CDI Severity Rising

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also associated with a higher mortality rate.

"The goal of the new guideline is to develop a better strategy for initially diagnosing the disease, and also a better management strategy in order to prevent the severe complications of CD that we're seeing," said Dr. Fishman, director of health care epidemiology and infection control and also of the Antimicrobial Management Program for the University of Pennsylvania Health System, Philadelphia.

The document defines a case of CDI by the presence of symptoms (usually diarrhea) and either a stool test that is positive for *C. difficile* toxins or toxigenic *C. difficile*, or colonoscopic or histopathologic findings that reveal pseudomembranous colitis. Severe CDI is defined as leukocytosis with a white blood cell count of at least 15,000 cells/mcL, or a serum creatinine level at least 1.5 times the premorbid level.

The first main section addresses epidemiology, with guidelines regarding the minimum data that should be collected for surveillance purposes and how the data should be reported. To increase comparability between clinical settings, case definitions should be used for health care facility (HCF)–onset, HCF-associated, and community-associated CDI.

Standardized reporting is needed to better track the disease, coauthor Dr. Stuart B. Johnson said in a separate interview at the meeting. "We emphasized standard reporting data so we can compare rates between hospitals. Right now everyone does it a little differently," said Dr. Johnson of Loyola University, Maywood, Ill.

A second section on diagnosis outlines the best testing strategy for diagnosing CDI in the clinical laboratory, along with additional options. Enzyme immunoassay (EIA), currently the most common testing method used in U.S. hospitals, is rapid but not very sensitive—75% at best—and therefore is "a suboptimal alternative" for diagnosis. Polymerase chain reaction testing appears to be a more rapid, sensitive, and specific test, but more data are needed before it can be recommended for routine testing, the document said.

"Most hospitals are using EIAs for toxin testing, but more and more data are showing these to be very insensitive. If you use it, you're going to miss cases," Dr. Johnson said in the interview. PCR "is probably going to take over EIA testing, but we need more data, so we weren't able to make a firm recommendation."

Testing of stool from asymptomatic patients is not recommended, including as a test of cure, nor is repeat testing of the same episode of diarrhea.

The panel's recommendation to use vancomycin instead of metronidazole is a key element of the new guidelines, Dr. Fishman said. "In the past, the standard therapy for CD has been metronidazole. But … in cases of severe disease, it is more appropriate to use oral vancomycin. That is one of the major significant differences [from the 1995] guidelines." However, Dr. Johnson noted, many hospitals continue to use metronidazole inappropriately for severe cases.

The recommendation for an initial episode of mild to moderate CDI is 500 mg metronidazole orally 3 times per day for 10-14 days. For an initial episode of severe CDI, 125 mg vancomycin should be given orally 4 times a day for 10-14 days. Treatment of the first recurrence is usually with the same regimen as the initial episode but should be stratified by disease severity. Metronidazole should not be used beyond the first recurrence or for long-term chronic therapy because of the risk of cumulative neurotoxicity.

The document's infection control and prevention guidelines address the most important measures to implement in the hospital during CDI outbreaks, including those for health care workers, patients, and visitors; environmental cleaning and disinfection; antimicrobial use restrictions; and the use of probiotics, which are not recommended due to limited data.

Implementation of the guidelines can be influenced by the size of the institution and by the financial resources and laboratory capacity available in the particular clinical setting. ■

Disclosures: *Dr. Fishman had no relevant financial disclosures. Dr. Johnson reported that he has served as an adviser to Genzyme, Viropharma, Salix Pharmaceutical, Romark Laboratories, and Acambis. Five of the other guideline coauthors reported similar disclosures, while two reported having none.*

MY TAKE

C. difficile Remains a Moving Target

C. difficile infection is a common clinical problem for hospitalists. It is notable that more severe strains of CDI are being detected, and that we now have new treatment guidelines that are based on the severity of the presenting illness. In the past, oral vancomycin was typically used only if metronidazole therapy failed, but oral vancomycin is now the standard for severe CDI.

Hospitalists also should be aware that ELISA toxin assays can be falsely negative, and that symptomatic patients may deserve treatment regardless of a "negative" test for CDI.

Overall, hospitalists should expect further changes in CDI over time. We must remain vigilant to new recommendations and guidelines regarding this common and potentially deadly disease.

