Decompressive colonoscopy with intracolonic vancomycin administration for the treatment of severe pseudomembranous colitis

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Abstract

Background: We explored the potential of early decompressive colonoscopy with intracolonic vancomycin administration as an adjunctive therapy for severe pseudomembranous *Clostridium difficile* colitis with ileus and toxic megacolon.
Methods: We reviewed the symptoms, signs, laboratory tests, radiographic findings, and outcomes from the medical records of seven patients who experienced eight episodes of severe pseudomembranous colitis with ileus and toxic megacolon. All seven patients underwent decompressive colonoscopy with intracolonic perfusion of vancomycin.
Results: Fever, abdominal pain, diarrhea, abdominal distention, and tenderness were present in all patients. Five of seven patients were comatose, obtunded, or confused, and six of the seven required ventilatory support. The white blood cell count was greater than 16,000 in seven cases (six patients). Colonoscopy showed left-side pseudomembranous colitis in one patient, right-side colitis in one patient, and diffuse pseudomembranous pancolitis in five patients. Two patients were discharged with improvement. Five patients had numerous medical problems leading to their death. Complete resolution of pseudomembranous colitis occurred in four patients. One patient had a partial response, and two patients failed therapy.
Conclusion: Colonoscopic decompression and intracolonic vancomycin administration in the management of severe, acute, pseudomembranous colitis associated with ileus and toxic megacolon is feasible, safe, and effective in approximately 57% to 71% of cases.

Key words: *Clostridium difficile* colitis — Colonic inflammation — Colonoscopy — Ileus — Vancomycin

With the development and widespread use of antibiotics, *Clostridium difficile* infection with diarrhea and pseudomembranous colitis are increasingly encountered in everyday clinical practice [10]. Oral vancomycin or oral or intravenous metronidazole commonly is used for treatment of this disease, proving to be more than 85% effective [34]. Less frequently, the infection can result in fulminant colitis, toxic megacolon, sepsis, and death [30]. In such severe cases, aggressive medical therapy frequently fails end surgery is required [18, 20]. Oral administration of vancomycin frequently is unsuccessful for patients with severe disease and ileus because adequate intracolonic drug concentrations cannot be achieved [2]. To avoid this, vancomycin has been administered by enema or rectal lavage [1, 7, 27]. However, rectal administration of vancomycin may result in increased concentration of the drug over only a portion of the infected colon [2]. Similarly, because less than 15% of intravenous metronidazole is excreted by fecal route, the drug may not be effective for patients with ileus [11, 21] Fig. 1.

For severe cases of pseudomembranous colitis, aggressive medical therapy possibly can prevent surgical intervention or serve as an alternative if surgery carries a high risk [30]. Colonoscopic decompression and subsequent intracolonic vancomycin administration through a fenestrated tube allows drug delivery directly to the site of inflammation and may serve as an attractive alternative therapeutic option. In this article, we report the feasibility, safety, and efficacy of colonoscopic decompression and intracolonic vancomycin administration in the management of severe, acute, pseudomembranous colitis associated with ileus and toxic megacolon.

Patients and methods

Eight cases of severe, postantibiotic, pseudomembranous colitis with ileus and toxic megacolon were studied. The colitis was defined as severe according to findings of toxic megacolon and ileus on plain radiographs accompanied by signs and symptoms of severe toxicity (fever, chills, dehydration, acidemia, high white blood cell count (WBC), and impaired mental status). All the patients were men with a mean age of 70 years

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Fig. 1. Plain abdominal radiograph taken shortly after colonoscopic decompression with placement of a colonic, fenestrated tube for subsequent intracolonic administration of vancomycin.

(range, 63–79 years) who presented with diarrhea, abdominal distention, pain, fever, and leukocytosis. Their comorbid conditions are summarized in Table 1. Diarrhea was defined as a change in bowel habits leading to more than five loose movements per day. *C. difficile* and its toxin were assayed using the enzyme immunoassay (ETA) test [14]. Plain abdominal radiographs and computed tomography (CT) scans were performed for diagnosis and monitoring of the disease course [10]. All the patients were treated with intravenous metronidazole without significant improvement of the clinical picture. Emergency colonoscopy and decompression was performed without prior lavage preparation, using a standard videocolonoscope (Olympus Corporation, Lake Success, NY, USA) and intravenous sedation with midazolam/meperidine under continuous cardiorespiratory monitoring. Cecal intubation was successful, showing colitis with pseudomembranes in all the patients.

