Nutrition support in acute pancreatitis: a systematic review of the literature
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CRD summary
This review assessed nutritional support for patients with acute pancreatitis. The authors concluded that enteral nutrition improved outcomes compared with parenteral nutrition in patients with severe acute pancreatitis. The authors’ conclusions appear to be supported by the evidence presented, but the inadequate reporting of study quality makes it difficult to assess the reliability of the results.

Authors’ objectives
To determine the optimal route and composition of nutritional support for patients with acute pancreatitis.

Searching
MEDLINE, the Cochrane CENTRAL Register and EMBASE were searched from 1966 to August 2005 using the reported search terms. Reference lists of retrieved studies and personal files were scanned.

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

Specific interventions included in the review
Studies that evaluated enteral nutrition (EN), parenteral nutrition (PN), standard treatment (STD; defined as no artificial nutritional support), or specific additives added to nutrition therapy were eligible for inclusion. Some of the included studies compared EN and PN with each other and with STD, while others compared EN or PN with and without additives. The additives evaluated in the included studies were probiotics, immune-enhanced EN formulas (contents included glutamine and arginine with and without omega-3 fatty acids, vitamins C, E and beta-carotene, and micronutrients), omega-3 polyunsaturated fatty acids, glutamine and modifications of glucose content. Some studies compared nasogastric with nasojejunal feeding or bolus versus continuous EN.

Participants included in the review
Studies of adults with acute pancreatitis were eligible for inclusion. The included studies involved patients admitted with acute pancreatitis and post-operative patients who had undergone surgery because of complications arising from acute pancreatitis. No further details of the participants were presented.

Outcomes assessed in the review
Specific inclusion criteria for the outcomes were not stated. The review assessed clinically important outcomes such as morbidity, length of hospital stay (LOS), infection, organ failure, noninfectious complications, need for surgical interventions, resolution of disease process and mortality. Surrogate outcomes were also assessed; these included nutritional markers, measures of inflammatory or immune response, and stress markers.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed on the basis of the following: randomisation; blinding; use of intention-to-treat analysis; methods used to select the patients; baseline comparability of the treatment groups; completeness of follow-up; adequacy of description of treatment protocol and cointerventions; and objectivity of the outcome measures. The maximum possible score appeared to be 14 points, but this was not explicitly reported.
Two reviewers independently assessed validity and resolved any disagreements by consensus.

**Data extraction**
Two reviewers independently extracted the outcomes and resolved any disagreements by consensus. For each study, the number of patients with each outcome of interest (or the mean value of the outcome measure with a measure of variance) was extracted. Risk ratios (RR) with 95% confidence intervals (CIs) were calculated for dichotomous outcomes and mean differences with 95% CIs for continuous measures. The authors of the primary studies were contacted for missing or unclear data where necessary.

**Methods of synthesis**
How were the studies combined?
The studies were grouped by interventions compared. Where two or more similar studies compared the same interventions using the same outcome measure, pooled RRs or weighted mean differences (WMDs) were calculated with 95% CIs using a random-effects maximum likelihood model. Otherwise, the studies were combined in a narrative.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared and I-squared statistics.

**Results of the review**
Twenty-seven RCTs were included (the total number of participants was not specified).

The mean quality score was 8.15 (range: 6 to 11).

Early EN versus PN (7 studies, including 5 studies in which patients were randomised within 48 hours of admission).

The meta-analysis showed that EN was associated with a significant reduction in infectious morbidity (RR 0.46, 95% CI: 0.29, 0.74, p=0.001; 7 studies; no significant heterogeneity) and hospital LOS (WMD -3.94 days, 95% CI: -5.86, -2.02, p<0.0001; 4 studies; heterogeneity was significant, p=0.03) compared with PN. There was no significant difference between treatments in mortality (based on 7 studies) or organ failure (based on 5 studies).

EN or PN versus STD.

EN versus STD: there was insufficient information from one small study (n=27) that lasted 4 days.

