Quick recovery of serum diamine oxidase activity in patients undergoing total gastrectomy by oral enteral nutrition
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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 present study compared enteral nutrition (EN) with peripheral supplements to total parenteral nutrition (TPN) in patients undergoing total gastrectomy for gastric cancer. In the TPN group, standard TPN was given from day 3. On day 8, patients started a liquid diet. In the EN group, EN was given from day 3 by mouth. The total calorific intakes each day were almost equal for the two groups. Each feeding protocol was reported in detail in the paper.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with gastric cancer undergoing a total gastrectomy with D1 or D2 lymphadenectomy were enrolled.

Setting
The setting was tertiary care. The economic study was performed in Japan.

Dates to which data relate
Patient enrolment took place between January 2001 and December 2002. The effectiveness and costs were reported from these data. The price year was not reported.

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

Link between effectiveness and cost data
The resource use data were based on the same patient sample as that used in the effectiveness study, and were collected prospectively.

Study sample
Fifty-two patients who underwent total gastrectomy at a single hospital were enrolled. Three patients were excluded because palliative surgery was performed, the primary tumour was unresectable, or metastatic disease was present. One patient who was randomised to the TPN group was also excluded because he developed severe heart failure. Thus, 48 patients were recruited and randomly assigned to either the EN group (n=27) or the TPN group (n=21). The male-to-female ratio was 19/8 in the EN group and 16/5 in the TPN group. (p=0.73). The mean age of the patients was 62 (+/-
10) years in the EN group and 65 (+/- 11) years in the TPN group, (p=0.25). No power calculations or sample selection were reported.

**Study design**

This was a randomised controlled trial (RCT) that was carried out in a single centre. The follow-up period was until hospital discharge. The randomisation method was not reported, nor was blinding of the outcome assessment. No patients were lost to follow-up. However, two patients in the EN group were withdrawn from treatment (one developed postoperative pancreatitis on postoperative day 3, while the other could not tolerate the supplement without vomiting). Their data were excluded from the analysis of retinol-binding protein (RBP) and diamine oxidase (DAO) activity, but they were included in the other analyses as members of the EN group.

**Analysis of effectiveness**

The authors reported that the analysis was based on 48 of the 52 intent to treat cohort, and gave reasons for the exclusion of 4 patients. The groups were comparable in terms of the site of the cancer, mean age, mean preoperative albumin concentration, duration of operation and operative blood loss. The authors did not specifically report a primary outcome, but serial measurements of serum concentrations of albumin and RBP were reported as nutritional parameters, in addition to DAO activity, an enzyme linked to mucosal integrity. Tolerance of the EN protocol and surgical complications were also assessed.

**Effectiveness results**

No significant differences were found at any point between the two groups for either albumin or RBP.

In both groups, serum DAO activity was lower than baseline on postoperative days 1 and 4.

In the TPN group, the level remained depressed until postoperative day 7.

In contrast, patients in the EN group showed quicker and more complete recovery of DAO activity than the TPN group on postoperative days 7 and 14.

On postoperative day 7, the mean (standard deviation) serum DAO activity was 8.1 (2.3) U/L in the EN group and 5.8 (2.3) U/L in the TPN group, (p=0.0078).

There were no deaths from the operation in either of the two groups.

The overall incidence of postoperative complications was reported to be similar in the two groups.

**Clinical conclusions**

EN had similar clinical outcomes to TPN. It could also possibly prevent intestinal atrophy in the patient who has to endure prolonged postoperative fasting.

**Measure of benefits used in the economic analysis**

No measure of benefit was reported. The study was thus classified as a cost-consequences analysis.

**Direct costs**

The only reported cost category included was that of treatment costs per hospitalisation. Discounting was not carried out, which was appropriate given the short time horizon of the study (i.e. less than two years). Neither the quantity/cost boundary nor the sources of the costs were specifically reported, although the data seem to have come from hospital administrative sources. The price year was not reported.
Statistical analysis of costs
Hospitalisation costs were compared statistically through the unpaired t-test.

Indirect Costs
No indirect costs were reported.

Currency
US dollars ($). No conversion method was reported.

Sensitivity analysis
No sensitivity analysis was reported.

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

Cost results
Hospital stay was shorter in the EN group (23.1 +/- 7.2 days) than in the TPN group (27.6 +/- 4.7 days), (p=0.0345). The mean treatment cost per hospitalisation during the hospital stay was smaller in the EN group ($1,193 +/- 51) than in the TPN group ($1,368 +/- 78), (p<0.0001).

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Enteral nutrition (EN) is an efficient way to provide nutrition to patients and possibly prevent intestinal atrophy in the patient who must endure prolonged postoperative fasting. The EN protocol is safe and well tolerated after total gastrectomy, and reduces patient discomfort by eliminating tubes and catheters. In addition, compared with total parenteral nutrition (TPN), EN reduces treatment cost and length of stay in the hospital.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The newer surgical techniques improve the anastomosis and allow the use of early EN instead of TPN. You should decide whether these two comparators are relevant in your setting as well.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The study design, an RCT, was appropriate given the study question. Although the study was an RCT, several caveats should be taken into consideration. In particular, the absence of power calculations to determine sample size and the treatment-completers-only basis for the analysis represented significant drawbacks. In addition, the failure to report the method of randomisation and blinding of the outcome assessment presented potential limitations to the reliability of the findings. All these factors could introduce bias into the results. The two patient groups were shown to be comparable in terms of the baseline criteria. The study sample should have been representative of all patients with gastric cancer undergoing a total gastrectomy with D1 or D2 lymphadenectomy, as there was no sample selection. The reader can examine the baseline criteria of the study sample to determine whether it appears representative of other populations with gastric cancer.
Validity of estimate of measure of benefit
No measure of benefit was reported. Thus, the study was classified as a cost-consequences evaluation.

Validity of estimate of costs
Although the perspective of the cost analysis was unclear, it appears that costs relevant to the hospital have been included. Too little detail on the costs was given, and only aggregated results of in-hospital treatment costs were reported. Since the authors did not break down the hospital costs, it was unclear whether they were all included. The costs and the quantities were not reported separately, which may hinder the reproducibility of the results. The resource use quantities were taken from a single study. No statistical, sensitivity, or any other kind of analysis of the quantities or prices was carried out. The year to which the prices referred was not stated, and this may hinder the generalisability of the results. These limitations may well influence the internal validity of the cost analysis.

Other issues
The authors made appropriate comparisons of their effectiveness results with those from other studies. The cost results were not compared, possibly because there were no studies considering clinical outcome and costs of EN and/or TPN protocols. The generalisability to other settings was not addressed. The authors did not present their results selectively, but the absence of follow-up after hospital discharge means that the authors’ conclusions do not completely reflect the scope of the analysis. The study considered depressed patients with gastric cancer undergoing a total gastrectomy and this was reflected in the authors' conclusions. The authors did not report any limitations of their study.

Implications of the study
According to the authors, this study supports early oral feeding after total gastrectomy with intact anastomosis, possibly preventing gastrointestinal atrophy. They believed this protocol should become the standard of care for nutritional support after total gastrectomy. The fact that this was a small trial conducted in a single centre, providing promissory but preliminary data, should be taken into consideration.

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