After decompression, a fenestrated tube (Wilson-Cook, Research Triangle, NC, USA) was positioned over a colonoscopically inserted guidewire, as previously described [29]. After radiologic confirmation of correct tube placement in the colon without evidence of perforation, the tube was perfused with vancomycin solution. The following protocol was followed: Vancomycin 1 g was dissolved in 1 l of sterile water. After this, 250 ml of this solution was administered through the colonic tube, which then was clamped for 3 h. This procedure was repeated every 6 h. The tube was connected to low intermittent suction for decompression between drug administrations. This therapy was continued until clinical improvement was achieved.

Resolution of pseudomembranous colitis was defined as complete if it was confirmed by autopsy or if the patients were discharged in good health with no clinical, radiographic, or laboratory findings of the disease. If patients had some decrease in WBC and no signs of ileus on plain radiographs or CT scan, but an abdomen that remained distended, the response was defined as partial. Nonresponders had minimal improvement or severe pancolitis on autopsy.

The specific details of the cases studies are delineated in the following sections.

Case 1

A 63-year-old Hispanic man was admitted because of acute renal failure, ascites and anasarca resulting from long-standing alcoholic cirrhosis, portal hypertension, and hepatic encephalopathy. At 2 weeks before admission, endoscopy showed an antral ulcer and *Helicobacter pylori* gastritis. Amoxicillin, clarithromycin, and lansoprazole were administered orally. In preparation for liver transplantation, therapy for ascites, renal failure, and encephalopathy was instituted. On the 16th hospital day, the patient became obtunded and leukocytosis developed (WBC, 21,000) with leftward shift. Intravenous piperacillin/tazobactam (Zosyn) was administered empirically. Two days later, abdominal pain, pronounced abdominal distention, and ileus had developed. The kidney and urinary bladder showed marked colonic and small intestinal dilation. Urgent colonoscopy showed diffuse pseudomembranous colitis. The EIA test results were positive for *C. difficile* toxin. A decompression tube was placed over a guidewire with its tip positioned in the hepatic flexure and perfused with vancomycin. Zosyn was discontinued, and intravenous metronidazole was initiated. The findings from colonic biopsies were consistent with pseudomembranous colitis. Within 48 h, the patient felt much improved. The ileus had resolved, and the WBC was 9,000. The colonic decompression tube was removed 6 days later. The next day, repeat colonoscopy showed partial resolution of the colitis. Oral vancomycin was continued.

The patient presented 2 weeks later with obtundation and septic shock resulting from abdominal panniculitis. Blood cultures were positive for *Pseudomonas aeruginosa.* Resuscitative efforts including pressors, broad-spectrum antibiotics, hemodialysis, and intravenous fluids failed to sustain him. Autopsy showed neither macroscopic nor histologic changes related to pseudomembranous colitis.

Case 2

A 65-year-old African American man was admitted because of jaundice, abdominal pain, and upper gastrointestinal bleeding. He had a long-standing history of alcoholism, with subsequent development of portal hypertension, splenomegaly, and esophageal varices. Endoscopy showed prominent esophageal varices that were bandligated. Intravenous octreotide and metoprolol were administered, and hemostasis was achieved. A fever to 39°C associated with bilaterally decreased breath sound developed, and bibasilar atelectasis was noted. *Klebsiella* was cultured from the sputum. Abdominal ultrasound showed ascites. Paracentesis showed ascitic fluid pleocytosis without microorganisms. Levofloxacin was initiated on hospital day 5.

On hospital day 7, tachypnea and acute ileus developed. A computed tomography (CT) scan of the abdomen showed colonic distention (cecal diameter, ~9 cm), minimal ascites, and pneumatosis intestinalis. The WBC was 10,800. Empirical intravenous Zosyn and metronidazole were administered. Urgent colonoscopy to the cecum showed pseudomembranous colitis with prominent features in the right colon. A decompression tube was placed over a guidewire with its tip positioned in the cecum and perfused with vancomycin over the ensuing 24 hours. Within 48 h the patient felt much improved. The ileus had resolved partially, and the WBC was 9,000. The EIA test results were negative for *C. difficile* toxin, and colonic biopsies showed nonspecific ulceration. Metronidazole was continued for 7 days, until complete clinical resolution.

