C. Difficile May Underlie Diarrhea in Women

BY DIANA MAHONEY
New England Bureau

TORONTO — Think *C. difficile* when evaluating severe or ongoing diarrhea in previously healthy young women, said Dr. Judith O'Donnell at the annual meeting of the Infectious Diseases Society of America.

Although healthy women of reproductive age in the community have traditionally been considered at low risk for infection with the *Clostridium difficile* bacteria, recent data from a Philadelphia hospital suggest a shifting epidemiology for *C. difficile*–associated disease.

From January to June of 2006, six otherwise healthy women between the ages of 18 and 47 were admitted to Hahnemann University Hospital for treatment of severe *C. difficile* infections. Of the six, three were pregnant, one had given birth three weeks before treatment, and two had recently undergone elective hysterectomies, said Dr. O'Donnell of Drexel University in Philadelphia. All of the women had taken antibiotics in the months before developing *C. difficile* infections, although in some cases, the antibiotic use was limited, she said.

The two women who underwent hysterectomy received two doses each of perioperative antibiotics. Two of the pregnant women had received outpatient antibiotic treatment for bacterial vaginosis and one received a single antibiotic dose following laparoscopic cholecystectomy. And the woman who had recently given birth was admitted for diarrheal disease 3 weeks after a caesarean delivery.

The absence of a common risk factor for infection suggests "these women likely contracted their infections outside of the hospital setting," said Dr. O'Donnell. The severity of disease they experienced suggests their infections were caused by a newer, hypervirulent strain of *C. difficile*.

Five of the six women had evidence of severe diffuse colitis on abdominal CT scans, and two of the six developed sepsis requiring treatment in the intensive care unit. One of the two women treated for sepsis died of complications from *C. difficile*–associated disease after undergoing a total colectomy, subsequent resection of a large portion of ileum when the sepsis did not resolve, and 14 days of intensive antibiotic therapy with intravenous metronidazole and oral and rectal vancomycin. The second septic patient responded to continuous colonic vancomycin infusion.

The remaining four patients responded to dual antibiotic therapy, "although two were subsequently diagnosed with a recurrence of *C. difficile* [infection], and one required a second hospitalization," she said.

Physicians treating women should be cognizant of the possibility of community-acquired *C. difficile* infection in this population, she said. Those providing obstetric and gynecologic care "should be thinking about this because it's not something they've seen very often, especially in pregnant patients." Dr. O'Donnell said she had no financial conflicts of interest related to the presentation. ■

Vancomycin Beats Metronidazole For Severe C. Difficile *Infection*

BY DIANA MAHONEY
New England Bureau

TORONTO — Vancomycin is a better first-line treatment for severe cases of diarrhea caused by *Clostridium difficile* infection than metronidazole, Dr. Melinda B. Davis said at the annual meeting of the Infectious Diseases Society of America.

In a prospective, placebo-controlled trial designed to compare the efficacy of vancomycin and metronidazole (Flagyl) for the treatment of *C. difficile*–associated diarrhea, 172 patients who tested positive for the *C. difficile* toxin A or B in the stool and had three or more loose stools per day or who had pseudomembranous colitis on endoscopy were randomized to receive 125 mg of liquid vancomycin and a placebo tablet or a 250-mg tablet of metronidazole and a placebo liquid for 10 days.

The cure rate in 31 patients with severe diarrhea in the vancomycin group was 97%, compared with 76% of the 38 patients in the metronidazole group.

After randomization, 22 patients were withdrawn from the study because of noncompliance, intolerance, loss to follow-up, or death before day 3 of therapy. Of the remaining 150 patients, 71 were in the vancomycin group and 79 were in the metronidazole group.

Patients were categorized with severe *C. difficile*–associated diarrhea if they had endoscopy-proven pseudomembranous colitis, if they required treatment in the intensive care unit, or if they had two of the following: fever, elevated white blood cell count, low albumin, or age older than 60 years. Diarrheal disease that did not meet these criteria was classified as mild.

The cure rate in the 31 patients with severe diarrhea in the vancomycin group was 97%, compared with 76% for the 38 patients with severe diarrhea in the metronidazole group, said Dr. Davis of the University of Illinois at Chicago. In those with mild diarrhea, including 40 patients on vancomycin and 41 on metronidazole, cure rates were similar, 98% and 90%, respectively. Patients were considered cured if the diarrhea resolved within 6 days of treatment initiation and if the resolution was sustained through day 10.

