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Epidemiology, clinical presentation, associated factors, and current trends in microscopic colitis

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ABSTRACT

Microscopic colitis has attracted the attention of internists and gastroenterologists due to its increasing incidence and the gaps in knowledge about the disease. Like other inflammatory bowel diseases, microscopic colitis frequently manifests as watery diarrhea, particularly in older patients, and significantly reduces their quality of life. This review aims to analyze the current understanding of microscopic colitis based on published studies. A literature search was conducted in PubMed and eLibrary.Ru (1976–2024) databases using the keywords *microscopic colitis* and *микроскопический колит*. Epidemiological data indicate an increasing incidence of microscopic colitis with global prevalence variability. The present study examines risk factors for microscopic colitis, including gut microbiota alterations, genetic determinants, and infectious factors, as well as the association of the disease with COVID-19. Significant risk factors for microscopic colitis include smoking and certain medications. The review discusses sex- and age-related characteristics of microscopic colitis, as well as the differentiation between collagenous and lymphocytic subtypes. According to most studies, the risk of developing microscopic colitis is associated with female sex and older age. The prevalence of collagenous colitis is notably higher among women than among men. The histological criteria, clinical presentation, and differential diagnosis of microscopic colitis are outlined, along with diagnostic criteria for incomplete forms of the disease. In addition, the study discusses non-invasive biomarkers of microscopic colitis and its associations with diseases of other systems, including autoimmune and cardiovascular conditions. Of particular interest is the frequent coexistence of microscopic colitis and celiac disease. Gaps in the knowledge of microscopic colitis are analyzed, and the issues of disease management, including achieving and maintaining clinical remission, are addressed. This review summarizes current evidence on microscopic colitis as a cause of unexplained watery diarrhea, particularly in older patients, including those in countries with low reported disease prevalence.

Keywords: microscopic colitis; collagenous colitis; lymphocytic colitis; diagnosis; epidemiology; therapy.

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Эпидемиология, клиническая картина, сопутствующие факторы и современные тенденции микроскопического колита

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АННОТАЦИЯ

Микроскопический колит привлекает внимание терапевтов и гастроэнтерологов ввиду возросшей его заболеваемости, а также парадокса знаний о нём. Микроскопический колит, как и другие воспалительные заболевания кишечника, часто вызывает водянистую диарею, особенно у пожилых пациентов, что существенно негативно сказывается на их качестве жизни. Цель обзора — анализ современных представлений о микроскопическом колите на основе публикаций. Проведён поиск публикаций в PubMed и eLibrary.Ru (1976–2024) по ключевым словам «микроскопический колит» и «microscopic colitis». Приведены данные эпидемиологических исследований, указывающих на повышение заболеваемости микроскопическим колитом с вариабельностью мировой распространённости. В статье рассмотрены факторы риска развития микроскопического колита, в том числе изменения микробиоты кишечника, генетические детерминанты, значение инфекционного фактора, включая связь с COVID-19. В ряду значимых факторов риска микроскопического колита признаются курение, приём ряда лекарственных препаратов. Обсуждаются половозрастные особенности развития микроскопического колита, включая дифференциацию для коллагенозного и лимфоцитарного подтипов. Риск развития микроскопического колита, по мнению большинства работ, ассоциирован с женским полом и старшим возрастом. Женщины более тропны к коллагенозному колиту, чем лимфоцитарному. Освещены гистологические критерии, клиническая картина и вопросы дифференциальной диагностики микроскопического колита. Приведены данные о критериях диагностики неполных форм микроскопического колита. Обсуждены неинвазивные маркеры микроскопического колита. Рассмотрена связь микроскопического колита с заболеваниями других систем, включая аутоиммунного, кардиологического профиля. Особого внимания заслуживает частое сочетание микроскопического колита и целиакии. Проанализированы текущие пробелы в знаниях о микроскопическом колите, поставлены вопросы рационального управления (достижения и удержания клинической ремиссии) микроскопическим колитом. В статье суммированы современные представления о микроскопическом колите как одной из причин необъяснимой водянистой диареи, особенно у пожилых пациентов, в том числе в странах с низким зарегистрированным уровнем заболеваемости.