Case 3

A 79-year-old white man was hospitalized because of worsening dyspnea and chest pain. He had a long-standing history of congestive heart failure, chronic obstructive pulmonary disease (COPD), renal insufficiency, and recurrent pneumonia. Empiric therapy with levofloxacin had been initiated 7 days before admission for clinically suspected pneumonia. Admission chest x-ray showed bibasilar pneumonia, bilateral pleural effusions, and emphysema. Intravenous Zosyn was substituted for levofloxacin.

On hospital day 9 the patient's respiratory status was improved. However, diarrhea, progressively severe abdominal distention, tenderness, and ileus developed. The WBC was 25,000, with leftward shift and toxic granulation. Abdominal radiographs showed colonic distention and wall thickening. Intravenous metronidazole and oral vancomycin were initiated. Emergency colonoscopy showed diffuse pseudomembranous colitis. The EIA test results were positive for *C. difficile* toxin. A decompression tube was placed over a guidewire with its tip positioned in the transverse colon

Table 1. Risk factors, comorbidity, and final outcome in the study population

	Cases							
	1	2	3	4	5	6	7	8
Alcoholic liver disease	+	+						
Renal insufficiency	Acute		Chronic	Chronic	Chronic			Chronic
Pneumonia		*Klebsiella*		*Klebsiella, Enterobacter cloaceae*	aspergillus			
Ascites	+	+		+				
Congestive heart failure			+	+				+
Chronic obstructive or restrictive pulmonary disease			+	+	+			+
Cellulitis								+
Corticosteroid use				+				+
Diabetes mellitus		+		+	+			+
Previous *C. difficile* colitis						+	+	
Sepsis	*Pseudomona aeruginosa*			*Staphylococcus fungus*				
Final outcome	Death	Recovery	Death	Death	Death	Recovery	Recovery	Death

and perfused with vancomycin. The cecum remained persistently distended. Despite intensive care efforts, progressive renal failure, acidosis, and refractory hypotension developed, and the patient died 15 h later without evidence of colonic perforation, as determined by radiologic criteria. No autopsy was performed.

Case 4

A 67-year-old white man was admitted because of congestive heart failure exacerbation, ascites, and anasarca. He had a long-standing history of restrictive lung disease, sleep apnea, atrial fibrillation, aortic valvular disease, alcoholism, and chronic renal insufficiency. Clinically, he was tachypneic and tachycardic, requiring ventilatory support. Chest x-ray showed pulmonary edema, bilateral pleural effusions, and left lower lobe consolidation. While the patient was under continuous respiratory support, staphylococcal bacteremia developed. His sputum cultures grew *Klebsiella* and *Enterobacter cloacae*. Intravenous vancomycin and ticarcillin/clavulanate (Timentin) were instituted.

Five days later, fever to 39°C, watery diarrhea, and marked abdominal distention had developed. Fungus was isolated from the blood. The WBC count was 50,300. Intravenous ceftazidime, fluconazole, and metronidazole were initiated. The patient developed progressive ileus and abdominal distention. Plain abdominal radiographs showed dilated colon to 10 cm with thickened haustrae. Urgent colonoscopy of the cecum showed pseudomembranous colitis with edema, friability, and exudation of mucopurulent material into the lumen. A decompression tube was placed over a guidewire with its tip positioned in the proximal transverse colon and perfused with vancomycin. Three days later, the WBC was 21,400, and an interval decompression of the transverse colon was noted by plain abdominal radiograph examination. Over the ensuing 3 days, the patient remained critically ill, febrile, and ventilator dependent. He died of aspiration pneumonia and heart failure. No autopsy was performed.

Case 5

A 74-year-old white man was admitted because of exacerbated chronic obstructive pulmonary disease and necrotizing pulmonary aspergillosis requiring ventilatory support and intravenous ceftriaxone. He had long-standing history of insulin-dependent diabetes, coronary artery disease, hypertension, and chronic renal insufficiency. Over the preceding 4 months he had suffered three episodes of *C. difficile* colitis that had responded well to intravenous metronidazole and oral vancomycin.

