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A population-based study of fatigue and sleep difficulties in inflammatory bowel disease

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Introduction

There is no known cure for Ulcerative Colitis (UC), but several agents are frequently used for control of inflammation. High doses of corticosteroids (CS) are administered in acute flares of UC and achieve a high response rate, but this success has the trade-off of a higher risk of complications after surgery. The anti-tumour necrosis factor (TNF)-α antibody infliximab (IFX) is now used in both induction and maintenance therapy for moderate to severe UC. The number of UC patients undergoing surgery after treatment with IFX is increasing. It has been hypothesized that IFX treatment may increase the risk of postoperative complications in patients with UC. Recent investigations have tried to assess this dilemma, with conflicting conclusions. A study on a 10-year experience from Belgium concluded that use of CS, but not IFX, increases the risk of early postoperative complications [1]. On the other hand, two large series globally comparing 132 patients who received IFX as a treatment before surgery with 692 who did not, found that IFX was associated with a higher rate of complications post surgery [2,3].

What are the key findings?

In the presented work Brengbak and colleagues performed a retrospective analysis of a database of patients undergoing surgery for UC within a 5-year period. They compared 20 patients who received IFX prior to surgery with 51 who were not treated with biologic agents. The main outcome measure was complications occurring within 30 days after surgery. The authors found no correlation between treatment with IFX 12 weeks prior to surgery and infectious postoperative complications. Interestingly, these were more likely to occur in patients receiving CS.

What was of interest in this study?

Even if the study design does not allow definitive conclusions to be drawn, preoperative patient assessment – which is a weakness of all previously published studies – is very well described.

The two groups were homogeneous as patients were selected using stringent criteria. A cut-off value of 90 days (12 weeks) between the last IFX infusion and primary surgery was chosen. Endoscopy was not performed to assess the Mayo score, resulting in a "partial Mayo score". However, the authors sufficiently explain their conduct in the text and also point out the weaknesses of the report. Two authors disclose a conflict of interest with an IFX distributor in Denmark; nevertheless, the study is well conducted and described, and the conclusions seem genuine, prudent and justified.

Although not included in the authors' aims, a longer follow-up period could be of interest to examine the long-term effect of IFX in patients undergoing surgery for UC. This investigation could take into account infectious as well as non-infectious complications.

Characteristics of studies investigating the association between Infliximab (IFX) and postoperative complications (source: G. Pellino)

STUDY	YEARS	PATIENTS	CONCLUSIONS	PRO & CON
Schluender et al *Dis Colon Rectum* 2007	2000-2005	17 IFX 134 NO IFX	IFX = NO IFX	- no preoperative assessment of disease activity
Selvasekar et al *J Am Coll Surg* 2007	2002-2005	47 IFX 254 NO IFX	IFX increases the odds of postoperative pouch related and infectious complications	- IFX group received higher dose of ASA, CS, 5-ASA
Mor et al *Dis Colon Rectum* 2008	2000-2006	85 IFX 438 NO IFX	IFX increases the risk of postoperative complications	- median last IFX infusion 13.5 wks → unlikely to mantain response > 12 wks
Ferrante et al *Inflamm Bowel Dis* 2009	1998-2008	22 IFX 119 NO IFX	IFX = NO IFX	+ 10-year survey - no preoperative assessment of disease activity
Couquet-Reinier et al *Surg Endosc* 2010	1999-2008	13 IFX 13 NO IFX	IFX = NO IFX Laparoscopy feasible after IFX	- small sample size - case-matched controls
Yang et al *Aliment Pharmacol Ther* 2010 metanalysis	1993-2008	132 IFX 553 NO IFX	IFX increases short-term total postoperative complications	- no associations between IFX and infectious or non-infectious complications when analysed separately
Gainsbury et al *J Gastrointest Surg* 2011	2005-2009	29 IFX 52 NO IFX	IFX = NO IFX hand-assisted laparoscopy feasible after IFX	- hand-assisted laparoscopy, failure of medical therapy, CS dose, MTX use, 6-MP use unequally distributed
Present study *J Crohns Colitis* 2011	2005-2010	20 IFX 51 NO IFX	IFX = NO IFX CS increase the risk of infectious postoperative complication	+ homogeneous groups + nice pre- and post-operative assessment + & - infectious ≠ non-infectious complications differences - partial Mayo score (endoscopy not routinely performed) - conflict of interest

References

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2. Selvasekar CR, Cima RR, Larson DW et al. Effect of infliximab on short-term complications in patients undergoing operation for chronic ulcerative colitis. J Am Coll Surg 2007;204:956-62.
3. Mor IJ, Vogel JD, da Luz Moreira A et al. Infliximab in ulcerative colitis is associated with an increased risk of postoperative complications after restorative proctocolectomy. Dis Colon Rectum 2008;51:1202-7.