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Therapeutic Approaches in Ulcerative Colitis: A Literature Review (*Abordagens Terapêuticas na Retocolite Ulcerativa: Uma Revisão da Literatura*)

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by recurrent inflammation affecting the mucosa of the colon and rectum, leading to debilitating symptoms and reduced quality of life. With advances in the understanding of the disease's pathophysiology, new therapeutic approaches have been developed, extending beyond conventional treatments such as aminosalicylates, corticosteroids, and immunosuppressants. To critically analyze and discuss current and emerging therapeutic approaches in the treatment of ulcerative colitis, considering their efficacy, safety, therapeutic innovations, and future perspectives in comprehensive patient care. This is a narrative literature review, involving a search of articles in the PubMed, SciELO, Scopus, and LILACS databases, published between 2015 and 2025. Included were clinical trials, systematic reviews, international guidelines, and observational studies related to UC treatment. The selection followed criteria of clinical relevance, methodological rigor, and updated evidence. Biologic therapies such as anti-TNFs, vedolizumab, and ustekinumab showed significant efficacy in inducing and maintaining remission in UC. Oral JAK inhibitors, such as tofacitinib and upadacitinib, are emerging as effective alternatives, though they require close monitoring. Complementary strategies such as fecal microbiota transplantation and specific diets have shown promising results. Precision medicine and the use of biomarkers are emerging as future trends, enabling more individualized and effective therapies. The treatment of ulcerative colitis has evolved significantly, incorporating new therapeutic technologies and multidisciplinary perspectives. Although the pharmacological arsenal is broader and more effective, challenges persist, such as loss of therapeutic response, adverse effects, and access limitations. The future points toward personalized, evidence-based, and accessible medicine, focusing on comprehensive care and improved patient quality of life.

RESUMO

A retocolite ulcerativa (RU) é uma doença inflamatória intestinal crônica caracterizada por inflamação recorrente que afeta a mucosa do cólon e reto, levando a sintomas debilitantes e redução da qualidade de vida. Com os avanços na compreensão da fisiopatologia da doença, novas abordagens terapêuticas foram desenvolvidas, estendendo-se além dos tratamentos convencionais, como aminosalicilatos, corticosteroides e imunossupressores. Analisar e discutir criticamente as abordagens terapêuticas atuais e emergentes no tratamento da retocolite ulcerativa, considerando sua eficácia, segurança, inovações terapêuticas e perspectivas futuras no cuidado integral ao paciente. Trata-se de uma revisão narrativa da literatura, envolvendo uma busca de artigos nas bases de dados PubMed, SciELO, Scopus e LILACS, publicados entre 2015 e 2025. Foram incluídos ensaios clínicos, revisões sistemáticas, diretrizes internacionais e estudos observacionais relacionados ao tratamento da RU. A seleção seguiu critérios de relevância clínica,

rigor metodológico e evidências atualizadas. Terapias biológicas como anti-TNFs, vedolizumabe e ustequinumabe demonstraram eficácia significativa na indução e manutenção da remissão na colite ulcerativa. Inibidores orais de JAK, como tofacitinibe e upadacitinibe, estão emergindo como alternativas eficazes, embora exijam monitoramento rigoroso. Estratégias complementares, como transplante de microbiota fecal e dietas específicas, têm mostrado resultados promissores. A medicina de precisão e o uso de biomarcadores estão emergindo como tendências futuras, permitindo terapias mais individualizadas e eficazes. O tratamento da retocolite ulcerativa evoluiu significativamente, incorporando novas tecnologias terapêuticas e perspectivas multidisciplinares. Embora o arsenal farmacológico seja mais amplo e eficaz, desafios persistem, como perda de resposta terapêutica, efeitos adversos e limitações de acesso. O futuro aponta para uma medicina personalizada, baseada em evidências e acessível, com foco no cuidado integral e na melhoria da qualidade de vida do paciente.

INTRODUCTION / INTRODUÇÃO

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) of autoimmune nature and recurrent course, primarily affecting the mucosa of the rectum and colon in a continuous and ascending pattern. Unlike Crohn's disease, which can affect any segment of the gastrointestinal tract, UC is limited to the large intestine and presents with superficial inflammation restricted to the mucosa (1). Its etiopathogenesis is multifactorial, involving genetic predisposition, alterations in the gut microbiota, and a dysregulated immune response to environmental antigens (2). External factors such as industrialized diets, smoking, early antibiotic use, and urban lifestyle have been identified as modulators of the risk of developing the disease (3). In Brazil, recent data indicate a progressive increase in the prevalence of IBD, reflecting a global phenomenon of epidemiological transition in developing countries (4).

