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REACTing Against Resistance: Fecal Microbiota Transplant Shows Safety and Promise in Long-Term Care Patients Cancer Risks in Familial Adenomatous Polyposis

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COLON

STRUCTURED ABSTRACT

Question: Among long-term acute care hospital (LTACH) patients colonized with multidrug-resistant organisms (MDROs), is fecal microbiota transplantation (FMT) superior to no treatment (contemporaneous controls) for safety and infection-related outcomes?

Design: Single-center, open-label, nonrandomized pilot clinical trial with contemporaneous untreated controls; enrollment April–December 2023; follow-up 6 months.

Setting: Academic-affiliated LTACH in Atlanta, Georgia (Southeastern US); median ~50-patient census and ~28-day length of stay.

Patients: Participants were adults aged ≥18 years whom had a perirectal or stool culture positive for a target MDRO (extended-spectrum β-lactamase [ESBL] Enterobacterales, carbapenem-resistant Enterobacterales [CRE], multidrug-resistant [MDR] Pseudomonas, vancomycin-resistant Enterococcus [VRE], or toxigenic Clostridioides difficile); able/willing to receive FMT via feeding tube or retention enema; willing to discontinue antibiotics, probiotics/other microbiota therapies, and proton pump inhibitors (PPIs) ≥1 day before FMT through Day 28. Participants were excluded if: pregnant or breastfeeding, had a compromised immune system (e.g., AIDS with CD4<200 and detectable HIV load, ANC<1000, recent intensive chemo/radiotherapy or hematopoietic cell transplant) or had an inability to discontinue PPI therapy.

Interventions: Healthy-donor fecal microbiota (50–100 g stool suspended in 250 mL normal saline with 9% glycerol) instilled via gastrostomy tube or enema; no antibiotic or bowel-prep conditioning.

Outcomes: Primary: frequency and severity of adverse events (AEs) graded by CTCAE v5.0; solicited AEs assessed daily through Day 7; unsolicited AEs through 6 months. Secondary: proportion MDRO-positive perirectal/stool cultures at Weeks 2 and 4 after FMT. MDROs included ESBL Enterobacterales, CRE, MDR Pseudomonas, VRE, and toxigenic C. difficile. Exploratory: bloodstream infection, intestinal pathogen dominance by metagenomics, antibiotic days of therapy, and healthcare utilization over the 6 months before vs after prevalence sampling.

Data Analysis: Descriptive summaries; Wilcoxon rank-sum for continuous variables; Fisher exact for proportions; 2-sided α=0.05. Difference-in-differences model for antibiotic days of therapy; analyses in R. (Trial not powered for formal hypothesis testing.)

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Results: Among 42 patients assessed (mean age ~64 years; 52% female overall), 10 received FMT and 32 served as contemporaneous MDRO-colonized controls. Routes among FMT recipients: 5 gastrostomy, 4 enema, 1 both (>30 days apart). No serious AEs were attributed to FMT; solicited post-FMT AEs were mild. At the final

visit, all FMT recipients remained MDRO culture–positive. Post hoc comparisons (underpowered) showed numerically fewer FMT recipients with positive blood cultures in the following 6 months (0/10 vs 6/32 [19%]; P=0.31), lower pathogen intestinal dominance (25% vs 50%; P=0.61), and fewer antibiotic days of therapy (median 12.6 vs 19.7 days per 1000 patient-days; P=0.38); a difference-in-differences analysis estimated 26 fewer antibiotic days per 1000 patient-days (95% CI, −64 to 12) after FMT.

Bottom line: In LTACH patients with MDRO colonization, single-dose FMT (via gastrostomy or enema) was acceptable and not associated with related serious adverse events (AEs); signals toward reduced bacteremia and antibiotic use did not reach statistical significance and warrant testing in larger randomized trials (**Table 1**).

