Early postoperative enteral immunonutrition: clinical outcome and cost-comparison analysis in surgical patients


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of an immunonutritional diet for early post-operative enteral feeding of patients undergoing operations for upper gastrointestinal (GI) cancer. The diet was supplemented with arginine, dietary nucleotides and omega-3 fatty acids.

Type of intervention
Treatment and supportive care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing major abdominal operations for upper GI cancer.

Setting
The setting was hospital. The economic analysis was carried out in the Departments of Surgery at the Universities of Bochum and Bonn, Germany.

Dates to which data relate
The data on effectiveness and resource use were gathered from a cohort of patients undergoing surgery between April 1992 and May 1994. The price year was 1995.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was performed retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 154 patients randomly assigned to either the immunonutrition group (n=77) or the placebo group (n=77). The mean age of the patients was 65.1 (standard deviation, SD=1.5) and 66.3 (SD=1.8) years in the immunonutrition and placebo groups, respectively. A total of 10 patients were excluded from the study; of these 10 patients, 2 refused to participate whilst the other 8 were ineligible due to insufficient intake of the enteral diet.
Study design
The study was a prospective, randomised, double-blind controlled trial carried out in three centres. The duration of the follow-up was until discharge. The study had no loss to follow-up. The investigators were kept blinded until the completion of the data analysis.

Analysis of effectiveness
The principle used in the analysis of effectiveness was intention to treat. The clinical outcome measures were:

- the total number of post-operative complications;
- details of post-operative complications, for example, septic complications, wound complications, pulmonary infection and urinary tract infection; and
- GI side-effects such as diarrhoea, bloating and abdominal cramps.

Post-operative complications were recorded in both the early phase, i.e. post-operative day 1 to 5, and in the late phase, i.e. after post-operative day 5. The study groups were found to be comparable in terms of demographic and prognostic features.

Effectiveness results
The immunonutrition group contained a total of 17 patients who experienced post-operative complications, compared with 24 patients in the placebo group; this observation was non significant. In the early phase, there were 12 patients suffering complications in the immunonutrition group and 11 patients in the placebo groups, whilst in the late phase, there were 5 and 13 patients in the immunonutrition and placebo groups, respectively, (p<0.05).

The total number of complicating events was 22 in the immunonutrition group versus 32 in the placebo group; this result was also non significant. In the late phase, there were 8 events in the immunonutrition group versus 17 events in the placebo group, (p<0.05).

The two study groups had similar and minimal cases of GI side-effects; no major cases occurred in either group.

Three patients died in the immunonutrition group versus 2 in the placebo group, i.e. a non significant result.

Clinical conclusions
The study showed that early post-operative enteral feeding is likely to reduce the number of late complications occurring in patients who have undergone major cancer operations. This finding confirms the assumption that a certain volume of immunonutrition, typically 5 to 6 L, has to be delivered over a post-operative period of 4 to 5 days before clinical efficacy can be expected.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. This study should, therefore, be classified as a cost-consequences analysis.

Direct costs
The costs were not discounted due to the short time frame considered in the study. Quantities were reported separately from the costs, and cost items were also reported separately. The cost analysis covered the costs for a 500-mL bottle of the immunonutrition and the standard diet, the nutrition costs for the experimental and placebo diet groups, and the costs related with the following complications:

- operative interventions, and emergency and anaesthetic procedures;
professional consultations and services related to complications;

artificial respiration and dialysis;

radiograph and sonography;

physiotherapy;

antibiotics and other complication-related medications.

A hospital perspective appears to have been adopted in the cost analysis. The source of resource use data was the medical records of the study patients. The source of cost data relating to professional services was the tariff of the German hospital association. Other cost data were obtained from the study hospital purchase prices. The date to which the price data referred was 1995.

Statistical analysis of costs
No statistical analysis of costs was performed.

Indirect Costs
Indirect costs were not considered.

Currency
German marks (DM). The exchange rate at the end of September 1995 was US$1 = DM1.4365.

Sensitivity analysis
No sensitivity analysis was conducted.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The total cost of complications for the 77 patients in the immunonutrition group was 83,654 DM, compared with 122,433 DM in the placebo group. The total cost for nutrition in the 77 patients was 17,456 DM, compared with 1,925 DM for the standard enteral diet. Overall, the use of an immunonutritional diet resulted in a saving of 23,248 DM.

Synthesis of costs and benefits
Costs and benefits were not combined since the use of the intervention was the dominant strategy.

Authors’ conclusions
Early enteral feeding with either the supplemented immunonutrition diet or the isonitrogenous, isocaloric placebo diet, was well tolerated in patients who underwent upper GI surgery. In patients who received the supplemented diet, a significant reduction in the frequency rate of late post-operative infectious and wound complications was observed. Thus, the treatment costs were substantially reduced in the immunonutrition group, as compared with the placebo group.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator was clear and justified by the authors.

**Validity of estimate of measure of benefit**
The effectiveness data were obtained from a double-blind randomised and multicentre study. The internal validity of the study is likely to be high given both the design of the study and the use of appropriate statistical analysis.

**Validity of estimate of costs**
Given the perspective of the analysis, all relevant direct costs were included. Resources used were obtained from actual data, and adequate details of methods of cost estimation were given. The external validity of the results may be increased by a sensitivity analysis.

**Other issues**
The issue of generalisability was partially addressed by the authors who discussed the different discharge policy applied in the USA and Germany.

Appropriate comparisons were made with other studies. In particular, the different results found with respect to other investigations, in terms of length of hospitalisation for patients receiving the experimental and placebo diets, were discussed and justified.

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