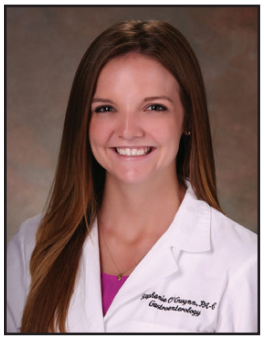
A Practical Approach to Managing Inpatient Acute Severe Ulcerative Colitis



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Hospitalized acute severe ulcerative colitis patients require a multidisciplinary team approach with a focus on early escalation of medical therapy and early surgical consultation. This review aims to provide a practical approach on the treatment of inpatient acute severe ulcerative colitis.

INTRODUCTION

Acute severe ulcerative colitis (UC) is a medical emergency requiring hospitalization and a multidisciplinary team approach involving a gastroenterologist and colorectal surgeon. North American UC cohort studies report that 18 to 25% of patients with UC will experience at least one flare requiring hospitalization.[1,2]

Severe UC is defined as having six or more bloody stools per day, tachycardia, fever, anemia (hemoglobin <10g/dL), and elevated erythrocyte sedimentation rate (ESR >30).[1]

Intravenous (IV) corticosteroids are the initial treatment for inpatient acute severe UC, however only two-thirds of patients will respond.[3] Predictors of nonresponse to IV corticosteroids are persistence of bloody stools and an elevated CRP on day 3 (≥8 stools/day or 3-8 stool/day plus CRP > 45 mg/L).[4] Up to 30% of patients admitted with an acute severe UC flare will require a colectomy. Early medical treatment and surgical consultation have been shown to decrease mortality rates in these patients.[3]

The purpose of this review is to provide a practical approach (Figure 1.) for the management of inpatient acute severe UC.

Day 1

On initial presentation, the patient should be hemodynamically resuscitated as appropriate.

1. *Stool Evaluation for Infectious Pathogens*

Patients should have stool samples assayed for Clostridium difficile (C. difficile) and cultured for bacterial pathogens. Patients with inflammatory bowel disease (IBD) concomitantly infected with C. difficile have longer hospitalizations, increase need for colectomy, and higher mortality rates.[5] The stool sample should be collected first, and if clinical suspicion for C. difficile infection is high, prophylactic oral

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vancomycin may be initiated. Oral vancomycin should be discontinued if C. difficile is negative. Routine use of antibiotics in the absence of infectious colitis is inappropriate.[6]

2. *Laboratory Evaluation*

On admission, labs should include complete blood count (CBC), basic metabolic panel (BMP), and albumin. C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) should be ordered to assess disease severity. Some patients may have a normal CRP despite having severe inflammation on endoscopy.

In preparation for possible biologic therapy, one should test for tuberculosis (QuantiFERON-TB Gold and chest x-ray), hepatitis B (hepatitis B surface antigen, hepatitis B surface antibody, and hepatitis B core antibody), and human immunodeficiency virus (HIV antibody). Some of these tests require several days to result; therefore, it is best to draw them on admission.

3. *Abdominal Radiograph*

Patients should have a baseline plain abdominal radiograph on admission to help identify conditions that require immediate surgical attention such as megacolon, pneumatosis intestinalis, and perforation. If the patient's clinical course changes at any time throughout the hospitalization, it is important to repeat the abdominal radiograph and compare it to the initial film.

4. *Endoscopic Evaluation*

A flexible sigmoidoscopy with biopsies should be done within the first 48 hours to assess disease severity and biopsy for cytomegalovirus (CMV). A bowel preparation and full colonoscopy is unnecessary in the acute setting and can increase the risk for megacolon and perforation.[7]

Biopsies for CMV should be done in the center of the ulceration. The gold standard for diagnosis is immunohistochemistry. CMV is considered significant if more than five inclusion bodies per high power field is seen. The preferred treatment for CMV colitis is IV ganciclovir.[8]

5. *Diet*

Patients should be allowed a normal diet throughout their hospitalization. There has been no evidence that complete bowel rest or total parenteral nutrition (TPN) improves inflammation or changes disease outcomes.[9] If a normal diet is not tolerated, enteral nutrition is indicated.

6. *Deep Venous Thrombus Prophylaxis*

Hospitalization and active inflammation increase an UC patient's risk for deep venous thrombosis (DVT). In a meta-analysis of eight randomized controlled trials, there was no significant increase in bleeding in patients treated with heparin during hospitalization for acute UC flares.[10] Therefore, despite having bloody stools, all hospitalized UC patients should receive DVT prophylaxis.

7. *First Line Medical Therapy*

IV corticosteroids (40 mg/day) should be initiated on admission. Studies have shown that there is no evidence to support increasing methylprednisolone beyond 60 mg/day and the benefits do not outweigh the risks when increasing the dose beyond 40 mg/day.[3]

Patients who fail to respond to IV corticosteroids by day 3, have poor outcomes and should be evaluated for surgery or rescue medical therapy. Steroid nonresponse is defined as ≥8 stools/day or 3-8 stools/day plus CRP > 45 mg/L on day 3.[4]

8. *Medications to Avoid and/or Stop During Hospitalization*

Aminosalicylates have been shown to cause paradoxical colitis in 3% of patients and therefore should be discontinued on admission.[11] Non-steroidal anti-inflammatory drugs (NSAIDs) can cause ulcers, increase risk for gastrointestinal bleeding, and can exacerbate flares and should be avoided.[12]

Narcotics increase morbidity and mortality in IBD patients.[13] It can also increase a patient's risk for megacolon. Narcotics are best avoided. Anti-diarrheals can also alter colonic motility and have no role in the treatment of UC.

