How to achieve deep remission in treatment of inflammatory bowel disease

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OBJECTIVE: This article investigates the methods of achieving deep remission of inflammatory bowel disease (IBD).

METHODS: Increasing recognition of the concept of quality of care is contributing to the evolution of treatment goals in patients with IBD from clinical response and remission (symptom control) toward deep remission. A change in the treatment goal requires a change in the treatment strategy. Optimization of conventional therapy, early treatment, use of the Lemann score, performance of double-balloon endoscopy, treatment using Traditional Chinese Medicine, and good communication between physicians and patients are needed to attain deep remission.

RESULTS: The above-mentioned methods can help to achieve deep remission.

CONCLUSION: Using the above methods, it will be possible to improve the prognoses of patients with IBD by minimizing complications and bowel damage and thereby changing the course of the disease.

INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn’s disease and ulcerative colitis, is a chronic, progressive, and destructive disease that is able to induce disability and severely influence affected patients’ quality of life. Although IBD is characterized by the alternate occurrence of remission and relapse, it may produce persistent inflammation, leading to progressive bowel damage and complications such as stricture, fistulae, and abscesses. These complications frequently require surgery, which may lead to further disability and higher mortality. Disability among patients with IBD is commonly underestimated, but decreased quality of life is well recognized among affected patients. The goals of IBD management were formerly focused on induction and maintenance of symptomatic responses, and little attention was paid to delay or even prevention of disease progression. However, increasing recognition of the concept of quality of care has led to the evolution of treatment goals in IBD from clinical response and remission (symptom control) toward deep remission. In clinical studies, "deep remission" means that treatment goals are evolving to encompass not only symptomatic but also mucosal remission, which is defined as a Crohn’s disease activating index (CDAI) of <150 and complete mucosal healing.
This paper explores the treatment changes that have developed with the evolution of the goals of IBD therapy and discusses the treatment methods necessary to reach the goal of deep remission.

EVOLUTION OF TREATMENT GOALS IN IBD

The evolution of treatment goals in patients with IBD is potentially changing the course of the disease, the expectations of patients and healthcare professionals, and the development of treatment plans. Twenty years ago, treatment methods for IBD were based on the symptoms of the patient, and the point of view that early treatment would lead to long-term maintenance of remission was put forward. This point of view has become the standard of treatment in the form of induction of remission and its subsequent maintenance. The provision of personalized medicine is now becoming possible through, for example, a better understanding of pharmacogenetics and therapeutic drug monitoring. In the future, treatment will be increasingly determined and optimized according to biotypes based on genetics, serology, proteomics, metabolomics, individual microbiology, etc. In addition, treatment goals have evolved toward mucosal healing with establishment and maintenance of deep remission. It is hoped that achieving these goals will lead to improvements in clinical outcomes, including quality of life, and reductions in disease-related complications and costs of surgery and hospitalization. Future goals may include avoidance of corticosteroids, prevention of extraintestinal complications, and decreased treatment costs.

Changing treatment goals requires variations in treatment strategies. In conventional approaches, immunomodulators are used with a bottom-up strategy based on clinical outcomes. At present, the aims include induction and maintenance of clinical remission, prevention of disease development and complications, optimization of surgical outcomes, and prevention of postoperative recurrence. Future approaches are likely to involve personalized treatments based on the patient’s prognosis as determined using biological predictors of response. Future goals will be to increase therapeutic effects, decrease treatment costs, and prevent disease.

HOW TO IMPROVE THE MANAGEMENT OF IBD TO ACHIEVE DEEP REMISSION

Advances in drug development have provided highly effective treatments to prevent bowel structure damage in patients with IBD, making deep remission a realistic goal. In fact, anti-TNF therapy achieved deep remission in a randomized placebo-controlled clinical study, which also indicates that deep remission is closely associated with a significant increase in quality of life and a significant decrease in the need for hospitalization.

However, translating these goals into everyday practice requires the implantation of optimized treatment strategies and ongoing monitoring of treatment outcomes. In addition, precise definition of the goals themselves is required, and the long-term benefits associated with their achievement need to be studied. Furthermore, although effective treatments are available, there remain many uncertainties about how best to use them.

Optimization of conventional therapy

Corticosteroids and immunomodulators have been used in the treatment of IBD for decades, and their effectiveness is highlighted by the fact that they are recommended by national and international guidelines. However, these agents also have some disadvantages. Although corticosteroids are very effective, they are not able to maintain remission, and their side effect profile makes their long-term use inappropriate. In addition, the slow action of immunomodulators may not be adequate to induce remission, and their long-term ability to modify disease has recently been questioned. Despite these shortcomings, corticosteroids and immunomodulators have been widely used in the treatment of IBD for many years. However, high-quality evidence to guide their precise use in terms of dosage, mode of administration, and duration of therapy is limited.

High-quality studies showing that corticosteroids effectively induced clinical remission in patients with IBD were published more than 30 years ago, and the efficacy of corticosteroids in IBD has been confirmed in Cochrane systematic reviews of controlled studies. However, once remission has been achieved, the goal is to maintain steroid-free remission. Despite inducing remission in most patients, a prolonged response to corticosteroids is observed in less than half of all patients. Importantly, corticosteroids are associated with substantial toxicity and should not be continued long-term.

Therefore, corticosteroids alone are inadequate for achieving the proposed treatment goal of deep remission. They should normally be supplemented and ultimately replaced by immunomodulators early in the treatment course.

Early treatment

The clinical features of IBD have changed in recent years, with a decreasing frequency of a purely inflammatory response and an increasing frequency of a penetrating disease leading to the need for surgery. Accordingly, to change the course of the disease, disease-modifying treatments must be prescribed early in the course of IBD before complications occur. There is now increasing clinical evidence to support the hypothesis that early treatment improves clinical outcomes in patients with IBD. Recent studies have also demonstrated that early treatment with anti-TNF therapy is associated with sustained steroid-free remission and complete mucosal healing.