Ключевые слова: микроскопический колит; коллагенозный колит; лимфоцитарный колит; диагностика; эпидемиология; терапия.

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INTRODUCTION

The past decade has witnessed an increasing incidence of microscopic colitis (MC), with a gradient toward older patients [1]. In some countries, the prevalence of MC exceeds that of peptic ulcer disease and Crohn's disease [2]. MC is characterized by the following clinicopathological triad: 1) chronic or intermittent watery diarrhea in the patient's history; 2) normal or near-normal findings on colonoscopy, including mild edema, erythema, and/or loss of vascular pattern; less commonly, observance of macroscopic changes such as pseudomembranes and a "cat scratch-like" appearance; 3) a pathognomonic microscopic pattern in the colonic biopsy.

The first descriptions of this novel inflammatory disease of the colonic mucosa, which is referred to as collagenous colitis, appeared in two independent reports in 1976 [3, 4]. Subsequent clinical and basic research validated the classification of collagen-associated inflammatory diseases of the gastrointestinal mucosa and their association with celiac disease and sprue-like disorders [5–12]. Our current understanding of collagenous inflammatory processes has evolved significantly. Growing evidence suggests that the risk factors for MC include infectious agents and the use of new pharmacological agents. Moreover, ongoing studies have explored the genetic susceptibility to MC and its association with celiac disease and other immune-mediated disorders [5]. However, several aspects of MC remain poorly understood.

The objective of the present review was to analyze the current concepts of MC based on the published literature. This review is intended for physicians and gastroenterologists to raise awareness about MC, its increasing prevalence, the necessity of histological verification for diagnosing watery diarrhea, and the importance of timely, rational, and relevant management strategies.

The literature search, selection, and quality assessment were conducted independently by three authors using the eLibrary.Ru and PubMed databases. The search included studies from 1976 to 2024 using the keywords *microscopic colitis* in both Russian and English languages. The literature review followed a three-stage process: screening by title and abstract and the full-text evaluation of potential studies. We excluded the abstracts, theses, and duplicate sources. A total of 60 sources were included in the descriptive review, comprising clinical studies, case reports, systematic reviews, and meta-analyses. The selected sources underwent content analysis, as well as historical and descriptive-analytical assessment. To identify any additional, previously unreported publications, reference lists were also examined.

DIAGNOSIS OF MICROSCOPIC COLITIS

MC is a chronic inflammatory disease of the colon that is characterized by chronic, watery, nonbloody diarrhea, and normal or nearly normal endoscopic findings [13]. MC is diagnosed by histological examination of colonic biopsy specimens obtained from at least six locations (three from the right and three from the left side of the colon) [14]. As per Langner et al., (2015) MC is histologically diagnosed in 12% of colonic biopsy samples from patients with nonbloody diarrhea [15]. Based on the characteristic morphological changes identified in the histological examinations, there are two main subtypes of MC: lymphocytic colitis (LC) and collagenous colitis (CC) [5].

Histological examination of LC revealed that the inflammatory infiltrate is primarily composed of lymphocytes, plasma cells, eosinophils, and scattered neutrophils [16]. The diagnosis of LC requires the visualization of ⩾20 intraepithelial lymphocytes (IELs) per 100 surface epithelial cells [15, 16]. In hematoxylin and eosin-stained specimens, IELs appear round with a compact, irregular nucleus and chromatin, while epithelial cells exhibit vacuolization and reduced mucin content, indicating regenerative or dystrophic changes [17].

LC can be further divided into two pathophysiological subtypes: channelopathy (associated LC, as characterized by impaired regulation of organic acid and ion transport) and inflammatory LC (results from immune responses to microbial metabolites). When compared to CC and classical inflammatory bowel diseases (IBDs), LC is associated with a less pronounced immune response [18].

