by the Centers for Disease Control and Prevention as an urgent public health priority, with an estimated 450,000 infections and 29,000 deaths per year in the United States.[2] Patients with cancer are particularly at high risk for both primary and recurrent CDI, along with complications such as toxic megacolon and treatment failure likely due to underlying immunosuppression and frequent use of broad-spectrum antibiotics.[3,4] Antineoplastic chemotherapy can also lead to an altered gut microbiome and promote CDI even in the absence of antibiotic drug exposure.[5]

Management of CDI is complicated by high rates of treatment failure in approximately 25% to 35% of the patients.[6] Despite appropriate first-line therapy, there is a greater than 60% risk of relapse after a second recurrence[7] because conventional antibiotic drug therapies such as vancomycin or metronidazole do not address the underlying gastrointestinal dysbiosis and, in fact, may worsen it. In 2 randomized clinical trials, Cornely et al[8]

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showed that response to oral vancomycin and fidaxomicin therapy was significantly lower in patients with cancer compared with those without cancer. In another study, malignancy was an independent risk factor for CDI recurrence (odds ratio = 2.66).[9]

Fecal microbiota transplant (FMT) is a safe and effective treatment in patients with recurrent CDI, with a success rate of approximately 90%.[10,11] Although immunocompromised patients are at increased risk for CDI, the use of FMT may be limited in this population because FMT clinical trials generally exclude immunocompromised patients due to concerns about its safety, particularly the theoretical risk of invasive infection through bacterial translocation.

Current evidence on the safety and efficacy of FMT in immunocompromised patients is limited. In 2014, Kelly et al[12] reported data from 15 published case reports or case series on the use of FMT in 80 immunocompromised patients. In this report, immunosuppression included a wide range of conditions, such as inflammatory bowel disease, solid organ transplant, and severe or end-stage chronic medical conditions, among others. However, there were only 7 patients with cancer who had received antineoplastic therapy concurrently or in the 3 months before FMT. Overall, they found that FMT was effective for CDI in this heterogeneous group of immunocompromised patients, with few severe adverse events (SAEs) and no infectious complications attributable to FMT.

In 2013, Rubin et al[13] reported 8 patients with cancer who were treated with FMT for recurrent CDI in a cohort of 75 patients. The rate of CDI relapse was higher at 50% compared with 21% for the entire cohort. No serious adverse events (AEs) directly related to FMT were reported. More recently, Webb et al[14] reported the use of FMT for CDI in 7 hematopoietic cell transplant (HCT) recipients, with only 1 of the 7 patients developing a recurrent CDI and no AEs.

Although evidence on the efficacy and safety of FMT in immunocompromised patients has started to emerge, data in patients with cancer and in the context of treatment with antineoplastic agents are still scant. Herein, we report a large case series from a single institution evaluating the efficacy and safety of FMT for recurrent CDI in patients with cancer treated with cytotoxic chemotherapies.

METHODS

Patients

A database of 452 consecutive patients with recurrent CDI who had received FMT at Mayo Clinic in Rochester, Minnesota, from August 1, 2012, through June 30, 2016, was reviewed. Patients were included in the study if they were 18 years or older at the time of FMT, had an underlying diagnosis of hematologic or solid malignancy, and had received cytotoxic chemotherapy before FMT. Patients were excluded from the analysis if they were treated only with surgery, endocrine therapy, or supportive care (n=15) or if they did not have a minimum of 60 days of post-FMT follow-up (n=2). Data regarding demographic characteristics, underlying malignancy, *C difficile* history, treatments, and clinical outcomes were retrospectively abstracted from electronic medical records. Timing of chemotherapy in relation to FMT was categorized as 12 weeks or less vs greater than 12 weeks before FMT. This study was approved by the Mayo Clinic Institutional Review Board.

Fecal Microbiota Transplant

The protocol for donor screening and FMT used at Mayo Clinic has been described previously.[15,16] Fresh stool from family/friend donors was used in 10 patients, and frozen stool from standard (unrelated) donors was used in 13 patients. Colonoscopy was performed on all the patients to instill approximately 50 g of donor stool emulsified in 250 mL of saline into the cecum. All FMT recipients were treated with a course of oral vancomycin that was stopped 24 hours before FMT. Telephone follow-up was conducted 1 week and 1 month after the procedure. Patients were surveyed regarding major symptoms, including diarrhea, constipation, nausea, abdominal cramps, and fecal urgency, as well as any new antibiotic drug use and infectious complications.

Clinical Outcomes and Definitions

Clinical resolution or relapse of CDI was determined based on post-FMT clinical course without routine testing for *C difficile* toxin.

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