Effectiveness of 5-aminosalicylic acid for maintaining remission in patients with Crohn's disease: a meta-analysis


Authors' objectives
To evaluate the effectiveness of 5-aminosalicylic acid (5-ASA) for maintaining remission in inactive Crohn's disease.

Searching
The Iowa Drug Information System database (1985 to 93), Current Contents (1991 to 1993) and MEDLINE (1990 to 1993) were searched for English language papers using the keywords 'Crohn's disease' and '5-aminosalicylic acid' (or 'mesalazine' or 'mesalamine'). In addition, reviews, textbooks and the reference lists of retrieved papers were reviewed and experts in the field contacted to identify any further publications.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing 5-ASA to placebo or no treatment were included.

Specific interventions included in the review
5-ASA with a dose range from 1 g per day to 3 g per day.

Participants included in the review
All patients had inactive Crohn's disease and received no concomitant therapy with adrenocorticosteroids, immunosuppressant, or other drugs potentially active for Crohn's disease. The duration of remission ranged from over 1 month to over 6 months. There was some variation in the disease sites between studies and a wide range in the proportions of operated patients.

Outcomes assessed in the review
Effectiveness was assessed in terms of relapse rates for both the treatment and control groups over a post-randomisation period of at least 6 months.

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

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

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

Methods of synthesis
How were the studies combined?
Two meta-analyses were performed: one using data from full-length papers only and one using data from both full-length papers and abstracts. For the first meta-analysis, the relapse-free actuarial curves were analysed to determine the distribution of the relapses and of the losses to follow-up stratified for each of the time intervals. For the second meta-analysis where insufficient data regarding time of relapse were provided by the study abstracts, the total number of
relapses was arbitrarily divided between the time period 0-6 months and 6-12 months, according to a ratio of 2.8:1 (the ratio found from the full-length papers), irrespective of the patients' assignment to the treatment or the control group. The Peto method of 'survival' meta-analysis was used to evaluate relapse-free survival (see Other Publications of Related Interest).

How were differences between studies investigated?
Differences between the studies were examined narratively.

Results of the review
Ten controlled trials were identified of which 8 were included in the review (468 patients received 5-ASA and 473 received placebo or no treatment). Four of these studies were available as full-length papers and 4 in abstract form only. One paper reported the results of 2 RCTs.

The meta-analysis of the five full-length papers showed that 5-ASA significantly reduced the frequency of relapse from 0 to 6 months (OR 0.56, 95% CI 0.37 to 0.84, p<0.01) and from 6 to 12 months (OR 0.47, 95% CI 0.33 to 0.67, p<0.001). The three trials providing data for the period 0 to 24 months also found a significant reduction in relapse from 5-ASA over the whole period (OR 0.53, 95% CI 0.38 to 0.74, p<0.001). The pooled relapse-free rates for the intervention versus control groups were: 91% vs. 77% at 6 months, 84% vs. 60% at 12 months, and 72% vs. 52% at 24 months.

Meta-analysis of all 10 papers showed similar results; the size of the effect resulting from 5-ASA was smaller but remained significant. Publication bias calculations indicated that a negative trial enrolling 1600 patient would be needed to overturn the results of these meta-analyses.

Cost information
A rudimentary cost analysis is presented in the discussion which concludes that the average cost of treating a relapse with 5-ASA is $4000 compared to the average cost of managing a relapse of $9000.

Authors' conclusions
Although there is some heterogeneity of the studies included, the meta-analyses demonstrates the effectiveness of 5-ASA for maintaining remission of Crohn's disease.

CRD commentary
This review is of adequate quality although more detail could have been provided in the paper. The literature search was adequate and the inclusion criteria and study details presented. The data syntheses appears to have been conducted in an appropriate manner although the validity of including data from studies published only in abstract form in the second meta-analysis is debatable. It is not clear why the literature searches of all three databases did not begin at the same point in time (1985). No validity assessment of the primary studies was mentioned in the review, which could introduce serious bias into the results of the meta-analysis, especially given the small sample sizes of the included trials. Further primary research may be required to fully evaluate the effectiveness of 5-ASA for preventing relapse of Crohn's disease.

Bibliographic details

PubMedID
8172139
Other publications of related interest

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Record Status
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.