On admission, the patient exhibited low-grade fever, watery diarrhea, diffuse abdominal pain, distention, and tenderness. Intravenous metronidazole as well as oral vancomycin and rifampin were administered empirically. Ceftriaxone was discontinued. The WBC was 85,300, with leftward shift and toxic granulation. The EIA test results were positive for *C. difficile* toxin. Plain abdominal radiographs showed marked small intestinal dilation consistent with paralytic ileus. Abdominal CT scan showed diffuse colonic wall thickening and stranding of the pericolonic and mesenteric fat consistent with inflammation. Fluid also was noted tracking along the perihepatic space, Morison's pouch, and right paracolic gutter. Emergency colonoscopy showed diffuse pseudomembranous colitis. A decompression tube was placed over a guidewire with its tip positioned in the cecum and perfused with vancomycin. The findings from colonic biopsies were consistent with pseudomembranous colitis.

Over the ensuing 4 days, the patient improved slightly. On hospital day 4, his WBC count was 16,200. *Pseudomonas* and *Staphylococcus aureus* were cultured from his sputum, and intravenous ciprofloxacin and vancomycin were initiated. Nine days later, small bowel ileus still was present on abdominal radiographs. The decompression tube was expelled. Repeat colonoscopy showed 75% improvement of the colitis, although edema, friability, and focal pseudomembranes still were present. A decompression tube was placed again over a guidewire with its tip positioned in the cecum and perfused with vancomycin. Within 48 h, the patient felt much improved. The ileus had resolved, and the WBC had decreased to 12,500. Mild diarrhea persisted.

Despite intensive care efforts, respiratory failure developed, and the patient died 2 weeks later. Autopsy showed severe bronchopneumonia, emphysema, and severe atherosclerotic cardiovascular disease. There was no evidence of pseudomembranous colitis.

Case 6

A 74-year-old white man was admitted with a 3-week history of diarrhea, nausea, and crampy abdominal pain. These symptoms had begun 3 days after he was started on oral dicloxacillin subsequently to drainage of a sebaceous cyst. His medical history was significant for hypertension, recurrent urinary tract infections, and pseudomembrenous colitis. On admission, the patient was febrile and had a markedly distended and tender

abdomen. The WBC was 17,500, with leftward shift. Occult bleeding was noted on rectal examination. Plain abdominal films showed colonic distention to a diameter of 11 cm as well as bowel wall edema and thickening. The patient was started on oral and intravenous metronidazole. A rectal tube was placed for low intermittent suction and decompression.

One week later, the WBC was 16,000. Abdominal radiographs showed a decrease in colonic dilation and small bowel gas distention. Colonoscopy showed severe, left-side pseudomembranous colitis. A decompression tube was placed over a guidewire and perfused with vancomycin. Three days later, abdominal films showed effective colonic decompression with a maximal colonic diameter of 6 cm. The WBC was 12,000. Two days later, oral vancomycin was substituted for oral metronidazole, and the colonic tube was removed. One week later, repeat colonoscopy showed normal mucosa in the ascending colon and mild edema and areas of erythema in the sigmoid colon. The patient continued to have low-grade fever and diarrhea.

One week later, on hospital day 26, a chest x-ray showed right lower lobe pneumonia. Levofloxacin was administered. Ten days later, recurrent fever, diarrhea, and leukocytosis to 21,000 with leftward shift developed. Oral vancomycin was initiated empirically and continued for 2 weeks until resolution of the patient's symptoms. Oral lactobacillus acidophilus and yogurt were administered.

Case 7

A 74-year-old white man (same patient as case 6 after 2 months of good health) was admitted to the hospital with fever to 103°F and a distended, tender abdomen. His WBC was 23,000, with leftward shift. The EIA test results were positive for *C. difficile* toxin. Oral vancomycin and intravenous metronidazole were administered. Abdominal radiographs demonstrated marked gaseous distention of the colon (maximal diameter, 13 cm), thumb-printing, and thickening of the left colon wall. Emergent colonoscopy without bowel preparation showed pseudomembranous colitis with sigmoid colon dilation. A decompression tube was placed over a guidewire with its tip positioned in the descending colon and perfused with vancomycin. One day later, the colonic tube was ejected spontaneously, and the patient became more distended. Repeat colonoscopy showed left-side pseudomembranous colitis. The decompression tube was replaced and perfused with vancomycin. Within 48 h, the patient felt much improved. His ileus had resolved, and his WBC was 11,500. Two weeks later, the patient was discharged home, where he remained in good health.

Case 8

A 67-year-old white man was admitted with a 6-day history of watery and bloody diarrhea, dehydration, and diffuse crampy abdominal pain. Oral cefazolin had been initiated 1 week before admission for the treatment of pain and cellulitis in his left foot after an injury. The patient's medical history was significant for coronary artery disease, congestive heart failure, diabetes mellitus, restrictive lung disease, and renal insufficiency.

