

The ultimate therapeutic goal: Establishing and maintaining quality of life

Remo Panaccione MD FRCPC

ARTICLE

Feagan BG, Yan S, Bala M, Bao W, Lichtenstein GR.
The effects of infliximab maintenance therapy on
health-related quality of life. *Am J Gastroenterol*
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ARTICLE SUMMARY

Outcomes in Crohn's disease clinical trials are traditionally reported in terms of remission and response rates according to the Crohn's Disease Activity Index (CDAI), which was developed as part of the National Cooperative Crohn's Disease Study (1). However, it has been argued that the CDAI does not measure the overall burden of the illness experienced by patients. An alternative is to assess the impact of a particular therapy on health-related quality of life (HRQL). HRQL not only measures the benefits of the therapy on disease symptoms but also is probably better at evaluating the trade-off between therapeutic efficacy and potential adverse effects.

Feagan and colleagues (2) report the results of the effects of infliximab on HRQL during the A Crohn's disease Clinical trial Evaluating infliximab in a New long-term Treatment regimen (ACCENT) I trial (3), which evaluated the long term effects of infliximab as maintenance therapy for patients with Crohn's disease. Quality of life was evaluated using a generic HRQL measure (the Short-Form-36 [SF-36]) and a disease-specific HRQL instrument (the Inflammatory Bowel Disease Questionnaire [IBDQ]). Scores were measured at baseline and throughout the trial, and various treatment regimens were compared in their ability to change HRQL scores from baseline.

All patients had significant impairment of HRQL at baseline. Following administration of infliximab, respondents reported immediate improvements in both the IBDQ and the SF-36 scores at week 2. Patients who received maintenance infliximab with either the 10 mg/kg or 5 mg/kg every eight weeks enjoyed significantly greater improvements in both SF-36 and IBDQ scores than did patients who received only one infusion of infliximab followed by placebo maintenance therapy. When

patients were evaluated at week 10, the three-dose induction regimen was more effective than the single dose in improving HRQL.

COMMENTARY

Infliximab has become an important treatment for patients with moderately severe and fistulizing Crohn's disease. Previous studies have demonstrated its ability to rapidly improve symptoms and induce remission (2,4,5). Most of these studies have focused on the agent's ability to reduce symptoms as measured by the CDAI, but there is debate as to whether this instrument truly captures the overall burden of illness experienced by patients with Crohn's disease. The CDAI does capture the severity of symptoms that arise from active disease. In our offices, we ask patients if their bowel movements have improved, if their abdominal cramping has diminished and if other symptoms have resolved. These questions are important to physicians but may underestimate the 'true benefit' of a particular therapy, because any adverse effects of drugs may impair a patient's quality of life.

The concept of HRQL refers to a person's or group's perceived physical and mental health over time. Physicians have often used HRQL instruments to measure the effects of chronic illness in their patients to better understand how an illness interferes with a person's day-to-day functioning. Measuring HRQL is particularly important in patients with Crohn's disease, because death is rare and serious complications are infrequent. The social and emotional components of the HRQL instruments are designed to assess the way the disease affects these predominantly young adults, their partners, children and colleagues. Previous studies have demonstrated that patients with Crohn's disease suffer from a marked impairment in quality of life (6). This study confirmed that HRQL was significantly worse in patients with Crohn's disease than in the general United States population. Therefore, the need to find an agent that rapidly improves and maintains HRQL is paramount.

Previous studies have demonstrated the ability of infliximab to improve HRQL after a single infusion (7). The present study again showed a rapid benefit in HRQL after the administration

Division of Gastroenterology, Department of Medicine, University of Calgary, Calgary, Alberta

Correspondence: Dr Remo Panaccione, University of Calgary, 3500 26th Avenue Northeast, Calgary, Alberta T1Y 6J4.

Telephone 403-943-5512, fax 403-943-4017, e-mail remo.panaccione@calgaryhealthregion.ca

of infliximab. An initial increase in IBDQ scores of approximately 40 points (greater than 16 points is considered clinically significant) occurred in all treatment groups by week 2 of the ACCENT I study. Improvement was seen in all four dimensions: bowel-related, systemic, emotional and social. More importantly, patients who received maintenance therapy were able to sustain this HRQL improvement. Correlation analyses demonstrated that the Mental Component Summary of the SF-36 was highly significantly correlated with the all dimensions of the IBDQ. This finding underscores the belief that Crohn's disease produces a high psychological burden.

This study also furthered knowledge in the methodology of studying patients with Crohn's disease by demonstrating a positive correlation between the SF-36 and the CDAI. This relationship between a traditional disease activity score and a generic HRQL score will allow for the comparison of general improvement across disease states in the future. Public health professionals use HRQL instruments to measure the effects of numerous diseases and short and long term disabilities in diverse populations. Monitoring of HRQL can identify subgroups with poor physical or mental health and help to formulate health care policies and interventions. This may lead to other important outcomes in patients with Crohn's disease, such as improved employment and decreased hospitalization rates (8).

This study by Feagan and colleagues not only demonstrates the benefits of maintenance infliximab on improving and maintaining HRQL but also reminds us how ill these patients are and how the disease disrupts all facets of their lives. If one

thinks of the patient holistically, the ability to improve and maintain HRQL should be the ultimate goal and the test that all therapeutic agents must pass.

Remo Panaccione MD FRCPC
Division of Gastroenterology, Department of Medicine
University of Calgary
Calgary, Alberta

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