

THE EFFECTIVE PHYSICIAN

Clostridium difficile Infection

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Clostridium difficile is the most common identified cause of infectious diarrhea in health care settings and causes 20%-30% of antibiotic-associated diarrhea. The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America recently published an updated guideline to improve the diagnosis and management of this common and costly nosocomial condition.

Conclusions

C. difficile infection (CDI) has been a common comorbidity in hospital and residential care patients for decades, but the incidence and virulence have increased with the emergence of the NAP1/B1/027 strain as a common entity in Canada and the United States since 2001. This strain has been associated with infection in patients considered "at risk" as well as in nontraditional risk groups, including healthy peripartum women and community-dwelling individuals without recent health care contact.

Risk factors for *C. difficile* disease include age over 64 years, prolonged hospitalization, exposure to antimicrobials (multiple antibiotics and longer courses increase risk), cancer chemotherapy, HIV infection, and gastrointestinal tract procedures.

In a recent study, more than 85% of patients with CDI had received antibiotics in the 28 days prior to illness.

Toxigenic culture is the most sensitive test to diagnose *C. difficile* colitis, but the requisite delay for this method makes the best diagnostic strategy uncertain. The combination of clinical criteria plus a cell cytotoxin assay is most useful in clinical management, and culture and typing are useful for epidemiologic study.

Expert opinion supports patient age, serum creatinine level, and white blood cell count to stratify the severity of CDI.

C. difficile spores are highly resistant to killing by alcohol. There are conflicting data on the effects of chlorhexidine hand wash vs. soap on *C. difficile* hand carriage.

Implementation

Chlorine-based (or other sporicidal) cleaners are recommended for decontamination of areas with elevated CDI rates; however, routine environmental screening is not recommended.

Minimizing the frequency, duration, and number of antibiotics prescribed is important to reduce the risk of CDI. Antimicrobial stewardship, specifically reduction in clindamycin and cephalosporin use, may help reduce the number of *C. difficile* infections. Although fluoroquinolone use is associated with NAP1/B1/027 *C. difficile* infection, there is insufficient evidence to recommend restriction of specific drugs within this class or this class of antibiotics.

Probiotics are not recommended for prevention of primary *C. difficile* infection.

Empiric treatment without testing (where testing is available) is not recommended, since only about 30% of hospitalized patients with antibiotic-associated diarrhea will have CDI. Testing for *C. difficile* (culture or toxin assay) should be performed only on diarrheal stool unless an ileus due to *C. difficile* is suspected. Repeated *C. difficile* testing during the

same diarrheal illness is not recommended.

Strict hand hygiene, gloves, gowns, and contact precautions in a private room are recommended for the duration of diarrhea in patients with CDI.

Initiation of empiric treatment for CDI pending stool toxin assay is appropriate when severe or complicated colitis is suspected. Treatment must be individualized in cases in which the stool toxin assay is negative.

Antibiotics associated with the development of CDI should be discontinued as soon as possible because their continuation may increase the risk of recurrence. Antiperistaltic medications should be avoided if possible.

Metronidazole (500 mg orally three times daily) is recommended for the initial episode of mild or moderate CDI; vancomycin (125 mg orally four times daily) is recommended for an initial severe episode. Treatment duration should be 10-14 days. CDI complicated by hypotension, ileus, or megacolon should be treated with high-dose vancomycin orally (and rectally as a retention enema in patients with an ileus) with or without intravenous metronidazole.

Subtotal colectomy with preservation of the rectum should be considered for severely ill patients with megacolon, sepsis, or bowel perforation. Serum lactate and leukocyte counts can be useful in stratifying the decision for surgery.

Based on historical data, up to 25% of patients treated for CDI have at least one recurrent episode; this rate is higher in patients over 65 years treated with metronidazole. Treatment of first recurrence of CDI usually is with the same agent as the initial episode; however, management based on disease severity should be stratified as for the initial episode.

Metronidazole should not be used beyond the initial recurrence or for long-term therapy. Second or later recurrences should be treated with vancomycin using a tapered or pulsed schedule.

