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CONCISE COMMENTARY

Concise Commentary: Treatment of Recurrent *C. difficile* Infection: A New Take on the Fecal–Oral Route

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Clostridium difficile infection (CDI) is the most common healthcare-associated infection in the USA [1]. Rates of multiply recurrent and antibiotic-resistant CDI are also increasing at an alarming rate [2]. Given this and the known effectiveness of fecal microbiota transplantation (FMT) in restoring the gut microbiota and preventing recurrence, the diverse modes of administration of FMT have been the focus of recent research [3]. "Lower administration" via enema, flexible sigmoidoscopy or colonoscopy seems to have the best efficacy, although these techniques might limit which providers can perform the procedure. Given this, orally administered capsules offer the broadest access to FMT. One potential issue with capsules is their release of colonic bacteria into the small bowel, with resultant proliferation, potentially causing small intestinal bacterial overgrowth and colonization of the small bowel with colonic flora.

In this issue of *Digestive Diseases and Sciences*, Allegretti et al. compare the safety, efficacy and engraftment patterns of two types of capsules with differing delivery mechanisms in outpatients with at least three documented episodes of CDI [4] defining cure as cessation of diarrhea and/or a negative CD stool antigen test. One, FMTgr, releases the transplant starting in the stomach, whereas FMTcr releases the transplanted material within the colon using coating technology to protect it during its passage through the stomach and small intestine. One cohort received either high-dose FMTgr (60 capsules) or low dose (30 capsules), whereas the other cohort received either high-dose FMTcr (30 capsules) or low dose (10 capsules). Patients were followed for 8 weeks following transplant. Cure rates were similar between cohorts with 75% (15/20) in FMTgr and 80.6% in FMTcr (25/31, $p = .063$). The small number of patients likely contributed to the trend seen as the colonic release form had a nonsignificantly higher rate of success. Most interestingly, the rates of engraftment, as measured by 16S metagenomic analysis of the pre- and post-transplant recipient microbiota compared with donor stool, the increase in microbial diversity and correction of dysbiosis, were superior in the cohort that received FMTcr. Even the low-dose FMTcr (10 capsules) contained a higher number of engrafter strains than either the low- or the high-dose FMTgr.

This study convincingly indicates the importance of this technological advancement where the material being transplanted is delivered directly to its colonic target via the oral route. Based upon the efficacy trend and the engraftment differences, it seems likely that with a larger trial, FMTcr will have fewer side effects and superior effectiveness. Future studies should include larger cohorts and more centers to allow better statistical power and more diverse patient populations to potentially reinforce these findings.

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