Effect of glutamine-enriched total parenteral nutrition in patients with acute pancreatitis

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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 use of total parenteral nutrition (TPN), supplemented with glutamine, for the management of patients with acute pancreatitis (AP). The parenteral feeding solution was administered for at least one week, and the amount and composition of TPN depended on the individual's characteristics. The composition of TPN comprised glucose, lipids, amino acids, nitrogen and glutamine.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with moderate to severe AP. This was diagnosed by the presence of a greater than three-fold increase of serum amylase concentrations and/or abdominal pain, typical finding in abdominal ultrasound, or computed tomography of the abdomen. Patients were excluded if they were pregnant, if they intended to eat within one week, or if they presented with renal failure (creatinine >150 mol/L). They were also excluded if they had received parenteral nutrition in the two weeks before the study.

Setting
The setting was a hospital. The economic study was carried out at the Department of Gastroenterology and Hepatology of the Hannover Medical School in Germany.

Dates to which data relate
Neither the dates nor the price year were reported.

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

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

Study sample
Retrospective power calculations were performed on a sample of patients treated in the 48 months before the beginning of the study. These showed that the present study had a power of 74% to show a statistically significant difference in a reduction of the TNP time between the two groups, and a power of 42% to show a statistically significant reduction in
the length of hospital stay (LOS).

Of all the patients (aged between 16 and 80 years) suffering from AP at the study hospital over a period of 26 months, a sample of 28 eligible patients was enrolled in the study. There were 14 patients in the group receiving TPN with glutamine (gln+) and 14 in the group receiving standard TPN (gln-). The patients in the gln+ group were aged 52.8 (+/- 17.3) years and 7 were men. The weight in this group was 68 (+/- 11.1) kg and the body mass index (BMI) was 23.4 (+/- 3.4) kg/m2. The patients in the gln- group were aged 54.8 (+/- 18.1) years and 9 were men. The weight in this group was 69.5 (+/- 11.3) kg and the BMI was 24.5 (+/- 3.4) kg/m2. It was not stated whether some of the patients refused to participate or were excluded for any reason from the initial study sample.

**Study design**
This was a prospective randomised controlled trial that was conducted in a single centre. The method of randomisation was not reported. Patients, nurses and physicians were unaware of the patients' allocation to the study groups. The length of follow-up appears to have been 14 days. No patient was lost to follow-up.

**Analysis of effectiveness**
All of the patients included in the study were taken into account in the effectiveness analysis (intention to treat). The primary health outcomes used in the analysis were LOS and duration of TPN. The secondary health outcomes were infectious complication rate and variations in nutritional and inflammatory parameters. For example, leucocytes, lymphocytes, C-reactive protein, soluble tumour-necrosis factor alpha-receptor-p75, lipase, BMI, albumin, transferrin, protein, amino acid, glutamine serum cholinesterase activity, alkaline phosphatase, and alanine aminotransferase. The study groups were shown to be comparable at baseline.

**Effectiveness results**
The median length of TPN was 10 days (interquartile range: 6 - 16) in the gln+ group and 16 days (interquartile range: 10 - 18) in the gln- group, (p<0.05).

The median LOS was 21 days (interquartile range: 14 - 32) in the gln+ group and 25 days (interquartile range: 19 - 40) in the gln- group. This difference did not achieve statistical significance, (p>0.05).

The infectious complication rate was 29% in the gln+ group and 36% in the gln- group. The difference was not statistically significant.

Lymphocytes (10^3/microL) changed significantly from 1.2 (+/- 0.6) to 1.9 (+/- 0.8) in the gln+ group, and from 1.5 (+/- 0.6) to 1.7 (+/- 0.6) in the gln- group.

Glutamine serum cholinesterase changed significantly from 3.3 (+/- 1.4) kU/L to 3.8 (+/- 1.5) kU/L in the gln+ group, and from 3.5 (+/- 0.9) kU/L to 3.7 (+/- 1.6) kU/L in the gln- group.

