Gastroenterology 2015;■:1–28

American Gastroenterological Association Institute Technical Review on the Medical Management of Microscopic Colitis

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Microscopic colitis (MC) is a cause of chronic diarrhea, and there are 2 subtypes: collagenous colitis (CC) and lymphocytic colitis (LC). The clinical features, symptoms, and responses to treatment are similar for both CC and LC. All meta-analyses conducted for this technical review tested for interaction (or a subgroup effect), and in every case there was no evidence of a subgroup effect. Therefore, in this review, the 2 subtypes are combined and considered together as MC. Information on pathophysiology was considered outside the scope of this review.

The prevalence of MC has been reported in recent studies to be 48 per 100,000 in Spain, 123 per 100,000 in Sweden, and 219 per 100,000 in Minnesota. MC is more common in people 60 years of age and older, and there is an apparent female preponderance. The clinical course of MC is variable; symptoms range from mild (a few loose stools daily) to severe (incapacitating watery diarrhea and abdominal pain). Symptoms can persist for months to years or spontaneously remit and then recur after months to years.

Diagnosis of MC is based on compatible histology from colonic mucosal biopsy specimens obtained during colonoscopy or flexible sigmoidoscopy. The distribution of colonic involvement can be patchy or segmental, so multiple random biopsy specimens are often required for diagnosis.

Quality of life is impaired in patients with MC in proportion to the degree of diarrhea, abdominal pain, urgency, and incontinence and to a similar degree to that reported for active irritable bowel disease. A diagnosis of MC does not increase mortality or the risk of colorectal cancer and only rarely requires surgery.

The goal of treatment of MC is to induce remission while minimizing potential adverse effects of therapy. Some patients remain asymptomatic after induction of remission and after discontinuing therapy and do not need maintenance treatment for MC. However, many patients have a symptomatic recurrence after discontinuation of treatment and should be considered for maintenance therapy. Medications that are used to treat MC include loperamide (an antidiarrheal agent); bismuth subsalicylate (an antimicrobial, anti-inflammatory agent); colesevelam, cholestyramine, and colestipol (bile acid binders); mesalamine (an anti-inflammatory agent); prednisone and budesonide (corticosteroids); azathioprine and methotrexate (immune suppressants); infliximab and adalimumab (biologic agents); and surgical interventions (diverting ileostomy and proctocolectomy with ileal pouch–anal anastomosis). Several of these therapies are used in clinical practice but have not been studied in clinical trials. These therapies are therefore not addressed directly in this technical review.

Methods

Focused Questions

The methods used to identify, select, and summarize the evidence are described at a question level. This technical review is not intended to be a review of all aspects of MC. Rather, it summarizes the evidence related to the following questions.

Question 1. What is the prevalence of MC? How many colon biopsy specimens should be obtained and from which areas of the colon? This question is for information and not a recommendation, and therefore it was not framed as a PICO (population, interventions, comparisons, and outcomes) question. The content of this question is included in the guideline only for information.

Question 2. In patients with MC (either LC or CC), which treatments are effective and safe for inducing remission of the disease, measured as clinical response, histological response, quality of life, and adverse events?

The population is adult patients with MC (either LC or CC). The interventions include bismuth subsalicylate, budesonide, cholestyramine, sulfasalazine, mesalamine, prednisone, azathioprine, metronidazole, methotrexate, infliximab, adalimumab, or any other medication described. The comparisons include any of the medications described as an intervention, compared in a head-to-head fashion or compared with placebo or no treatment. The outcomes include clinical response, histological response, quality of life, and adverse events according to the outcome description in the included studies.

Abbreviations used in this paper: **CC, collagenous colitis; CI, confidence interval; GIQLI, Gastrointestinal Quality of Life Index; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LC, lymphocytic colitis; MC, microscopic colitis; MD, mean difference; PICO, population, interventions, comparisons, and outcomes; RR, relative risk; SIBDQ, Short Inflammatory Bowel Disease Questionnaire.**

0016-5085/$36.00
http://dx.doi.org/10.1053/j.gastro.2015.11.006

Question 3. In patients successfully treated for MC (either LC or CC) and in remission of symptoms, which treatments are effective and safe for maintaining clinical remission of the disease, measured as maintenance of clinical response, maintenance of histological response, time to relapse, quality of life, and adverse events?

