Enteral nutrition and corticosteroids in the treatment of acute Crohn's disease in children

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Authors' objectives
To compare the effectiveness of enteral nutrition and corticosteroids in the treatment of acute Crohn's Disease in children.

Searching
MEDLINE (from 1966 to July 1999) and the Science Citation Index were searched. Additional studies were located by manual searching of abstracts (1990 to 1999) from ESPGHAN, NASPGN, and the American Gastroenterology Association (AGA), scanning of reference lists of review articles and meta-analyses, and by examination of recent book chapters and their bibliographies; leaders in the field were also contacted. The following search terms were used: 'Crohn's disease', 'enteral nutrition', 'child' (less then 18 years), 'clinical trial', 'diet', 'food' (formulated), 'steroids' and 'aminosalicylic acids'. There were no restrictions on publication type or language.

Study selection
Study designs of evaluations included in the review
Clinical trials of randomised, semi-randomised (consecutive allocation), and non-randomised (equal disease activity and distribution at treatment onset) design with a minimum 3-week treatment period were included. Observational studies, case series, studies in which patients were randomised more than once, and preliminary reports later published in full, were excluded.

Specific interventions included in the review
In terms of selection criteria, studies comparing enteral nutrition with corticosteroids in the treatment of Crohn's disease were included. In the included studies, the steroid doses used ranged between 0.2 and 2.4 mg/kg per day. In relation to the daily calorie intake, the following were used in the included studies: 75 kcal/kg; 50 to 80 kcal/kg; 100 to 140% of the reference nutrient intake (RNI); and calorie intake in accordance with the recommended dietary allowance (RDA). Studies of nutritional supplements, or the use of enteral nutrition to prolong remission were excluded.

Participants included in the review
Studies recruiting participants aged under 18 years and suffering from acute Crohn's Disease (newly diagnosed or relapsed) were included. Adult studies including paediatric patients were excluded.

Outcomes assessed in the review
The main outcome of interest was objective assessment of remission, with percentage remission reported for each treatment group. Data were also examined with respect to speed of remission reduction, duration of remission, nutritional end points, and height velocities.

How were decisions on the relevance of primary studies made?
All authors (n=4) examined the papers. However, the authors do not state whether examination was independent, or describe methods for resolving disagreements.

Assessment of study quality
No systematic assessment of validity was undertaken.

Data extraction
Data previously agreed to be relevant by all authors, were extracted from each article by two independent reviewers. Findings were compared and consensus reached among all authors by re-reading the manuscripts. All data were
extracted on an intention to treat basis. Authors of primary studies were contacted when necessary to clarify remission criteria and randomisation methods.

**Methods of synthesis**

How were the studies combined?
Fixed-effect and random-effects models were used to generate a pooled relative risk (RR) and 95% confidence intervals (CIs). Data on remission reduction, duration of remission, nutritional end points, and height velocities were combined in a narrative summary.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Cochran Q statistic, where a p-value of less than 0.05 was considered to represent significant heterogeneity. A Galbraith plot was used to visually detect inter-trial heterogeneity. Initially, the pooled RR was estimated for the 5 RCTs, then sensitivity analyses were performed by adding the semi-randomised and non-randomised studies. The number of studies required for a statistically-significant result in favour of steroid therapy was calculated.

**Results of the review**

Seven studies (n=194) were included: 5 of randomised design (randomised controlled trials, RCTs), 1 semi-randomised design and 1 non-randomised design.

The 7 studies were found to be homogeneous.

Pooled data from 5 RCTs (n=147): pooled RR 0.95 (95% CI: 0.67, 1.34). Heterogeneity Q statistic was 0.46 (d.f.=4, p=0.98). The pooled RR for all 7 studies was 0.982 (95% CI: 0.73, 1.33; Q=0.82, d.f.=6, p=0.991). For both analyses, identical values were obtained when using fixed- and random-effects models.

It was estimated that 10 further studies, identical in both size and outcome to the largest reported included study (n=68), would be required for a significant RR to be achieved in favour of steroid therapy: RR=0.86 (95% CI: 0.74, 0.99; Q=0.83, d.f.=14, p=1.0).

In terms of remission reduction, duration of remission, nutritional end points, and height velocities, the only significant between-group difference was found for height velocities achieved at short-term follow-up. Findings from 3 studies showed that the children receiving enteral nutrition had a significantly higher mean height velocity score at 3 and 6 months.

**Authors' conclusions**

There is no difference in efficacy between enteral nutrition and corticosteroid therapy in the treatment of acute Crohn's disease in children. Improved growth and development, without the adverse effects of steroid therapy, make enteral nutrition a better choice for first-line therapy in children with active Crohn's disease.

**CRD commentary**

Adequate details were given of the selection criteria used for primary studies, and some study details were provided in tables and text. The methods of pooling were appropriate. At least two reviewers were involved in selecting papers and extracting data. The search strategy would have benefitted from the inclusion of other electronic databases; as it stands, some relevant reports may have been omitted from the review. However, the authors attempted to estimate the impact of publication bias. No systematic method of validity assessment was reported, although the authors did attempt to assess the impact of including semi-randomised and non-randomised studies in the meta-analysis. Caution should be applied when interpreting the review's findings and the authors' conclusions, since the validity of each individual included study is not discussed.
Implications of the review for practice and research

Practice: The authors state that 'Enteral nutrition is as effective as steroids in achieving a remission in children with active Crohn's disease. In view of the benefits of dietary therapy on growth, development, and probably the gut mucosa, an enteral diet should be recommended as first-line therapy in all children with active Crohn's disease'.

Reviewer's comment: Some caution is required in interpreting these findings since the validity of each individual included study is not discussed.

Research: The authors state that 'Allocation of funds and enrolment of patients, even if randomised, to studies merely supporting current good-quality evidence is inappropriate'.

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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.