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REVIEW ARTICLE

Treating beyond symptoms with a view to improving patient outcomes in inflammatory bowel diseases☆

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Abstract

Background and aims: Treatment goals in inflammatory bowel diseases are evolving beyond the control of symptoms towards the tight control of objectively-measured gastrointestinal inflammation. This review discusses the progress and challenges in adopting a treat-to-target approach in inflammatory bowel diseases.
Methods: Evidence from the literature that highlights current thinking in terms of treating-to-target in patients with inflammatory bowel diseases is discussed.
Results: Monitoring for objective evidence of inflammation using endoscopy, cross-sectional imaging or laboratory biomarkers may be a useful approach in inflammatory bowel diseases; however, setting the appropriate treatment goal remains a challenge. Deep remission (a composite of symptom control and mucosal healing) may now be a realistic target in Crohn's disease; however, it remains to be proven that achieving deep remission will modify the long-term disease course. Assessing prognosis at an early stage of the disease course is essential for the development of an appropriate management plan, with the rationale of adapting treatment to disease severity. An algorithm has been proposed for

Abbreviations: CDI, colour doppler imaging; CEUS, contrast-enhanced ultrasound; CRP, C-reactive protein.

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the treatment of early Crohn's disease that involves early treatment with immunosuppressants and tumour necrosis factor antagonists, in the hope of preventing structural bowel damage.
Conclusions: Treating beyond symptoms will require a clear management plan influenced by disease severity at presentation, clinical and biological prognostic factors, achievement and maintenance of clinical and biological remission and pharmacoeconomics.

Contents

1. Introduction

Early and optimised treatment to meet specific targets is key to preventing tissue damage and ultimately physical disability in a number of chronic and progressive diseases including hypertension, type 2 diabetes mellitus and rheumatoid arthritis.[1–3] This treat-to-target approach has been facilitated by the development of algorithms based on therapeutic targets (which are modified to be more or less stringent in high-risk patient groups); adoption of a frequent monitoring policy where treatment is continually optimised until the target is reached; and recognition of early disease states.[2,4,5] In inflammatory bowel diseases (IBD), current therapeutic goals focus on induction and maintenance of clinical remission and prevention of complications of both the disease and the treatment. However, it is increasingly recognised that inflammatory activity persists even in the absence of gastrointestinal symptoms, leading to progressive accumulation of bowel damage including fistulae, abscesses and strictures in Crohn's disease (CD),[6,7] and fibrosis, dysmotility and colorectal neoplasm in ulcerative colitis (UC).[8–10] Treatment goals in IBD are therefore evolving beyond the control of symptoms alone towards the sustained control of gastrointestinal inflammation, measured objectively by endoscopic, radiologic and laboratory parameters.

2. Setting appropriate treatment goals in IBD

The ideal treatment goal in any chronic disease is one that is clearly defined, achievable with medical or surgical therapy, predictive of long-term outcomes, affordable, non-invasive and relevant across disease subtypes, with a low test-to-test variability.

In most current clinical practice, the primary goal of IBD treatment is to induce and maintain clinical remission, with therapeutic decision-making driven by the presence or absence of clinical symptoms.[11–13] However, achieving this goal does not necessarily determine the clinical course of the disease nor prevent long-term disease sequelae. Monitoring for objective evidence of inflammation using endoscopy, cross-sectional imaging or laboratory biomarkers may be a more useful approach; however, setting the appropriate goal remains a challenge (Table 1).

Biomarkers, such as C-reactive protein (CRP) and faecal calprotectin, may be useful for measuring disease activity and guiding therapeutic decisions.[14–17] However, test-to-test variability, relevance across subtypes of IBD and ability to predict long-term outcomes need to be more fully evaluated. Achieving mucosal (endoscopic) healing is an important prognostic feature of IBD treatment[18,19] and prospective studies are required to determine whether this outcome is a feasible and necessary treatment goal. While a validated definition of mucosal healing in IBD is still lacking, working definitions are beginning to evolve. Laboratory markers may also provide a surrogate measure of mucosal healing, although more work is required to validate this approach.

With the advent of biologic therapies, it has become apparent that deep remission (a composite of symptom control and mucosal healing) may now be a realistic target in CD.[20–22] The definition of deep remission should include considerations for both early and late disease,[19] with early disease including more stringent criteria. Patients diagnosed late in the course of CD, those who already have pre-existing disease complications or those who have required surgical treatment may not be capable of achieving an absence of clinical symptoms as a result of irreversible structural damage inflicted by the CD itself or by surgical resection.