CLINICAL UPDATE

Current Developments in the Treatment of *Clostridium difficile* Infection

Highlights in *Clostridium difficile* Infection From the World Congress of Gastroenterology at ACG 2017

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Severe Refractory *Clostridium difficile* Infection Successfully Treated With Combination of Fidaxomicin, Vancomycin, and Fecal Microbiota Transplantation

The combination of fidaxomicin (Dificid, Merck), vancomycin, and fecal microbiota transplantation (FMT) successfully treated severe refractory *Clostridium difficile* infection (CDI) in a patient who had previously failed initial FMT. The results of a case study were presented in a poster by Dr Weiming Ryan Yan at the World Congress of Gastroenterology at ACG 2017.

An 82-year-old woman was admitted to a hospital after presenting with abdominal pain and diarrhea. She had a history of cellulitis on the lower extremities, chronic lymphedema, and morbid obesity, and had recently been treated with antibiotics. She developed septic shock, acute renal failure, and hypoalbuminemia, and was found to have CDI. Results of a computed tomography showed extensive wall thickening of the left colon.

Treatment with oral vancomycin showed initial improvement, but continued abdominal pain and watery diarrhea was followed up with a colonoscopy with FMT (OpenBiome). The left colon was found to have severe pseudomembranous colitis, and vancomycin was reinitiated. A repeat FMT performed 5 days later demonstrated a resolved pseudomembrane and diminished diarrhea. The original symptoms reappeared after 10 days, and a second computed tomography showed extensive colitis, particularly on the right colon; a colonoscopy for a third FMT confirmed pseudomembranous colitis on the right colon. Treatment with fidaxomicin was then initiated. The right colon membrane subsided upon a fourth colonoscopy with FMT. The patient was placed on a taper-and-pulse course of vancomycin for 8 weeks following fidaxomicin and has been in remission for CDI for 2 months following treatment.

Yan WR. Fecal microbiota transplantation (FMT) bridging with fidaxomicin and vancomycin for severe refractory *Clostridium difficile* infection (CDI). Presented at: the World Congress of Gastroenterology at ACG 2017; October 13-18, 2017; Orlando, FL. Poster P148.

No Relationship Between Adverse Outcomes of *Clostridium difficile* Infection and Antibiotic Treatment Regimen Among Patients With Inflammatory Bowel Disease

There is no significant difference among the various antibiotic treatments for CDI and infection-related adverse outcomes, such as severity, in patients with inflammatory bowel disease (IBD), according to results of a study presented in a poster by Dr Dipesh Solanky and colleagues at the World Congress of Gastroenterology at ACG 2017. The type of antibiotic used to treat CDI in this patient population also did not influence the rate of adverse events of IBD flares, subsequent CDI episodes, CDI-related hospitalization, or colectomy at 1-year follow-up.

The investigators collected data from patients with CDI and IBD between 2008 and 2013. They looked at the rates of IBD flares (ie, symptom recurrence, exacerbation, or persistence with negative stool CDI), subsequent episodes of CDI (ie, symptom return with a positive stool test following completion of CDI therapy), management and severity of CDI, hospitalizations related to CDI, and colectomy at 1 year post-CDI. Severe CDI was defined as a white blood cell count greater than 15,000/µL or serum creatinine at least 1.5 times baseline. Complicated CDI was defined as bowel perforation, admission to an intensive care unit, hypotension, ileus, megacolon, shock, or bowel resection for IBD management at the time of active CDI. Descriptive statistics and one-way analysis of variance composed the statistical analyses.

Of the 137 IBD patients included in the study, 51% had ulcerative colitis, 46% had Crohn's disease, and 3% had indeterminate colitis. Seventy-one percent of patients

had mild-moderate CDI, and 14% and 15% had severe or complicated infection, respectively. Within the mild-moderate cohort, 29% of patients were treated with vancomycin, 42% with metronidazole, and 28% with a vancomycin/metronidazole combination. Within the severe cohort, 21% received vancomycin, 42% received metronidazole, and 32% received both medications. Within the complicated cohort, 10% were treated with vancomycin, 43% with metronidazole, and 47% with both medications. No significant difference was observed among the various CDI treatments and the rate of IBD flares (P=.54), subsequent CDI episodes (P=.56), infection severity (P=.27), hospitalizations related to CDI (P=.15), and colectomy (P=.42) 1 year post-CDI.

