

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Management of Hospitalized Patients With Ulcerative Colitis



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G&H What are the indications for hospitalization of patients with ulcerative colitis?

LB Patients with ulcerative colitis (UC) who have failed or have not responded to oral corticosteroid-based therapy as outpatients usually have to be admitted to the hospital for inpatient supervised care.

G&H What are the goals of hospitalization?

LB The goals are to avoid disease complications (such as perforation) and unnecessary infections that could occur when patients stay on corticosteroids for the long term in the outpatient setting, assess disease severity, exclude infections or other compounds, induce remission with rapidly acting and very efficacious medications, determine response, and decide the need for colectomy if medical therapy fails.

G&H When these patients are admitted to the hospital, which laboratory tests and examinations are usually performed?

LB Laboratory tests should include a complete blood count, liver function tests, and a complete metabolic profile, including albumin levels and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate, which should all be performed almost daily. Stool samples should be examined to check for infections such as *Clostridium difficile*, which may make symptoms worse. A score for stool frequency and the presence of blood in stool should be kept. A computed

tomography scan of the abdomen may be necessary, especially if a patient has signs suggestive of peritonitis or toxic megacolon. It is also important to check that patients have undergone tuberculin testing and are up-to-date on their vaccinations to determine that they do not have any latent infections before they are treated with rescue medications. Sometimes an urgent unprepped sigmoidoscopy with minimal air insufflation and biopsy needs to be considered to assess endoscopic severity of the disease and rule out cytomegalovirus colitis.

G&H Which rescue medications are usually given to patients hospitalized for UC?

LB When these patients are admitted, they are first given intravenous corticosteroids for approximately 3 to 5 days. It is then important to monitor inflammatory markers such as CRP and the frequency of stool every day for the next several days. If the CRP level and stool frequency do not drop by the third to fifth day, the patient is probably not going to respond to medical therapy. At this point, surgery may have to be considered. When a patient's CRP level and stool frequency decrease, rescue medications can be administered. The rescue medications most commonly used are infusions of infliximab (Remicade, Janssen) and cyclosporine. Depending upon the treating physician's experience, either of these medications may be used initially; sometimes, they have even been used sequentially with relatively safe outcomes. Deep vein thrombosis prophylaxis with subcutaneous low molecular weight heparin should be started on admission.

G&H Is it possible to predict which patients will respond to the initial corticosteroid therapy?

LB There is usually no way of knowing in advance whether patients will respond. The main reason for response is that the intravenous formulation of the corticosteroid therapy given in the hospital usually consists of a higher dose than the oral medication that patients

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take at home. A downward trend of inflammatory markers, decreased frequency of bloody diarrhea, decreased urgency, and improved stool consistency are the usual indications of response. Several indices, such as the Oxford Index, have been used to determine that most patients who do not experience a decrease in inflammatory markers and improvement in stool consistency within 3 to 5 days do not usually do well and will require surgery.

G&H How effective are the rescue medications for these patients?

LB They are usually very effective when given to the appropriate patient at the appropriate dose. If a patient's CRP level does not seem to be decreasing, usually he or she has very severe disease and will most likely require surgery. When treating a patient, it is important to determine how well the patient may respond to rescue medications by testing for albumin levels in the case of infliximab and testing for renal function and cholesterol levels in the case of cyclosporine. Patients who have low albumin levels tend to require higher doses of infliximab. Traditionally in the outpatient setting, patients start infliximab therapy with a dose of 5 mg/kg at day 0 and then are given another 5 mg/kg at 2 weeks and then at 6 weeks. If the patient is doing well, maintenance therapy will be at the same dose every 8 weeks. However, when patients are in the hospital, if albumin levels are low (most doctors use a cutoff of less than 2.5 g/dL), a 5-mg/kg formulation would not be given; instead, the

dose would be 10 mg/kg. This is because patients with severe UC have low albumin owing to profound diarrhea, so they will be losing a lot of the drug through stool. Patients with severe disease have high levels of tumor necrosis factor (TNF), which tends to consume the anti-TNF drug that they receive. Thus, doctors have to give these patients more medication and do not have to wait for 2 weeks to do so. It may be fine to give them another 10 mg/kg after a week. If patients start responding over time, the doctor may then decide to keep them on the 10-mg/kg dose or return them to the traditional 5-mg/kg dose. For patients taking cyclosporine, cholesterol levels will determine dosage between 2 and 4 mg/kg.

G&H When, specifically, is surgery indicated?

LB There are several absolute indications for surgery. If a patient has toxic megacolon, medical therapy will not work, so the patient should go straight to surgery. With toxic megacolon, the patient has severe inflammation, fever, a well-dilated colon (>8 cm, usually involving the transverse colon), a distended abdomen, and persistent tachycardia. Another indication for surgery is the presence of a perforation. Finally, if a patient is losing so much blood that it cannot be replaced fast enough, then the patient must go to surgery. The decision for surgery should not be delayed under these circumstances.

When patients do not have absolute indications for surgery, doctors must make a clinical judgment call to decide whether they should try treating the patients with more medicine to induce a possible response or send them to surgery.

G&H What measures can be undertaken to try to prevent the development of *C difficile* infection in patients hospitalized for UC?

