Maintenance of remission among patients with Crohn's disease on antimetabolite therapy after infliximab therapy is stopped

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Introduction

Infliximab (IFX) has dramatically changed the approach to the management of patients with Crohn's Disease (CD) [1]. IFX induces rapid and profound endoscopic healing, improves quality of life and allows patients to avoid hospitalisation and surgery [2]. The ACCENT I [3] and ACCENT II [4] trials have shown that scheduled maintenance therapy with IFX is superior to episodic therapy in maintaining response and remission both in luminal and in fistulising CD. Nonetheless, approximately 60% of patients cannot reach remission and 25–40% of patients on an IFX maintenance regimen experience a loss of response to the drug [5].

It has been demonstrated that the combination of IFX and azathioprine is more effective than IFX alone in inducing steroid-free remission and mucosal healing of the bowel in luminal CD in patients not treated previously with azathioprine. The Study of Biologic and Immunomodulator Naive Patients in Crohn's Disease (SONIC) also showed that IFX monotherapy is significantly better at inducing steroid-free remission and mucosal healing than azathioprine alone in azathioprine-naive patients [6].

It is important, however, to determine whether IFX therapy can be safely interrupted in patients with CD who have undergone a period of prolonged remission, and the timing of IFX withdrawal in patients who receive combination therapy is one of the most controversial topics in IBD management.

What this paper is about?

This interesting prospective multicentre cohort study included 20 centres in France and Belgium between March 2006 and December 2009. The paper analyzed the time to relapse after IFX discontinuation in CD patients who achieved a corticosteroid-free remission for at least 6 months as a result of the combination of IFX and antimetabolite therapy (azathioprine, 6-mercaptopurine, methotrexate). In addition, the authors identified factors associated with a low risk of relapse. 115 CD patients of the GETAID cohort were treated with scheduled IFX and antimetabolite for 1 year. In patients achieving steroid-free remission (CDAI 250 or between 150 and 250 with a 70-point increase from baseline over two consecutive weeks), with a total relapse rate of 43.9% +/- 5% and 52.2% +/- 5.2% in the first and second year, respectively.

The following were identified as relapse risk factors: male sex, the absence of surgical resection, leucocyte counts >6x109 /L, levels of haemoglobin 5 mg/L and faecal calprotectin >300 µg/g. Patients were graded according to the risk of relapse: patients presenting no more than two of the above risk factors had a 15% likelihood of relapse within 1 year. 40 patients who relapsed were also re-started on IFX therapy and were assessed for response to treatment 30 days after the first IFX re-treatment up to the third infusion. Therapy was effective in inducing remission in 37/40 (93%) and 39/40 (98%) showed a clinical response. IFX re-treatment proved itself to be safe and was well tolerated by all patients.

Conclusion

The study shows that approximately 50% of patients with CD who were on an antimetabolite agent and IFX for 1 year and in corticosteroidfree remission for at least 6 months experienced a relapse within 2 years after discontinuation of IFX. However, patients with a low risk of relapse can be identified using a combination of clinical and biological markers. The study group under examination was characterised by extremely heterogeneous risk factors for debilitating disease, from endoscopic grading to smoking. However, those features seemed not to represent risk factors for relapse. Finally, a control group of patients continuing combination therapy is needed.

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