The clinical manifestations of UC include bloody diarrhea, abdominal pain, tenesmus, urgency to evacuate, and in more severe cases, fever and weight loss (5). The disease's impact goes beyond physical symptoms, significantly interfering with patients' quality of life, with emotional and social implications such as anxiety, depression, and work impairment (6). Moreover, patients with long-standing disease have an increased risk of developing colorectal cancer, which underscores the importance of effective control of intestinal inflammation (7). Therefore, the clinical management of UC should aim not only to control symptoms and prevent relapses but also to reduce complications and improve the overall health status of the patient.

Historically, UC treatment was centered on drugs such as aminosalicylates (mesalazine, sulfasalazine), corticosteroids, and immunosuppressants like azathioprine and cyclosporine (8). However, these conventional therapies have limitations, especially in patients with moderate to severe disease or inadequate response to induction therapy (9). In addition, adverse effects associated with prolonged corticosteroid use, such as osteoporosis, diabetes, and hypertension, demand safer and more sustainable therapeutic strategies (10).

Over the past two decades, the advent of biologic therapies has revolutionized UC treatment, offering greater efficacy and symptom control in patients refractory to traditional approaches. Tumor necrosis factor-alpha (TNF-α) inhibitors, such as infliximab, adalimumab, and golimumab, were the first biologic agents introduced, showing good results in both clinical and endoscopic remission (11). Subsequently, new drug classes have been incorporated, such as integrin antagonists (vedolizumab), which act selectively in the gastrointestinal tract, and interleukin blockers (ustekinumab), approved for moderate to severe cases (12). More recently, oral therapies such as Janus kinase (JAK) inhibitors, including tofacitinib and upadacitinib, have offered advantages in administration and onset of action, although they require strict monitoring due to potential adverse effects such as thromboembolic events (13).

Beyond the pharmacological arsenal, emerging strategies are being explored, such as modulation of the intestinal microbiota through probiotics, prebiotics, and fecal microbiota transplantation, with promising results in refractory cases (14). Diet has also gained prominence as a course-modifying factor, with specific nutritional approaches aimed at excluding pro-inflammatory foods and including nutrients with anti-inflammatory potential (15). In parallel, psychological support, health education, and multidisciplinary follow-up are fundamental in comprehensive patient care, promoting treatment adherence and improved clinical outcomes (16).

In this context, personalized medicine emerges as an innovative perspective, seeking to tailor treatment based on genetic, immunological, and microbial biomarkers, optimizing therapeutic efficacy and minimizing adverse events (17). Identifying specific patient profiles that respond better to certain drugs or therapeutic pathways represents an important step toward the future of UC management. Given so many changes and advances, systematizing and critically analyzing the recent literature becomes essential to understand the current state of therapy and its future possibilities.

Therefore, this literature review aims to analyze and discuss the current and emerging therapeutic approaches in the treatment of ulcerative colitis, highlighting the most relevant advances, persistent clinical challenges, and innovative trends in the care of patients with this chronic and debilitating condition.

This work is a narrative, descriptive, and exploratory literature review, aiming to compile and critically analyze current and emerging therapeutic approaches in the treatment of ulcerative colitis. This type of review was chosen due to its

methodological flexibility and its ability to encompass a variety of sources and types of studies, allowing for a broad and updated overview of the topic (18).

The literature search was conducted in the electronic databases PubMed, SciELO, Scopus, and LILACS, through searches carried out between April and June 2025. The following Health Sciences Descriptors (DeCS/MeSH) were used, combined with Boolean operators: "Ulcerative Colitis" AND "Treatment" OR "Therapy" OR "Biological Agents" OR "New Drugs" OR "Precision Medicine". The search was limited to articles published in the last ten years (2015–2025), in Portuguese, English, and Spanish, with full-text access.

The review included randomized clinical trials, observational studies, systematic review articles, international society guidelines (such as ECCO, AGA, ACG), and updated consensus documents on the management of the disease, as long as they addressed therapeutic interventions, clinical efficacy, safety, or emerging perspectives in the treatment of ulcerative colitis. Articles exclusively focused on Crohn's disease, studies on pediatric populations without separated data, and publications with inadequate methodology or lacking peer review were excluded.