The investigators suggest that prospective studies are needed regarding optimal CDI management among patients with IBD.

Solanky D, Pardi DS, Loftus EV Jr, Khanna S. *Clostridium difficile* infection in inflammatory bowel disease patients: influence of antibiotic choice on adverse outcomes. Presented at: the World Congress of Gastroenterology at ACG 2017; October 13-18, 2017; Orlando, FL. Poster P2135.

Opioid Use for *Clostridium difficile* Infection Associated With Longer Hospital Stays and Increased White Blood Cell Counts

Use of opioids in patients with CDI is associated with an increased hospital length of stay (LOS) and higher white blood cell counts, according to results of a follow-up study presented in a poster by Dr Elizabeth S. John and colleagues at the World Congress of Gastroenterology at ACG 2017. Opioid use in patients with CDI has also been linked to increased rates of in-hospital mortality and infection severity.

The investigators examined the medical records of 302 patients who had been clinically diagnosed with CDI and who had a LOS of more than 3 days during a single year. Patients assigned to the opioid group (n=175; 58%) were given more than 10 mg of an opioid, equivalent to a dose of morphine. Patients who received less than 10 mg were assigned to the no-opioid group (n=127; 42%). Regression analyses were used to estimate the adjusted associations between the use of opioids and indicators of CDI severity, mortality, and LOS. Regression covariates included comorbidities, demographic characteristics, prior use of antibiotics, use of acid-suppressive medication, and the source of infection (ie, hospital or community).

On average, patients in the opioid group were more likely to have severe or complicated CDI than patients in the no-opioid group (54.8% vs 39.3%; adjusted odds ratio, 1.82; P=.023). The opioid group also expressed higher rates of complicated CDI alone (12.6% vs 5.5%; adjusted odds ratio, 3.76; P<.001). Additionally, in-hospital mortality was more frequent (23.1% vs 11.1%) and average LOS was longer (25.1 vs 15.3 days) among the opioid group vs the no-opioid group. Statistically significant differences were found between opioid use and components of CDI severity, white blood cell count elevation, and creatinine rise.

John ES, Huss B, Moradi D, et al. A follow-up study about opioids in *Clostridium difficile* infections: lengthening the road to recovery and hospital stays. Presented at: the World Congress of Gastroenterology at ACG 2017; October 13-18, 2017; Orlando, FL. Poster P103.

Fecal Microbiota Transplantation Effective in Patients With Severe or Complicated *Clostridium difficile* Infection

FMT is effective in managing patients with severe or complicated CDI and should be considered early in the disease course for symptom resolution and avoidance of colectomy, according to results of a case series presented in a poster by Dr Joseph Alukal and colleagues at the World Congress of Gastroenterology at ACG 2017.

The study cohort consisted of 4 patients with fulminant CDI (confirmed via stool polymerase chain reaction) who were admitted to an intensive care unit for septic shock from CDI colitis (n=2), acute kidney failure (n=1), or respiratory failure (n=1). All 4 patients were on oral vancomycin and intravenous metronidazole; 1 patient was also on fidaxomicin, and 2 patients received a vancomycin enema. CDI was refractory to antibiotic treatment; thus, patients underwent FMT (OpenBiome) either via nasogastric tube (n=3; 100 cc of slurry) or via percutaneous endoscopic gastrostomy tube (n=1; 200 cc of slurry).

Two patients continued oral vancomycin post-FMT, and 1 patient continued a combination of oral vancomycin and intravenous metronidazole. One patient discontinued treatment. Symptom resolution and improvement of abdominal pain and diarrhea occurred in 100% of patients in an average of 5.25 days post-FMT (range, 2-8 days). One patient experienced recurrence of CDI at 90 days owing to the use of antibiotic treatment for chronic obstructive pulmonary disease.

Alukal J, Laster J, Tabbaa O, Rastogi P, Mattar MC. Efficacy of fecal microbiota transplant (FMT) in severe/complicated *Clostridium difficile* infection (CDI): a case series. Presented at: the World Congress of Gastroenterology at ACG 2017; October 13-18, 2017; Orlando, FL. Poster P1820.