CC generally has a benign course; however, one of its serious complications is intestinal perforation following colonoscopy [19]. The diagnostic criterion for CC is subepithelial collagen band thickening (⩾10 μm), as confirmed histologically [15, 16]. Collagen deposits may be observed in capillaries, erythrocytes, and lymphocytes [20]. The degree of epithelial damage in CC is more pronounced than in LC. A relevant hallmark morphological feature is the desquamation of epithelial cells from the subepithelial collagen layer. While an increase in IELs can be observed in CC, the counts do not reach the levels recorded in LC. The lamina propria undergoes cellular composition changes, including mononuclear infiltration and, in rare cases, active crypt inflammation with crypt abscess formation, resembling IBD-associated changes [21].

Mogilnaya et al. (2019), in a study analyzing biopsy samples from patients with irritable bowel syndrome (IBS) (n = 23), reported that, in CC, the pathogenetic mechanism involves fibroblasts of the colonic lamina propria, whereas, in LC, the key feature is the dynamics of CD4+ and CD8+ T-cell subpopulations [22].

In addition to the previously mentioned subtypes, some studies [1, 13–16] have described additional subtypes of MC, namely incomplete CC and incomplete LC. Incomplete MC is suspected in patients presenting with clinical signs of MC, but whose biopsy samples do not fully meet the histological criteria for LC or CC. Fiehn et al. (2024) proposed diagnosing incomplete LC when 10–20 IELs per 100 epithelial cells were detected and incomplete CC when the collagen band thickness was 5–10 μm, with mildly increased mononuclear inflammation in the lamina propria [23].

EPIDEMIOLOGY AND RISK FACTORS OF MICROSCOPIC COLITIS

Over the past 15 years, epidemiological studies have demonstrated a rising trend in the incidence and prevalence of MC, particularly in North America and Europe [24]. According to the European clinical guidelines (UEG/EMCG, 2021), the estimated prevalence of MC is 119.4 cases per 100,000 population [95% CI 72.9–165.9] [16]. In Denmark, MC incidence has reached 24.6 cases per 100,000 people [25], surpassing that of ulcerative colitis (18.6 cases per 100,000) and Crohn's disease (9.1 cases per 100,000) [26]. A study on MC subtypes reported the following prevalence rates per 100,000 population: CC, 50.1 cases (95% CI 13.69–76.5) and LC, 61.7 cases (95% CI 48.2–75.3). The annual incidence of MC was 11.4 cases per 100,000 people (95% CI 9.2–13.6) [15].

Several studies have highlighted that MC primarily affects individuals over 60 years of age [27–29]. The highest age-adjusted incidence rates for both men and women were observed in the 60–69-age group [27]. Miehlke et al. reported a predominantly female prevalence of MC, with a peak incidence occurring between the sixth and eighth decades of life [16]. In a cohort study, Fernández-Bañares et al. (2016) found that individuals aged ⩾65 years had an increased risk of developing MC (hazard ratio [HR] 5.25; 95% CI 3.81–7.24) [28]. Furthermore, the risk of CC was significantly higher in individuals aged >65 years (OR 8.3; 95% CI 6.2–11.1) and females (OR 2.8; 95% CI 2.0–3.7) [29]. Another study reported that being ⩾65 years of age increases the risk of developing CC (95% CI 3.9–4.0) and LC (95% CI 3.8–4.4) by 4.1 times. However, MC has also been diagnosed in 25% of patients aged <45 years and cases of CC have been documented in children [30].

Women show a stronger predisposition to CC, with the risk being three times greater than in men (95% CI 2.92–3.19), whereas LC risk is 1.92 times greater in women (95% CI 1.53–2.31) [23]. Among women aged ⩾65 years, the risk of CC was 3.6-times greater (95% CI 3.4–3.9), while the risk of LC was 3.3-times greater (95% CI 3.0–3.6) compared to that in women aged <65 years [27]. In clinical guidelines incorporating 19 studies, female sex was also identified as a significant risk factor for MC development (OR 2.52; 95% CI 2.28–2.79) [16].

