Defined-formula diets versus steroids in the treatment of active Crohn's disease: a meta-analysis

Authors' objectives
To compare the effectiveness of defined-formula diets versus steroids for the treatment of active Crohn's disease.

Searching
Sources searched included the Iowa Drug Information System from January 1985 to June 1995 using the index terms 'Crohn's disease', 'steroids', 'defined-formula diet', 'elemental diet' and 'polymeric diet'. Current Contents from October 1991 to June 1995, and the MEDLINE database from January 1990 to June 1995 were searched, as were reviews, textbooks, reference lists of all trials found and abstract books of the main international congresses and symposia held between January 1992 and April 1995. Experts in the field were contacted. Only trials published in English were considered.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) evaluating the effectiveness of defined formula diets alone in comparison with a control group treated with steroids were included. If effectiveness was assessed in terms of remission rates in treatment and control groups, the end point was evaluated after a minimum of 10 days and a maximum of 8 weeks after initiation of treatment. Trials which combined the use of steroids and sulphasalazine (or related drugs) were included. Six studies were excluded for the following reasons: study was not a RCT, exclusively paediatric patients were studied (2 studies), treatment duration was 1 week, patients did not have active disease and one study was thought to contain duplicated data.

Specific interventions included in the review
Diets studied were polymeric diets using Edanec HN, elemental diets using Vivonex TEN, semi-elemental diets including Vital HN, Peptisorb and Survimed. The diets were given orally or by nasogastric tube. The duration of diet therapy ranged from 10 days to 6 weeks. Steroids given included prednisolone in doses from 35 mg/day to 52.5 mg/day, prednisolone in doses ranging from 52.5 mg/day to 70 mg/day and methylprednisolone in doses ranging from 12 mg/day to 48 mg/day. Some steroid groups also received sulphasalazine 3 g/day.

Participants included in the review
Adults with active Crohn's disease were studied. The definition of Crohn's disease varied between studies and included a Crohn's disease activity index (CDAI) greater than 150, simple activity index and a combination of symptoms and laboratory indices with Van Hees activity index greater than 120.

Outcomes assessed in the review
The main outcome assessed was the occurrence of a treatment failure. All patients who failed to achieve a remission were considered to be treatment failures. In studies based on simple activity index, remission was defined as the patient scoring 0 or 1.

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 reviewers performed the data extraction. For each study, the odds ratio of the risk of treatment failure and the 95% confidence limits were calculated with the method of Woolf.

Methods of synthesis
How were the studies combined?
The pooled odds ratio (OR) of the relative risk (RR) of treatment failure in patients given steroids compared to those receiving defined formula diets was calculated using the fixed-effect method of Mantel-Haenszel and the random-effects model of DerSimonian and Laird. The 95% confidence limits of the Mantel-Haenszel odds ratio were estimated using the Breslow Day method. Pooled rates of treatment failure were computed as the ratios of total crude data and by the method of Laupacis et al. The percentage reduction of risk and the number-needed-to-treat (NNT) were calculated. The data were reanalysed after excluding patients who failed after treatment with defined formula diets because of intolerance, side-effect or non-compliance, after including a non-randomised trial, and after including a trial in which patients allocated to the defined formula diet arm also received a regime of non-absorbable antibiotics.

How were differences between studies investigated?
Heterogeneity was assessed using the methods described by Collins.

Results of the review
Seven RCTs (353 patients) were used to compare the effectiveness of defined formula diets with steroids.

Treatment failure: pooled OR using Mantel-Haenszel = 0.35 (95%CI: 0.23, 0.53; P < 0.001); pooled OR using DerSimonian and Laird = 0.44 (95%CI: -0.08, 0.94; P = 0.03).

Using Mantel-Haenszel method: NNT = 4.5 (95%CI: 3.6, 6.9); Percentage risk reduction = 22% (95%CI: 14.5%, 27.9%).

Using DerSimonian and Laird: NNT = 5.5 (95%CI: 2.4, 66); percentage risk reduction = 18.2% (95%CI: 1.5%, 42.4%).

The number of null studies required to lead to statistical non-significance: using Mante-Haenszel = 23; using DerSimonian and Laird = 11.

Heterogeneity (Collins method) chi-squared = 5.1, df = 6, P > 0.50. No significant inter-trial heterogeneity.

Reanalysis after excluding patients who failed on diet therapy due to intolerance, side-effects, non-compliance: pooled OR using Mantel Haenszel = 0.46 (95%CI: 0.27, 0.79; P = 0.005); pooled OR using Der Simonian and Laird = 0.56 (95%CI: -0.03, 1.15; P = 0.14).

Reanalysis after including non-randomised trial: pooled OR using Mantel Haenszel = 0.43 (95%CI: 0.30, 0.64; P < 0.001). Number of null studies required for non-significance = 15.

Authors' conclusions
The administration of defined formula diets without concurrent steroids seems to have poor effectiveness in the treatment of adults with active Crohn's disease. These diets have a limited effectiveness also in the sub-group of patients who are not intolerant to this form of feeding.

CRD commentary
This is a clearly-written and presented review which includes an extensive literature search, defined inclusion criteria for primary studies, statistical analysis which involved a fixed-effect and a random-effects model, assessment of publication bias and inter-trial heterogeneity, sensitivity analysis and a discussion of the limitations of the review. The
authors mention the possibility of bias induced by the increased sense of well-being in patients treated with steroids and the dependence of the Crohn's disease activity index upon this measure, thus producing the potential for some bias in favour of steroids. The authors report that a meta-analysis by Griffiths of enteral nutrition as primary treatment of active Crohn's disease gave similar results.

The literature search, though extensive, was limited to English language publications and some relevant studies may have been omitted. No details are given of the methods used either to select studies for inclusion or to extract data. There is no assessment of the validity of the primary studies. The authors decided not to include quality scores in the design of the meta-analysis arguing that there is, at present, no agreement on how one can handle quality scores after calculating them. Fuller details of the participants would have been welcome to allow assessment as to the generalisability of the results. Five of the seven primary studies had fewer than fifty participants.

The authors conclusions are supported by the evidence given for the population studied.

Implications of the review for practice and research
The authors state that there is limited information about the effectiveness of a combination of diet and steroids.

Bibliographic details

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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.