Mesenteric fat as a source of C reactive protein and as a target for bacterial translocation in Crohn's disease

Laurent Peyrin-Biroulet, Florent Gonzalez, Laurent Dubuquoy, Christel Rousseaux, Caroline Dubuquoy, Cecilia Decourcelle, Alain Saudemont, Mickael Tachon, Elodie Beclin, Marie-Francoise Odou, Christel Neut, Jean-Frederic Colombel, Pierre Desreumaux

Gut. 2012 Jan;61(1):78-85.

DIRK P. VAN ASSELDONK
Department of Gastroenterology and Hepatology
VU University Medical Center
Amsterdam, The Netherlands

Dirk P. van Asseldonk
was born in 1982 and lives in Amsterdam. He is currently performing his training in Gastroenterology at the Alkmaar Medical Centre and working on his PhD thesis that includes clinical and pharmacological studies concerning thiopurine treatment in IBD.

Introduction

A substantial number of patients with acute severe ulcerative colitis are glucocorticoid resistant. Before cyclosporine (CsA) and infliximab (IFX) were introduced as rescue therapies colectomy rates were 46% at 3 months and 64% at 10 years.(1) Both CsA and IFX are effective in reducing colectomy rates to around 36%.(2;3)

It is not clear whether one of these drugs is superior to the other, although a single infusion of IFX seems less effective than CsA induction therapy. (4) On the other hand, preliminary results of a randomized controlled trial comparing CsA (2 week intravenous (IV) infusion followed by a daily oral formulation) with scheduled IV IFX (Week 0, 2, 6 followed by every 8 weeks) show equal clinical response rates and colectomy rates at 1 and 14 weeks.(5) Long-term data, including data on the role of antimetabolite co-treatment are awaited.

What does this study add to the literature?

This nice retrospective monocenter cohort study compares CsA and IFX as rescue therapies for corticosteroid refractory acute severe ulcerative colitis. Two historical cohorts with a minimum follow-up of 12 months were compared in regard to colectomy rates and number of relapses requiring hospitalization; one treated between 1994 and 2003 with CsA (daily 2 mg/kg IV for 14 days followed by daily 5 mg/kg in oral formulation for a maximum of 3 months) and the other treated from 2004 to 2011 with IFX (week 0, 2 and 6 followed by every 8 weeks 5 mg/kg IV). Provided that patients were not previously proven intolerant of or resistant to azathioprine (AZA), in CsA treated patient AZA was initiated (2.5 mg/kg) together with the CsA oral formulation, whereas in IFX treated patients AZA was initiated soon after the last IFX infusion.

A total of 65 patients were included, 35 of whom received CsA and 30 IFX. After 3 months 28.5% (10/35) and 17% (5/30) underwent colectomy in the CsA and IFX treated group, respectively (p=0.25). At 12 months the colectomy rate rose to 48% in the CsA group while in the IFX group it remained 17% (p=0.01). The 1-2-3 year cumulative colectomy rates were 48%, 54%, and 57% in the CsA group, and 17%, 23%, and 27% in the IFX group. Between the groups there was no difference in the number of relapses requiring hospitalization. In addition, there were no serious adverse events in either group, nor was there any difference in adverse events. In the overall population high levels of CRP, no AZA use and extensive disease were related to the risk of colectomy.

The remarkable differences in colectomy rates must be interpreted with some caution. Firstly, 12 out of 25 initial CsA responders did not receive AZA concomitantly or successively due to previous intolerance or resistance. Nine (75%) of them underwent colectomy, suggestive of the importance of co-treatment. Secondly, there seems to be a fair chance of selection bias as none out of the seven patients who failed IFX treatment due to adverse events, and were treated only with mesalazine (n=5) or AZA (n=2), underwent colectomy.

Conclusion

This study shows that CsA and IFX as rescue therapy for patients with corticosteroid refractory acute severe ulcerative colitis seems to be equally effective in avoiding colectomy at 3 months, while at 12 months IFX seems to be more effective. In regard of adverse events there are no differences.

Concomitant or successive AZA treatment seems to be of major importance for effective CsA treatment. Data from randomised prospective studies are awaited to establish whether CsA or IFX is more effective in avoiding colectomy on the longer term.

References

1. Gustavsson A, Halfvarson J, Magnuson A et al. Long-term colectomy rate after intensive intravenous corticosteroid therapy for ulcerative colitis prior to the immunosuppressive treatment era. Am J Gastroenterol 2007;102(11):2513-9.
2. Arts J, D'Haens G, Zeegers M et al. Long-term outcome of treatment with intravenous cyclosporin in patients with severe ulcerative colitis. Inflamm Bowel Dis 2004;10(2):73-8.
3. Filippi J, Allen PB, Hebuterne X et al. Does anti-TNF therapy reduce the requirement for surgery in ulcerative colitis? A systematic review. Curr Drug Targets 2011;12(10):1440-7.
4. Sjoberg M, Walch A, Meshkat M et al. Infliximab or cyclosporine as rescue therapy in hospitalized patients with steroid-refractory ulcerative colitis: A retrospective observational study. Inflamm Bowel Dis 2012;18(2):212-8.
5. Laharie D, Boureille A, Branche J et al. Ciclosporine versus infliximab in acute severe ulcerative colitis refractory to intravenous steroids: a randomized study. Journal of Crohn's and Colitis 2012;1:A12.