On admission, the patient presented with diffuse abdominal distention and tenderness, leukocytosis with leftward shift (WBC, 24,900 on admission and 41,500 on hospital day 2). A CT scan with contrast showed mild ascites and diffusely thickened colonic wall consistent with pancolitis. The ascending and rectosigmoid colon were most seriously affected, and the small bowel was mildly dilated. Emergency colonoscopy showed diffuse pseudomembranous colitis. A decompression tube was placed over a guidewire with its tip positioned in the transverse colon and perfused with vancomycin. Intravenous metronidazole and vancomycin were administered. After limited foot debridement, the patient's cellulitis was clinically improving. Four days later, he felt much improved. His WBC had decreased to 26,200. His abdomen was much less distended and mildly tender.

On hospital day 7, the patient became progressively lethargic, with development of rebound tenderness and worsening abdominal distention. Subtotal colectomy with a Hartman's pouch and ileostomy was performed. At 12 h after surgery, hypotension and hemodynamic instability had developed. Cardiopulmonary resuscitation was initiated, and repeat laparotomy was performed. Massive hemoperitoneum was noted secondary to a bleeding splenic artery, and the patient died. Pathology showed typical pseudomembranous colitis (summit lesion) without evidence of perforation.

Results

In four of the seven reported patients, pseudomembranous colitis developed while they were in the hospital. All the patients had a history of antibiotic use (cephalosporin, levofloxacine, amoxicillin, clarithromycin, ticarcillin, and dicloxacillin) within 2 to 3 weeks of presentation. In addition to antibiotic use, two of the seven patients were receiving concomitant corticosteroid therapy. The presenting symptoms and signs are shown in Table 2. Fever (>38°C) and diarrhea were manifested in four patients. The abdomen was distended and tender in all the patients. Five of the seven patients were obtunded, confused, or in coma, and six of the seven required tracheal intubation for mechanical ventilatory support.

Laboratory evaluation showed a WBC greater than 16,000 in seven cases (six patients). Only one patient had a WBC within the normal range throughout his disease course. Six of the patients had a positive EIA test result for *C. difficile.* Abdominal radiographs were performed for all the patients, and abdominal CT scan was performed for three patients. These imaging studies showed that megacolon was present in five patients, and that combined small and large bowel dilation and isolated small bowel dilation was present in two patients. Distended colon with thumb-printing was identified in one patient, with wall-thickening in three patients. The CT findings of pseudomembranous colitis included colonic wall-thickening, stranding of pericolic and mesenteric fat, and pneumatosis intestinalis. Colonoscopy showed left-side pseudomembranous colitis in one patient, right-side colitis in one patient and diffuse pseudomembranous pancolitis in five patients. Two patients were discharged with improvement, whereas five patients had numerous medical problems leading to their deaths.

Resolution of pseudomembranous colitis was considered complete in four patients (57%) who had complete resolution of pseudomembranous colitis by laboratory, radiographic, and clinical findings as well as by colonoscopy or autopsy. One patient (14%) had some features of pseudomembranous colitis and was defined as a partial responder. Two patients (29%) did not respond to therapy.

Discussion

This article describes the presentation, clinical evolution, and management of eight cases of fulminant pseudomembranous colitis with colonoscopic decompression and intracolonic vancomycin administration. The reported data suggest that this approach is feasible and safe in the management of severe, acute, pseudomembranous colitis associated with ileus and toxic megacolon. With a complete or partial success rate of 57% to 71%, this approach appears to be an important therapeutic alternative in the management of these severe cases.

C. difficile colitis after antibiotic therapy is increasingly common, accounting for most cases of nosocomial diarrhea [10]. Cephalosporins, penicillin, lincomycin, clindamycin, and ampicillin are most commonly involved, but virtually almost all antibiotics have been implicated [14, 22]. Although fulminant pseudomembranous colitis occurs in only 3% of patients, it leads to serious complications including