Day 2

1. *Clinical Assessment and Laboratory Evaluation*

Clinical response should be assessed based on the trend in the number of stools, blood in stools, and CRP.

2. *Colorectal Surgery Consultation*

Early colorectal surgery consultation is important. Surgery should be considered as an equal option to rescue

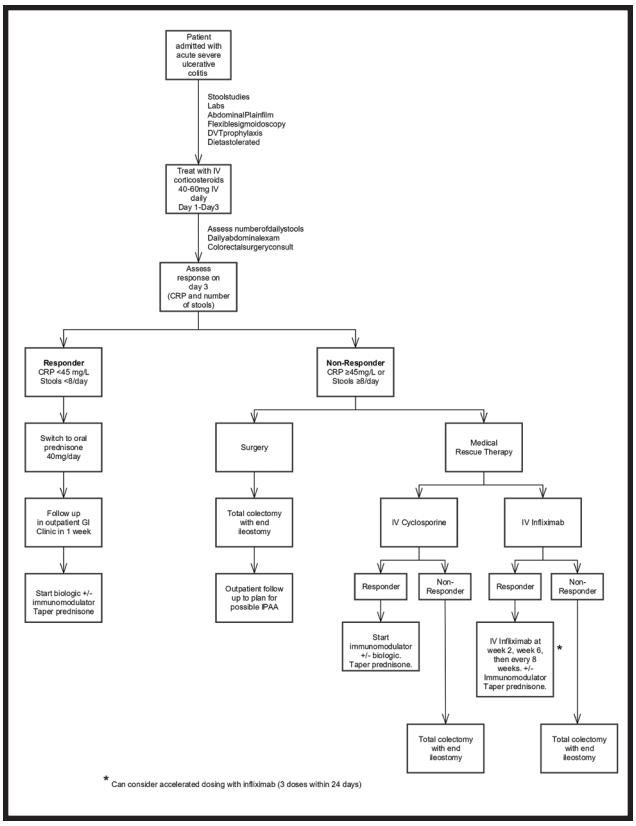

Figure 1. Approach to Treatment of Hospitalized Adult Patients with Severe Ulcerative Colitis

medical therapy in a patient who is not responding to IV corticosteroids. Early discussions about all possible options (medical versus surgical) between the patient, colorectal surgeons, and gastroenterologists will ensure optimal patient care.

Day 3

1. *Clinical Assessment and Laboratory Evaluation*

On day 3, response to IV corticosteroids will help to determine if rescue (medical or surgical) therapy is needed. Those patients that are responding to IV corticosteroids as defined by less than 8 stools per day with an appropriate downtrend in CRP can be switched to oral prednisone (40 mg daily). These patients should be discharged on oral prednisone (40 mg daily) with close outpatient gastroenterology follow up (preferably within one week). At follow up, maintenance therapy should be initiated (biologic and/or immunomodulator) and prednisone should be tapered.

Patients who fail to respond to IV corticosteroids by day 3, as defined by ≥8 stools/day or 3-8 stool/day plus CRP > 45 mg/L, should consider rescue medical therapy versus surgery.[4]

2. *Rescue Medical Therapy*

Either IV cyclosporine or infliximab is an appropriate choice as rescue therapy for patients who are failing IV corticosteroids and should be given on days 3-5.[14] The choice of medication depends on the center's expertise. Response should be assessed within 5-7 days after receiving rescue medical therapy.[15] If no clinical response by day 7, surgery is indicated.

Patients who respond to IV cyclosporine should be switched to oral thiopurines for maintenance therapy.[16] Combination therapy with a biologic may be required. Patients who respond to a single infusion of infliximab should complete induction doses at week 2 and week 6 followed by maintenance therapy every 8 weeks. Combination therapy with an immunomodulator should be considered.[17]

Low albumin levels and elevated CRP have been associated with lower infliximab serum levels due to rapid drug clearance.[18] Studies have also found that infliximab is lost in the stool in the setting of severe inflammation resulting in lower serum infliximab levels.[19] Therefore, higher and more frequent doses of infliximab may be required in patients with acute severe UC with elevated CRP levels and hypoalbuminemia. A recent retrospective study found that accelerated infliximab dosing (infliximab 5mg/kg, 3 doses within a median of 24 days) was associated with lower rates of colectomy compared to standard infliximab induction doses (infliximab 5mg/kg at week 0, 2, and 6).[20]

3. *Surgical Management*

Indications for surgery include toxic megacolon, perforation, massive bleeding, nonresponse to IV corticosteroids by day 3, and nonresponse to rescue medical therapy with cyclosporine or infliximab. The surgery of choice is a total colectomy with end-ileostomy and Hartmann's pouch.[21] An ileal pouch-anal anastomosis can be considered three to six months after the initial colectomy.

CONCLUSION

All patients with acute severe UC flares requiring hospitalization should receive IV corticosteroids on admission. C. difficile infection is common and should be treated with oral vancomycin. An early multidisciplinary team approach is critical to ensure optimal patient outcomes. Early rescue medical therapy or surgery is indicated if patients do not respond to IV corticosteroids by day 3.

Other biologics have not been thoroughly studied as rescue medical therapies. Future research should aim to characterize the use of other biologic and biosimilar agents in the setting of an acute severe ulcerative colitis flare requiring hospitalization. ■

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