PN versus STD: PN given within 24 hours of admission significantly increased LOS (16 versus 10 days, p<0.04) and non significantly increased the time to a clear liquid diet (10 versus 6 days, p=0.8) compared with STD (based on 1 study in 55 patients with generally mild pancreatitis). PN given later (24 to 48 hours after 'liquid resuscitation') significantly reduced overall complications (52.4% versus 91.3%, p<0.01), hospital LOS (28.6 versus 39.1 days, p<0.05) and mortality (14.3% versus 43.5%, p<0.05) compared with STD (based on 1 study with 44 patients with severe acute pancreatitis).

Post-operative EN versus PN or STD. EN versus PN: there was insufficient information from one small study (n=22).

EN versus STD: the meta-analysis showed that EN reduced mortality compared with STD in patients who had required surgery for complications of acute pancreatitis, but the reduction was not statistically significant (RR 0.26, 95% CI: 0.06, 1.09, p=0.06; based on 2 studies with 71 patients).

Addition of supplements.

EN plus supplements versus EN alone: individual studies reported benefits (including reductions in mortality, LOS and complications) from adding arginine, glutamine, omega-3 polyunsaturated fatty acids and probiotics to EN compared with EN alone.
PN plus supplements versus PN alone: supplementing PN with parenteral glutamine did not significantly reduce overall complications (RR 0.68, 95% CI: 0.42, 1.09, p=0.11; based on 3 studies). Two studies reported reduced hospital LOS with glutamine supplementation, but in only one was the reduction statistically significant.

Tolerance to EN.

One small study (n=28) reported a non statistically significant reduction in the proportion of patients with no pain relapse (0% versus 27%) and LOS (12 versus 21 days) for nasojejunal feeding compared with oral feeding. One study (n not stated) reported no significant differences between nasogastric versus nasojejunal feeding. One small study (14 patients following surgery for the complications of acute pancreatitis) reported that bolus EN significantly increased the volume, bicarbonate content and enzyme output of the pancreas in comparison with continuous EN infusion (p<0.05).

Cost information
Five of the included studies evaluated costs and reported reduced costs (ranging from 2 to 7 times lower) for EN compared with PN. Four studies did not define 'costs'; the fifth study defined cost according to charges to patients. In 2 studies the reduction in costs was statistically significant ($2,756 versus $394, p=0.004 and $3,294 versus $761, p<0.005).

Authors' conclusions
EN improves outcomes compared with PN in patients with acute pancreatitis. Better outcomes are achieved by starting EN early in the course of severe acute pancreatitis. The addition of supplements to EN and PN may further improve outcomes.

CRD commentary
The review addressed a series of questions that were reasonably well defined in terms of the participants, interventions and study design; the outcomes assessed in the review were stated clearly. Several relevant sources were searched, but no attempts to locate unpublished studies were reported; this raises the possibility of publication bias. It was unclear whether any language restrictions had been applied, so the potential for language bias could not be assessed. Methods were used to minimise reviewer errors and bias in the assessment of validity and extraction of data, but it was not clear whether similar steps were taken when selecting the studies. Validity was assessed using specified criteria but only the composite score was presented, making it difficult for readers to judge the study validity for themselves.

Only studies that were similar were pooled. Statistical heterogeneity was assessed. Many studies had small sample sizes, which resulted in small numbers being included in the meta-analyses. The authors' conclusions regarding the superiority of EN over PN appear to be supported by the evidence presented, but the lack of adequate reporting of study quality makes it difficult to assess the reliability of the results. The cautious conclusions about additives seem appropriate.

Implications of the review for practice and research
Practice: The authors recommend that EN is to be preferred over PN for patients admitted with acute severe pancreatitis; that in patients with severe acute pancreatitis where it is not possible to use EN, feeding with PN should not be started for at least 5 days after hospital admission; and that the initiation of EN may be considered even in patients with severe advanced disease.

Research: The authors did not state any implications for further research.

Bibliographic details

PubMedID
Other publications of related interest
This additional published commentary may also be of interest. Carreazo NY, Ugarte K, Bada C. When should we start oral intake in children with severe acute pancreatitis? Evid Based Nurs 2008;11:39-40.

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Biomarkers /analysis; Costs and Cost Analysis; Enteral Nutrition /methods; Hospitalization; Humans; Length of Stay; Nutritional Support /economics; Pancreatitis /surgery /therapy; Parenteral Nutrition /methods; Postoperative Care; Randomized Controlled Trials as Topic; Stress, Physiological; Time Factors; Treatment Outcome

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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.