The population is adult patients successfully treated for MC (either LC or CC) and in remission of symptoms. The interventions include budesonide, a thiopurine agent (azathioprine), or any other intervention described in the literature for maintaining remission of MC. The comparisons include head-to-head comparisons among any of the interventions identified, placebo, or no treatment. The outcomes include maintenance of clinical response, maintenance of histological response, time to relapse, quality of life, and adverse events, as described in the included studies.

A summary of the focused questions and PICO components is shown in Table 1.

Definition of the Relative Importance of Outcomes

After defining the included outcomes for each focused question, an online survey was circulated among panel members participating in this review. In this survey, participants were asked to rank the outcomes according to their relative importance. The process was conducted individually and independently. In the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, the relative importance of an outcome is defined on a scale from 1 (least important) to 9 (most critical); those rated from 1 to 3 are defined as of limited importance, from 4 to 6 as important, and from 7 to 9 as critical.[1] The panel was not aware of the quality of the evidence for each of the outcomes at the moment of assessing their importance. The results of the determination of the relative importance of the outcomes are shown in Table 2.

Study Selection Criteria and Search Strategy per Question

Question 1. What is the prevalence of MC? How many colon biopsy specimens should be obtained and from which areas of the colon?

Study selection criteria. We included studies recruiting patients with both LC and CC. For estimation of the prevalence of the disease, we selected studies based on populations of patients with chronic diarrhea. These studies also provided a description of the diagnostic test used, number of biopsy specimens obtained, and areas of the colon from which biopsy specimens were obtained. We excluded editorial letters, comments, notes, or case reports.

Search strategy and databases. We searched Ovid MEDLINE, Ovid EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and the Cochrane Database of Systematic Reviews from inception to August 2014. The search strategy included terms such as "microscopic colitis," "colonoscopy," and "biopsy," among others. There was no restriction by language or status of publication. For more details about the search strategy, see Appendix 1.

Question 2. In patients with MC (either LC or CC), which treatments are effective and safe for inducing remission of the disease, measured as clinical response, histological response, quality of life, and adverse events?

Study selection criteria. We included studies that recruited participants with a confirmed diagnosis of MC, irrespective of whether the patients had CC or LC. In addition, the studies provided information about the effectiveness and safety profile of any medication to treat these conditions compared with other interventions in a head-to-head comparison or placebo. For this question, we excluded studies reporting on the effect of interventions for maintaining remission of MC, because these studies are covered in question 3. Given that we were anticipating scarce evidence to answer this question, we included both randomized controlled trials and observational studies during the initial screening process. Good-quality observational studies were included in the review along with the controlled trials.

Search strategy and databases. We searched Ovid MEDLINE from 1946 to July week 4 2014, Ovid EMBASE from 1980 to 2014 week 31, the Cochrane Central Register of Controlled Trials (CENTRAL) to June 2014, and the Cochrane Database of Systematic Reviews from 2005 to June 2014. The search strategy included terms describing the disease and all medications available for inducing remission of MC. There was no restriction by language. We excluded editorial letters, comments, notes, or case reports. For more details about the search strategy, see Appendix 2.

Question 3. In patients successfully treated for MC (either LC or CC) and in remission of symptoms, which treatments are effective and safe for maintaining clinical remission of the disease, measured as maintenance of clinical response, maintenance of histological response, time to relapse, quality of life, and adverse events?

Study selection criteria. We included treatment trials for patients with a confirmed diagnosis of MC, including both CC and LC, who were in clinical remission. Studies were selected that included information about the effectiveness and safety profile of any medication to maintain remission. We included interventions for maintaining remission compared with other interventions or placebo. We excluded studies reporting on the effect of interventions for inducing remission of MC because those studies were addressed in question 2. Because we anticipated scarce evidence to answer this question, we initially included both randomized controlled trials and observational studies. Good-quality observational studies were included in the review along with the controlled trials.

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