Reference

Cohen S.H., et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). Infect. Control Hosp. Epidemiol. 2010;31:431-55.



DR. GOLDEN (left) is professor of medicine and public health and DR. HOPKINS is program director for the internal medicine/pediatrics combined residency program at the University of Arkansas, Little Rock. Write to Dr. Golden and Dr. Hopkins at our editorial offices or imnews@elsevier.com.

Hepatic Encephalopathy Diagnostic Test Effective

BY BRUCE JANCIN

FROM THE ANNUAL INTERNATIONAL LIVER CONGRESS

VIENNA — The same brief, Web-based neuropsychologic test used by all National Football League teams to assess players for the effects of concussion appears to be advantageous for the diagnosis of minimal hepatic encephalopathy.

The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT v4.0) is a well-validated, computer-based neuropsychologic test that takes about 10 minutes. It's available in 13 languages, can be administered by anybody in the office, and produces immediate results without need of a clinical neuropsychologist to interpret the scores, Dr. Michel H. Mendler explained at the congress, sponsored by the European Association for the Study of the Liver.

"ImPACT could become a new standard for minimal hepatic encephalopathy testing, both in routine clinical practice and to evaluate treatments," said Dr. Mendler, a gastroenterologist at Loma Linda (Calif.) University.

Minimal hepatic encephalopathy (MHE) is a greatly underdiagnosed neurocognitive disorder present in 60%-80% of patients with cirrhosis. It results in impaired quality of life, increased work disability, and impaired driving. If unchecked, MHE can progress to overt hepatic encephalopathy, a more serious neuropsychiatric syndrome characterized by cognitive and motor deficits that often require hospitalization.

MHE includes deficits in mental processing speed, fine motor skills, memory, complex attention, constructive abilities, and visual-spatial orientation. These deficits are subtle and require neuropsychologic testing for diagnosis.

Conventional neuropsychologic testing is complex, lengthy, and requires interpretation by a specialist Dr. Mendler said. A widely used alternative is paper-and-pencil testing using several psychometric tests, such as Digit Symbol and Number Connection tests A and B. But the results of these tests are confounded by the substantial practice effect with repeated testing.

In contrast, ImPACT (www.impacttest.com), which was developed by neuroscientists at the

University of Pittsburgh, generates an unlimited number of alternate forms, avoiding the practice effect, Dr. Mendler said.

He compared ImPACT with paper-and-pencil testing in 90 cirrhotic patients with no history of overt hepatic encephalopathy and 131 matched healthy controls. ImPACT scores identified 25 of 90 cirrhosis patients as having abnormal results consistent with MHE; paper-and-pencil testing identified 16, only 10 of whom were also ImPACT-positive.



Cognitive impairment is cumulative with the number of acute episodes of overt hepatic encephalopathy.

DR. SANYAL

In addition, ImPACT identified 12 of 74 paper-and-pencil test-negative patients as having MHE. Seven of 131 healthy controls were ImPACT-positive, a significantly lower false-positive rate than with paper-and-pencil testing, which was positive in 19 controls.

In a separate study presented at the congress, Dr. Arun Sanyal reported that the severity of chronic cognitive impairment is cumulative with the number of acute episodes of overt hepatic encephalopathy (OHE), underscoring the importance of early detection, prompt treatment, and preventive therapy.

Fifty cirrhosis patients were followed for a mean of 13 months after their first hospitalization for OHE. The severity of their deficits in working memory, attention, psychomotor speed, and response inhibition was highly correlated with the number of OHE episodes.

The implication is that the metabolic derangements that cause OHE might also induce chronic neurologic injuries that aren't readily reversible, according to Dr. Sanyal, professor of medicine and chairman of the division of gastroenterology, hepatology, and nutrition at Virginia Commonwealth University, Richmond. ■

Disclosures: Dr. Mendler's study was funded by a research grant from Salix Pharmaceuticals Ltd. He has no other financial relationship with the company nor any financial interest in the ImPACT test. Dr. Sanyal is a consultant to Salix.