in patients with ulcerative colitis; however, the role of topical mesalamine in CD, although commonly used, is of limited benefit.

Corticosteroids. Corticosteroids are used primarily for the treatment of flares of CD. Conventional corticosteroids are effective for reducing the signs and symptoms of active CD and induction of remission in patients with moderately to severely active CD. Oral formulations may be used for mild to moderate disease, whereas systemic corticosteroids are used for moderate to severe disease. Conventional corticosteroids are not consistently effective to enable patients to achieve mucosal healing. They have historically been used as a "bridge" to permit symptom control until immunomodulators and/or biologic agents become effective and enable mucosal healing.

Although not as effective as conventional oral corticosteroids such as prednisone, controlled ileal release (CIR) budesonide may be effective for short-term relief of symptoms of mild-to-moderate CD in patients whose disease is confined to the terminal ileum and right colon. CIR budesonide is a pH-dependent ileal release oral corticosteroid formulation with high topical activity and low systemic bioavailability (~10–20%). CIR budesonide has been demonstrated to be effective in randomized placebo controlled trials for treatment of active mild-to-moderate ileocecal CD (183,184). The lesser efficacy of CIR budesonide is balanced against the agent's release profile, limited to the ileum and right colon, and its topical activity with extensive first-pass effect, minimizing systemic exposure to corticosteroid effects.

Antimicrobial therapy. In patients with CD it is hypothesized that the development of chronic intestinal inflammation is caused by an abnormal immune response to normal flora in genetically susceptible hosts. The involvement of bacteria in CD inflammation has provided the rationale for including antibiotics in the therapeutic armamentarium. The precise mechanisms whereby broad-spectrum antibiotics are beneficial in the treatment of a subset of CD patients are uncertain. Several proposed mechanisms of efficacy include direct immunosuppression (e.g., metronidazole), elimination of bacterial overgrowth, and abolishment of a bacterially mediated antigenic trigger.

Although widely used in the past, the primary role of antibiotics for the treatment of luminal CD is not established. Metronidazole is not more effective than placebo at inducing remission in patients with CD (185,186). Ciprofloxacin has shown similar efficacy to mesalamine in active CD, but has not been shown to be more effective than placebo to induce remission in CD. Neither of these agents has been shown to heal the mucosa in patients with active luminal CD (186–189). Broad-spectrum antibiotics are used for the treatment of pyogenic complications (e.g., intra-abdominal and mesenteric abscesses) in patients with CD.

Metronidazole may be helpful to prevent postoperative recurrence in CD. Its efficacy is increased over placebo when used in combination with azathioprine. Ornidazole has been more helpful than placebo to prevent postsurgical recurrence of clinical and endoscopic CD. In addition, a novel enteric form of rifaximin may be of benefit for mild-to-moderate CD (190) (see Maintenance section for a detailed description).

The relationship of mycobacterial disease to the development of CD has been extensively evaluated. The absence of mycobacteria in all tissue examined (even when assessed by PCR) and the lack of significant patient disease benefit when treated with multidrug regimens has led to the recommendation that antimycobacterial therapy should not be used to treat patients with active CD. Antimycobacterial therapy has not been shown to be effective for induction or for maintenance of remission or mucosal healing in patients with CD (191,192).

Diet. Some studies suggest that dietary therapies, including elemental, semielemental, and defined diets, may be effective in some patients with CD, including reduction of objective indicators of mucosal inflammation. These benefits, however, are not durable, with symptoms and active inflammation reoccurring upon resumption of an unrestricted diet. Therefore, dietary therapies may be considered as an adjunct to other therapies in induction therapy (193). Patients deemed to be at low risk for progression of disease may be treated with nonspecific therapies directed at symptoms, but must be followed carefully for signs of disease worsening or progression.

Provided that the goal of treatment is the normalization, or at least substantial improvement, of objective indicators of mucosal inflammation, providers can avoid the pitfall of inadequate disease treatment that, over time, will culminate in progression of disease and the occurrence of important complications even if they choose expectant observation and treatment directed to alleviating symptoms.

Moderate-to-severe disease/moderate-to-high-risk disease

Corticosteroids

Recommendations

17. Oral corticosteroids are effective and can be used for short-term use in alleviating signs and symptoms of moderate to severely active Crohn's disease (194) (strong recommendation, moderate level of evidence).
18. Conventional corticosteroids do not consistently achieve mucosal healing and should be used sparingly (weak recommendation, low level of evidence).

Systemic corticosteroids are ineffective for maintenance therapy in patients with CD. Topical corticosteroids, although commonly used in CD, are of limited benefit (Summary Statement).

Patients experiencing moderate-to-severe symptoms, or who have features of moderate to high risk of progression and complication, require treatment with more effective agents. Conventional corticosteroid treatment, such as prednisone and methylprednisolone given orally or, for more severe disease, intravenous corticosteroids are effective in alleviating signs and symptoms of a flare. However, even short-term use may be accompanied by important adverse events, such as bone loss, mood disorder, insomnia, hypertension, elevated blood glucose,