LB When any patient is admitted, stool samples should be checked for *C difficile* infection so that it can be treated early. If a patient stays in the hospital for a long time, stool samples should be sent every 3 days to look for *C difficile*, as this is a ubiquitous organism, especially in a hospital setting. To prevent *C difficile* infection from developing, the best advice to give others, from patients to healthy people, is to make sure that their hands are washed with soap and water very well every time they come into contact with anyone in the hospital. Researchers are trying to develop a vaccine, but none is available for use currently.

G&H If hospitalized UC patients are infected with *C difficile*, how should they be treated?

LB Patients with inflammatory bowel disease (IBD) who are infected with *C difficile* are considered to be a special population. Therefore, while most people with *C difficile* infection are treated with metronidazole, most patients with this infection who also have UC are treated with vancomycin. Vancomycin has been shown to work better in patients with both conditions than in patients with only *C difficile*. In addition, a new drug on the market is fidaxomicin (Dificid, Merck), which is also effective for patients with both IBD and *C difficile*. There are also several research trials currently being conducted on *C difficile* toxin antibodies that may be helpful in the management of these patients.

G&H How can pain be managed in UC patients who are hospitalized?

LB Doctors should stay away from using nonsteroidal anti-inflammatory medications in patients who have IBD, as these drugs tend to make the disease worse.

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Long-term use of narcotics should also be avoided in patients with IBD. Acetaminophen usually tends to be good at controlling pain; however, doctors often do not give enough of this medication due to its potential hepatotoxicity. Tramadol and anxiolytics have been found to be very useful in UC patients admitted to the hospital. In most people, the pain ideally goes away once the disease is well controlled.

G&H Do hospitalized UC patients have any special nutritional or dietary needs?

LB Although there is currently no specific diet that patients with IBD should follow, there are a few dietary considerations that should be kept in mind. While there have not been any randomized, controlled trials, epidemiologic studies have suggested that people who eat food that is high in fat, specifically trans fat, tend to be predis-

posed to IBD. In addition, people who eat food that is high in fiber tend not to get Crohn's disease, and those who have a diet high in vegetables tend not to get UC. If a patient has a flare, it is best to avoid high-fiber and -fat diets. Patients in remission can eat most foods, although it may be best to steer patients toward a high-fiber diet, which is the only diet that has currently been suggested to be beneficial to patients with IBD.

It is also important that hospitalized UC patients drink as much replacement fluids (water and Gatorade) as possible because these patients tend to become dehydrated due to their diarrhea. At the same time, they should be careful about drinking coffee and tea, as these drinks act as diuretics and will make the patients lose weight and become dehydrated in the long term. Energy drinks have also been tried because hospitalized patients often feel fatigued and tired, but these drinks contain a lot of caffeine. In addition, carbonated drinks produce uncomfortable gas and alcohol, and sugary drinks lead to worsening of diarrhea.

G&H Are there any special considerations that should be kept in mind when managing hospitalized UC patients?

LB As previously mentioned, when patients are in the hospital, it is always important to monitor their inflammatory markers closely, as this is one of the most objective ways of knowing whether a patient is responding. In addition, inflammatory markers usually increase when a flare occurs. Thus, inflammatory markers can be used to monitor patient progress. If the CRP level does not respond, the patient's erythrocyte sedimentation rate can also be monitored for inflammation.

It is also important that patients are hospitalized early. Many times, patients might look like they are well, but they are actually not well; in fact, 30% of patients who present looking well have colonoscopic findings that suggest otherwise. For some patients, the first time they visit a doctor is when they have complications. It is better to admit patients early and find out that they do not have severe disease than admit patients late when the disease is very advanced. Another option is sending patients to a center of excellence for IBD, instead of admitting them to any hospital, because they will receive the most appropriate therapy there.

G&H When can hospitalized UC patients be discharged, and how should they be monitored thereafter?

LB Patients can leave the hospital once their UC is well controlled and a plan is in place for maintenance therapy

and monitoring of their response for the long term. Patients who are treated with infliximab and respond can continue on infliximab for maintenance. Some patients are treated with cyclosporine, but it must be noted that this drug is usually used for induction of remission as a bridge to another therapy that can be used long term, such as an immunomodulatory or biologic agent.

Once these patients are out of the hospital, they can be followed like most nonhospitalized UC patients. They should be seen frequently in clinics, and inflammatory markers, including fecal calprotectin, should be monitored to prevent the patients from flaring if possible. It is better to prevent a flare than to wait for one to occur. Even if patients are not being seen regularly, markers should be checked whenever possible to see how well they are doing.

G&H What are the most important research needs in this area?

LB One of the most significant needs is developing a system of indices to determine how severe or mild a patient's disease is and how high the risk of colectomy is. Currently, in the world of IBD, we do not have an objective set of indices to determine whether a patient has severe, moderate, or mild disease. Truelove and Witts' classification can be used but was created decades ago. Hospitalization (par-

ticularly multiple times) should be factored into disease severity but currently is not. The impact of the disease on the patient's quality of life, what medications they have tried and failed, and other measures of intestinal damage should be assessed. More objective measures, such as colonoscopy findings, should also play a role, although when admitting a patient, this information might not be known yet. Various researchers are working on indices, but none have been validated yet.

Another need is the development of point-of-service laboratories that can provide blood test results in a matter of hours instead of days. Normally, blood test results take up to a week in outpatient settings and several days when the patient is in the hospital. Obtaining faster blood results would let doctors adjust drug doses faster, which would result in better management of patients.

Dr Baidoo has no relevant conflicts of interest to disclose.

Suggested Reading

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