

ACG Clinical Guideline: Ulcerative Colitis in Adults

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Erratum

In the Conflict of Interest section of the article, the Financial Support subsection should have stated that “No support was provided for this work.” The publisher regrets any confusion this misstatement may have caused.

The corrected Potential Competing Interests subsection for Dr Kornbluth is as follows: “Asher Kornbluth is a consultant for Salix Pharmaceutical, Shire Pharmaceutical, Proctor and Gamble Pharmaceutical, Centocor, and Prometheus Laboratory and has received research support from Salix Pharmaceutical, Proctor and Gamble Pharmaceuticals, and Centocor Inc. He is also on the Speaker’s Bureau of Salix Pharmaceutical, Shire Pharmaceutical, Proctor and Gamble Pharmaceutical, Centocor, Prometheus, and Axcan Pharmaceutical.”

Also in the Conflict of Interest section, Dr Sacher’s Potential Competing Interests statement was not included. It is as follows: “David Sachar serves as expert witness for the plaintiffs in litigation claiming that isotretinoin was a cause of their inflammatory bowel disease. He has no other conflicts of interest to report.”

Abstract

Guidelines for clinical practice are aimed to indicate preferred approaches to medical problems as established by scientifically valid research. Double-blind placebo controlled studies are preferable, but compassionate-use reports and expert review articles are used in a thorough review of the literature conducted through Medline with the National Library of Medicine. When only data that will not withstand objective scrutiny are available, a recommendation is identified as a consensus of experts. Guidelines are applicable to all physicians who address the subject regardless of specialty training or interests and are aimed to indicate the preferable but not necessarily the only acceptable approach to a specific problem. Guidelines are intended to be flexible and must be distinguished from standards of care, which are inflexible and rarely violated. Given the wide range of specifics in any health-care problem, the physician must always choose the course best suited to the individual patient and the variables in existence at the moment of decision. Guidelines are developed under the auspices of the American College of Gastroenterology and its Practice Parameters Committee and approved by the board of trustees. Each has been intensely reviewed and revised by the Committee, other experts in the field, physicians who will use them, and specialists in the science of decision analysis. The recommendations of each guideline are therefore considered valid at the time of composition based on the data available. New developments in medical research and practice pertinent to each guideline will be reviewed at a time established and indicated at publication to assure continued validity. The recommendations made are based on the level of evidence found. Grade A recommendations imply that there is consistent level 1 evidence (randomized controlled trials), grade B indicates that the

evidence would be level 2 or 3, which are cohort studies or case–control studies. Grade C recommendations are based on level 4 studies, meaning case series or poor-quality cohort studies, and grade D recommendations are based on level 5 evidence, meaning expert opinion.

Introduction

Ulcerative colitis (UC) is a chronic disease characterized by diffuse mucosal inflammation limited to the colon. It involves the rectum in about 95% of cases and may extend proximally in a symmetrical, circumferential, and uninterrupted pattern to involve parts or all of the large intestine. The hallmark clinical symptom is bloody diarrhea often with prominent symptoms of rectal urgency and tenesmus. The clinical course is marked by exacerbations and remissions, which may occur spontaneously or in response to treatment changes or intercurrent illnesses (1, 2). UC affects approximately 500,000 individuals in the United States with an incidence of 8–12 per 100,000 population per year; the incidence has remained relatively constant over the last five decades (3–8).

The disease accounts for a quarter million physician visits annually, 30,000 hospitalizations, and loss of over a million workdays per year (9). The direct medical costs alone exceed four billion dollars annually, comprising estimated hospital costs of over US\$960 million (10, 11) and drug costs of \$680 million (11).

Diagnosis and Assessment

Recommendation

1. In a patient presenting with persistent bloody diarrhea, rectal urgency, or tenesmus, stool examinations and sigmoidoscopy or colonoscopy and biopsy should be performed to confirm the presence of colitis and to exclude the presence of infectious and noninfectious etiologies. Characteristic endoscopic and histologic findings with negative evaluation for infectious causes will suggest the diagnosis of UC.

Approach to Management

Recommendation

1. Goals of treatment are induction and maintenance of remission of symptoms to provide an improved quality of life, reduction in need for long-term corticosteroids, and minimization of cancer risk.

Management of Mild-Moderate Distal Colitis

Recommendations

1. Patients with mild to moderate distal colitis may be treated with oral aminosalicylates, topical mesalamine, or topical steroids (Evidence A).
2. Topical mesalamine agents are superior to topical steroids or oral aminosalicylates (Evidence A).
3. The combination of oral and topical aminosalicylates is more effective than either alone (Evidence A).
4. In patients refractory to oral aminosalicylates or topical corticosteroids, mesalamine enemas or suppositories may still be effective (Evidence A).
5. The unusual patient who is refractory to all of the above agents in maximal doses, or who is systemically ill, may require treatment with oral prednisone in doses up to 40–60 mg per day, or infliximab with an induction regimen of 5 mg/kg at weeks 0, 2, and 6, although the latter two agents have not been studied specifically in patients with distal disease (Evidence C).