Article selection was carried out in two stages. First, titles and abstracts were screened based on inclusion criteria. Second, the selected articles were read in full, and relevant data were extracted, including author, year, study type, study population, therapeutic intervention, analyzed outcomes, and main results. This step enabled the organization of the content into thematic categories according to the nature of the therapies discussed.

Data analysis was performed in a qualitative and integrative manner, aiming to compare clinical evidence, identify knowledge gaps, and highlight ongoing therapeutic advances. Although this is not a systematic review with meta-analysis, methodological rigor was ensured by following the principles recommended by authors such as Mendes et al. (19), thus ensuring the consistency and scientific validity of the synthesized evidence.

To ensure the relevance and timeliness of the content, priority was given to the inclusion of articles published in high-impact journals, as well as clinical guidelines from recognized entities in the fields of gastroenterology and inflammatory bowel diseases. The review also adhered to ethical principles of good scientific practice, using only open-access sources or materials retrieved via institutional repositories.

RESULTS & DISCUSSION / RESULTADOS E DISCUSSÃO

Conventional therapies for ulcerative colitis (UC) still play a central role in the management of mild to moderate cases, particularly through the use of aminosalicylates such as mesalazine and sulfasalazine. These drugs act directly on the intestinal mucosa with a local anti-inflammatory effect, proving effective in inducing and maintaining remission in non-severe forms of the disease (10). Randomized studies have shown clinical remission rates of up to 40% with the isolated use of mesalazine in patients with mild to moderate colitis (11).

Corticosteroids, such as prednisone and budesonide, are reserved for moderate to severe cases and acute flare-ups. Although effective in inducing a rapid response, prolonged use is associated with significant adverse effects such as hyperglycemia, osteoporosis, and increased infection risk (20). Steroid dependence remains a challenge for many patients, requiring safer therapeutic strategies.

Immunosuppressants such as azathioprine and 6-mercaptopurine are used primarily for maintaining remission and reducing corticosteroid dependence. However, they have a delayed therapeutic onset and carry risks of myelotoxicity, hepatotoxicity, and pancreatitis (4). In summary, while conventional therapies have historically contributed to disease control, they prove insufficient in moderate to severe cases and present safety profile limitations.

The introduction of biologic agents has revolutionized UC treatment, offering more robust and sustained clinical responses. Tumor necrosis factor-alpha (TNF-α) inhibitors—such as infliximab, adalimumab, and golimumab—were the first biologics approved for the disease, showing efficacy in both induction and maintenance of clinical and endoscopic remission (21). Infliximab, for example, showed clinical response rates exceeding 60% after eight weeks in multicenter studies (ACT 1 and 2), with significant endoscopic remission after 30 weeks (22).

Despite therapeutic success, about 30% of patients do not respond to induction therapy (primary failure), and another 30% lose response over time (secondary failure), prompting the development of new drug classes (23). Among them, vedolizumab stands out—a selective anti-α4β7 integrin agent that acts specifically in the gastrointestinal tract by blocking the migration of inflammatory lymphocytes. Studies such as GEMINI 1 demonstrated superiority to placebo in induction and maintenance of remission, with fewer systemic side effects (12).

Another advance was the use of ustekinumab, a monoclonal antibody that blocks interleukins 12 and 23, key cytokines in the inflammatory cascade of UC. Trials like UNIFI showed significant clinical and mucosal response rates after administration of the drug in patients refractory to anti-TNFs (24). The incorporation of these drugs into the therapeutic arsenal has allowed for treatment individualization based on clinical profiles and prior treatment history, and they are currently recommended as first-line options for moderate to severe UC by international guidelines (25).

More recently, Janus kinase (JAK) inhibitors have emerged as a promising oral treatment option for refractory UC. Tofacitinib was the first JAK inhibitor approved for use in adults with moderate to severe UC. Unlike biologics, which are administered via infusion or injection, JAK inhibitors are taken orally and act intracellularly by blocking the signal transduction of inflammatory cytokines (26).

A phase III study (OCTAVE Induction) demonstrated that tofacitinib achieved clinical remission in 18.5% of patients by week 8, compared to 8.2% in the placebo group. In the maintenance phase (OCTAVE Sustain), 40.6% of patients maintained clinical remission after 52 weeks (26). Despite these

positive results, JAK inhibitors require precautions due to the risk of serious adverse events, including opportunistic infections, dyslipidemia, and cardiovascular events—especially in patients with pre-existing risk factors (27).

