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AGA SECTION

American Gastroenterological Association Institute Guideline on the Medical Management of Microscopic Colitis

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This document presents the official recommendations of the American Gastroenterological Association (AGA) Institute on the medical management of microscopic colitis. The guideline was developed by the AGA Clinical Guidelines Committee and approved by the AGA Governing Board. It is accompanied by a technical review that is a compilation of clinical evidence from which these recommendations were formulated.[1]

Microscopic colitis is characterized by chronic watery diarrhea caused by inflammation in the colon and diagnosed by colonic biopsy. With a predilection for those 60 years of age or older, it comprises 2 subtypes, lymphocytic colitis and collagenous colitis; there is a female predominance in the latter. The reported prevalence of microscopic colitis ranges from 48 to 219 per 100,000.[1] Microscopic colitis is not associated with increased mortality, although symptoms can lead to impaired quality of life. Unlike other inflammatory colitides, there is no evidence that the persistence of histological inflammation portends long-term unfavorable outcomes such as colorectal cancer or need for surgery. Accordingly, the goal of medical therapy reflected in these recommendations is to relieve symptoms and improve quality of life while minimizing drug-related adverse effects. Because outcomes did not differ between lymphocytic colitis and collagenous colitis in the technical review, the recommendations in this guideline do not distinguish between subtypes of microscopic colitis.[1]

This guideline focuses on the medical treatment of microscopic colitis and does not specifically address its diagnosis, surgical management, or the appropriateness of screening for associated autoimmune disorders. Because microscopic colitis occurs in 7.5% of patients undergoing evaluation for chronic diarrhea, it would be prudent when assessing these patients with endoscopy to perform colonoscopy with biopsies of multiple segments of the colon. If for any reason flexible sigmoidoscopy is performed instead of colonoscopy, it is important to obtain biopsy specimens from the descending colon in addition to those from the rectosigmoid colon because biopsy specimens from the latter may not reveal the disease in some cases. Moreover, when patients with microscopic colitis have ongoing symptoms despite medical therapy, coexisting causes of chronic diarrhea such as celiac disease should be considered. The persistence of residual bowel symptoms may also reflect coexisting or postinflammatory functional bowel disorders. Patients with refractory symptoms should also avoid potential medication triggers such as nonsteroidal anti-inflammatory drugs, proton pump inhibitors, and selective serotonin reuptake inhibitors.

The guideline was developed using a process outlined elsewhere.[2] Briefly, the AGA process for developing clinical practice guidelines incorporates best practices of guideline development as outlined by the Institute of Medicine.[3] The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to prepare the background summary of evidence, develop the technical review, and assess the certainty of the evidence and grade the strength of the recommendations.[4] Optimal understanding of this guideline will be enhanced by reading applicable portions of the technical review. The guideline panel and the authors of the technical review met in person on April 25, 2015, to discuss the quality of evidence (Table 1) and consider other factors relevant for the risk/benefit assessment of the recommendations. The guideline authors subsequently formulated the recommendations. Although quality of evidence was a cardinal factor in determining the strength of the recommendations (Table 2), the balance between benefit and harm, patients' values and preferences, and resource utilization was also taken into consideration.

Recommendation 1. In patients with symptomatic microscopic colitis, the AGA recommends treatment with budesonide over no treatment for the induction of clinical remission. *Strong recommendation, moderate quality of evidence.*

A meta-analysis of 6 randomized clinical trials showed clear benefit of budesonide in inducing clinical response,

Abbreviations used in this paper: AGA, American Gastroenterological Association; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

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Table 1. GRADE Definitions of Quality of Evidence

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect

with 5 studies also showing histological response. Two studies also showed improvement in quality of life, although the difference did not reach statistical significance. Patients treated with 9 mg of budesonide daily were more than twice as likely to achieve clinical remission over an average of 7 to 13 days when compared with no treatment (relative risk, 2.52; 95% confidence interval, 1.45–4.4). The risk of serious adverse events is low with budesonide. Because of the highly favorable risk/benefit profile and convenience of once-daily dosing, budesonide should be considered first-line therapy for the treatment of microscopic colitis. However, because budesonide is expensive, alternative therapies may also be considered if cost is a determining factor. In general, it is not necessary to perform colonoscopy to assess histological response. However, for patients who have residual symptoms after treatment with budesonide, normal colonic biopsy specimens may be suggestive of coexisting irritable bowel syndrome or celiac disease. Cessation of budesonide can be considered after 8 weeks of therapy. One-third of patients will remain symptom-free thereafter and not require maintenance therapy, which mitigates long-term cost issues with the drug.

Recommendation 2. In patients with symptomatic microscopic colitis, the AGA recommends treatment with budesonide over mesalamine for the induction of clinical remission. *Strong recommendation, high quality of evidence.*

A high-quality clinical trial provided direct evidence that budesonide should be considered first-line therapy over mesalamine whenever possible. Patients with symptomatic microscopic colitis who were treated with budesonide 9 mg daily were nearly twice as likely as those treated with mesalamine 3 g daily to achieve clinical and histological remission, and there was no statistically significant difference in occurrence of adverse events.

Recommendation 3. In patients with symptomatic microscopic colitis in whom budesonide therapy is not feasible, the AGA suggests treatment with mesalamine over no treatment for the induction of clinical remission. *Conditional recommendation, moderate quality of evidence.*

Moderate-quality evidence from a single randomized clinical trial suggests that mesalamine therapy is associated with a lower likelihood of achieving clinical response when compared with no treatment (odds ratio, 0.74; 95% confidence interval, 0.44–1.24), although this was not statistically significant. Thus, due to serious imprecision, the benefit of mesalamine in achieving clinical remission is uncertain. Although not directly comparable, it should be noted that in 2 other clinical trials in which mesalamine was administered in the control arm, the clinical response rate was 84% and 87%, while in a third it was 44%. Because of the uncertain balance between benefits and potential harms, mesalamine is recommended conditionally as a potential second-line therapy that can be used under select circumstances. A trial of mesalamine may be appropriate for patients who have a contraindication or had a poor response to budesonide or those who have a strong preference against using it. Because costs are similar between mesalamine and budesonide, it is not likely to be a determining factor.

Recommendation 4. In patients with symptomatic microscopic colitis in whom budesonide therapy is not feasible, the AGA suggests treatment with bismuth salicylate over no treatment for the induction of clinical remission. *Conditional recommendation, low quality of evidence.*

Table 2. GRADE Definitions of Strength of Recommendation

	For the patient	For the clinician
Strong	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
Conditional	The majority of individuals in this situation would want the suggested course of action, but many would not.	Different choices will be appropriate for different patients. Decision aids may well be useful in helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.

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