Glutamine dipeptide for parenteral nutrition in abdominal surgery: a meta-analysis of randomized controlled trials
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CRD summary
This review evaluated the effectiveness of standard isonitrogen parenteral nutrition supplemented with glutamine dipeptide in patients undergoing abdominal surgery. Glutamine dipeptide decreased infection rate and length of hospital stay and improved nitrogen balance. The reliability of these conclusions is questionable given the lack of information about review methodology and the possible inappropriate pooling of data.

Authors' objectives
To evaluate the effectiveness of glutamine dipeptide as a supplement to parenteral nutrition (PN) in patients undergoing abdominal surgery.

Searching
MEDLINE (via PubMed) (1966 to April 2006), EMBASE (1980 to April 2006) and ISI Web of Knowledge (Science Citation Index) (April 2006) and the Cochrane Library (April 2006). 'Literature reference proceedings' were also handsearched (it was not clear whether this referred to conference proceedings). The search terms were reported.

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 comparing standard isonitrogen PN and PN supplemented with glutamine dipeptide were eligible for inclusion. The included trials supplemented patients with 0.18 to 0.5 g/kg glutamine dipeptide per day and lasted between 5 and 7 days.

Participants included in the review
Studies of adult patients undergoing abdominal surgery were eligible for inclusion. The included studies were conducted in Europe and Asia.

Outcomes assessed in the review
Inclusion criteria for the outcomes were not stated. The outcomes assessed in the review were post-operative cumulative nitrogen balance, post-operative infection and length of hospital stay.

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

Assessment of study quality
The Jadad scale was used to assess methodological quality and a score greater than two was used to indicate high quality. The authors did not state how the validity assessment was performed.

Data extraction
Two reviewers independently extracted the data and decisions were resolved by the research team. Post-operative infection was expressed as an odds ratio (OR) and the length of hospital stay and post-operative cumulative nitrogen balance were expressed as weighted mean differences (WMDs), along with their 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis. WMDs and ORs were combined using either a fixed-effect or random-
effects model.

How were differences between studies investigated?
Differences between the studies were investigated using a chi-squared test for statistical heterogeneity.

**Results of the review**
Nine RCTs (n=373) were included in the review.

**Post-operative cumulative nitrogen balance.**

The WMDs of 6 RCTs (n=238) were combined. The chi-squared test indicated significant statistical heterogeneity between studies (p<0.00001). Glutamine dipeptide use in PN was associated with a statistically significant improvement in cumulative nitrogen balance (WMD 8.35, 95% CI: 2.98, 13.71, p=0.002).

**Post-operative infection.**

The ORs of 5 RCTs (n=215) were combined. The chi-squared test indicated no significant heterogeneity between the studies. Glutamine dipeptide use in PN was associated with a statistically significant reduction in infective events (OR 0.24, 95% CI: 0.06, 0.93, p=0.04).

**Length of hospital stay.**

The WMDs of 6 RCTs (n=291) were combined. The chi-squared test indicated significant heterogeneity between the studies (p<0.00001). Glutamine dipeptide use in PN was associated with a statistically significant reduction in length of hospital stay (WMD 3.55, 95% CI: -5.26, -1.84, p<0.00001).

The authors reported that no serious adverse effects were reported in the included studies, but gave no further details.

**Authors' conclusions**
Post-operative PN supplemented with glutamine dipeptide is effective and safe in terms of decreasing the infection rate and length of hospital stay, and improving nitrogen balance.

**CRD commentary**
The research question was well defined but, although the inclusion criteria were clear with regards to the study design and intervention, there were no criteria relating to the outcomes; this may have resulted in subjective decisions regarding inclusion. The authors searched four relevant databases but did not investigate publication bias. The validity of the individual studies was assessed, but was not taken into account in the discussion of the results. Two independent reviewers extracted the data. However, the authors did not specify how decisions about inclusion were made or how the validity assessment was performed, so it is not known whether further steps were taken to minimise bias or error in the review process.

The authors assessed heterogeneity between the studies, which was statistically significant for two of the three outcomes investigated; the pooling of these studies in a meta-analysis may therefore have been inappropriate. Also, there was insufficient detail of the individual studies to enable an assessment of how clinically similar they were. The evidence provided appears to support the authors' conclusions about effectiveness, but there was no analysis to support conclusions concerning the safety aspect of supplementation. The reliability of the authors' conclusions is questionable given the lack of information about review methodology and the possible inappropriate pooling of data.

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

Research: The authors stated that further high-quality trials in children and in patients with severe conditions are required. Mortality and hospital cost should be considered in future RCTs of sufficient size and with rigorous design.
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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.