Treatment Options Differ in Initial, Recurrent *C. difficile*

BY BRUCE JANCIN

ESTES PARK, COLO. — The treatment success rate for metronidazole in *C. difficile*–associated disease has dropped off, compared with that of vancomycin, since the disease epidemiology changed around the year 2000, but the drug retains a highly useful role for this infection.

Metronidazole's falloff in efficacy since the rise of community-acquired *C. difficile*–associated disease (CDAD) has been largely at the severe end of the disease spectrum, where vancomycin is now the drug of choice. In milder cases, metronidazole retains a respectable 90%-plus success rate, Dr. Mary Bessesen said at a conference on internal medicine sponsored by the University of Colorado.

Keeping vancomycin in reserve for severe cases of CDAD makes sense because the emergence of vancomycin-resistant enterococci is a real concern, whereas metronidazole-resistant *C. difficile* remains rare. Plus, vancomycin is expensive. "In our pharmacy, vancomycin costs $18 per capsule," noted Dr. Bessesen, chief of infectious diseases at the Denver VA Medical Center.

Vancomycin remains the sole Food and Drug Administration–approved drug for CDAD, but metronidazole is recommended by so many textbooks and guidelines that its use can't be criticized, she continued.

The most common dose of vancomycin is 125 mg four times daily. The drug is safe for use in pregnancy and during breastfeeding. It's also well-tolerated when given long term, an important consideration in recurrent CDAD. In contrast, chronic use of metronidazole can result in neuropathy.

The natural history of CDAD is that 20% of patients will relapse after a first episode resolves. Retreatment with the same agent used in the initial episode will cure half of first-time relapsers; the other half will have a second relapse. Subsequent relapses are more difficult to manage. More than 60% of patients who have a third relapse will later have a fourth.

An oral vancomycin taper can be useful in managing multiple relapsers. It consists of 125 mg four times daily for 14 days, then 125 mg b.i.d. for 7 days, 125 mg once daily for 7 days, 125 mg once every other day for 8 days, and finally 125 mg once every 3 days for 15 days.

Two randomized clinical trials have shown a 50% reduction in the CDAD recurrence rate with the use of the probiotic *Saccharomyces boulardii*. It is widely used in Europe, where it has regulatory approval, but it is not FDA-approved. Cases of invasive disease have been associated with the probiotic, so Dr. Bessesen generally avoids the therapy in immunocompromised patients.

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DR. BESSESEN

Antibiotic resistance is not the cause of recurrent CDAD. Most patients are at home when they have a recurrence, so it's vital to minimize the risk of reinfection by instructing the family to decontaminate their home using a 10% bleach solution (1 cup of bleach in 1 gallon of water) to clean all hard surfaces.

Other agents with activity against *C. difficile* have limited roles. Nitazoxanide is similar in efficacy to metronidazole and is an alternative in cases of metronidazole intolerance. Rifaximin is approved for treating traveler's diarrhea and has been used for recurrent CDAD; it's not recommended as initial therapy because resistance emerges in a single-step mutation. "My personal experience with rifaximin has been less favorable than reported in case series in the literature," Dr. Bessesen noted. Tigecycline, described in a few case reports, is "an additional agent for desperate cases," she said. ■

Acute Abdomen May Be Symptom of C. difficile

BY BRUCE JANCIN

ESTES PARK, COLO. — One of the major diagnostic challenges in community-acquired *Clostridium difficile*–associated disease is that it can present without diarrhea or a history of recent antibiotic use—and with symptoms closely mimicking acute appendicitis.

"I have actually seen a patient go to appendectomy when in fact the problem was unrecognized community-acquired *C. difficile*–associated disease," Dr. Mary Bessesen said at a conference on internal medicine sponsored by the University of Colorado.

"*C. difficile* tends to preferentially involve the cecum, so patients can present with very typical right lower quadrant pain, tenderness, leukocytosis, and look for all the world like appendicitis," explained Dr. Bessesen, chief of infectious diseases at the Denver VA Medical Center.

Abdominal imaging is extremely useful in making the distinction in these patients without diarrhea.

This is a high-stakes diagnostic dilemma. Patients with community-acquired *C. difficile*–associated disease (CDAD) who present without diarrhea are at the severe end of the disease spectrum. Moreover, if they present with ileus they can't produce a specimen for diagnostic testing. "These are the most difficult and lethal cases because the CDAD is not recognized and the patients are so ill," she noted.

The ileus can range in severity from mild to toxic megacolon requiring surgery. Under the latter circumstances, rectal vancomycin can be colon-saving. It is given by inserting a Foley catheter into the rectum, inflating the balloon, instilling 500 mg of intravenous vancomycin in 100 cc of normal saline, then clamping the catheter. This is repeated every 6 hours.

The negative predictive value of most lab tests for *C. difficile* is so poor that often the best strategy when suspicion runs high is to treat empirically for the infection while waiting 5-7 days for the results of culture, the most sensitive test available.

Some encouraging recent developments in lab testing may make it possible to avoid empiric therapy. In a not-yet-published study, a *C. difficile* glutamate dehydrogenase assay had a sensitivity approaching that of culture (negative predictive value above 98%), and a turnaround time of an hour or less. And a commercially available *C. difficile* real-time PCR assay developed by BD GeneOhm had negative predictive values of 97% and 99% in two recent studies (J. Clin. Microbiol. 2009;47:373-8; J. Clin. Microbiol. 2009;47:1276-7).

"We haven't adopted the PCR assay at our hospital because it costs about $80. If the cost comes down it might become an excellent system," Dr. Bessesen said.

Postoperative Ileus Requires More Tests, Inflates Costs

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — Postoperative costs for patients who develop an ileus after colectomy are almost double those for patients without this complication, a retrospective study indicates.

"It's already established that a postoperative ileus increases length of stay, but the economic impact has been hard to quantify," Dr. Theodor Asgeirsson said at the annual meeting of the American Society of Colon and Rectal Surgeons.

In a review of 191 colectomies performed at the Ferguson Clinic in Grand Rapids, Mich., starting in July 2007, Dr. Asgeirsson and his colleagues found that postoperative ileus incidence was 26%, including 41 primary cases and 10 secondary cases. A primary postoperative ileus was defined as three episodes of emesis in 24 hours and/or insertion of a nasogastric tube during the index admission. A secondary ileus was associated with intra-abdominal complications. Nineteen patients in the primary ileus group and one in the secondary group required a nasogastric tube.

Development of an ileus affected slightly more than one-quarter of patients, and was associated with 39% of total care costs in the study, said Dr. Asgeirsson, a researcher at the clinic.

During index admissions, the total cost for patients with a postoperative ileus was $31,629 vs. $17,626 for those without this complication, a statistically significant difference. "Surprisingly, this was not significantly different for secondary postoperative ileus," Dr. Asgeirsson said.

The total readmission cost for postoperative ileus patients was $8,742 vs. $12,946 for non-ileus patients. Readmission for gastrointestinal failure, including nausea, vomiting, and/or poor oral intake, was also considered ileus, unless small bowel obstruction was identified. In contrast, non-ileus patients were readmitted for more serious adverse events, he said.

When asked whether total costs were higher only because patients with a postoperative ileus had longer stays, Dr. Asgeirsson said no. "When these patients get readmitted for a delayed postop ileus, the team usually wants to rule out the worst, such as anastomosis," he said. "We are doing a lot of diagnostic tests that increase costs." ■