Table 2. Clinical features of patients with fulminant pseudomembranous colitis

					Cases			
	1	2	3	4	5	6	7	8
Age (years)/gender	63/male	65/male	79/male	67/male	74/male	74/male	74/male	67/male
Mental status	Obtunded	Coma	Obtunded	Obtunded	Obtunded	Normal	Normal	Normal
Symptoms/signs		Not obtainable						
Pain	+		+	+	+	+	+	+
Fever	−	+	−	+	+	+	+	−
Distention	+	+	+	+	+	+	+	+
Diarrhea	−	−	+	+	+	+	−	+
WBC count[a]	21,000	10,800	25,000	34,200	85,300	16,000	23,000	46,500
C. difficile toxin assay	+	−	+	+	+	−	+	+
Radiography	Marked colonic and small intestinal dilation	Small bowel and large bowel dilation	Colonic distention with air/fluid level and wall thickening	Colon dilated to 10 cm, thickened haustra	Marked small bowel dilation	Colonic distention to 11 cm, bowel wall edema and thickening	Colonic distention to 11 cm, thumb-printing and wall thickening	Mild dilation of small bowel, no evidence of colon dilation
CT scan	ND	Colonic distention (cecum ~9 cm), ascites, pneumatosis, intestinalis	ND	ND	Diffuse colonic wall thickening, mesenteric and pericolic fat stranding	ND	ND	Diffusely thickened colonic wall, ascites
Colonoscopy								
Pseudomembranes	Diffuse	Segmented (right colon)	Diffuse	Diffuse	Diffuse	Segmented (left colon)	Segmented (left colon)	Diffuse
Decompression	Hepatic flexure	Transverse colon	Transverse colon	Proximal transverse colon	Cecum	Transverse colon	Descending colon	Transverse colon
Treatment								
M IV	+	+	+	+	+	+	+	+
V PO	+	−	+	−	+	+	+	+
Response to treatment	Complete	Complete	No response	Partial	Complete	Complete	Complete	No response
Final outcome	Death	Recovery	Death	Death	Death	Recovery	Recovery	Death
Autopsy	No evidence of PMC	ND	ND	ND	No evidence of PMC	ND	ND	Severe PMC

[a] WBC was obtained at the time of decompressive colonoscopy before intracolonic vancomycin administration.
WBC, white blood cell count; CT, computed tomography; ND, not done; M, metronidazole; IV, intravenous; V, vancomycin; PO, orally; PMC, pseudomembranous colitis.

perforation, prolonged ileus, megacolon, and death, particularly in elderly and immunocompromised patients [30]. Risk factors for *C. difficile* colitis include old age, prolonged use of antibiotics, renal failure, obstructive pulmonary disease, and conditions that impair host-immune defenses, such as steroid use and diabetes [4, 16, 23]. Whereas increasing age has been recognized as one of the most important risk factors for the acquisition of *C. difficile,* preexisting renal disease, diabetes, steroid use, and prolonged hospital stay increase the risk of acquiring *C. difficile* colitis [16]. Renal disease in particular has been associated with increased mortality from *C. difficile* colitis [12]. Of the reported patients, 71% had acute or chronic renal insufficiency. The mortality of these patients was 100%. Diabetes was present in four of the seven patients (57%) and steroid use in two of the seven patients (28%), contributing to their immunocompromised state. Three of the seven patients (42%) had severe COPD, and one had restrictive lung disease (Table 1).

Pseudomembranous colitis can cause acute abdomen even in the absence of diarrhea. Recognition of pseudomembranous colitis in such patients by emergency colonoscopy with or without decompression and early initiation of intravenous metronidazole therapy against *C. difficile* may obviate the need for surgery and contribute to improved overall management [16, 33]. It has been shown that intravenous metronidazole (500 mg every 6 h) will result in therapeutic luminal concentrations in the inflamed colon [3]. However, metronidazole excretion takes place mainly in the upper part of the gastrointestinal tract, with approximately 14% of intravenous metronidazole being excreted in feces. Therefore, this regimen may not be effective for patients with ileus [15, 19, 21, 26]. Because of such unpredictable drug delivery in cases of ileus or toxic megacolon, intravenous metronidazole may be supplemented with vancomycin administered by nasogastric tube or enema [27]. Other alternatives include colostomy or ileostomy for direct instillation of medication [1].