Despite the ongoing research, the exact etiology and pathogenesis of MC remain unclear; however, it is generally recognized as a multifactorial disease [16, 31, 61]. Potential triggers contributing to MC include immune-inflammatory reactions to bile salts, bacterial toxins, and drugs, as well as the possible involvement of autoimmune processes.

Epidemiological studies have consistently identified smoking as a major risk factor for MC [31–34]. For instance, Larsson et al. (2016) reported associations between MC and female sex (OR 3.57; 95% CI 2.22–5.74), smoking (OR 2.29; 95% CI 1.66–3.84), and high alcohol consumption (OR 1.89 for the highest quartile; 95% CI 0.82–4.33, $p_{\text{for trend}} = 0.032$) [31]. These findings align with those of Burke et al. (2018), who reported a higher risk of MC in current smokers (OR 2.52; 95% CI 1.59–4.00) and former smokers (OR 1.54; 95% CI 1.09–2.17). Moreover, the risk increased with longer smoking duration (OR 2.52; 95% CI 1.59–4.00, $p = 0.001$), but decreased after smoking cessation (OR 0.57; 95% CI 0.36–0.91, $p = 0.017$). Current smoking was more strongly associated with CC (OR 3.68; 95% CI 1.94–6.97) than with LC (OR 1.71; 95% CI 0.83–3.53) [32]. A meta-analysis (2019) of seven studies confirmed a higher risk of MC in active smokers compared to that in never-smokers (OR 2.99; 95% CI 2.15–4.15). The study also noted that the risk of MC persisted even after smoking cessation (OR 1.63; 95% CI 1.37–1.94) [33]. Another meta-analysis (8 studies, n = 1,461) demonstrated an increased risk of MC in active smokers (OR 3.58; 95% CI 2.51–5.11), as well as a higher risk of CC (OR 4.43; 95% CI 2.68–7.32) and LC (OR 3.64; 95% CI 2.46–5.38) [34].

Infectious factors

The role of infectious triggers in the pathogenesis of MC remains debatable. For instance, Khalili et al. (2021) identified an increased risk of MC following infectious gastroenteritis (OR 2.63; 95% CI 2.42–2.85). The following pathogens were significantly associated with an increased risk of MC: *Clostridium difficile* (OR 4.39; 95% CI 3.42–5.63), norovirus (OR 2.87; 95% CI 1.66–4.87), and *Escherichia* species (OR 3.82; 95% CI 1.22–11.58). They also report an association between gastrointestinal infections and the risk of MC, which was stronger for the CC subtype (adjusted odds ratio [aOR] 3.23; 95% CI 2.81–3.7; $p = 0.005$) compared to LC (aOR 2.51; 95% CI 2.28–2.76; $p = 0.005$) [35]. Several studies have also described an association between severe COVID-19 and MC (OR 1.27; 95% CI 1.08–1.49), particularly CC (OR 1.72; 95% CI 1.29–2.28), but not LC (OR 1.11; 95% CI 0.91–1.36) [36].

Role of gut microbiota imbalance

In their study on the microbiota of individuals with MC, Millien et al. found an increased abundance of the proinflammatory *Desulfovibrionales* family and a reduced presence of the beneficial *Corynebacteriaceae* family. In addition, an increased abundance of the genus *Actinomyces* was observed in patients taking proton-pump inhibitors, as well as an increase in the class *Bacilli* in patients using nonsteroidal anti-inflammatory drugs (NSAIDs) [38]. Another study described gut microbiome dysbiosis in MC patients, characterized by an increased prevalence of proinflammatory bacteria such as *Proteobacteria*, *Alistipes*, and *Collinsella* as well as reduced levels of *Faecalibacterium prausnitzii (Ruminococcaceae)* [39]. Sequencing data further confirmed qualitative shifts in the microbiota composition of MC patients relative to that of healthy individuals, particularly in terms of the depletion of *Clostridiales* and the enrichment of *Prevotella* [40].

