Application of perioperative immunonutrition for gastrointestinal surgery: a meta-analysis of randomized controlled trials


CRD summary
This review evaluated the clinical effectiveness of peri-operative immunonutrition and its effect on post-operative immunity in patients with gastrointestinal cancers. Compared with standard diet, immunonutrition was found to decrease post-operative infection and reduce the length of hospital stay through increasing humoral and cellular immunity. Poor reporting of the study methodology means that the authors' conclusions should be viewed with caution.

Authors' objectives
To evaluate the clinical effectiveness of peri-operative immunonutrition and its effect on post-operative immunity in patients with gastrointestinal cancers.

Searching
MEDLINE (via PubMed) (1966 to 2006), the Cochrane Library (2006), EMBASE (1980 to 2006) and ISI Web of Knowledge (2006) were searched; some search terms were reported. Literature reference proceedings were also handsearched (it was unclear whether this referred to conference proceedings). Only studies reported in the English language were included.

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 in which a peri-operative immunonutrition diet (supplemented with two or more nutrients including arginine, glutamine, omega-3 polyunsaturated fatty acids (PUFA) and ribonucleic acids) was compared with a standard diet were eligible for inclusion. The included studies evaluated diets supplemented with arginine, ribonucleic acids and omega-3 PUFA; glutamine, arginine and omega-3 PUFA; and arginine and omega-3 PUFA. The last time of immunonutrition varied from 7 days pre-operatively to 10 days post-operatively.

Participants included in the review
Hospitalised adult patients with abdominal cancer undergoing gastrointestinal surgery, including gastrectomy, pancreatico-duodenectomy and colectomy, were eligible for inclusion. The patients included had upper gastrointestinal operations, gastrectomies, pancreatico-duodenectomies and colectomies for cancer.

Outcomes assessed in the review
The outcomes assessed were mortality, length of hospital stay, post-operative infection, immune markers (total lymphocytes, CD4, CD8, IgG, IL6, IL2 and CRP levels), adverse events and hospital cost.

How were decisions on the relevance of primary studies made?
Two reviewers independently identified relevant studies.

Assessment of study quality
Methodological quality was assessed using the Jadad scale, a 5-point scale evaluating features such as randomisation, blinding and allocation concealment. The authors did not state how the validity assessment was performed.

Data extraction
Two reviewers independently extracted the data.

Methods of synthesis

How were the studies combined?
The outcome measures were pooled in a fixed-effect or random-effects meta-analysis to generate odds-ratios (ORs), weighted mean differences (WMDs) and 95% confidence intervals (CIs).

How were differences between studies investigated?
A chi-squared test was used to assess statistical heterogeneity.

**Results of the review**
Thirteen RCTs (n=1,269) were included in the review. Six were double-blinded (n=627).

Compared with standard diet, immunonutrition had a statistically significant positive effect on post-operative infection rate in 11 trials (OR 0.41, 95% CI: 0.30, 0.54, p<0.00001), length of hospital stay in 8 trials (WMD -3.48, 95% CI: -4.70, -3.26, p<0.00001), total lymphocytes in 3 trials (WMD 0.40, 95% CI: 0.21, 0.59, p<0.0001), CD4 levels in 3 trials (WMD 11.39, 95% CI: 6.20, 16.58, p<0.0001), IgG levels in 2 trials (WMD 1.07, 95% CI: 0.46, 1.67, p=0.0005) and IL6 levels in 5 trials (WMD -201.83, 95% CI: -328.53, -75.14, p<0.002).

The effect of immunonutrition on mortality and CD8, IL-2 and CRP levels, compared with standard diet, was not statistically significant.

The authors stated that no significant side-effects were reported.

**Cost information**
The authors reported that 2 trials found hospital costs were lower in patients taking the immunonutrition diet.

**Authors’ conclusions**
Immunonutrition is effective and safe. It decreases post-operative infection and reduces the length of hospital stay through increasing humoral and cellular immunity in post-operative patients, compared with standard diet. Further research in children and critically ill patients undergoing gastrointestinal surgery is required.

**CRD commentary**
The review question was clear in terms of the participants, intervention and study design of interest. However, inclusion criteria were not stated for the outcomes of interest. The authors searched four relevant databases and performed some handsearches, but it is unclear whether they attempted to identify unpublished studies, which may have increased the possibility that some relevant studies were not included. Publication bias was not assessed. Only English language studies were included, which might have introduced language bias. Two reviewers independently identified and extracted relevant papers, thereby minimising the potential for errors and bias in the review process. The validity of the individual studies and statistical heterogeneity were assessed, but the results of these were neither reported nor considered in the discussion of the results. Few details of the individual studies were provided in this review. Poor reporting of the included studies and the validity and heterogeneity of the studies means it is not possible to assess the suitability of combining them in meta-analysis. The authors’ conclusions should therefore be viewed with caution.

**Implications of the review for practice and research**
Practice: Immunonutrition should be recommended.

Research: Further trials of children undergoing gastrointestinal surgery and patients that are critically ill and undergoing gastrointestinal surgery are needed. Factors such as pre-operative nutritional status, prevention of administration of antibiotics and standardisation of type of operation should be considered.

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