Albumin increased significantly from 30 (+/- 7.3) g/L to 36 (+/- 5.2) g/L in the gln+ group, and from 32 (+/- 7) g/L to 32 (+/- 7.3) g/L in the gln- group.

Transferrin changed from 43 (+/- 12.4) mmol/L to 51 (+/- 16.7) mmol/L in the gln+ group, and from 47 (+/- 12.4) mmol/L to 39 (+/- 12.1) mmol/L in the gln- group.

Protein changed from 59 (+/- 8.1) g/L to 72 (+/- 5.2) g/L in the gln+ group, and from 65 (+/- 10.5) g/L to 68 (+/- 7.8) g/L in the gln- group.

The remaining parameters were not statistically different across the study groups.

**Clinical conclusions**
The effectiveness analysis showed that TPN supplemented with glutamine had beneficial effects on the clinical course.
of patients with AP. In comparison with standard TPN without glutamine, it led to a shorter time of nutrition, an increase in serum proteins (indicating an improved anabolic response), and a trend towards shorter LOS.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used. A cost-consequences analysis was therefore performed.

Direct costs
Discounting was irrelevant since the costs were incurred over a short period of time. The unit costs were not reported separately from the quantities of resources. The economic evaluation included only the costs of the TPN components (solutions and materials). The cost/resource boundary adopted in the study was not reported. The resources used were estimated on the basis of trial data, while the unit costs were derived from a published study. No price year was reported.

Statistical analysis of costs
Standard statistical analyses of the costs were conducted to test for statistical significance; median values and interquartile ranges were reported.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Euros.

Sensitivity analysis
No sensitivity analyses were conducted.

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

Cost results
The daily cost was higher in the gln+ group (78 +/- 25.7 euros) than in the gln- group (55 +/- 19.3 euros), (p<0.01). However, the total costs per patient were not statistically different (929 +/- 586 euros versus 981 +/- 507 euros) due to the shorter LOS in the gln+ group.

Synthesis of costs and benefits
Not relevant as a cost-consequences analysis was conducted.

Authors' conclusions
The introduction of glutamine within total parenteral nutrition (TPN) was beneficial. In addition, compared with standard TPN without glutamine, it improved the patient's response to therapy without increasing the costs.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. TPN without glutamine was selected since it represented the
standard nutritional approach in patients with AP. You should decide whether it represents a widely used intervention in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis of the effectiveness used a randomised controlled trial, which was appropriate for the study question. The study sample was representative of the study population. The study groups were shown to be comparable at baseline and statistical analyses were conducted when estimating the effectiveness. Retrospective power calculations were performed. These issues tend to increase the internal validity of the analysis. However, the authors stated that their analysis was underpowered to detect statistically significant differences in terms of secondary outcomes, such as complication rates. The method of randomisation was not reported.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the economic analysis. The analysis was therefore categorised as a cost-consequences study.

**Validity of estimate of costs**

The perspective adopted in the study was not stated. Only the costs strictly related to the components of the solutions used for TPN were included in the analysis. The unit costs were not reported separately from the quantities of resources used and no price year was given, thus presenting difficulties for reflation exercises in other settings. Statistical analyses of the costs were performed, but the cost estimates were specific to the study setting as no sensitivity analyses were conducted.

**Other issues**

The authors compared their findings with those from other studies, but did not address the issue of the generalisability of the study results to other settings. No sensitivity analyses were performed, thus further limiting the external validity of the analysis. The study considered patients with AP and this was reflected in the conclusions of the analysis. The authors commented on the potential limitation of a study with limited power in the effectiveness analysis.

**Implications of the study**

The authors suggested that their findings support the use of parenteral nutrition supplemented with glutamine in patients suffering from AP. Future research should be based on a larger population and focus on sub-groups of patients with and without pancreatic necrosis.

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