Genetically determined risk factors

Several studies [41, 42] have demonstrated an increased prevalence of LC in individuals carrying the HLA-A1 and HLA-DRW53 genotypes, whereas the HLA-DQ2 genotype has been

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associated with a lower prevalence of CC. For instance, Stahl et al. (2020) identified an association between three HLA alleles (HLA-B × 08:01, HLA-DRB1 × 03:01, and HLA-DQB1 × 02:01) of the 8.1 haplotype and an increased risk of CC. These alleles were linked to other immune-mediated diseases, including celiac disease [40]. Norén et al. (2018) reported an association between MC development and single nucleotide polymorphisms in genes that reduce the expression of tight junction proteins, specifically: rs1234224 in *PTEN* (OR 1.70; 95% CI 1.23–2.34; $p = 0.001$) and rs17417230 in *MAGI1* (OR 1.58; 95% CI 1.14–2.19; $p = 0.006$) [40].

Drug-induced risk factors

The present findings linking MC development to medication-use have prompted some authors to introduce the term "drug-induced MC" [41].

According to relevant clinical guidelines (2021), MC has been linked to the use of proton-pump inhibitors (OR 2.95; 95% CI 1.82–4.80) owing to an increased risk after 4–12 months of use (OR 4.69; 95% CI 3.58–6.13), selective serotonin-reuptake inhibitors (OR 2.98; 95% CI 2.35–3.78), and NSAIDs (OR 2.40; 95% CI 1.99–2.89) [16].

CLINICAL PRESENTATION AND DIFFERENTIAL DIAGNOSIS OF MICROSCOPIC COLITIS

Verhaegh et al. (2021) reported that, within the first year of MC diagnosis, 34% of the patients experienced relapses, while 15% developed a chronic active form, which was associated with a reduced quality-of-life [42]. The following symptom prevalence was established in MC: abdominal pain (50%–70%), nocturnal diarrhea (25%–50%), flatulence and an urge to defecate (70%), urinary incontinence (40%), weight loss (up to 50%), and fatigue (50%–60%) [43]. Among the hospitalized individuals diagnosed with MC, 87.7% presented with diarrhea, 26.3% reported abdominal pain, 17.5% had acute kidney injury, 17.5% experienced rectal bleeding, 16.4% reported vomiting, and 7.0% experienced syncope or collapse [44]. Munck et al. (2023) identified bile acid malabsorption diarrhea in 36% of all MC cases (34% in CC, 28.5% in LC) [45]. During a 1-year follow-up, individuals diagnosed with MC reported the following symptoms: nocturnal stools (15%), abdominal pain (28%), weight loss (32%), and fecal incontinence (21%) [46].

MC must be differentiated from IBS with predominant diarrhea (IBS-D). Approximately one-third of individuals with MC report symptoms resembling IBS-D, including abdominal pain associated with defecation, altered stool consistency, or changes in bowel movement frequency [47]. Rusu et al. (2023) reported that 11.2% of individuals initially diagnosed with IBS-D were ultimately diagnosed with MC, with LC being more prevalent than CC [48]. Moreover, Songtanin et al. (2023) demonstrated that the fecal calprotectin levels were significantly elevated in MC patients compared to that in the corresponding controls (95% CI 0.3–1.0; $p = 0.001$), suggesting that fecal calprotectin measurement can act as a noninvasive marker for diagnosing MC in cases of chronic diarrhea [49].

COMORBIDITIES ASSOCIATED WITH MICROSCOPIC COLITIS

According to Barta et al., 45.28% of individuals diagnosed with MC have a concurrent autoimmune disease [50]. A separate study identified a 1.83-fold increased risk of developing rheumatoid arthritis among MC patients compared to the general population (adjusted relative risk [aRR] 1.83; 95% CI 1.39–2.41) [51]. In addition, Kang et al. (2023) found that type 1 diabetes was 80% more prevalent among MC patients than among the general population. This association was stronger for CC (OR 2.15; 95% CI 1.70–2.71) than for LC (OR 1.62; 95% CI 1.37–1.92) [52].

