The clinical value of parenteral immunonutrition in surgical patients

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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 authors assessed parenteral nutrition (PN) in surgical patients. Three strategies were compared:

(A) standard PN;

(B) standard PN supplemented with intravenous glutamine (Dipeptiven; Fresenius-Kabi) at a dose of 2.0 mL/kg per day; and

(C) standard PN supplemented with intravenous omega-3-unsaturated fatty acids (Omegaven; Fresenius-Kabi) at a dose of 1.0 mL/kg per day.

PN was prepared as All-in-One admixtures comprising Aminoplasmal 10% and 15% (B Braun) or Aminomel (Baxter) amino acid solutions, fatty acid emulsions (Lipofundin MCT/LCT 10% and 20%; B Braun), and glucose (10, 20 and 40% solutions).

Type of intervention
Secondary prevention of malnutrition and immune system-related problems in post surgical patients.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients operated on for gastric carcinoma. Stringent inclusion criteria were used:

age 18 to 90 years;

total or subtotal gastrectomy for gastric cancer;

Karnoffsky grade > 60;

contraindication or lack of possibility of enteral nutrition after surgery;

no alternations of nutritional status or malnutrition of minor grade; and

indication of PN after gastrectomy.

The exclusion criteria included confirmed malnutrition of severe grade, recent history of severe heart, lung, kidney or liver failure, and a history of recent immunosuppressive therapy. Further exclusion criteria were confirmed metastases to central nervous system, contradictions for PN, and unexplained diarrhoea or vomiting.

Setting
The setting was secondary care (Department of General GI Surgery). The economic study was carried out at the Jagiellonian University in Cracow, Poland.

**Dates to which data relate**

The effectiveness and resource use data were obtained between January 2001 and August 2003. The prices seemed to relate to the same period of time, although this was not explicitly stated.

**Source of effectiveness data**

The effectiveness data were derived from a single study.

**Link between effectiveness and cost data**

The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

**Study sample**

The authors used patients operated on for gastric carcinoma in the study setting during the timescale of the trial (n=105). All 105 patients were randomly allocated to one of the three groups. There were 35 patients in group A (standard PN), 34 in group B (standard PN supplemented with intravenous glutamine) and 36 in group C (standard PN supplemented with intravenous omega-3-unsaturated fatty acids. Fifteen patients were excluded after initial enrolment for various reasons (4 from group A, 5 from group B and 6 from group C). The remaining 90 patients (43.3% female; mean age 61.9 years) were split between the three study groups (n=30 in each group). There was no report that power calculations were carried out to estimate the influence of chance on the results. The sample included patients who were already at risk of malnutrition and so provided an appropriate sample to assess the impact of parenteral immunonutrition.

**Study design**

The analysis was based on a randomised controlled trial (RCT) that was carried out in a single medical centre. The method and unit of randomisation were not reported. The patients were followed for 12 days after the operation. The authors did not report any loss to follow-up for any reason. There was no report that blinding was carried out, and it would have been especially difficult in this analysis.

**Analysis of effectiveness**

It was unclear whether the patients were analysed according to intention to treat or treatment completers. The primary health outcomes were albumin, prealbumin, total lymphocyte count (TLC), rate and type of complications, kidney and liver function, and treatment tolerance. The authors reported that age, gender, performance status, disease characteristics, surgical procedure, amount of blood or plasma, and albumin transfusion were comparable in all three groups.

**Effectiveness results**

Treatment tolerance was satisfactory with no reported side effects. In no case was intolerance the reason for early PN termination.

The authors reported that there were no significant differences amongst the groups in terms of albumin or TLC, although immunonutrition enabled faster TLC growth during the postoperative period, p>0.05. There were also no significant differences in postoperative complications (group A versus group B, p= 0.13; group A versus group C, p=0.2) and hospital length of stay, despite stay being shorter in the immunonutrition groups than in the standard groups).

A statistically significant difference was observed in plasma prealbumin concentrations between groups B or C and A,
The differences in postoperative complications were not statistically significant between groups.

The results indicated correct liver and kidney function.

**Clinical conclusions**
The authors concluded that immunostimulating PN helps to reduce the rate of infectious complications. Immunonutrition has no influence on surgical complications and liver and kidney function.

**Measure of benefits used in the economic analysis**
There was no summary measure of health benefit. Therefore, the authors carried out a cost-consequences analysis.