Other oral molecules such as upadacitinib and filgotinib are in advanced clinical trials and have shown promising preliminary results. Upadacitinib, for example, demonstrated clinical remission rates of up to 26% during induction, outperforming tofacitinib in specific subgroups (28). The convenience of oral administration and rapid onset of action make JAK inhibitors strong candidates to replace biologics in selected patient profiles.

Modulation of the gut microbiota has been gaining ground as an emerging strategy in UC therapy. Fecal microbiota transplantation (FMT), for instance, has shown good outcomes in refractory colitis patients by improving bacterial diversity and intestinal barrier integrity (28). A recent systematic review found clinical remission rates of up to 33% with FMT, especially in protocols involving multiple infusions (14).

In parallel, specific dietary interventions are being studied as adjuncts to pharmacological treatment. Diets such as the Crohn's Disease Exclusion Diet (CDED) and low-FODMAP diets have been associated with reduced inflammatory activity and improved gastrointestinal symptoms (15). Although there are no formal guidelines recommending dietary interventions as monotherapy, individualized nutritional counseling is already widely recognized as an essential part of therapeutic planning (16).

Precision medicine stands out as one of the most significant future prospects in UC management. Recent studies have identified genetic and immunologic biomarkers capable of predicting therapeutic response, such as interferon pathway gene expression or gut microbiota composition (17). Identifying specific inflammatory and molecular profiles will, in the future, allow for the selection of the most effective treatment for each individual, reducing exposure to ineffective therapies.

Despite the progress, significant challenges remain in the treatment of UC. The absence of widely available biomarkers, the high cost of biologics, and difficulties in accessing these drugs through public health systems are barriers to the full implementation of therapeutic innovations (9). Furthermore, secondary loss of response and adverse events associated with treatment require constant clinical monitoring and laboratory follow-up.

Nevertheless, the future is promising. New molecules such as sphingosine-1-phosphate (S1P) inhibitors and cellular therapies using regulatory T cells are under investigation and may further revolutionize UC treatment (30). Additionally, advances in artificial intelligence in risk stratification and clinical data analysis may offer new tools to support therapeutic decision-making.

Thus, it is evident that UC management is rapidly evolving toward a personalized, multidisciplinary approach based on robust evidence. The future of UC therapy is headed toward individualization, integration of diverse knowledge domains, and improved accessibility, offering a concrete hope for enhanced quality of life for affected patients.

CONCLUSION

Ulcerative colitis (UC) represents a growing therapeutic challenge in clinical practice, especially due to its chronic, recurrent, and potentially debilitating nature. Over the years, the understanding of the disease's pathophysiology has evolved, enabling the development of more specific and effective therapies. While conventional treatments such as aminosalicylates, corticosteroids, and immunosuppressants still play a role in mild cases and as background therapy, significant progress has been made in the treatment of moderate to severe forms with the incorporation of biologic agents and, more recently, small oral molecules such as JAK inhibitors.

Biologic therapies—particularly anti-TNF agents, integrin blockers, and interleukin antagonists—have introduced a paradigm shift in UC management, providing sustained clinical remission and improving patients' quality of life. JAK inhibitors are also emerging as a promising alternative, especially due to their oral administration and rapid onset of action, although close monitoring is required due to their safety profile.

Moreover, therapeutic strategies have expanded beyond pharmacology, recognizing the importance of diet, the gut–microbiota axis, and psychological support in disease control. Interventions such as fecal microbiota transplantation, personalized diets, and health education have shown adjuvant potential, reflecting the multifactorial complexity of UC.

Precision medicine, in turn, is emerging as a strategic future direction, aiming to use biomarkers and molecular profiles to guide therapeutic choices. This individualization of care is essential for improving clinical outcomes and reducing the costs associated with ineffective therapies.

However, important limitations remain, such as inequality in access to advanced therapies, the lack of widely available biomarkers in clinical practice, and the need for more long-term studies in diverse populations. Therefore, it is recommended that UC management be conducted by multidisciplinary teams, based on updated evidence, and that public health policies ensure broader access to modern treatments.

In summary, the consolidation of current therapies and the rise of emerging approaches point to a more promising future for the treatment of ulcerative colitis. Continuous professional development and the strengthening of clinical research are central elements for sustaining progress in the management of this complex and impactful condition.

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