A French multicenter prospective study identified significant associations between MC and age >50 years (OR 3.1; 95% CI 1.6–5.9), autoimmune diseases (OR 5.5; 95% CI 2.5–12.0), and the use of NSAIDs (OR 3.7; 95% CI 2.1–6.6) [53]. Madisch et al. observed that autoimmune disorders were more common among CC patients (48.4%) than among LC patients (29.6%) receiving corticosteroids, antibiotics, bismuth, or 5-aminosalicylates. Regular NSAID use has also been reported by 18.6% of CC patients and 17.6% of LC patients [54]. Autoimmune thyroid diseases were diagnosed in 10%–20% of MC patients, while celiac disease was detected in 5%–25% [49].

Bergman et al. (2023) reported that MC developed at a younger age in individuals diagnosed with celiac disease (53.7 ± 18.9 years vs. 62.1 ± 16.5 years, $p = 0.49$). The authors observed an 11.6-fold increased risk of MC in individuals with celiac disease (95% CI 9.8–13.8) [5]. The coprevalence of MC and celiac disease has been estimated at 6%, particularly in refractory cases [16]. Patients with celiac disease have a 50- to 70-fold increased risk of developing MC, while celiac disease is diagnosed in 2%–9% of all MC patients [51]. Roth et al. (2024) identified a 6.06-fold greater risk of celiac disease in LC compared to that in CC [52]. Another study confirmed the association between MC and celiac disease, reporting an 8.3-fold increased risk (OR 8.276; 95% CI 5.888–11.632, $p < 0.001$). The prevalence of MC among celiac patients was 6.2% (95% CI 4.1–9.2; $p < 0.001$), with CC in 1.6% of cases (95% CI 0.7–3.5; $p < 0.001$) and LC in 4.3% of cases (95% CI 3.1–5.9; $p < 0.001$) [53].

Roth and Ohlsson (2024) reported that MC and celiac disease co-occurred at the onset in 50% of all cases. The prevalence of celiac disease was higher in LC (12.1%) than in CC (3.3%; $p = 0.05$) and in single-episode MC compared to refractory MC (12.9% vs. 2.3%; $p = 0.01$). Glucocorticoids were more frequently used in CC (37.0%) than in LC (21.2%; $p = 0.037$). After adjusting for the smoking status, celiac disease was positively associated with LC (OR 4.222; 95% CI 1.020–17.469; $p = 0.047$) and inversely associated with refractory MC (OR 0.210; 95% CI 0.042–1.506; $p = 0.058$) [52].

Altawili et al. (2024) examined 6,836 MC patients, which included 179 with celiac disease, and found a strong association between MC and celiac disease (OR 22.69; 95% CI 19.55–26.33; $p < 0.0001$). They found that the mortality rates were higher in MC patients with celiac disease than in those without (2.79% vs. 0.99%; $p = 0.019$), signifying celiac disease as an independent risk factor for mortality in MC patients [54].

Forss et al. reported that MC patients had an increased risk of major adverse cardiovascular events, including ischemic heart disease, congestive heart failure, and stroke (OR 1.27; 95% CI 1.21–1.33) [55]. Moreover, Hong et al. (2023) reported a moderate association between MC and ischemic heart disease ($p = 0.02$) [56].

APPROACHES TO THE MANAGEMENT OF PATIENTS WITH MICROSCOPIC COLITIS

The primary goal of therapy for MC, irrespective of its subtype (LC or CC), is to achieve clinical remission, with maintenance therapy and quality-of-life improvement as secondary objectives [43]. As the significance of achieving histopathological remission is unclear, repeat biopsies are not recommended for patients demonstrating clinical improvement [51]. A key aspect of MC management involves modifying the potential risk factors, including smoking cessation and discontinuing medications that exhibit a chronological association with diarrhea onset [33, 35].