However, the identification of patients with early IBD in clinical practice remains a challenge because no for-
mal definition exists. An international consensus has been established to develop a formal definition of early IBD. The agreed-upon definition is a disease duration of <18 months in the absence of the use of disease-modifying agents. General acceptance of such a definition will help establish the widespread use of an optimized treatment strategy.

**New indices in IBD management**

Several assessment tools are available for evaluating IBD symptoms, including the CDAI and Harvey-Bradshaw index, but these are often not used routinely in clinical practice. However, the Lemann score is clinically useful and can reflect both the extent and severity of digestive damage. To assess the extent of damage, the digestive tract is considered to be divided into segments: the upper tract comprises 3 segments, the small bowel comprises up to 20 segments, the colon and rectum comprise 6 segments, and the anus is considered to be 1 segment.

As a first step in assessing the severity of damage, each segment is evaluated separately for strictures, penetrating lesions, and a history of surgery or other procedures. Each section is graded from no damage to the most severe damage corresponding to resection, and based on this evaluation, a score from 0 to 10 is attributed to each segment.

In the second step, the score per organ is calculated, which is the sum of the scores in all segments in the organ. Thus, the score per organ would be 0 to 30 for the upper tract, 0 to 200 for the small bowel, 0 to 60 for the colon/rectum, and 0 to 10 for the anus.

Finally, the scores obtained for each organ are summed to give an overall score for the entire digestive tract. The Lemann score is independent of the diagnostic technique used and allows patients to be assessed at different clinical stages regardless of surgical history or whether they have limited or extensive disease.

**Role of endoscopy in daily clinical practice**

Endoscopy plays a key role in the monitoring of IBD. It allows for assessment of the extent and severity of the disease, aids treatment decisions, and detects signs of progression.

Double-balloon endoscopy (DBE) allows for complete examination of the small bowel, which is important for determining the extent of mucosal healing. Furthermore, it may also be used for biopsies or therapeutic interventions (such as balloon dilatation of strictures) during DBE. This means that DBE may offer an alternative to surgery for some patients. DBE has been successfully used to dilate strictures, while endoscopy does not have this function.

**Use of Traditional Chinese Medicine**

Acupuncture, a popular procedure in Traditional Chinese Medicine (TCM), has a long history of medical treatment in China and other Asian countries. It has been increasingly performed as a complementary and alternative medical therapy for patients with IBD in the last 10 to 15 years. Satisfactory results and positive effects of both acupuncture and acupuncture combined with Chinese herbal medicine decoctions have been reported.

According to TCM theory, spleen "damp-heat", which is present in many patients with mild to moderate IBD, cannot strongly promote blood circulation, easily resulting in "blood stasis". Combined wind and damp-ness is found to adversely interfere with "Yang Qi", inducing blood stagnation and resulting in thrombosis and stagnant cold-dampness.

The TCM treatment principles for IBD are regulation of Qi activity, promotion and improvement of blood circulation, and invigoration of the spleen. TCM therapy has shown definite effectiveness. At the same time, because TCM methods involve a long-term treatment course, they greatly contribute to achieving the aim of deep remission. In addition, if patients have erosions that are confined to the colon, even the left-sided colon and mainly ulcerative colitis, treatment comprising enemas or Chinese medicine suppositories would be adopted. Such treatments can not only directly reach the erosions, but also have long-term effects. In TCM, they are now regarded as important complementary methods for patients with IBD.

**Good communication between physicians and patients**

Good communication between physician and patients is a cornerstone of effective disease management. After diagnosis of IBD, patients are likely to feel great uncertainty about their future. They may be concerned about the impact of the disease and its treatment on their daily life, employment prospects, ability to have children, and later need for hospitalization and surgery. By proactively discussing these issues, physicians and the patients can begin to build confidence and establish an open and long-lasting relationship of trust.

Clear communication regarding the benefits and risks of alternative management strategies and therapeutic options is essential throughout the physician-patient relationship. However, physicians must keep in mind that the management goals that are important to the patient and the benefits or risks assessed by the patient may differ from their own. To help reconcile the two perspectives, the physician must clearly communicate issues such as the rationale for a long-term management plan, the impact of disease progression, steroid dependence, common and rare potential complications of surgery, etc. At every decision point, the potential risk of the treatment (development of complications, need for surgery, and nutritional problems) must be carefully balanced against those of overtreatment (anti-TNF-induced toxicity and potential impact on quality of life).

**CONCLUSION**

IBD is characterized by sustained inflammation that
may affect any part of the gastrointestinal tract. Chronic uncontrolled inflammation can lead to the development of complications such as stenosis and fistulae, resulting in irreversible structural bowel damage that is not amenable to medical therapy. Such damage is often associated with the need for surgical removal of bowel segments. Even during clinical remission, subclinical inflammation may persist and is largely unrecognized, increasing the risk of complications. Treating physicians must recognize the disconnect between symptoms and the presence of inflammation, and periodic evaluation of disease activity should be routinely conducted. It is hoped that complete control of inflammation bowel segments. Even during clinical remission, subclinical inflammation may persist and is largely unrecognized, increasing the risk of complications. Treating physicians must recognize the disconnect between symptoms and the presence of inflammation, and periodic evaluation of disease activity should be routinely conducted. It is hoped that complete control of inflammation, timely use of appropriate therapy, strict control of complications, and minimization of bowel damage will change the course of the disease, improve prognosis, and increase the quality of life of affected patients.

REFERENCES