Medical Management of Diverticular Disease

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Abstract

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This article reviews the current literature supporting the non-surgical options for treatment in acute uncomplicated diverticulitis, complicated diverticulitis, and options for prevention of recurrent diverticulitis.

Diverticulosis is an extremely common malady in the adult population of the Western culture. The reported incidence shows a significant increase with age. Patients younger than 40 years have an incidence of less than 20%, whereas the incidence of diverticulosis is greater than 65% in patients older than 65 years, and greater than 70% in patients older than 80 years. Though the incidence of diverticulosis is extremely high, the incidence of symptomatic disease is significantly lower, with reported rates of diverticulitis occurring in 15 to 25% of afflicted patients. Of all the patients with diverticulosis, only 0.5% go on to require operative intervention.¹ Therefore, diverticulosis and diverticulitis are diseases that are primarily managed medically. There are multiple options and guidelines for the treatment of symptomatic uncomplicated diverticular disease (SUDD, Hinchey class 0 to 1a), as well as for complicated diverticular disease. There are multiple treatment options, including dietary modification for the prevention of recurrent diverticular disease, with varying rates of success.

Medical Therapy for Acute Uncomplicated Diverticulitis

Acute Diverticulitis is encompassed by a broad range of clinical scenarios ranging from pericolic inflammation (Hinchey 1a) to fecal peritonitis (Hinchey 4). For patients with purulent peritonitis (Hinchey 3) and feculent peritonitis (Hinchey 4), the practice paradigm is geared toward operative management. There is little debate with the more severe cases of diverticulitis, as there is a general consensus in the literature that these patients require operative intervention. For patients with Hinchey I-II, there has been a trend toward less invasive management.

Traditional treatment of mild acute diverticulitis has centered on antibiotics, pain control, and bowel rest. These tenets of therapy have recently been called into question. In the most recent guidelines published by the American Gastroenterological Association Institute, the recommendation for treatment of acute diverticulitis without abscess formation is selective administration of antibiotics based upon patient characteristics rather than the routine use of antibiotics.² They categorize these recommendations as conditional, based on low quality of evidence. These recommendations are based upon the AVOD Trial³ and the DIO-BOLO Trial.⁴ In the Sweden and Iceland AVOD trials, 623 patients with CT proven Hinchey I diverticulitis were randomized to standard antibiotic therapy versus no antibiotic therapy. Their results showed that there was no clinically significant difference in the failure of conservative therapy or in recurrence in one year. In the Dutch DIABOLO trial, 528 patients with CT proven Hinchey I diverticulitis were randomized to antibiotic therapy versus observation alone. There was no significant difference in time for complete recovery, nor was there a significant difference in recurrence rate at 6 months.

There is still definite controversy about whether or not antibiotics are indicated. The American Society of Colorectal Surgeons recommends treatment of acute uncomplicated diverticulitis with dietary modification and oral or IV antibiotics aimed at gram negative rods and anaerobic bacteria. In their recommendations they state that outpatient management is acceptable as long as there are no underlying patient factors that require admission.⁵ Though the American Gastroenterological Association Institute recommendations for selective administration of antibiotics are considered conditional, as they are

currently based upon only two multicenter randomized controlled trials, there is increasing evidence that no antibiotics are as effective as IV or oral antibiotic administration for Hinchey I diverticulitis.⁶ In a systematic review article from the European Society of Coloproctology, they give level 1B recommendations that antibiotics for uncomplicated diverticulitis are unnecessary for otherwise healthy patients. For immune compromised, pregnant, septic, and poorly conditioned patients, the recommendation is for 4 days of antibiotics. They also recommend oral antibiotics over intravenous antibiotics.⁷

Although there is currently no consensus on whether or not antibiotics are indicated for acute uncomplicated diverticulitis, there is consensus that the majority of patients do not go on to have serious complications no matter the treatment pathway selected. Further research is required to develop a consensus on the adequate mode and length of therapy for uncomplicated Hinchey I diverticulitis.

Medical Therapy for Complicated Acute Diverticulitis

Hinchey class II-IV diverticulitis is not well managed by antibiotics alone. The appropriate interventional and surgical modality for pelvic abscess through feculent peritonitis is outside the scope of this discussion. However, following appropriate invasive intervention, there is a need for continued antibiotic therapy. Unfortunately, the length of antibiotic therapy for complicated acute diverticulitis is not well studied. The traditional practice has been to treat patients with antibiotics for 7 days or until signs and symptoms of sepsis have been resolved.⁸ This practice has been recently challenged by literature not specific to diverticulitis, but generalized to intra-abdominal infections. In the STOP IT trial published in the *New England Journal of Medicine* in 2015 they looked at randomized 518 patients with a complicated intra-abdominal infection following adequate source control to either antibiotic therapy until 2 days after the resolution of fever, leukocytosis, and ileus for a maximum of 10 days, or 4 calendar days. The outcomes in the two groups were not significantly different for surgical site infection, recurrent intra-abdominal infection, or death. The average length of antibiotic therapy was 8 days for the control group and 4 days for the experimental group.⁹ This trial was not specific to diverticulitis; however, the results did include 177 patients with colonic source of intra-abdominal infection. Though this is only a single randomized trial, it does open the discussion for shorter courses of antibiotics. Significant further research needs to be completed in this area for consensus recommendations.

Medical Therapy for the Prevention of Recurrent Diverticulitis

There is some evidence that patients with diverticulosis but no diverticulitis have regions of colitis within and around the diverticulum.¹⁰ This has led to a belief that there is overlap between inflammatory bowel disease and diverticulosis. Because of this, there has been significant research into

whether or not 5-aminosalicylic acid (mesalamine) can be of some benefit for the prevention of acute diverticulitis as well as reducing the severity of acute diverticulitis. Mesalamine is an anti-inflammatory medication used to treat ulcerative colitis. The mechanism of action is not completely understood; however, it is thought to decrease prostaglandin and cytokine production, inhibit neutrophil chemotaxis, and promote a mucosal barrier effect.¹¹

Mesalamine has been trialed in both the acute phase of diverticulitis, as well as a preventive medication for recurrent episodes of diverticulitis. In a trial out of Italy,¹² authors looked at 50 patients who were admitted with uncomplicated diverticulitis. Twenty patients were treated with mesalamine, and 30 patients were not. All were treated with antibiotics. The mesalamine group had a faster reduction in C-reactive protein (CRP) which was correlated to decreased levels of inflammation. The mesalamine group also tolerated a diet faster than the group without mesalamine. Though this was a small study, it was able to show that mesalamine may help with the reduction of inflammation in uncomplicated diverticulitis and may aid in a faster recovery.

Though there were initial thoughts that mesalamine may be beneficial for the prevention of recurrent diverticulitis, recent mesalamine versus placebo trials have failed to show a benefit. In the PREVENT1 and PREVENT2¹³ trials, two identical phase III trials were completed. The PREVENT1 trial included 590 patients and PREVENT2 included 592 patients. Patients who had diverticulitis without colonic resection within 6 weeks were included. Patients were randomized to receive mesalamine versus placebo for 104 weeks. Recurrence rates in the placebo and mesalamine groups were not significantly different, and the proportion of patients eventually requiring surgery was not different between the two groups.

At this point, the current literature does not support the use of mesalamine to prevent future episodes of acute diverticulitis.

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