**Direct costs**
A very basic costing analysis was carried out, and the perspective from which it was approached was not reported. The authors estimated the total cost of parenteral treatment (presumably drug costs) and the cost of the stay in hospital over the course of the clinical study. These estimates were not broken down into their constituent parts, and the costs and the quantities were not reported separately. The sources of the cost data were not reported. As the study took place over 12 days, there was no need to discount any cost estimates. No price year was reported, which is important as the clinical study occurred over a period in excess of two years and, therefore, some reflation of prices would have been necessary.

**Statistical analysis of costs**
The costs were treated deterministically. No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not estimated.

**Currency**
Polish zlotych (PLN) and Euros (Euro). The conversion rate was not reported.

**Sensitivity analysis**
No sensitivity analyses were reported.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The cost of parenteral treatment was reported to be significantly higher in group C, reaching PLN 32,780 (Euro 6,689).

The authors reported that the costs in group B were greater than standard treatment alone. However, the actual treatment costs for groups A and B were not reported.

The total cost of a hospital stay (including PN costs) was PLN 39,480 (Euro 8,400) in group A, PLN 40,170 (Euro 8,546) in group B and PLN 49,580 (Euro 10,550) in group C.
Synthesis of costs and benefits
The costs and benefits were not combined as the study was a cost-consequences analysis.

Authors' conclusions
The cost of immunostimulating treatment based on omega-3-unsaturated fatty acids is higher than the cost of standard parenteral nutrition (PN), and the difference exceeds potential profits from shorter hospital stay. The authors doubted whether Omegaven was cost-effective, but suggested that Dipeptiven was more cost-effective because of the slightly lower number of complications and only a slightly higher cost.

CRD COMMENTARY - Selection of comparators
The authors compared patients receiving standard PN, standard PN supplemented with intravenous glutamine, and standard PN supplemented with intravenous omega-3-unsaturated fatty acids. The authors suspected that the two supplemented diets would improve the immune system and so reduce postoperative complications and improve patient well-being. The choice of the comparator, standard PN, was justified by illustrating the clinical benefit that can be gained from supplemented PN. You should decide if the comparators represent available practices in your own setting.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The study design, an RCT, was appropriate for the study question. Randomisation helped reduce any systematic biases between the patients groups. The study sample included all patients attending a medical centre who met the inclusion criteria. Therefore, the study sample should be representative of the study population since there was no sample selection. The patients were compared at analysis and shown to be comparable. The lack of reported methods of randomisation and blinding during the outcome assessment presented potential threats to the reliability of the findings. Another weakness of the analysis was that no sample size was determined in the planning phase of the study, and no power calculations were reported. This introduces the possibility that the results may be prone to bias.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was therefore categorised as a cost-consequences analysis, and the reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
Very few details of the costing, including the perspective from which it was conducted, were reported. The perspective could not have been societal as the indirect costs were not included. Therefore, the analysis appears to have been carried out from the perspective of the health care provider. Given this perspective, it would appear that no relevant costs were omitted from the analysis. Sources for the unit costs and separate resource use data would have enhanced the reader's ability to interpret the results and key cost drivers, and hence to draw their own conclusions with regards to the cost results. Some statistical analysis of the costs, or a sensitivity analysis, would also have enabled the reader to assess the robustness of the results to changes in key variables. The lack of a reported price year will hinder any future reflation exercises and prevent comparisons with other technologies assessed at different time periods. The costs were not discounted since they were all incurred during less than one year.

Other issues
The authors made extensive comparisons of their own results with those of other authors. The comparisons considered studies that reinforced their own results and those that had conflicting results. In the latter case, reasons for such differences were well explored. The issue of generalisability was addressed with the authors acknowledging that the study only involved patients without severe malnutrition and that the results may differ substantially (in favour of supplemented PN) when patients with severe malnutrition are treated. The results were not presented selectively and the conclusions reflected the scope of the analysis. It would have been useful had the authors gone a step further and
assessed whether the additional cost of supplemented PN was justified by the observed difference in prealbumin, particularly with reference to other treatments used in their setting. The authors stated that the main limitation was the specific patient group enrolled and thus the limited generalisability of the study.

**Implications of the study**
The authors did not make any explicit recommendations for changes in policy or practice. They also did not recommend any further research.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
15906909

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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