



REVIEW IN GASTROENTEROLOGY

Advances for improved diagnosis of microscopic colitis in patients with chronic diarrhoea[☆]



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Abstract Microscopic colitis is a generic term that includes 2 main forms, collagenous colitis and lymphocytic colitis, and describes a form of inflammatory bowel disease with a chronic and relapsing course. The incidence of microscopic colitis is between 2 and 8 times higher in women than in men, although age, more than sex, increases the risk of collagenous colitis (odds ratio [OR] 8.3 for age ≥ 65 vs. < 65 and OR 2.8 for women). The main symptom is chronic non-bloody watery diarrhoea. Other common symptoms include abdominal pain (50%–70%), with the result that many patients with microscopic colitis meet criteria for irritable bowel syndrome. Colonoscopy with multiple colonic biopsies is currently recommended, as histological changes are the main characteristic feature. The colonic mucosa is macroscopically normal, although certain minimal endoscopic abnormalities have been described.

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PALABRAS CLAVE

Colitis microscópica;
Colitis colágena;
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Diagnóstico
endoscópico;
Criterios histológicos

Colitis microscópica: avances para una mejor identificación en los pacientes con diarrea crónica

Resumen Colitis microscópica es un término genérico que incluye 2 formas principales, colitis colágena y colitis linfocítica, que describe una forma de enfermedad inflamatoria intestinal con curso crónico y recidivante. La incidencia de colitis microscópica es entre 2 y 8 veces más alta en mujeres que en hombres; sin embargo, la edad contribuye más que el sexo en el riesgo de colitis colágena (OR 8,3 para edad ≥ 65 vs. < 65 años y OR 2,8 para sexo femenino). El síntoma principal es la diarrea crónica acuosa, no sanguinolenta. Otros síntomas frecuentes incluyen el

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dolor abdominal (50-70%), lo que hace que muchos pacientes con colitis microscópica cumplan criterios de síndrome de intestino irritable. Hoy en día se recomienda la realización de una colonoscopia, con toma de biopsias escalonadas en todos estos pacientes, ya que el diagnóstico es principalmente histológico. La mucosa colónica suele ser macroscópicamente normal, aunque se han descrito alteraciones endoscópicas mínimas.

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Concept of microscopic colitis

Microscopic colitis (MC) is a generic term that includes two main forms, collagenous colitis (CL) and lymphocytic colitis (LC), and describes a form of inflammatory bowel disease (IBD) characterised by:

1. Chronic or intermittent non-bloody watery diarrhoea.
2. Macroscopically normal or almost normal colonic mucosa assessed by colonoscopy.
3. Characteristic histopathological findings.

In 1993, French and American research groups suggested the use of MC as a generic term to cover any type of colitis in which there were histological, but not endoscopic or radiological, abnormalities. This later became the generic term for the two main entities, known as CC and LC,¹ which are characterised clinically by chronic non-bloody watery diarrhoea. Nevertheless, some authors consider that CC and LC should be regarded as histological subtypes of the same disease, and not as different entities,² a hypothesis that is widely debated.³

There are few studies on the clinical course of patients with MC, but the disease is considered to be characterised by chronic or intermittent diarrhoea and recurrent symptoms. Although the colonic mucosa is macroscopically normal in most patients, it can present mild oedema and erythema. Mucosal tears or fractures and an abnormal vascular pattern have also been described occasionally, especially in patients with CC. MC is characterised by microscopic findings that differ for CC and LC, and which are specific to each entity. These aspects will be discussed in detail in the following sections.

Epidemiology: incidence of microscopic colitis and frequency in patients with chronic diarrhoea

Ten population-based studies on the incidence of CC and/or LC in five European countries (Sweden, Iceland, Denmark, the Netherlands and Spain) and two North American countries (United States and Canada) have been published⁴⁻¹⁴ (Table 1). Four of these studies reported that the incidence had increased over several decades¹⁵⁻¹⁹. The incidence of CC in northern Europe and North America varies from 5.2 to 10.8 ($\times 100,000$ person-years), and in Spain from <1 to 2.9. Unfortunately, no studies have been conducted in other

southern European countries to determine whether there are north-south differences in incidence. The incidence of LC varies from 4 to 19 ($\times 100,000$ person-years) in northern Europe and North America, and from 2.3 to 16 in Spain.

Studies that have assessed trends in the incidence of MC have observed an increase in the frequency of both CC and LC in recent decades.^{7,8,10,14} This could be due to a real increase in incidence as well as a better understanding of the disease.²⁰

Several epidemiological studies have shown that the incidence of MC is between 2 and 8 times higher in women than in men.^{4,7,14,19,21} Furthermore, MC is a disease that can be diagnosed at any age, although it has been observed more often in elderly patients.^{4,6-19} It has been suggested that age contributes more than sex to the risk of CC (OR 8.3 for age ≥ 65 vs. <65 years and OR 2.8 for women),¹³ and that age ≥ 65 years increases the risk of developing CC/LC 4.1-fold (95% CI: 3.9-4.4 for CC and 95% CI: 3.8-4.4 for LC).¹² Finally, it has been reported that 25% of patients with CC are under 45 years of age at diagnosis,¹⁵ and cases of MC have been described in the paediatric population.²²⁻²⁶

Various studies have also determined the frequency of diagnosis of MC in patients with a history of chronic or intermittent non-bloody watery diarrhoea and normal colonoscopy in whom other causes of these have been excluded, observing MC in 4%-29% of cases.^{7,9,16-18,27-36} However, the diagnostic protocols prior to colonoscopy with biopsies are not reported in most studies and, therefore, these may not be comparable. Similarly, the causes of chronic diarrhoea may differ according to geographical region. Nevertheless, it is notable that cases of MC have been described in practically all areas of the world (Fig. 1). The frequency of MC in patients with chronic watery diarrhoea increases with age; thus, the frequency of MC in men over 70 or in women over 50 was around 20% in two studies, giving an incidence of MC of 9.5% and 13.7% if the entire age group is considered.^{9,17}

Advances in diagnosis

Clinical diagnosis

Clinical symptoms: symptom guide

As mentioned, the main symptom of MC is chronic non-bloody watery diarrhoea, which can be recurrent or intermittent. Other common symptoms include abdominal pain (50%-70%), nocturnal diarrhoea (25%-50%), meteorism,

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