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REVIEW ARTICLE

New Trends in Inflammatory Bowel Disease

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Abstract Inflammatory bowel disease (IBD) is a chronic idiopathic inflammatory disease of the gastrointestinal (GI) tract. In the past decade a shift in the treatment paradigm of IBD has ensued. The availability of drugs capable of inducing mucosal healing, combined with the recognition that IBD is not an intermittent disease, but rather a progressive one causing bowel damage and disability, led us to a more stringent strategy. Tailored therapy with more aggressive treatment in high-risk patients, treating beyond symptoms, intervening early before damage occurs, optimizing therapeutic regimens, and actively pursuing sustained remission and sustained control of inflammation are strategies that are slowly being incorporated in our clinical practice. Furthermore, new drugs targeting different immunological pathways, such as vedolizumab, have recently been approved and therefore more therapeutic resources for patients failing anti-tumour necrosis factor alpha (anti-TNFα) agents will be available.

The future years look promising for IBD. Hopefully the new trends in IBD management, combined with new drugs, will make possible to change the course of disease and provide better therapy and quality of life for patients suffering from this disabling disease.

PALAVRAS CHAVE
Colite Ulcerosa;
Doença de Crohn;
Doença Inflamatória Intestinal;
Terapia Molecular Dirigida;
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Novas Estratégias Terapêuticas na Doença Inflamatória do Intestino

Resumo A doença inflamatória intestinal (DII) é uma doença idiopática crónica e incapacitante do trato gastrointestinal. Na última década tem-se assistido a uma modificação nas estratégias de abordagem e tratamento do doente com DII. O desenvolvimento de fármacos potentes com capacidade de induzir a cicatrização da mucosa, aliado ao reconhecimento do carácter progressivo da doença, com dano intestinal irreversível e compromisso da qualidade de vida, conduziu à adoção de estratégias mais rigorosas. Tem-se assistido à incorporação de novas estratégias na prática clínica atual, tais como terapêutica individualizada mais agressiva em doentes com mau prognóstico mais precocemente, uso de outros objetivos terapêuticos para além da remissão

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sintomática, intervenção precoce para evitar o desenvolvimento de dano intestinal irreversível, optimização da terapêutica com objetivo de alcançar a remissão sustentada e o controlo da inflamação. Adicionalmente, a aprovação de novos fármacos com ação em vias imunológicas alternativas, como o vedolizumab, permitirá alargar o espetro terapêutico no doente não respondedor a agentes anti-factor de necrose tumoral alfa.

O futuro parece promissor na área da DII. É expectável que as novas estratégias de abordagem do doente com DII, aliadas ao desenvolvimento de novos fármacos, permitam alterar o curso natural da doença, evitando o dano intestinal irreversível e possibilitando a melhoria da qualidade de vida destes doentes.

1. Introduction

In the past years, inflammatory bowel disease (IBD) has witnessed major advances both at the fundamental and clinical levels. Key discoveries in disease's pathogenesis led to the development and refinement of therapeutic strategies paving the way for a new era in targeted drug development.[1]

Therapeutic management in IBD has also suffered a major shift in the past years. The traditional paradigm of gradually introducing the least toxic but less powerful drugs and repeated courses of steroids has progressively moved to favour the early introduction of immunomodulation and most recently biologic therapy, in order to modify the natural history of disease.[2]

The discovery and introduction of anti-TNFα agents have constituted a major breakthrough for patients and clinicians. These novel therapies offer the ability to induce and maintain remission, heal the mucosa, and reduce surgeries and hospitalizations.[3] However, many patients will still be refractory to treatment or loose response over time. Therefore, therapeutic drug monitoring, as a way of optimizing anti-TNFα use, has been an area of intensive research. Furthermore, new drugs are expected to hit the clinic. Vedolizumab, an anti-integrin, is eagerly awaited for patients who have failed anti-TNFα and it has shown to be able to induce and maintain remission in patients with Crohn's disease (CD) and ulcerative colitis (UC).

We are increasingly using prognostic and predictive factors at diagnosis and during follow-up to guide our therapeutic decisions. We now recognize that in order to block disease progression, it is crucial to intervene early before damage occurs.

In this review we will briefly discuss new therapies in IBD, and we will focus on new trends that are emerging in the treatment of IBD patients, with the goal of optimizing current therapeutic strategies and blocking disease progression.

2. Prognostication in IBD

IBD is a heterogeneous condition with a highly variable clinical course, with some patients following a mild course while others experience early and aggressive disease progression.[4–6] Therapeutic strategies in IBD result from a delicate and difficult balance between benefits and risks of more aggressive therapies. Early treatment with immunomodulators and/or anti-TNFα is expected to change the natural history of disease, especially for CD, but with the risk of overtreating some patients with mild-moderate disease who would not need such intensive therapy. Therefore, the possibility of patient profiling using prognostic factors at diagnosis (including clinical, laboratory and imaging criteria) for the selection of the best suited candidates for early aggressive therapies is of main importance (Tables 1 and 2).[7,8]

Several definitions of poor prognosis in CD have been suggested. Disabling CD was arbitrarily defined by Beaugerie et al[9] in 2006 by the presence of at least one of the following criteria in the 5-year period after diagnosis: More than two steroid courses and/or steroid dependency; further hospitalization after diagnosis for flare up or complications of the disease; presence of disabling chronic symptoms; need for immunosuppressive therapy; and intestinal resection or surgery for perianal disease. In a recent meta-analysis[8] including 1961 patients,[9–11] the demographic and clinical characteristics associated with significantly higher risk of developing disabling disease at five years after initial diagnosis were: young age (<40 years) at diagnosis, initial requirement of steroids for treating the first flare and perianal disease.[8]

In 2012, Zallot and Peyrin-Biroulet[12] suggested a different definition for complicated IBD. Complicated CD was defined as the presence of bowel damage (stricture, abscess and/or fistula) and/or the requirement for surgery and/or the presence of extra-intestinal manifestations. Clinical factors associated with complicated CD include young age at diagnosis, small bowel disease (ileal and/or ileocolonic), upper gastrointestinal extent, stricturing or penetrating behaviour, perianal disease, severe endoscopic lesions (deep ulcerations) at index colonoscopy and smoking.[12–16]

Complicated UC was defined as the development of colon cancer and/or the need for surgery (colectomy) and/or the presence of extra-intestinal manifestations.[12] Clinical predictors for complicated UC include young age at diagnosis, male gender, extensive colitis, severe disease activity at diagnosis, high histological inflammation score, the presence of primary sclerosing cholangitis, steroid use and steroid resistance.[4,12,13,17–21]