The first-line therapy for inducing clinical remission in MC is budesonide, as confirmed by multivariate analysis (OR 25.0; 95% CI 2.63–238.10, $p = 0.0052$). Budesonide therapy resulted in clinical remission in 100% of patients with histopathological remission, whereas only 11.8% of those with persistent histological inflammation achieved remission ($p = 0.0002$) [57]. Malik et al. (2024) also reported a higher rate of clinical remission at 6 weeks in MC patients receiving budesonide (relative risk [RR] 2.46; 95% CI 2.27–2.67) than in those receiving mesalamine (RR 2.24; 95% CI 1.95–2.57). This effect persisted at 8 weeks (RR 2.29; 95% CI 2.14–2.45 and RR 1.7; 95% CI 1.41–2.05, respectively; $p = 0.003$) [58]. Accordingly, considering the high recurrence rate following short-term budesonide therapy, maintenance treatment should be considered [57].

In cases of refractoriness or intolerance to budesonide in MC patients, additional agents may be considered for induction and maintenance of clinical remission, including loperamide, diphenoxylate/atropine, mesalazine, bismuth subsalicylate, prednisolone, bile acid sequestrants, or immunomodulators, as per the circumstances [59].

The efficacy of vedolizumab and anti-TNF-α therapies in steroid-refractory MC remains an emerging area of study, necessitating large-scale clinical trials [60]. A meta-analysis (2023) of 14 studies (n = 164) demonstrated the benefit of vedolizumab and TNF-α inhibitors in achieving clinical remission with acceptable safety profiles in steroid-refractory MC, as follows: vedolizumab 63.5% (95% CI 0.483–0.776; $p = 0.08$), infliximab 57.8% (95% CI 0.3895–0.7571; $p = 0.7541$), and adalimumab 39.3% (95% CI 0.0814–0.7492; $p = 0.02$). The maintenance remission rates were as follows: vedolizumab 65.9% (95% CI 0.389–0.889; $p = 0.02$), infliximab 45.3% (95% CI 0.1479–0.7747; $p = 0.36$), and adalimumab 32.5% (95% CI 0.000–0.8508; $p = 0.14$). The incidence of treatment-related adverse events requiring discontinuation was 12.2% for vedolizumab, 32.9% for infliximab, and 23.0% for adalimumab [60].

CONCLUSION

MC is increasingly recognized as an urgent clinical concern and is frequently diagnosed via histopathological evaluation of colonic biopsies in patients with diarrhea, particularly in elderly populations. As such, MC warrants equal attention to other immune-mediated IBDs in the pursuit of sustained remission. Despite the advancements in MC research, several unresolved questions remain. Fundamental research holds promise for elucidating the etiology and pathogenesis of MC. Identifying MC triggers, such as gut microbiota dysbiosis, cytokine imbalance, and genetic predisposition, paves the way for preventing MC development, thereby devising new rational therapeutic strategies and achieving sustained remission or potential cure. Currently, no validated severity grading system exists for MC, and the use of noninvasive biomarkers (e.g., fecal calprotectin, lipocalin) requires further validation for disease activity prediction. The only way to verify MC is through colonoscopy with multiple biopsies, followed by extensive histopathological evaluation. The choice of treatment is thus largely determined by symptom severity, with the primary goal of inducing symptomatic remission while minimizing the potential side effects and improving the patients' quality-of-life in the short term. Budesonide remains the first-line therapy for induction and maintenance of remission, albeit the uncertainties persist regarding the optimal duration of maintenance therapy and the best preventive strategies. As such, an important challenge remains the subset of MC patients who are resistant to budesonide, highlighting the limitations of currently available treatment options and the need for the development and implementation of novel therapeutic strategies.

ADDITIONAL INFORMATION

Authors' contribution. R.R.S. — resources, formal analysis, investigation, writing — original draft; D.G.I. — investigation, formal analysis, methodology; E.V.K. — conceptualization, visualization, formal analysis, investigation, writing — review and editing, supervision, validation, data curation, project administration. Thereby, all authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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Вклад авторов. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией). Наибольший вклад распределён следующим образом: Р.Р.С. — ресурсы, анализ, исследование, создание черновика; Д.Г.И. — исследование, анализ, методология; Е.В.Х. — концептуализация, визуализация, анализ, исследование, редактирование рукописи, общее руководство, проверка, обработка и управление результатами, администрирование проекта.
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