Systematic review of postoperative complications in patients with inflammatory bowel disease treated with immunomodulators

Subramanian V, Pollok R C, Kang J Y, Kumar D

CRD summary
The review investigated whether patients who had surgery for Crohn’s disease or ulcerative colitis had increased post-operative complications if taking immunomodulator drugs such as azathioprine, 6-mercaptopurine, cyclosporin, methotrexate or infliximab at the time of surgery. The authors concluded that the limited available evidence did not prove a higher complication rate in these patients. This limited, negative conclusion appears likely to be reliable.

Authors’ objectives
To investigate whether patients with inflammatory bowel disease (IBD), either ulcerative colitis (UC) or Crohn’s disease (CD), who continue taking immunomodulator drugs when undergoing abdominal surgery have increased post-operative complications.

Searching
The authors searched PubMed and EMBASE from inception to August 2005), as well as other sources (Ingenta, Zetoc and Ovid); the search terms were reported. References of selected articles were also handsearched.

Study selection

All study designs appear to have been eligible for inclusion. The included studies were all retrospective observational studies.

Specific interventions included in the review
Studies were eligible for inclusion if they reported outcomes associated with individual immunomodulator drugs. The immunomodulator drugs used in the included studies were azathioprine, 6-mercaptopurine, cyclosporin, methotrexate and infliximab. These were sometimes taken in combination with corticosteroids (with some controls being on corticosteroids as well).

Participants included in the review
IBD patients treated with immunomodulator drugs who underwent abdominal surgery without discontinuation of the drug were eligible for inclusion in the intervention group. The included patients had CD or UC. The patients in the control groups were frequently taking corticosteroids and in some cases were taking a different immunomodulator.

Outcomes assessed in the review
Studies that included post-operative infective or total complication rates associated with the use of individual immunomodulator drugs were eligible for inclusion. The specific post-operative complications tracked varied between studies.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Data on complications in the immunomodulator and control groups were used to calculate the odds ratio and 95% confidence interval for each type of complication (infectious and total) where possible.

**Methods of synthesis**
- **How were the studies combined?**
  The studies were combined in a narrative summary. The authors grouped studies where patients took similar immunomodulatory drugs.

- **How were differences between studies investigated?**
  Differences between the studies were simply listed or mentioned.

**Results of the review**

Eleven studies (n=1,497) were included.

Azathioprine and 6-mercaptopurine.

Of five studies, none showed increased total complications, and the two studies that tracked them did not show increased infectious complications. One study published in abstract form reported that an increased risk of anastomotic complications and of further surgery was associated with the use of azathioprine or 6-mercaptopurine in patients with CD.

Cyclosporin.

Five studies (two without a control group) did not show added risk. In studies without a control group this was judged by comparison with the complication rates from other studies.

Infliximab.

Three controlled studies of post-operative outcomes in patients who received infliximab did not show increased total complications. The one study which reported them did not show increased infectious complications.

**Cost information**

One study (n=30) found that in patients with UC requiring immediate colectomy, the costs were higher in those treated with cyclosporin than in those not receiving cyclosporin.

**Authors' conclusions**

The limited existing evidence does not support the belief that there is an increased risk of post-operative complications after IBD surgery when patients are taking immunomodulator drugs.

**CRD commentary**

The review addressed a clear question in terms of the patients, interventions and outcomes. It appears that all study designs were eligible for inclusion. Relevant electronic databases and other sources were searched and the search terms reported. It was not mentioned whether any language restrictions were applied. The study selection and data extraction processes do not appear to have been done in duplicate to minimise bias, and a quality assessment and evaluation of publication bias were not performed. Two included studies were published only in abstract form. The table of included studies had incomplete data on some outcomes, reporting total complication rates for patients on immunomodulators and a control group, but not reporting on specific complication occurrence by group. Two studies had no control group, so the reviewers compared complication rates in these studies with those published elsewhere. The review reported
sufficient details about patient conditions and surgeries in individual studies when available.

Although studies included in the review were weak and the review had methodological limitations, the authors' limited, negative conclusion - that available evidence does not prove an increased rate of post-operative complications in IBD patients on immunomodulators - appears likely to 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 larger controlled studies, with well-defined standardised criteria for outcomes, are needed.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.