Intracolonic Vancomycin for Adjunctive Treatment of Severe *Clostridium difficile* Colitis: Indications and Precautions

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**ABSTRACT**

Treatment of severe *Clostridium difficile* colitis can be challenging. The most important first step in treatment is cessation of the inciting agent, most commonly via antibiotics, if this is deemed to be medically appropriate. For mild diseases, this is often sufficient for full recovery. For severe diseases, antimicrobial therapy directed against *C. difficile* is required. Oral metronidazole therapy for 10-14 days has been regarded as the first-line therapy, while oral vancomycin is recommended as the second-line therapy. Controlled trials are lacking for patients with fulminant colitis who may not tolerate oral therapy. Surgical intervention is indicated for patients who are not responding to medical treatment or when colonic perforation or toxic megacolon is suspected. For patients with severe *C. difficile* colitis who are not candidates for surgical intervention, administration of adjunctive intracolonic vancomycin has been used with success. We, herein, have summarized the evidence on indications and precautions of intracolonic vancomycin as an adjunctive treatment for severe *C. difficile* colitis. (*J Infect Dis Antimicrob Agents* 2005;22:21-6.)

**Clinical Scenario**

The patient was a 43-year-old Thai male, with a history of non-Hodgkin’s Lymphoma, with diffuse abdominal pain and a fever lasting four days. He had received chemotherapy (CHOP regimen) four weeks prior to admission. Upon admission, his temperature was 38.2°C, his blood pressure was at a level of 80/50 mmHg, his pulse rate was 128/min, and he had hypoactive bowel sound. Initial laboratory tests showed white blood cell counts of 22,500 cells/µL, blood urea nitrogen of 39 mg/dL (reference range, 10-20 mg/dL), and a creatinine of 2.1 mg/dL (reference range, 0.4-1.5 mg/dL). After fluid resuscitation, the patient was treated with intravenous cefoperazone-sulbactam for presumed sepsis and metronidazole for presumed *Clostridium difficile* colitis. The patient’s stool tested positive for *C. difficile* toxin by Bartels’ cytotoxicity assay. His hospital course was complicated by candidemia and hospital-acquired pneumonia. His abdominal computed tomography is shown in Figure 1.

The patient remained hypotensive and required vasopressure agents and ventilator support for the next...
five days. Flexible sigmoidoscopy revealed diffuse pseudomembranes, and antibiotics were changed to parenteral metronidazole, intracolonic vancomycin (ICV) (1 g administered rectally every 8 hours), intravenous ciprofloxacin and amphotericin B. After nine days of treatment, the patient showed continued clinical improvement, the fungemia was resolved and he was extubated. The dosage of intracolonic vancomycin was tapered to every 12 hours, while parenteral metronidazole was changed to oral metronidazole. He was discharged and continued on oral metronidazole for another two weeks. On follow-up, he was doing well without any evidence of ongoing infection or recurrence of disease.

INTRODUCTION

C. difficile colitis has been identified as a leading cause of nosocomial infectious diarrhea in adults. Nosocomial C. difficile infection is associated with significant increase in morbidity, mortality, length of hospital stay, and attributable costs.1-13 The spectrum of clinical presentations of C. difficile colitis varies from mild diarrhea to life-threatening pseudomembranous colitis (PMC) with toxic megacolon, diffuse ileus, and possible perforation. The natural history and factors contributing to the development of C. difficile colonization and diarrhea are summarized in Figure 2. In severe C. difficile diseases, treatment with standard oral or intravenous therapy has been limited by inadequate therapeutic intracolonic drug concentrations and ongoing toxin production.14-16 Although rarely reported, pancolectomy has been used as a surgical intervention for severe cases of C. difficile colitis.17-19-20 Several anecdotal reports suggest successful treatment of severe C. difficile colitis with adjunctive ICV.21-31 We have summarized the historical perspectives of adjunctive ICV, along with the clinical indicators and precautions of adjunctive ICV treatment for severe C. difficile colitis.
Historical Perspective on Adjunctive ICV Therapy

Adjunctive ICV was first recommended by George and colleagues for use in patients with ileus or toxic megacolon associated with *Clostridium difficile* toxin production. The first report of successful adjunctive ICV for *C. difficile* colitis was made by Griebie and Adams, in a patient who had severe ileus and colonic obstruction after head and neck surgery. Subsequent anecdotal reports and case series suggest that 20 of 24 (83.3%) episodes of *C. difficile* colitis have shown evidence of clinical benefit with adjunctive ICV. An our case report suggests that adjunctive ICV may be an effective alternative to pancolectomy in a patient with severe *C. difficile*-associated pancolitis.

Indications, Administration, Dosing and Duration

Current data suggest the use of ICV as an “ad-
junct” to the standard regimens for treatment of patients with persistent or severe *C. difficile* diarrheal disease or colitis. Potential adjunctive ICV candidates include patients with persistent infection (inadequate response to the standard regimens after several days), those with severe ileus resulting in cessation of diarrhea and impaired oral intake, and those with clinical progression to fulminant colitis. Among the reports in the literature, the administration of ICV has varied from instillation via an 18-French Foley catheter or soft 6-French pigtail catheter as a 60-minute retention enema, via enema or lavage rectum, colostomy or ileostomy, or to instillation during decompressive colonoscopy. As with most observational studies, the duration and dosing intervals of ICV have varied, although 2-3 g/day of ICV, with dosing intervals of 4-12 hours, appeared safe and effective in the majority of patients evaluated. The time to the clinical response has varied from 2 to 17 days.

**PRECAUTIONS**

The evidence to support the use of adjunctive ICV in patients with persistent or severe *C. difficile* colitis remains anecdotal. To date, no randomized controlled trials has compared adjunctive ICV with other enema formulations. The effectiveness of adjunctive ICV treatment for right-sided and transverse colitis is limited. While some reports have suggested successful treatment outcomes, Shetler and colleagues suggested failure of ICV treatment in these circumstances. Since oral administration of vancomycin for treatment of *C. difficile* colitis can lead to a significant serum level in the presence of renal failure, serum vancomycin monitoring seems prudent for patients with this clinical scenario. Notably, adjunctive ICV has not been associated with the acquisition of the enteric vancomycin-resistant enterococci (VRE). Nevertheless, the attributable risks of bacteremia associated with ICV therapy and treatment impact on VRE colonization could not be determined from that study.

**CONCLUSION**

Existing evidence suggests the use of ICV as an “adjunct” to the standard regimens in selected patients with persistent or severe *C. difficile* colitis. Until additional data are available, clinicians should carefully select dosing intervals and durations of treatment that are tailored to the particular patient. Further studies are needed to delineate the role of ICV.

**References**

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