Advanced enteral therapy in acute pancreatitis: is there a room for immunonutrition? A meta-analysis
Petrov MS, Atduev VA, Zagainov VE

CRD summary
This review assessed whether adding glutamine, arginine or omega-3 fatty acids to standard enteral feeding improved rates of infection, mortality or hospital stay in patients with acute pancreatitis. It concluded that no beneficial effect was gained. Although the review was generally well conducted, the conclusions may be overstated due to the small number of studies and small sample size.

Authors' objectives
To determine whether enteral nutrition enhanced with glutamine, arginine or omega-3 fatty acids was clinically superior to standard enteral formulas in patients with acute pancreatitis.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE and MEDLINE were searched from 1 January 1990 to 1 December 2007. Search terms were provided. No language restrictions were applied. The references of the original articles were examined for further studies, as were abstracts from two major gastroenterological meetings (2001 to 2007).

Study selection
Randomised controlled trials (RCTs) of patients with acute pancreatitis in which enteral nutrition supplemented with glutamine, arginine, omega-3 fatty acids or nucleotides alone or in combination (immunonutrition) was compared with enteral feeding with no supplementation (standard enteral nutrition). Outcomes of interest were total infectious complications, in-hospital mortality and length of hospital stay.

In the immunonutrition groups, supplemented nutrients were omega-3 fatty acids alone, glutamine and arginine, or all three substances combined. Patients who received omega-3 fatty acids alone mostly had mild pancreatitis; those who received combination supplements were mostly suffering from severe pancreatitis. Enteral feeding was initiated either within 24 hours of admission or 72 hours from onset; duration of nutrition ranged from five days to over 17 days.

Inclusion criteria were applied independently by two authors.

Assessment of study quality
Study quality was assessed with a previously published quality scale that included items relating to randomisation, analysis, blinding, patient selection, comparability of groups at baseline, extent of follow-up, treatment protocol, co-interventions and outcomes. The resulting quality score could range from 0 to 14 points.

Quality data were extracted independently by two authors.

Data extraction
Data on number of events per group were extracted for the mortality and infectious complications outcomes. Data on mean length of hospital stay were extracted. Additional data were supplied by two study authors.

Data were extracted independently by two reviewers.

Methods of synthesis
Studies were combined using random-effects meta-analysis. A weighted analysis was performed, but the weight used was not described. For infectious complication and mortality, risk ratios (RR) with 95% confidence intervals (CIs) were
estimated. Estimates of hospital stay were combined using the mean difference method. The $I^2$ test was used to assess heterogeneity; $I^2$ of greater than 0.2 indicated significant heterogeneity. Funnel plots were used to explore any publication bias.

**Results of the review**
Three RCTs with a total of 78 participants were included in the review. Quality scores were 6, 8 and 11 out of a possible 14. No evidence of publication bias was identified from the funnel plots.

No statistically significant benefit from immunonutrition was identified in terms of either total infectious complications or mortality (both assessed in all three RCTs). No heterogeneity was identified for either of these outcomes. Length of hospital stay was assessed in two RCTs; no significant benefit from the intervention was identified, but statistically significant heterogeneity was reported ($I^2=57.2$).

**Authors’ conclusions**
Supplementation of enteral feeding with glutamine, arginine and/or omega-3 fatty acids did not clinically benefit patients with acute pancreatitis.

**CRD commentary**
This review had a clear objective and clearly stated and relevant inclusion criteria. The search appeared thorough (three major databases supplemented with review of reference lists). Attempts were made to minimise language and publication biases. Adequate study details were provided and allowed the reader to assess the similarity of included studies and generalisability of results. However, only the overall validity score was given and no presentation or discussion of individual quality items (such as adequacy of allocation concealment or blinding) was given, which made a detailed assessment of individual study validity impossible. The review process was clearly described and adequate attempts were made to minimise reviewer bias by using two independent reviewers at all key stages. The use of random-effects meta-analysis was appropriate; however, the authors did not acknowledge the low power of the test for heterogeneity given the small number of studies in the analyses. The assessment of publication bias from a funnel plot of only three studies was also unlikely to be reliable. The review was well conducted in terms of its methodology and generally good attempts were made to minimise bias and error. However, the conclusions did not adequately reflect the results of the review: the results did not show any evidence of benefit from enteral feed supplementation, but this may be due to the small number of studies and sample sizes of those studies and is not equivalent to providing evidence of no benefit as the authors’ imply.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that continued refinement of intra-luminal therapy may potentially have an exciting clinical implication in acute pancreatitis. A large scale RCT may be needed to investigate alternative enteral feed supplementations.

**Funding**
Not stated.

**Bibliographic details**


**PubMedID**
18325863

**DOI**
10.1016/j.ijsu.2008.01.003
Original Paper URL
http://www.journals.elsevierhealth.com/periodicals/ijsu/article/S1743-9191(08)00013-7/abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Arginine /administration & dosage; Enteral Nutrition; Fatty Acids, Omega-3 /administration & dosage; Glutamine /administration & dosage; Humans; Pancreatitis /therapy

AccessionNumber
12008106832

Date bibliographic record published
23/12/2008

Date abstract record published
20/01/2010

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.