INFECTIONOUS DISEASES

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BOSTON – Single-dose intravenous immunoglobulin may be an effective adjunctive therapy for patients with severe C. difficile colitis without evidence of rectal involvement.

BY DIANA MAHONEY

In a review of 15 patients with C. difficile colitis who were unresponsive to standard therapy with metronidazole, vancomycin, and/or other agents, adjunctive treatment with a single dose of intravenous immunoglobulin (IV Ig) led to clinical remission in 87% of the cases, reported lead investigator Dr. Benvenido G. Yangco of the Infectious Disease Research Institute in Tampa.

“Thirteen of the 15 patients had improvement or resolution of diarrhea, fever, and leukocytosis and were eventually discharged from the hospital,” he said. “One patient who demonstrated initial improvement was readmitted to the hospital 1 month later for recurrent C. difficile diarrhea. After the third dose of IV Ig, the remaining 11 patients who had a repeat C. difficile toxin test remained negative after IV Ig and have maintained clinical improvement to date.”

The patients included in this review were treated between January 2009 and July 2010 and were C. difficile cytotoxin positive with diarrhea, abdominal pain, distention, fever, leukocytosis, radiographic or colonoscopic evidence of colitis, and persistent or recurrent clinical manifestations despite receiving metronidazole (12 patients), vancomycin (13 patients), nitazoxanide (13 patients), and probiotics (9 patients), Dr. Yangco explained. The patients’ mean age was 77 years.

Of the 15 patients, 2 received a single IV Ig dose of 200 mg/kg/dose, two a single 400 mg/kg dose. Among the patients receiving the higher dose, two underwent colectomy. One of these patients, whose colectomy was related to colorectal cancer, had resolution of C. difficile, and the other patient died, Dr. Yangco reported. The authors found that patients had adverse effects from the IV Ig treatment.

The findings are clinically relevant given the dramatic increases in the incidence and severity of C. difficile colitis in recent years and the substantial clinical outcomes observed with standard therapies, despite the relative nonexistence of C. difficile resistance to these drugs in vitro, he said. Dr. Yangco attributed the clinical/microbiological discrepancy to low or waning antibody antibody levels in patients with C. difficile colitis.

Passive high-immunoglobulin therapy with IV Ig in patients who don’t respond to standard treatment has been used since 1991, and its efficacy has been reported in small case series and observational studies, no controlled trials of IV Ig therapy approval have been completed to date, said Dr. Yangco. “It should be noted that the IV Ig doses in the published studies vary from 200 to 1,250 mg/kg for 1-5 consecutive days or once every 3 weeks for 2-3 doses, and in those reports there was no standardized dose and no possible efficacy observed with IV Ig,” he said. “None of the published studies has discouraged its use.”

Although the findings of the current study are limited by the small number of patients and the retrospective design, the results of this study support the use of IV Ig for the treatment of severe, recurrent C. difficile “warrants further investigation in prospective, controlled studies,” Dr. Yangco stressed.

“IT is very likely that [the high cost of IV Ig is] an obstacle to its use—might be offset in these patients by the benefits associated with sustained clinical improvement, including shorter hospital stays and fewer readmissions.”