Meta-analysis: pre-operative infliximab treatment and short-term post-operative complications in patients with ulcerative colitis

Yang Z, Wu Q, Wu K, Fan D

CRD summary
The review found that preoperative infliximab appeared to increase short-term postoperative complications among patients with ulcerative colitis, possibly due to an increased risk of postoperative infection. In view of limitations in the review, including a suboptimal search, lack of randomised studies, failure to report study quality, and wide differences between the studies, the authors' conclusions may not be reliable.

Authors' objectives
To assess the effect of preoperative infliximab on short-term postoperative complications among patients with ulcerative colitis.

Searching
PubMed was searched from 1950 to September 2009. Search terms were reported. Reference lists of eligible studies were checked. The search was restricted to fully published studies in English.

Study selection
Controlled observational studies that reported short-term (within 30 days) complications among patients with ulcerative colitis treated with preoperative infliximab were eligible for inclusion. Studies were required to report infectious complications (e.g. wound infection, sepsis, abdominal abscess, peritonitis) or total complications (e.g. intestinal obstruction, thromboembolism, gastrointestinal haemorrhage).

Some studies in the review included participants with bowel disorders other than ulcerative colitis (e.g. Crohn's disease, unclassified inflammatory bowel disease). In all studies, participants with ulcerative colitis received corticosteroids, with or without other medications. In the infliximab group, the time period between the final infliximab infusion and surgery varied, and in some cases was more than 12 weeks.

The review reported non-infectious complications, as well as the pre-specified outcomes.

The authors did not state how many reviewers performed the selection.

Assessment of study quality
Studies with contemporaneous intervention and control groups, and few significant differences in demographic or clinical variables, were considered high quality.

Two reviewers independently assessed study validity, with disagreements resolved by consensus.

Data extraction
Odds ratios (ORs) were extracted or calculated from event rates in the two groups, with 95% confidence intervals (CIs). Attempts were made to contact the authors of one study for more information.

Two reviewers independently extracted the data, with disagreements resolved by consensus or by discussion with a third reviewer.

Methods of synthesis
Studies were combined to calculate pooled odds ratios and 95% confidence intervals, using the DerSimonian and Laird random-effects model. Heterogeneity was assessed using the $\chi^2$ and I$^2$ tests. The Begg and Egger tests were used to assess publication bias.
Results of the review
Six studies were included in the review (n=1,119 patients, range 21 to 413); five of these studies (n=706 patients) had data suitable for meta-analysis. Three of the studies reported disparities between the groups at baseline (e.g. in age, disease severity, use of immunosuppressants other than infliximab). Duration of follow up was 30 days (where stated).

There was no statistically significant difference between the infliximab preoperative treatment group and the control group in the rate of post-operative infectious complications (four studies, n=685 patients) or non-infectious complications (three studies, n=544 patients). There was a significantly increased rate of total complications (four studies, n=565 patients) in the infliximab preoperative treatment group (OR 1.8, 95% CI 1.12 to 2.87). There was significant statistical heterogeneity for the analysis of infectious complications ($\chi^2 p=0.015$), but not for the other analyses.

There was no evidence of publication bias.

Authors’ conclusions
Preoperative infliximab appeared to increase short-term postoperative complications among patients with ulcerative colitis, possibly due to an increased risk of postoperative infection.

CRD commentary
The objectives and inclusion criteria of the review were clear. Only the PubMed database (which includes MEDLINE) was searched; the search was also limited by language and publication status. This meant that some studies may have been missed and that the review was prone to language and publication biases. Publication bias was not evident on formal testing, but the power of such testing was low due to the small number of included studies. Steps were taken to minimise the risk of reviewer bias and error by having more than one reviewer assess study validity and extract the data, but it was unclear whether such precautions were taken with study selection.

No information was reported about the quality of individual studies; study quality was not mentioned in the interpretation of review findings. It was also unclear whether all participants included in analysis had ulcerative colitis. The studies differed widely with respect to their populations, concomitant medications and types of complication reported. Consequently, it was questionable whether they were sufficiently similar to pool, and difficult to determine the reliability or applicability of the review findings. The authors advised some caution in the interpretation of their results, noting that the infliximab group may have had more serious disease than the control group (causing confounding in the review), and that the findings were possibly underpowered due to lack of data.

In view of several limitations in the review, including a suboptimal search, lack of randomised studies, failure to report study quality and heterogeneity between the studies, the authors’ conclusions may not be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that well-powered prospective studies are needed to determine the effect of preoperative infliximab on postoperative complications among patients with ulcerative colitis.

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