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Fecal Transplant via Retention Enema for Refractory or Recurrent *Clostridium difficile* Infection

Clostridium difficile infection (CDI) is the leading cause of nosocomial infection and its rates continue to rise. In the United States, the incidence of CDI tripled between

1996 and 2005 (31 per 100 000 vs 84 per 100 000).¹ This has been accompanied by an increase in disease severity, with mortality rates of up to 6.9%.² In addition, nosocomial CDI increases the cost of otherwise matched hospitalizations by 4-fold.³

Metronidazole therapy failure rates for uncomplicated CDI have risen from 2.5% to higher than 18% since 2000.¹ Recurrence rates are as high as 50% in patients older than 65 years and exceed 60% after 2 or more recurrences.^{1,4} Accordingly, fecal transplant (FT) serves as an alternative approach. While antibiotics can further disrupt the microbiome, FT aims to reconstitute healthy flora. In uncontrolled case series, clinical resolution rates following FT are 73% to 100% in recurrent or refractory CDI.⁵⁻⁷ Most reports have evaluated FT via nasogastric tube and colonoscopy, which are cumbersome and costly.^{6,7} This report describes FT via retention enema in patients with refractory or recurrent CDI.

Methods. Patients. Case records were reviewed for 27 patients who underwent FT via retention enema. Inclusion criteria were (1) laboratory-confirmed *C difficile* toxin using enzyme immunoassay with no other cause for diarrhea; (2) refractory CDI (defined as ongoing diarrhea despite antimicrobial treatment) or recurrent CDI (defined as symptom resolution for at least 2 days after discontinuation of treatment with recurrence of diarrhea); and (3) complete clinical and laboratory documentation by medical chart or telephone review.

FT Donor Screening. Two healthy volunteers served as donors and were evaluated for transmissible pathogens. Blood was screened for hepatitis B surface antigen, hepatitis C antibody, *Helicobacter pylori* and syphilis serologic markers, human immunodeficiency virus types 1 and 2, and human T-lymphotropic virus types I and II. Stool was processed for enteric bacterial pathogens, *C difficile* toxin, and ova and parasites. The donors took no antibiotics for 6 months prior to stool donation.

FT Protocol. All CDI therapy was discontinued at least 24 hours prior to FT. Approximately 150 g of fresh stool collected was emulsified in 300 mL of sterile water. The supernatant component was administered rectally by enema. If diarrhea recurred within 7 days, the procedure was repeated.

Results. The mean age was 69.4 years (range, 26-87 years) with 14 male subjects (52%) and 22 in-patients (81%). Subjects had a mean duration of diarrhea of 152.6 days. Fever and abdominal pain were documented in 29.6% and 74.1%, respectively.

Prior CDI therapies and clinical outcomes following FT are outlined in the **Table**. The mean cumulative antibiotic exposure before FT included 24.9 days of metronidazole therapy; 54.6 days of vancomycin monotherapy; 13.6 days of vancomycin taper; and 9.9 days of combined therapy with metronidazole and vancomycin.

After FT, 25 of 27 (93%) experienced clinical resolution. Of these, 22 resolved within 24 hours of transplant. Five patients underwent a second FT because of ongoing diarrhea; 3 had symptom resolution and 2 continued to experience diarrhea despite 2 FTs. There were no relapses or adverse events in the cohort that success-

Table. Treatment and Clinical Outcomes in 27 Patients Treated With Fecal Transplant for CDI

Patient No.	CDI Treatment in Total Days					Fecal Transplant	
	Metronidazole Monotherapy	Vancomycin Monotherapy	Metronidazole + Vancomycin	Vancomycin Taper Protocol	Probiotics	Clinical Outcome	Days of Resolution
1	18	17	Resolution	663
2	45	63	Resolution	682
3	19	...	42	Resolution	687
4	14	19	Resolution	687
5 ^b	1	12	34	Resolution	692
6	7	...	15	15	...	Resolution ^a	467
7	14	601	Resolution	431
8	1	14	23	Resolution ^a	390
9	24	Resolution	579
10	17	Resolution	555
11	150	42	Resolution	695
12	14	221	Resolution	371
13	76	323	...	200	30	Resolution	627
14	28	14	...	63	...	Resolution	627
15 ^a	14	7	Treatment failure ^a	NA
16	14	19	Resolution	173
17	14	17	Resolution	194
18	42	...	10	Resolution	176
19	14	14	...	58	...	Resolution	51
20	14	7	Resolution	159
21	7	13	Resolution	263
22	14	7	...	31	...	Resolution	600
23	43	...	10	Resolution	268
24	14	15	75	Resolution	243
25	28	48	Resolution	268
26	58	...	48	Resolution	134
27 ^a	9	...	13	Treatment failure ^a	NA

Abbreviations: CDI, *Clostridium difficile* infection; NA, not applicable; ellipses, patient not administered this treatment.

^aRequired 2 fecal transplants.

^bReceived intravenous immunoglobulin.

fully underwent FT, with a mean follow-up at 427.3 days after transplant.

