**Budesonide in the treatment of Crohn's disease: a meta-analysis**  
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**Authors’ objectives**  
To perform a meta-analysis to assess the effectiveness and safety of oral budesonide for inducing remission in active Crohn’s disease and for preventing relapse in Crohn’s disease with medically- or surgically-induced remission.

**Searching**  
MEDLINE (from initiation to date of search) was searched using the following MeSH terms: ‘budesonide’ and ‘Crohn’ or ‘inflammatory bowel disease’. A manual search of review articles and proceedings from major gastrointestinal meetings (1993-1999) was also performed, and the bibliographies of retrieved articles searched. Only results fully reported in journal articles were included. No language restrictions were reported.

**Study selection**  
Study designs of evaluations included in the review  
Double-blind randomised controlled trials (RCTs) which reported sufficient information to allow an intention-to-treat analysis to be performed.

Specific interventions included in the review  
Budesonide (9mg) administered with prednisolone (40 or 48mg) was compared to conventional corticosteroids or placebo.

Participants included in the review  
Individuals (>18yrs) with active or quiescent Crohn’s disease.

Outcomes assessed in the review  
Well-defined outcomes including the induction of remission, prevention of clinical relapse, prevention of endoscopic recurrence after surgery, prevention of clinical recurrence after surgery and evaluation of corticosteroid-related adverse effects.

How were decisions on the relevance of primary studies made?  
Three authors decided on the relevance of the studies.

**Assessment of study quality**  
The criteria proposed by Chalmers (see Other Publications of Related Interest nos.1-2) were used although the authors do not state what the criteria were and the data were not reported individually for the five included studies. For each trial the total score was expressed as a percentage of the maximum possible score. The authors do not state how many of the reviewers performed the validity assessment.

**Data extraction**  
Data were extracted blindly and independently onto a standardised form by three of the authors and disagreements were resolved by consensus. The following information was recorded: demographics of study population, study design, control treatment, definition of outcomes, and frequencies of each end-point. Authors were not contacted for missing or additional data.

**Methods of synthesis**  
How were the studies combined?  
Therapeutic effects in the form of risk differences (RD) (i.e. the difference in event rates between the treatment and
control groups) were pooled using the DerSimonian and Laird random-effects model (see Other Publications of Related Interest no.3). Data were quoted with 95% confidence intervals (CIs) where applicable and the number needed to treat (NNT) with 95% CI calculated. Results were also analysed in terms of odds ratios (ORs). Statistical significance was set at the 5% level.

How were differences between studies investigated?
Heterogeneity was assessed using the Q statistic of DerSimonian and Laird (see Other Publications of Related Interest no.3). Due to the lack of power of the Q test, studies were considered heterogeneous if \( P<0.10 \). A visual display representing the results on a L’Abbe plot (see Other Publications of Related Interest no.4) was also used.

Results of the review
Twelve double-blind RCTs (overall number of participants not reported).

Active Crohn's disease (n=6 studies):
Budesonide was less effective than conventional corticosteroids for inducing remission of active Crohn’s disease (pooled RD=-8.5%, 95% CI: -16.4, -0.7, \( p=0.02 \), n=4 studies and 621 participants), corticosteroid-related adverse events were reduced (RD=-22.4%; 95% CI: -32, -12.8%, \( P<0.001 \)). No significant heterogeneity was detected chi-squared=1.89, \( P=0.595 \). Budesonide was significantly superior to placebo for inducing remission after 8wks of treatment (RD=22.5%; 95% CI: 10.6, 34.3); and significantly superior to mesalazine for inducting remission within 16wks (RD=27.1%; 95% CI: 13.3, -40.8%).

Quiescent Crohn's disease (n=6 studies):
Budesonide was as effective as placebo for preventing relapse in medically induced remission (RD=-0.8%, 95% CI: -9.9, 8.3, \( P=0.42 \), n=4 studies and 449 participants). No significant heterogeneity was detected chi-squared=1.01, \( P=0.798 \). Similarly budesonide was as effective as placebo for preventing endoscopic recurrence in surgically induced remission (RD=-3.5%, 95% CI: -16.9, 9.8, \( P=0.30 \), n=2 studies and 212 participants). The pooled risk difference for preventing clinical recurrence was -3.0 (95% CI: -15.0, 8.8, \( P=0.33 \)). No significant heterogeneity was detected.

Corticosteroid-related adverse effects (n=6):
In the long-term treatment, budesonide had an occurrence rate of corticosteroid-related adverse effects similar to placebo (RD=5.3%, 95% CI: -3.9, 14.5, \( P=0.30 \), n=6 studies and 661 participants). However, there was significant heterogeneity chi-squared=9.96, \( P=0.076 \). If two trials with particularly low occurrences of adverse events are removed from the analysis, the remaining trials are homogeneous, chi-squared=2.66, \( P=0.447 \) (RD was not stated).

Authors' conclusions
Budesonide is significantly less effective than conventional corticosteroids for inducing remission in active Crohn's disease, but the risk of corticosteroid-related adverse effects is significantly reduced. Budesonide is not effective in preventing relapse of Crohn's disease after medically- or surgically-induced remission.

CRD commentary
This is a well-presented review with clearly stated inclusion/exclusion criteria. The search for studies only included one electronic database although manual searches of journals and bibliographies were performed. However, there is a risk of publication bias as only full reports of data published in journals were included. Studies' inclusion and data extraction were performed by multiple authors. The quality of the studies was also assessed although the number of authors involved in this process was not stated. In addition, the quality of the five included studies was reported individually.

The data were pooled appropriately after investigating heterogeneity both visually and statistically. However, the authors do not state the RD for adverse effects when the two studies responsible for causing heterogeneity were removed from the analysis. In view of the data presented the authors' conclusions and implications would appear to be reasonable.
Implications of the review for practice and research

Practice: The authors state that 'budesonide is less efficacious than conventional corticosteroids for inducing remission in active Crohn's disease, but the occurrence rate of corticosteroid-related adverse events is significantly lower'. In addition' despite their efficacy in active disease there is no evidence that prolonged low-dose corticosteroid therapy will prevent symptomatic relapse in Crohn's disease in remission'.

Research: The authors state that 'the finding of a slight benefit (of budesonide) in patients who underwent surgery primarily for disease activity need further evaluation'.

Bibliographic details

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Oral; Administration, Topical; Anti-Inflammatory Agents /administration & dosage /adverse effects /therapeutic use; Budesonide /administration & dosage /adverse effects /therapeutic use; Crohn Disease /drug therapy; Double-Blind Method; Glucocorticoids; Humans; Randomized Controlled Trials as Topic

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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.