A systematic review of the role of immunonutrition in patients undergoing surgery for head and neck cancer

Stableforth W D, Thomas S, Lewis S J

**CRD summary**
This review assessed whether perioperative immunonutrition had a role in the treatment of head and neck cancer and concluded that length of hospital stay was improved, but clinical complications were not. In light of small sample sizes, a lack of good quality data and uncertainty over parts of the review process, the authors' conclusions should be interpreted with caution.

**Authors' objectives**
To assess whether perioperative immunonutrition had a role in the treatment of head and neck cancer.

**Searching**
PubMed, EMBASE and Cochrane Central Register of Controlled Trials were searched (no dates were given); search terms were reported. Reference lists were searched for additional studies. Unpublished data were sought from pharmaceutical companies and authors of relevant trials.

**Study selection**
Randomised controlled trials (RCTs) that compared polymeric nutritional supplements with immunonutritional additives to a control group that received traditional care (intravenous fluids) or polymeric nutritional supplements in patients receiving head and neck surgery for cancer were eligible for inclusion. Most included trials compared polymeric feeds with immunonutrition. Pre-operation supplementation ranged from >5 days to 10 days. Post-operation supplementation was >10 days in most studies; only a small number of studies used pre-operation supplementation in addition to post-operation supplementation. Outcomes included biochemical or immunological changes, wound infections, fistula formation, mortality, length of postoperative hospital stay and quality of life. Mean patient age ranged from 55 to 63 years in the control groups and 59 to 63 years of age in the active groups. Mean body mass index (BMI), where reported, ranged from 23.2 to 25.1 in the control groups and 22.1 to 26.2 in the active groups.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

**Assessment of study quality**
Study quality was assessed using: method of randomisation; allocation sequence and concealment; use of power calculation; blinding; and use of intention-to-treat analysis.

The authors did not state how the validity assessment was performed.

**Data extraction**
Odds ratios (ORs) and 95% confidence intervals (CI) were calculated for postoperative complications and mean differences and 95% CI for length of postoperative stay. Authors of included trials were contacted to provide further information where necessary.

Two reviewers independently extracted the data, which was checked by a third reviewer; disagreements were resolved through consensus.

**Methods of synthesis**
Pooled OR and weighted mean differences (WMDs) and their 95% CI were calculated using a random-effects model. Heterogeneity was assessed using the X² test. Significant heterogeneity was defined as p<0.05.
Results of the review
Ten RCTs (n=605, range 29 to 129) were included. Allocation concealment was reported in seven studies. Most studies were double-blinded. Nine studies were analysed as intention-to-treat. Where stated, duration of follow up was generally less than 12 weeks.

A statistically significant reduction in length of postoperative stay of 3.5 days (95% CI: 0.7 to 6.3, p<0.01; six studies) was observed for patients who received perioperative immunonutrition compared to control. There were no significant reductions observed for clinical complications. The ORs for: wound infection was 0.66 (95% CI: 0.22 to 1.93; three studies); fistula formation was 0.55 (95% CI: 0.15 to 1.99; five studies) and mortality was 1.18 (95% CI: 0.32 to 4.32; three studies). Quality of life measures revealed no evidence of improvements with pre- or postoperative immunonutrition compared with control. No significant heterogeneity was observed.

Authors’ conclusions
Perioperative immunonutrition was associated with reduced lengths of hospital stay. Clinical complications were not reduced.

CRD commentary
The review question and inclusion criteria were clear. A limited literature search was undertaken. It was unclear whether language restrictions were applied and language bias could have been present. Unpublished studies were sought through contacting authors and drug companies. More than one reviewer was involved in data extraction, but it was unclear whether this extended to study selection and hence it was unclear whether appropriate methods were used to reduce error and bias throughout the review process. An assessment of study quality was undertaken. Most included RCTs were small and contained less than 50 participants. In light of the diversity of interventions and variable clinical populations (acknowledged by the authors) it was unclear whether meta-analysis was appropriate in this review. Heterogeneity was assessed and found to be absent from the analyses. The authors’ conclusions were reasonable based on the evidence presented, but small sample sizes and small numbers of events mean that the analysis may have been underpowered to detect a reduction in complications.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that a suitably powered clinical trial was required before firm recommendations could be made on the use of immunonutrition in head and neck cancer patients postoperatively.

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