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C. difficile *Infection Surpasses MRSA in Community Hospitals*

BY MIRIAM E. TUCKER

ATLANTA — Hospital-onset *Clostridium difficile* infection was more common than infection due to methicillin-resistant *Staphylococcus aureus* in a study of 28 community hospitals.

The finding comes from an analysis of data from the Duke Infection Control Outreach Network. The analysis also showed that health care–associated *C. difficile* infection (CDI) occurs approximately as often as health care–associated bloodstream infections or combined device-related infections, Dr. Becky Miller reported at the 2010 International Decennial Conference on Healthcare-Associated Infections.

Many infection control initiatives have targeted methicillin-resistant *Staphylococcus aureus* (MRSA) and have not been aimed at CDI. Also, most of the previous studies on health care–associated infections were done at large tertiary care facilities rather than smaller community hospitals where most U.S. patients receive care. "We feel that studies done in community hospitals are relevant from an epidemiologic standpoint," said Dr. Miller, an infectious disease fellow at Duke University, Chapel Hill, N.C.

In an analysis of more than 3 million patient-days during the 24-month period from Jan. 1, 2008, through Dec. 31, 2009, there were 847 cases of hospital-onset, health care facility–associated CDIs and 680 cases due to MRSA. (For brevity, Dr. Miller referred to these as nosocomial infections during her presentation.)

There were 838 cases of hospitalwide bloodstream infection, 251 cases of ICU catheter-associated bloodstream infections, 132 cases of ICU ventilator-associated pneumonia, and 298 cases of ICU catheter-associated urinary tract infection.

The rate of nosocomial CDI was 0.28/1,000 patient-days, while the rate of nosocomial infection due to MRSA was 0.23/1,000 patient-days and the rate of hospitalwide bloodstream infections was 0.28/1,000 patient-days. The rate of nosocomial CDI was about 25% higher than the rate of such infections due to MRSA, and about 25% higher than the rate of combined ICU device-related infections. The CDI rate also was about as common as hospitalwide nosocomial bloodstream infections, Dr. Miller reported.

In an interview, Dr. Miller said MRSA declined steadily during the 5-year period from 2005 through 2009, while CDI declined initially until 2007, then rose and surpassed MRSA in 2009. "Development of effective prevention strategies for this emerging infection is needed," she said. ■

Disclosures: *Dr. Miller stated that she had nothing to disclose.*

Infusion May Help Prevent Recurrence of *C. difficile*

BY MICHELE G. SULLIVAN

A fully humanized monoclonal antibody infusion given along with antibiotics decreased the rate of recurrent *Clostridium difficile* infections by 72%, compared with placebo in a phase II trial.

The active infusion, which contained antibodies against *C. difficile* toxins A and B, was significantly better than placebo regardless of whether patients had experienced one or multiple previous infections and regardless of whether they were infected with the epidemic or nonepidemic strain, Dr. Israel Lowy and his colleagues reported (N. Engl. J. Med. 2010;362:197-205).

The placebo-controlled, randomized trial included 200 patients who had experienced diarrhea associated with a positive *C. difficile* stool test within 14 days of enrollment. All were taking either metronidazole or vancomycin at baseline. Their mean age was 63 years, although the range was wide (20-101 years), said Dr. Lowy, senior director of clinical science and infectious disease at Medarex, the company developing the antibody, and his colleagues.

Patients in the active group received a 2-hour infusion of 200 mL normal saline containing 10 mg of *C. difficile* antibody CDA1 and 10 mg of antibody CDB1 per kilogram of body weight. Patients in the placebo group received an infusion of 200 mL normal saline.

The patients recorded their stool count daily over the 84-day study. The primary end point was lab-confirmed recurrence of *C. difficile* infection. Secondary end points included the days until resolution of the initial infection, severity of the initial infection, and antibiotic failure.

Recurrence of infection occurred in significantly fewer patients in the active group than in the placebo group (7% vs. 25%). Recurrent diarrhea also occurred in significantly fewer patients in the active group (28% vs. 50%).

The antibody infusion did not significantly affect the severity of diarrhea during the initial episode, nor the number of days until the initial episode resolved. It also had no significant effect on antibiotic failure. ■

Disclosures: *The study was sponsored by Medarex and MassBioLogics. Dr. Lowy is a patent holder of the antibody infusion. Dr. Lowy and several coauthors are Medarex employees and coinventors of the infusion. One coauthor received research funds from MassBioLogics.*