Maintenance of Remission in Distal Disease

Recommendations

1. Mesalamine suppositories are effective in the maintenance of remission in patients with proctitis, whereas mesalamine enemas are effective in patients with distal colitis when dosed even as infrequently as every third night (Evidence A).
2. Sulfasalazine, mesalamine compounds, and balsalazide are also effective in maintaining remission; the combination of oral and topical mesalamine is more effective than either one alone (Evidence A).
3. Topical corticosteroids including budesonide, however, have not proven effective for maintaining remission in distal colitis (Evidence A).
4. When all of these measures fail to maintain remission in distal disease, thiopurines (6-mercaptopurine (6-MP) or azathioprine) and infliximab (Evidence A), but not corticosteroids, may prove effective (Evidence B).

Management of Mild-Moderate Extensive Colitis: Active Disease

Recommendations

1. Patients with mild to moderate extensive colitis should begin therapy with oral sulfasalazine in daily doses titrated up to 4–6 g per day, or an alternate aminosalicylate in doses up to 4.8 g per day of the active 5-aminosalicylate acid (5-ASA) moiety (Evidence A).
2. Oral steroids are generally reserved for patients who are refractory to oral aminosalicylates in combination with topical therapy, or for patients whose symptoms are so troubling as to demand rapid improvement (Evidence B).
3. 6-MP and azathioprine are effective for patients who do not respond to oral steroids, and continue to have moderate disease, and are not so acutely ill as to require intravenous therapy (Evidence A).
4. Infliximab is an effective treatment for patients who are steroid refractory or steroid dependent despite adequate doses of a thiopurine, or who are intolerant of these medications. The infliximab induction dose is 5 mg/kg intravenously at weeks 0, 2, and 6 weeks (Evidence A).
5. Infliximab is contraindicated in patients with active infection, untreated latent TB, preexisting demyelinating disorder or optic neuritis, moderate to severe congestive heart failure, or current or recent malignancies.

Management of Mild-Moderate Extensive Colitis: Active Disease

Recommendations

1. Once the acute attack is controlled, a maintenance regimen is usually required, especially in patients with extensive or relapsing disease. Sulfasalazine, olsalazine, mesalamine, and balsalazide are all effective in reducing relapses (Evidence A).
2. Patients should not be treated chronically with steroids. Azathioprine or 6-MP may be useful as steroid-sparing agents for steroid-dependent patients and for maintenance of remission not adequately sustained by aminosalicylates, and occasionally for patients who are steroid dependent but not acutely ill (Evidence A).
3. Infliximab is effective in maintaining improvement and remission in the patients responding to the infliximab induction regimen (Evidence A).

Management of Severe Colitis

Recommendations

1. The patient with severe colitis refractory to maximal oral treatment with prednisone, oral aminosalicylate drugs, and topical medications may be treated with infliximab 5 mg/kg if urgent hospitalization is not necessary (Evidence A).
2. The patient who presents with toxicity should be admitted to hospital for a course of intravenous steroids (Evidence C).
3. Failure to show significant improvement within 3–5 days is an indication for either colectomy (Evidence B) or treatment with intravenous cyclosporine (CSA; Evidence A) in the patient with severe colitis. Long-term remission in these patients is significantly enhanced with the addition of maintenance 6-MP (Evidence B).
4. Infliximab may also be effective in avoiding colectomy in patients failing intravenous steroids but its long-term efficacy is unknown in this setting (Evidence A).

Surgery

Recommendations

1. Absolute indications for surgery are exsanguinating hemorrhage, perforation, and documented or strongly suspected carcinoma (Evidence C).
2. Other indications for surgery are severe colitis with or without toxic megacolon unresponsive to conventional maximal medical therapy, and less severe but medically intractable symptoms or intolerable medication side effects (Evidence C).

Management of Pouchitis

Recommendations

1. Patients who develop typical symptoms and signs of pouchitis after the IPAA should be treated with a short course of antibiotics (Evidence A).
2. Controlled trial studies show efficacy for metronidazole in a dose of 400 mg three times daily, or 20 mg/kg daily, or ciprofloxacin 500 mg twice daily (Evidence A).
3. Other etiologies mimicking pouchitis include irritable pouch syndrome, cuffitis, CD of the pouch, and postoperative complications such as anastomotic leak or stricture. Inadequate evidence exists to recommend routine surveillance of the pouch for dysplasia or adenocarcinoma (Evidence C).

Cancer Surveillance

Recommendations

1. After 8–10 years of colitis, annual or biannual surveillance colonoscopy with multiple biopsies at regular intervals should be performed (Evidence B).
2. The finding of HGD in flat mucosa, confirmed by expert pathologists' review, is an indication for colectomy, whereas the finding of LGD in flat mucosa may also be an indication for colectomy to prevent progression to a higher grade of neoplasia (Evidence B).