Early nasogastric enteral nutrition for severe acute pancreatitis: a systematic review
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CRD summary
The authors concluded that early nasogastric enteral feeding was potentially effective and safe for severe acute pancreatitis, but that evidence was scanty and more research is needed. The review was reasonably well-conducted and these cautious conclusions appear justified.

Authors' objectives
To determine the effectiveness and safety of early nasogastric enteral nutrition for severe acute pancreatitis.

Searching
The Cochrane Central Register of Controlled Trials (Issue 2, 2006) and PubMed (1966 to 2006) were searched with no restriction on publication language. Search terms were reported. References from relevant articles were handsearched.

Study selection
Randomised controlled trials (RCTs) using an early nasogastric enteral nutrition route through a nasogastric tube for patients with severe acute pancreatitis were eligible for inclusion. Included trials were required to use specified criteria to make the diagnosis (Atlanta classification; Apache II, Ranson and/or Balthazar computer tomography criteria). Controls were required to receive nutritional support via a conventional route designed to rest the pancreas, such as total parenteral nutrition, nasojejunal tube or jejunostomy tube. Other medical and surgical co-interventions (listed in the review) were permitted. The primary outcome measure was overall mortality. Other outcomes of interest were hospital stay, complications and safety including re-feeding pain recurrence and adverse events. There were no limitations by patient age, race or gender or by acute pancreatitis aetiology.

Participants in the included trials had acute pancreatitis diagnosed by a variety of clinical and biological criteria and by severity scoring tools. The inclusion criteria for severity ranged from an Apache score of at least 6 to at least 8 points. Exclusion criteria varied between trials but included: age under 18 years; pregnancy; delayed presentation; shock; and acute pancreatitis associated with surgery, bowel disease or chronic pancreatitis. Control interventions used in the review included total parenteral nutrition and nasogastric enteral nutrition.

The authors did not state how the papers were selected for the review or how many reviewers performed the selection.

Assessment of study quality
Study validity was assessed using Cochrane criteria to examine the adequacy of reported allocation concealment, blinding and use of intention to treat analysis. The Jadad five point scale was also used (a score of 5 points indicating highest quality). Validity was assessed by two reviewers working independently, with disagreements resolved by discussion with a third reviewer.

Data extraction
For dichotomous data, risk ratios and 95% confidence intervals (CIs) were calculated from the number of events in each group. For continuous variables, mean differences between the two groups and 95% CIs were calculated.

Data were extracted by two reviewers working independently, with disagreements resolved by discussion with a third reviewer.

Methods of synthesis
Data were combined to calculate pooled risk ratios and weighted mean differences, with 95% confidence intervals, using a fixed-effect model. Statistical heterogeneity was assessed using the $\chi^2$ test. Subgroup and sensitivity analyses (by intervention type and trial quality) were used to investigate differences between the studies.
Results of the review
Three randomised controlled trials (RCTs) were included in the review (n=131 patients; range 31 to 50; 67 in the early nasogastric enteral nutrition group and 64 in the conventional nutrition route group). None of the trials used blinding. Two trials reported satisfactory methods of randomisation and two reported both adequate allocation concealment and use of intention to treat analysis. Jadad scores were 2 or 3 points. Withdrawal rates ranged from 3 to 6%.

Early nasogastric enteral nutrition versus controls: Pooling of data showed no statistically significant difference between the groups in overall mortality (risk ratio 0.76, 95% CI: 0.37 to 1.55; p=0.45, three RCTs, n=131 patients). For other effectiveness outcomes, pooling of data showed no statistically significant difference between the groups in: length of hospital stay (one RCT, n=31 patients); infective complications, multiple organ deficiency syndrome (two RCTs, n=81 patients); intensive care unit admission (two RCTs, n=100 patients); or conversion to surgery (two RCTs, n=81 patients). No statistically significant heterogeneity was detected for any analysis.

Safety: Pooling of data showed no statistically significant difference between the groups in: recurrent re-feeding pain (two RCTs, n=81 patients); diarrhoea, tube displacement or severe complications requiring withdrawal of tube feeding (two RCTs, n=81 patients).

Subgroup and sensitivity analyses did not change the statistical significance of any of the findings.

Authors’ conclusions
Early nasogastric enteral nutrition was potentially effective and safe for management of severe acute pancreatitis, but evidence was scanty and more research is needed.

CRD commentary
The objectives and inclusion criteria of the review were clear, except that definition of the term "early" would have been helpful. Relevant sources were searched for studies without language restriction. However, as only two databases were searched and it did not appear that specific efforts were made to locate unpublished studies, it is possible that some trials might have been missed. Publication bias was not formally assessed. Relevant criteria were used to assess study validity and steps were taken to minimise bias by having more than one reviewer independently undertake validity assessment and data extraction. It is not clear whether similar steps were taken to select trials for inclusion in the review. Appropriate statistical techniques were used to combine trials, assess statistical heterogeneity and explore differences between the trials. Also, the authors acknowledged the potential biases associated with small sample sizes and the differences in the primary trials’ inclusion criteria for acute pancreatitis severity. The review was reasonably well-conducted and the authors' cautious conclusions appear justified.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that large high quality randomised controlled trials are needed to establish the effectiveness, safety and cost-effectiveness of early nasogastric enteral nutrition for management of severe acute pancreatitis. The optimum time to commence oral re-feeding needs to be established.

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