Early enteral nutrition in acutely ill patients: a systematic review

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Authors' objectives
To evaluate the effect of early enteral nutrition on the outcome of critically ill and injured patients.

Searching
MEDLINE was searched from 1966 to August 2000 using the following terms: 'enteral nutrition' (explode) and 'early or immediate or delayed' and 'randomized controlled trials' (publication type) or 'controlled clinical trials' or 'clinical trials, randomized'. The bibliographies of all selected articles and reviews that included information on enteral feeding were examined for other articles. The authors also reviewed their personal files and contacted experts in the field.

Study selection
Study designs of evaluations included in the review
Randomised clinical trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Comparisons of early versus delayed institution of enteral nutrition were eligible for inclusion. Early enteral nutrition was defined as the initiation of enteral feeds within 36 hours of admission to the hospital, or within 36 hours of surgery. Delayed enteral nutrition was defined as nutritional support that was initiated after 36 hours following admission to the hospital, or after 36 hours following surgery.

Early enteral nutrition protocols in the included studies were small bowel tube (range: less than 2 hours to less than 36 hours), jejunostomy (range: less than 2 hours to less than 24 hours), oral (less than 24 hours), orogastric tube (less than 6 hours), and orogastric tube/small bowel tube (less than 24 hours). The formulas used included: elemental diet; standard isocaloric; hypercaloric; nutrition supplement; immune-enhancing diet; blended liquid diet; and liquid diet. The caloric intake varied between trials.

Participants included in the review
Studies in hospitalised adult post-operative, trauma, head-injured, burn or medical intensive care unit (ICU) patients were eligible for inclusion. The included studies were in abdominal surgery, trauma, head-injury and burns patients. No studies of medical ICU patients were found.

Outcomes assessed in the review
Studies that reported at least one of the following primary outcome variables were eligible for inclusion: the number of infections, the total number of non-infectious complications, the length of hospital stay, and hospital mortality.

How were decisions on the relevance of primary studies made?
The studies were selected independently by two reviewers.

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

Data extraction
The data were extracted independently by two reviewers. The data extracted from each study included: date and author; the number of participants; enteral nutrition protocol and formula; caloric intake or percentage of goal (control versus intervention); and results for each outcome variable. Where the standard deviation for mean hospital stay was not reported, this was computed from the observed mean differences and the test statistics, or by using reported P-values and tables for the normal distribution.
Methods of synthesis
How were the studies combined?
Infections, complications and mortality were treated as binary variables; length of hospital stay was treated as a continuous variable. A meta-analysis using a random-effects model was used to calculate the pooled relative risk (RR) or weighted mean difference (WMD) with 95% confidence intervals (CIs).

How were differences between studies investigated?
Subgroup analyses were performed for post-operative, trauma, head-injury and burn groups; these were selected because they represent the main clinical populations included in the trials. Heterogeneity between trials was tested using a chi-squared test, where a P-value of less than or equal to 0.05 indicated significant heterogeneity.

Results of the review
Fifteen RCTs (n=753) were included.

Overall (12 trials, n=603), the risk of infection was significantly lower among patients who received early enteral nutrition (RR 0.45, 95% CI: 0.30, 0.66, P=0.00006). Statistical heterogeneity between the trials was significant (P=0.049). Seven of the 12 trials were in abdominal surgery patients (n=388), 2 in trauma patients (n=81), 2 in head-injury patients (n=114), and one in burns patients (n=20).

Overall (9 trials, n=520), no significant difference was shown in non-infectious complications (RR 0.82, 95% CI: 0.56, 1.19, P=0.3). Statistical heterogeneity between the trials was significant (P=0.047). Six of the 9 trials were in abdominal surgery patients (n=355), one in trauma patients (n=63), one in head-injury patients (n=82), and one in burns patients (n=20).

Overall (12 trials, n=489), the length of hospital stay was significantly shorter in the enteral nutrition group (WMD -2.22 days, 95% CI: -3.63, -0.81, P=0.002). Statistical heterogeneity between the trials was significant (P=0.0012). Eight of the 12 trials were in abdominal surgery patients (n=346), 2 in trauma patients (n=91), one in head-injury patients (n=32), and one in burns patients (n=20).

Overall (6 trials, n=296), no significant difference was shown in mortality (RR 0.74, 95% CI: 0.37, 1.48, P=0.4). Statistical heterogeneity between the trials was not significant (P=0.92). Three of the 6 trials were in abdominal surgery patients (n=131), one in trauma patients (n=63), one in head-injury patients (n=82), and one in burns patients (n=20).

Authors' conclusions
While the results support the experimental data demonstrating the benefit of the early initiation of enteral feeding, they must be interpreted with some caution because of significant heterogeneity between the studies.

CRD commentary
The review addressed a clear question in terms of the intervention, comparator, participants and outcomes. The studies were selected by two independent reviewers to minimise bias. Only one database was searched along with bibliographies and personal files; it is possible that some studies could have been missed due to language, publication and citation bias. The data were extracted by two independent reviewers to minimise errors. The included trials were presented in tabular format. However, there was no information concerning the participants’ underlying risk, the control interventions were not described, and some of the outcome measures reported were not explicitly defined (e.g. infections, other complications). The methodological quality of each included study was not assessed or taken into account in the analyses. The meta-analysis was conducted with appropriate methods, although pooling the results from such clinically heterogeneous trials is of questionable clinical relevance. The authors discussed possible reasons for the statistical heterogeneity observed, but they did not explore any of these in their analyses.

The evidence presented supports the authors' conclusion that their results should be interpreted with caution; however, it does not convincingly support their conclusion of benefit associated with early versus delayed initiation of enteral
feeding.

**Implications of the review for practice and research**

Practice: The authors state that current data supports the use of early enteral nutritional support in critically ill patients.

Research: The authors state that a large multicentre double-blind randomised study would provide more definitive evaluation of the benefits of early enteral feeding. Also, an additional study of critically ill medical patients is required, and that additional studies addressing the site of feeding would be of clinical value.

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