Oral administration of vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis [9]. It is minimally absorbed and found in cecal concentrations of 427 mg/g (after a dose of 0.5 g) [11]. Unfortunately, this therapy is unsuccessful in patients with paralytic ileus. Because of the poor intestinal motility, an adequate intracolonic vancomycin concentration cannot be achieved [2]. Rectal vancomycin in conjunction with intravenous metronidazole has been proposed as an alternative regimen for patients unable to take oral medication [27]. When given intravenously, vancomycin is excreted in the urine (90%) and does not reach effective concentrations the bowel lumen [19]. Patients with severe ileus can be given vancomycin-retention enemas (500 mg of vancomycin in 100 ml of normal saline) [27]. However, vancomycin enema is effective only for treating left colon disease [2]. Five of the seven reported patients (71%) had pseudomembranous pancolitis, and one had right-side infection that would not have been treated adequately with rectal therapy alone.

Colonoscopic decompression with introduction of a fenestrated colonoscopic overtube transanaly during colonoscopy was found to be effective treatment for recurrent colonic distention [8]. In 1993, Pasic et al. [29] reported the use of an elastic pigtail catheter during diagnostic colonoscopy with subsequent intracolonic vancomycin to treat antibiotic-associated pseudomembranous colitis in a patient with paralytic ileus. This allows delivery of vancomycin in adequate amounts to the site of inflammation to inhibit *C. difficile.* These authors administered vancomycin an initial dose of 2 g directly into the colon, followed by a 100-mg dose every 6 h combined with an additional 100 mg after every watery stool, continuing such therapy for 7 to 14 days [28, 29]. Because of colonic inflammation and the potential for systemic absorption of vancomycin, intracolonic vancomycin dosage must be reduced in patients with renal and hepatic impairment to prevent serum concentrations exceeding 30 to 40 mg/l with consequent neurotoxicity and nephrotoxicity [28]. We used the same approach in treating our patients, dissolving 1 g of vancomycin in 1 l of sterile water and administering 250 ml of this solution through the colonic tube. Considering that a vancomycin concentration of 5 mg per 1 ml or less inhibits and destroys *C.difficile,* we thought that this was adequate, safe, and effective therapy [13, 19].

Even in the best medicosurgical milieu, the management of fulminant pseudomembranous colitis remains very challenging. Surgical intervention using subtotal colectomy with diverting ileostomy is generally considered when patients fail to respond to therapy in 48 to 72 h or exhibit signs of organ failure, a worsening CT scan, or signs of peritonitis [5, 20, 24, 25, 30, 32]. Prompt and timely colectomy is warranted and required in 65% to 100% of patients with fulminant disease. Overall mortality after surgical treatment ranges from 35% to 80%, reflecting the poor clinical condition of these patients at the time of emergency surgery [16, 18, 20, 24]. Mortality is highest in patients with fulminant colitis or perforation who are elderly, who have received immunosuppressives or antibiotics for more than 7 days, who have underlying malignancies, or who have a delay in the diagnosis [16, 24, 30]. Jobe at al. [16] found that the factor most associated with mortality was the length of the time from onset of symptoms to treatment, the delay being nearly 10.7 days for those who died of their disease, as compared with 5.4 days for survivors. At laparotomy, the external appearance of the colon often is deceptively normal or even thickened and should not influence the decision to perform subtotal colectomy to remove the septic focus [16, 20]. In the reported patients, surgical intervention was considered to have the highest risk because of their clinical state and comorbid medical conditions.

Bacteriological confirmation of *C. difficile* infection is not always feasible in cases of pseudomembranous colitis [31]. In this study, we encountered two cases in which repeat EIA testing to detect toxin A produced negative results at least twice, and the tissue culture assay for cytotoxin (toxin B) was not performed because it requires specialized referral laboratories. It is therefore possible that these cases were induced by toxin A–negative/toxin B–positive *C. difficile* strains recognized more recently [6, 17].

In terms of clinical response, we found that the most important and consistent sign predicting a favorable outcome in such severely ill patients was the WBC. With effective therapy, the WBC significantly decreased within 2 days and normalized within 7 to 10 days. Patients exhibiting a persistently elevated WBC (>20,000) either did not have

complete resolution of pseudomembranous colitis or had another source of infection/sepsis.

In conclusion, *C. difficile* colitis should be considered part of the differential diagnosis in any patient presenting with an acute abdomen or with diarrhea who has received prior antibiotics. Physicians should be able to recognize patients at risk and perform early colonoscopy, considering possible decompression/intracolonic vancomycin therapy. Such intervention is feasible, safe, and efficacious in 57% of cases. It remains the single best method for minimizing the morbidity and mortality of colectomy used to manage *C. difficile* colitis. However, the actual efficacy and safety of this approach could be addressed only by a randomized, controlled clinical trial.

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