Outcome	FMT Group (n=10)	Control Group (n=32)	*P* value	Interpretation
Serious adverse events related to FMT	**0**	—	—	No FMT-related serious AEs reported
Any adverse event (solicited, ≥7 days)	Mild, transient GI symptoms only	—	—	FMT well tolderated
MDRO colonization at final visit	**10/10 (100%)**	**32/32 (100%)**	—	Persistent MDRO colonization in all participants
Bloodstream infection within 6 mo	**0/10 (0%)**	6/32 (19%)	0.31	Trend toward fewer BSIs after FMT
Pathogen intestinal dominance	**25%**	50%	0.61	Numerically lower in FMT group
Antibiotic COT per 1,000 patient-days	**12.6**	19.7	0.38	Fewer antibiotic DOTs post-FMT
Difference-in-differences: DOT change (95% CI)	**−26 days (−64 to +12)**	Reference	—	Suggests reduced antibiotic exposure after FMT

Table 1. Clinical and microbiologic outcomes in the REACT trial comparing fecal microbiota transplantation (FMT) with contemporaneous controls among long-term acute care patients colonized with multidrug-resistant organisms (MDROs). FMT was well tolerated with no related serious adverse events and showed numerical reductions in bloodstream infections and antibiotic use, though not statistically significant. BSI, bloodstream infection; CI, confidence interval; DOT, days of therapy; GI, gastrointestinal.

*Dominance defined by metagenomic relative abundance > 30% of any MDRO species in stool.

COMMENTARY

Why Is This Important?

FAP is a difficult population to study because it is relatively rare, although it's clinical presentation is quite dramatic due to the burden of colorectal polyps. Many studies on FAP harken back to historical studies before the advent of routine high-definition colonoscopies for screening, as reflected in the increasing incidence of aFAP over time.[1] It is thus helpful to have a more contemporary description of cancer risks and outcomes in both cFAP and aFAP.

Key Study Findings

With presumed standard-of-care prophylactic colectomies and surveillance colonoscopies (in the United States), most FAP patients will fortunately not develop cancer, although the risk overall is still markedly higher than the average-risk patient without FAP.

There is still a subset of FAP patients that can develop rectal cancer after colectomy, thus frequent flexible sigmoidoscopy of the residual rectum (typically every 6-12 months depending on polyp burden) remains important.[2] The burden of duodenal adenomas is still substantial, particularly in the cFAP population, although we still do not fully understand risk factors for duodenal adenocarcinoma otherwise.

Caution

This study does not account for surveillance procedures such as colonoscopy prior to colectomy, as well as surveillance flexible sigmoidoscopy/pouchoscopy (for those with an ileorectal anastomosis or ileo-anal pouch anastomosis) or ileoscopy (for those with an end ileostomy) after colectomy. Prior studies have observed that the risk of ileal adenomas is higher in those with a pouch compared to end ileostomy, which would be an important risk factor to understand given its potential impact on choice of surgery.[3] It is also curious that only about half of patients underwent surgery, which may be from inadequate observation time (i.e. the colectomy has not happened) rather than non-operative colonoscopic management of polyp burden, which is seldomly feasible with substantial resource and colonoscopic burden.[4]

FAP patients are not typically recognized as high risk for pancreatic adenocarcinoma in national guidelines.[5-7] As the authors note, these patients did not undergo genetic re-evaluation to assess for comorbid pathogenic variants. To recognize this as a FAP-associated cancer, future studies must account for differences in other risk factors for pancreatic cancer (alcohol, tobacco, chronic pancreatitis etc.). Finally, the study did not examine desmoid disease, which is a leading cause of

morbidity and mortality in FAP patients despite its non-malignant nature.

My Practice

Upon meeting a newly diagnosed FAP patient, I counsel the patient that although the risk of colorectal cancer is high, the risk can be dramatically reduced with colectomy and subsequent frequent lower endoscopies. Prior to colectomy, I find that the removal of most diminutive/small adenomas and counting the exact number of polyps is practically less useful. Given that the majority of FAP patients require extended or total colectomy, I perform colonoscopy with several diagnostic goals in mind: 1) masses concerning for cancer or advanced polyps; 2) estimating whether the rectal burden of polyps is "endoscopically manageable" over time with repeat procedures; 3) define the anatomic extent of endoscopically "un-manageable" polyposis in collaboration with colorectal surgery to inform whether the patient is a candidate for an ileorectal or even ileosigmoid anastomosis to improve post-operative quality of life. Finally, I do stress to the patient that even after surgery, frequent lower endoscopies are still critical to avoid the risk of rectal cancer.

For Future Research

Larger studies incorporating endoscopic data is still needed to understand how to manage the upper intestinal manifestations of FAP such as duodenal or gastric neoplasia, as well as medication interventions to help manage those with advanced duodenal neoplasia given the morbidity associated with duodenectomy.

Conflict of Interest

The author has no reported conflicts of interest.

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