The effects of supplemental glutamine dipeptide on gut integrity and clinical outcome after major escharectomy in severe burns: a randomized, double-blind, controlled clinical trial

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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 parenteral supply of glutamine (gln) dipeptides following extensive eschar excision on severe burns was assessed. The patients received an alanyl-glutamine dipeptide solution (Dipeptiven; Fresenius Kabi, Germany) at a dose of 0.5 g/kg body weight (bw) per day, which corresponded to 0.35 g L-glutamine per kg bw/day.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised burn patients aged between 20 and 50 years. Patients were included if they had a burn size of 30 to 50%, or third-degree injuries ranging from 15 to 25% of the total body surface. Patients were also included if they were free from respiratory injury or smoke inhalation, multi-trauma, septicaemia, diabetes, chronic renal disease and liver disease.

Setting
The setting was secondary care. The economic study was carried out in Beijing, China.

Dates to which data relate
The dates when the effectiveness and resource use data were collected were not reported. 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 effectiveness data and the cost data were derived from the same patient sample. The costing was carried out prospectively.

Study sample
Power calculations were not reported. Thirty burn patients were enrolled in the study, and were randomly assigned to two groups. Fifteen patients received the standard parenteral nutrition solution (control group) and 15 received the parenteral nutrition solution with gln dipeptide supplementation (test group). The patients in the control group had a
mean age of 33.4 (+/- 8.1) years and a bw of 65.8 (+/- 6.8) kg). The patients in the test group had a mean age of 34.6 (+/- 7.8) years and a bw of 63.7 (+/- 5.1) kg.

**Study design**
The study was a prospective, randomised, double-blind clinical trial that was conducted in a single centre. Random tables were used for randomisation. The follow-up period to assess the clinical outcomes was 12 days for both groups.

**Analysis of effectiveness**
The basis of the analysis was intention to treat. The primary health outcomes assessed were:

- the plasma gln concentrations,
- the gut permeability, expressed as the lactose/mannitol (L/M) ratio,
- the plasma endotoxin levels,
- the wound healing time,
- the rate of infectious complications, and
- the survival rate.

There were no statistically significant differences in general characteristics and burn size between the two groups at baseline.

**Effectiveness results**
The plasma gln concentrations were below the reference value for healthy Chinese (659 +/- 35 micromol/L) in both groups prior to the operation. One and 12 days after the operation, plasma gln increased significantly with gln dipeptide supplementation in comparison with the control group. The plasma gln levels were 431.3 (+/- 52.7) versus 321.0 (+/- 40.7) micromol/L after 1 day, (p=0.001), and 532.1 (+/- 48.9) versus 397.8 (+/- 38.7) micromol/L after 12 days, (p=0.001).

Prior to the operation, the L/M ratios in both groups were higher than the reference value for healthy Chinese (0.022 +/- 0.0016). One day after the operation, the ratio in the gln group was significantly lower than the control group (0.138 +/- 0.039 versus 0.175 +/- 0.022; p=0.003).

Prior to the operation, the plasma endotoxin levels in both groups were higher than the reference value for healthy Chinese (0.016 +/- 0.0086 EU/mL). One and 12 days after the operation, the gln group had lower concentrations than the control group. The plasma endotoxin levels were 0.097 (+/- 0.029) versus 0.121 (+/- 0.028) EU/mL after 1 day, (p=0.026), and 0.112 (+/- 0.026) versus 0.141 (+/- 0.045) EU/mL after 12 days, (p=0.043).

The wound healing time was significantly lower in the gln group than the control group (32.1 +/- 3.3 versus 36.6 +/- 5.7 days; p=0.012).

The rate of infections in the gln group (n=3, 13%) was lower than that seen in the control group (n= 4, 26%). A statistical evaluation was not possible.

The skin graft survival rate 12 days after the operation was similar in both groups (control group 92.7% versus gln group 93.1%; p=0.86).

**Clinical conclusions**
Supplementation with gln dipeptide was associated with enhanced gln plasma concentrations, and decreased gut
permeability, endotoxin levels and wound healing times, in severe burn patients.

**Measure of benefits used in the economic analysis**
No summary measure of benefit was used. The study was therefore considered to be a cost-consequences analysis.

**Direct costs**
The costs were calculated at discharge from hospital. Discounting was not carried out as the costs were incurred during less than 2 years. The total costs for each group were reported, but there were not details of the categories of costs included in the analysis. It would appear that only the hospital costs were assessed. The unit costs and the quantities were not analysed separately. The resource use data were taken from the patients' records. The source of the unit costs was not given. The dates (of the effectiveness and resource use data) and price year were not reported.

**Statistical analysis of costs**
The costs were expressed as mean values +/- the standard deviation, and were analysed using the Wilcoxon test.

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

**Currency**
Chinese renminbi (RMB) or Yuan. The conversion to US dollars ($) was $1 = RMB 8.27.

**Sensitivity analysis**
No sensitivity analysis was reported.

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

**Cost results**
The total cost of hospitalisation was RMB 45,300 +/- 5,500 ($5,436 +/- 660) for the control group and RMB 41,400 +/- 3,400 ($4,968 +/- 408) for the gln group, (p=0.029).

The cost of parenteral nutrition was $376 (+/- 3.13) for the control group and $1,152 (+/- 9.12) for the gln group, (p=0.001).

**Synthesis of costs and benefits**
Not relevant as no summary measure of benefit was derived.

**Authors' conclusions**
Parenteral nutrition supplemented with glutamine (gln) dipeptide is helpful in enhancing plasma gln and reducing serum endotoxin concentrations. In addition, it improves gut permeability, ameliorates wound healing following extensive eschar excision, and decreases the cost of hospitalisation.

**CRD COMMENTARY - Selection of comparators**
The authors explicitly justified the choice of the comparator. The standard parenteral nutrition solution reflects the
standard approach after eschar excision of burns patients in the authors' setting. You should judge whether this comparator is relevant in your setting, or whether other comparators could also have been relevant.

**Validity of estimate of measure of effectiveness**
The analysis was based on a prospective randomised double-blind clinical trial, which was appropriate given the study question. A statistical analysis was conducted to compare the groups at baseline, and the methods of randomisation and blinding were reported. The study sample appears to have been representative of the study population. However, the lack of power calculations and the subsequent small sample size meant that it was unclear whether the study sample was sufficiently large to prove a statistically significant difference in health outcomes.

**Validity of estimate of measure of benefit**
The authors did not derive a measure of health benefits. The reader is referred to the comments in the ‘Validity of estimate of measure of effectiveness’ field (above).

**Validity of estimate of costs**
Although the perspective adopted was unclear, it appears that categories of costs relevant to the hospital perspective have been included. The total cost of hospitalisation and the cost of the parenteral nutrition solution were reported, but no additional details of the cost analysis were given. The costs and the quantities were not reported separately, which will hamper the extrapolation of this analysis to other settings. The resource use quantities were taken from a single study and a statistical analysis was carried out. The source of the unit costs was not reported. No statistical or sensitivity analysis of the prices was carried out, and this limits the interpretation of the results. The failure to report the price year also limits any future reflation exercises. Discounting was appropriately not carried out since all the costs were incurred during less than 2 years. Currency conversions were undertaken to reflect US dollar results, and the conversion rate was appropriately reported.

**Other issues**
The authors compared their clinical results with those from other studies, but they did not compare the economic results with other economic studies. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. However, the authors did not seem to be aware of the limited usefulness of the cost analysis they presented. The authors reported no limitations to their study.

**Implications of the study**
The authors did not make any specific recommendations for changes in policy or practice and/or the need for further research.

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