Meta-analysis of enteral nutrition as a primary treatment of active Crohn's disease
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Authors' objectives
To compare the treatment of Crohn's disease by liquid diet therapy and corticosteroids using meta-analysis, and to assess the importance of formula composition to efficacy.

Searching
MEDLINE and EMBASE were searched from 1976 to 1994 and from 1984 to 1994, respectively; Gut, Gastroenterology and Journal of Paediatric Gastroenterology and Nutrition were handsearched from January 1991 to May 1994. Abstracts submitted to major gastroenterological meetings, bibliographies of retrieved articles and the authors' personal files, were also examined. The search strategy was given.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) of a minimum of 2 weeks' duration, which compared one type of liquid diet with another or with corticosteroids, were included.

Specific interventions included in the review
Efficacy of liquid diets versus corticosteroids: the liquid diets were categorised as elemental, semi-elemental or polymeric. The elemental diets included formulations of amino acids; the semi-elemental group included formulations of amino acids plus oligopeptides; and the polymeric group included intact milk protein. These were compared to corticosteroid therapy which included treatment with prednisone, sulphasalazine (SASP) or metronidazole (MTZ).

Efficacy of elemental versus non-elemental liquid diet therapy: the actual diets used were Elemental 028, Vivonex HN and Vivonex TEN, Trisorbon, Realmentyl (R), Nutrison (N), Enteral 400, Peptamen and Peptide 2+.

Participants included in the review
Patients with active Crohn's disease were included. No sex or age data were given.

Outcomes assessed in the review
The percentage of patients achieving remission with treatment was the main outcome measure.

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 validity of the included studies was assessed in terms of design, implementation and analysis. The overall index of trial quality was weighted as follows: design, 0.60; analysis, 0.30; presentation of results, 0.10. Studies were not excluded on the basis of this quality score, instead the final score for each study is given and studies are listed in order of quality from highest to lowest. The quality of included studies is also described. Quality assessment was performed independently by three assessors using the criteria outlined by Chalmers et al. (see Other Publications of Related Interest). Assessments were made blinded to authors, institution and journal of publication.

Data extraction
The data were extracted independently by two reviewers with any discrepancies resolved by discussion. The outcome data were extracted on an intention-to-treat basis.
Methods of synthesis
How were the studies combined?
Pooled odds ratios (ORs) were calculated with 95% confidence intervals (CIs), though the type of meta-analysis method employed is not stated. The quality scores were not used as weights in the meta-analysis.

How were differences between studies investigated?
Heterogeneity among the ORs was examined using the Breslow-Day test, and for both primary meta-analyses the included studies were found to be homogenous (p>0.50 in both cases). ORs of individual trials were also plotted graphically to confirm homogeneity. Sensitivity analyses were carried out to examine the effect of excluding various trials on the overall results.

Results of the review
Thirteen trials including a total of 547 patients were identified for inclusion: 8 comparing enteral nutrition with corticosteroids (n=413) and 5 comparing 2 types of enteral nutrition (n=134).

Liquid diet therapy versus corticosteroids:
Enteral nutrition was found to be inferior to corticosteroids (pooled OR 0.35, 95% CI: 0.23, 0.53). 21% of patients randomised to nutritional therapy did not complete the trials because of intolerance of formulated food. 8% of patients who were administered liquid diet nasogastrically did not tolerate therapy. A secondary meta-analysis of studies excluding patients who dropped out because of intolerance, but including early treatment failures who were withdrawn, still showed worse efficacy for dietary treatment (OR 0.57, 95% CI: 0.35, 0.94). Only one study reported outcomes in subgroups of patients classified according to anatomic location of disease, so no analysis was possible to determine whether response to therapy varied with site of inflammation. However, exclusion of the 2 trials with the highest proportion of isolated Crohn's colitis did not alter the overall results. Subgroup analyses were also carried out based on the nature of the protein and the quantity of fat in the formula. In all but one study the formulas contained no complete proteins and derived less than 10% of their calories from fat, and the exclusion of one trial of a polymeric diet did not significantly affect the overall results. The pooled analysis comparing low-fat elemental or low-fat semi-elemental diet to corticosteroids also showed nutritional therapy to be less effective (OR 0.34, 95% CI: 0.22, 0.52). No significant effect was found in a comparison between elemental diet and corticosteroids, though CIs were wide (OR 0.45, 95% CI: 0.17, 1.16). Two studies examined maintenance of remission at 1 year and no difference between treatments was found: approximately two-thirds of both treatment groups had relapsed. However, the total number of patients in this subgroup analysis was small.

Elemental versus non-elemental liquid diet therapy: the meta-analysis showed no difference in efficacy between therapies (OR 0.87, 95% CI: 0.41, 1.83). Three studies provided long-term follow-up data and no difference was found between dietary therapies, though the total number of patients included in the analysis was small (OR 1.83, 95% CI: 0.64, 5.19).

Authors' conclusions
Corticosteroids are more effective than enteral nutrition in the treatment of active Crohn's disease. There is no evidence of a difference in efficacy between elemental and non-elemental preparations, though this may be due to small sample sizes in the subgroup analyses.

CRD commentary
The thorough examination of the quality of the included trials indicates this is a good quality review, and the subgroup analyses suggest that the finding of greater efficacy for corticosteroids is robust. However, details of the baseline characteristics of the included patients would have helped assess the generalisability of the results.

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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.