Authors' objectives
To compare enteral nutritional support supplemented with key nutrients versus standard enteral nutritional support to determine the effects on morbidity and mortality rates and hospital stay.

Searching
Manual and computerised searches (MEDLINE) of published literature from January 1990 to February 1998 were carried out and reference lists of relevant publications were reviewed.

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

Specific interventions included in the review
Enteral nutritional support supplemented with key nutrients including L-arginine, n-3 essential fatty acids, RNA, L-glutamine, branched chain amino acids (e.g. Impact and Immun-Aid); standard enteral nutritional support. In seven studies experimental and control diets were isonitrogenous and isocatonic diets.

Participants included in the review
Patients with critical illnesses requiring enteral nutritional support including trauma, laparotomy and burns patients, patients with sepsis and patients requiring surgery (e.g. for upper and lower GI cancer).

Outcomes assessed in the review
Incidence of major infectious complications (wound infection, intraabdominal abcess, pneumonia, septicemia), nosocomial pneumonia alone (in view of the common occurrence and importance of hospital acquired respiratory tract infections) and death. For the definition of infectious complications in the papers studies, either clear criteria were detailed or the authors referred to previously published definitions. For the purposes of this meta-analysis, these were comparable between the studies examined. The length of rehabilitation time (time spent in hospital or intensive care unit) was also used as an outcome where provided.

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

Assessment of study quality
Validity was assessed using a three-point scale, taking into account sources of systematic errors of bias: selection, performance, attrition, and detection biases as previously described in Mulrow and Oxman 1997 (see Other Publications of Related Interest no.1). Studies were categorised as A (low risk of bias), B (moderate risk of bias) or C (high risk of bias). The validity ratings were not taken into account in the meta-analysis. Two independent observers assessed each study and differences were agreed by consensus.

Data extraction
Two reviewers independently abstracted the data and differences were agreed by consensus. Data were extracted concerning patient numbers and type, time of initiation of feeding, type of supplemented nutrition, stated nutritional goals, nutritional intake achieved, weight loss before the study and power calculations.
**Methods of synthesis**

How were the studies combined?
Odds ratios (ORs) and 95% confidence intervals (95% CI) were pooled for each outcome using a fixed-effect model. Weighted mean differences were used for the length of hospital stay. Separate analyses were carried out including only those studies with patients undergoing surgery for GI cancer.

How were differences between studies investigated?
Heterogeneity was assessed using a chi-square test.

**Results of the review**

Eleven RCTs including a total of 1009 participants.

Major infectious complications: All studies (n=9) OR=0.47 (95% CI: 0.32, 0.70), chi-square = 7.50, p = non-significant. GI cancer studies only (n=6) OR=0.47 (95% CI: 0.30, 0.73), chi-square = 3.55, p = non-significant.

Nosocomial pneumonia: All studies (n=8) OR=0.91 (95% CI: 0.53, 1.56), chi-square = 7.50, p = non-significant. GI cancer studies only (n=4) OR=0.71 (95% CI: 0.32, 1.60), chi-square = 6.10, p = non-significant.

Death rate: All studies (n=11) OR=1.77 (95% CI: 1.00, 3.12), chi-square = 3.32, p = non-significant. GI cancer studies only (n=6) OR=1.53 (95% CI: 0.44, 5.37), chi-square = 2.28, p = non-significant.

Length of hospital stay: All studies (n=8) weighted mean difference (WMD)=-2.491 days (95% CI: -3.993, -0.990), chi-square = 4.73, p = significant (text of results states p = non-significant, but figure and conclusions state p is significant). GI cancer studies only (n=5) WMD=-2.365 days (95% CI: -3.94, -1.171) (text of review states 95% CI: -3.94, -0.8), chi-square = 1.91, p = significant (text of results states p = non-significant, but figure and conclusions state p is significant).

Length of stay in intensive care: All studies (n=3) WMD=-0.251 days (95% CI: -1.380, 0.878), chi-square = 2.48, p = non-significant. Only one of the studies looked at GI cancer patients and this showed no significant difference between the two types of nutrition.

**Authors’ conclusions**

This meta-analysis has demonstrated that nutritional support supplemented with key nutrients results in a significant reduction in the risk of developing infectious complications and reduces the overall hospital stay in patients' critical illness and in patients with gastrointestinal cancer. However, there is no effect on death. These data have important implications for the management of such patients.

**CRD commentary**

This review answers a well-defined research question using clearly explained methodology. The studies were quality assessed and the data extracted independently by two reviewers. Heterogeneity between the studies was also assessed prior to appropriately combining the studies in a meta-analysis. Separate analyses were carried for GI cancer patients. However, the use of odds ratios instead of relative risks may give misleading results for outcomes where the event rate is high (e.g. for infection rates). There are also discrepancies within the different sections of the text, and between the text and figures with regards to the significance of the results and the 95% CIs. The review may also have missed relevant data by only searching one database and the possibility of publication bias cannot be ruled out as no attempt was made to locate unpublished material. In view of these comments the findings of the study should be interpreted with caution.

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

Practice: The authors state that the ‘data have important implications for the management of such (patients requiring enteral nutritional support) patients’.
Research: The authors state that 'when considering length of overall hospital stay, the combined results of all studies demonstrated a significant reduction when all patients were analysed together, and also when patients with GI cancer were examined separately. This could have major financial implications. However, a cost/benefit analysis comparing total costs for all patients needs to be done in this context'. In addition 'further well-designed studies (with adequate statistical power), focusing on defined patient groups, with a clearly defined supplemented nutritional regimen, appropriate control nutritional supplement, and precise outcome measures are now urgently required to confirm that supplemented nutritional supplementation has beneficial effects on clinical outcome in critically ill patients. Lastly, when reporting the results of randomised studies, the guidelines described in the Consolidated Standards of Reporting Trials (CONSORT) statement should be followed to allow better interpretation of trial results'.

Bibliographic details

PubMedID
10203078

Other publications of related interest

This additional published commentary may also be of interest. Posani T. Review: supplemented enteral nutrition reduces infectious complications and length of hospital stay in patients with critical illness. Evid Based Nurs 2000:3;23.

Indexing Status
Subject indexing assigned by NLM

MeSH
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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.