In severe and mild disease, relapse rates were higher among patients treated with metronidazole compared with those treated with vancomycin. The rate of disease recurrence within 21 days of successful treatment completion in those with severe disease was 10% in the vancomycin group and 21% in the metronidazole group. For those with mild disease, 5% of those on vancomycin and 8% of those on metronidazole relapsed.

Dr. Davis reported no financial disclosures with respect to her presentation. ■

Antihistamines, Decongestants of No Help in Otitis Media With Effusion

Antihistamines and/or decongestants have no benefit for children who have otitis media with effusion, a Cochrane review of medical literature has concluded.

In fact, children who used them experienced an 11% spike in side effects such as gastrointestinal upset and drowsiness, compared with those who did not use them.

"Because we found no benefit for any of the studied interventions for any of the outcomes measured, and we found harm from the side effects of the interventions, we recommend practitioners not use antihistamines, decongestants, or antihistamine/decongestant combinations to treat otitis media with effusion in children," wrote the researchers, led by Dr. Glenn Griffin of Quinte West Medical Center in Trenton, Ont. They noted that the findings mirror the current joint guidelines on the management of otitis media with effusion (OME) from the American Academy of Family Physicians, the American Academy of Otolaryngology–Head and Neck Surgery, and the American Academy of Pediatrics (Pediatrics 2004;113:1412-29).

Dr. Griffin and his associates studied 15 randomized, controlled trials of 1,516 children with OME that compared antihistamines, decongestants, or a combination of the two and that appeared in the medical literature through March 2006. Studies that randomized children based on acute otitis media were not included in the analysis (Cochrane Database Syst Rev. 2006;[4]:CD003423). The researchers found no benefit of taking decongestants alone or in combination with antihistamines in terms of being cured within 1 month, lessening hearing loss, risk of OME recurrence, development of otitis media, and the need for tympanostomy.

Six studies in the analysis measured side effects of medications. In these, 17% of children who received decongestants alone or in combination with antihistamines suffered side effects such as gastrointestinal upset and drowsiness, compared with 6% of children who took placebo, a difference of 11%. The researchers estimated that for every nine children treated with the drugs, one would be harmed.

Dr. Griffin and his associates acknowledged that a key limitation of the review was the small number of studies found. "However, we were unlikely to miss studies given our comprehensive search, and we found many more than the previous systematic review on this topic," they wrote.

—Doug Brunk

Bilateral Infections, History Flag Those At Risk for Hard-to-Treat Otitis Media

SAN FRANCISCO — Several factors can help guide empiric therapy for acute otitis media by flagging patients at higher risk for infection with multiple organisms or resistant organisms, Dr. Mendel E. Singer said in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Patients with bilateral infection, those with a history of acute otitis media, or patients infected in the fourth quarter of the year may warrant high-dose aminopenicillin therapy rather than low doses, said Dr. Singer, an epidemiologist at Case Western Reserve University, Cleveland.

He and associates retrospectively analyzed pooled data from 14 studies of patients aged 3-36 months treated at Soroka University Medical Center, Beer Sheva, Israel, for acute otitis media from 1994 to 2004. In 967 patients, 23% were infected with multiple pathogens. Of the 63% of patients with bilateral ear infections, 53% were more likely to have multiple pathogens than were those with unilateral infections, he said at the meeting, sponsored by the American Society for Microbiology.

Analysis of drug resistance in a subset of 333 patients infected with *Streptococcus pneumoniae* found that 33% had organisms resistant to the treatment drug. Data showed high rates of resistance to trimethoprim-sulfamethoxazole (in 67% of patients treated with these drugs) and to the cephalosporins cefdinir, cefaclor, or cefuroxime (in 59% of patients treated with these). There was moderate resistance to azithromycin (in 23%) and to low-dose regimens of the aminopenicillins amoxicillin or amoxicillin clavulanate (in 16% of patients given these drugs). Only 1% of isolates treated with high-dose aminopenicillins were resistant to therapy.

S. pneumoniae was 32% more likely to be drug-resistant in girls than in boys. A history of prior acute otitis media nearly tripled the risk for resistant *S. pneumoniae.* Infection in the fourth quarter of the year doubled the risk for resistance.

The data suggest that patients with any of these risk factors might best be treated empirically with high-dose amoxicillin or amoxicillin-clavulanate, Dr. Singer said. Patients without these characteristics may respond sufficiently to low doses of these drugs or to treatment with the other medications used in the study. Dr. Singer has no affiliations with the companies that market the drugs discussed.

—Sherry Boschert