Comment. According to small, uncontrolled studies, the FT success rate is 89% (98 of 110 patients).⁵⁻⁸ These reports are limited by heterogeneity in delivery modality, publication bias, and small sample sizes. However, the success of FT in refractory and recurrent CDI cannot be overlooked.

There is no consensus on the ideal delivery modality for FT. Previous reports, including the 2 largest series to date, have evaluated nasogastric or colonoscopic infusion.^{6,7} However, retention enema is a less invasive, more economical, and more feasible option for both hospitalized and ambulatory patients. In addition, this modality averts some of the risks of nasogastric intubation or colonoscopy, including gastrointestinal perforation.^{7,9} Despite its advantages, there have been few data on FT via retention enema.

To our knowledge, this is the largest reported series of patients treated with FT for refractory or recurrent CDI. Although our subjects had a significant burden of disease with prolonged cumulative antimicrobial therapy, our results demonstrate a robust treatment effect, with 25 of 27 cases (93%) responding clinically to FT. In addition, there were no reported adverse events or complications.

Unlike previous cohorts, this study population was bal-

anced by sex. In the largest study of FT by colonoscopy, 17 of 19 patients were female.⁶ Similarly, the largest series using nasogastric intubation, had 13 women among 18 patients.⁷ We report our positive findings with some caution. Delivery by enema may be limited in those unable to retain the infusate. Five elderly patients required another FT, while treatment failed in 2. We speculate that this relates to attenuated sphincter tone in elderly patients. Also, this study was not controlled, and outcome assessment was not blinded. Nonetheless, a strong placebo effect seems unlikely in subjects with prolonged and severe symptoms.

In conclusion, FT via retention enema appears to be an effective and safe treatment for patients with recurrent or refractory CDI.

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Improvement in Revascularization Time After Creation of a Coronary Catheterization Laboratory at a Public Hospital

Time to revascularization is a major predictor of outcomes during the treatment of ST-segment elevation myocardial infarction (STEMI).¹ As such, a door-to-balloon (DTB) time of less than 90 minutes is an important quality standard. Among nearly 5000 acute care hospitals in the United States, fewer than 25% have percutaneous coronary intervention (PCI) facilities, resulting in a significant proportion of patients with STEMI being transferred for PCI.² Despite targeted efforts nationally, these institutions rarely achieve revascularization standards.³ In addition, public hospitals charged with serving as regional default health care facilities for the uninsured may disproportionately struggle to meet guidelines when transferring for PCI. Revascularization data for these institutions, however, are lacking from the current literature.³⁻⁶ In the present study,

we determined DTB times for patients with STEMI presenting to a public hospital previously reliant on transferring for PCI and examined whether creation of a 24-hour cardiac catheterization laboratory (CCL) improved revascularization times.

Methods. San Francisco General Hospital (SFGH) is a public tertiary care hospital serving as the region's only level 1 trauma center. Before October 2008, SFGH operated a single CCL without 24-hour PCI services and transferred patients with STEMI to 4 PCI facilities within a 5-mile (8-km) radius. A protocol was established that involved emergency physicians initiating transfer to the PCI facilities and an on-site coordinator arranging for transportation and direct admission. Prehospital electrocardiographs (ECGs) were not obtainable, and thrombolytic agents were reserved for when no PCI centers were available. After October 2008, SFGH created an on-site 24-hour PCI facility with emergency physicians responsible for activation of the CCL.

We enrolled consecutive patients between April 2005 and October 2008 with a clinical diagnosis of STEMI, successful transfer for angiography, and available data for all time intervals. Patients revascularized at SFGH after October 2008 required similar criteria and were consecutively enrolled until equaling the number of transfer patients. Data were collected retrospectively from hospital medical charts using a standardized set of data definitions. Univariate analyses were performed using the Fisher exact test for categorical data and unpaired *t* tests for continuous data. The Wilcoxon rank sum test was used for time comparisons that were skewed. All tests were 2-tailed, and $P < .05$ was considered significant.

Results. Patients were primarily male (79%), with a mean (SD) age of 57 (11) years. Transfer patients had an increased prevalence of diabetes (40% vs 17%; $P = .03$) and a lower rate of family history of cardiac disease (24% vs 52%; $P = .01$). Otherwise, there were no significant differences in age, sex, cardiac risk factors, and illicit drug use between groups ($P > .05$ for all comparisons). More than 90% of both groups had insurance at enrollment. Patients also presented similarly in regards to chief complaint and location of ST-segment elevations on ECG. Two transfer patients received thrombolytic agents and both required rescue PCI.

All patients received angiograms and similar propor-

For editorial comment see page 98

tions of transfer and nontransfer patients received PCI (67% and 81%; $P = .21$). Median time intervals are shown in the **Figure**. For transfer patients, median door-to-catheterization (DTC) and DTB times were 184 minutes (interquartile range [IQR], 155-231 minutes) and 200 minutes (IQR, 166-242 minutes), respectively, with no patients revascularized in less than 90 minutes. With the 24-hour PCI facility, median DTC and DTB times decreased to 50 minutes (IQR, 34-89 minutes) and 84 minutes (IQR, 68-113 minutes), respectively, with 65% revascularized in less than 90 minutes ($P < .001$ for both compared with transfers). Off-hours revascularization