The effect of supplemental enteral glutamine on plasma levels, gut function, and outcome in severe burns: a randomized, double-blind, controlled clinical trial


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 glutamine-enriched enteral nutrition for patients suffering from severe burn injury. Glutamine (gln) is an essential amino acid related to the normal function of the immunologic system and intestinal tract. In this study, gln was given as the dipeptide of alanyl-gln, the dose of which provided 0.35 g gln/kg body weight per day.

Type of intervention
Rehabilitation.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals aged 18 to 50 years, with burns ranging in size from 50 to 80% of the total body surface burn, and third-degree injuries of between 20 and 40%. The inclusion criteria also stipulated no presence of respiratory injuries and no presence of smoke inhalation.

Setting
The setting was a hospital. The economic analysis was performed in China.

Dates to which data relate
The dates during which the effectiveness evidence and resource use were gathered were not given. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was performed on the same samples of patients as those used in the effectiveness study. It appears that the costing was performed prospectively, although this was not explicitly stated.

Study sample
No power calculations to determine the sample size were conducted. A total of 41 patients were enrolled sequentially in the study. The patients were enrolled in the study only after informed consent had been obtained. One patient was excluded because of early death. The final sample included 40 patients randomised to receive either gln-enriched enteral nutrition (n=20) or standard enteral nutrition (n=20). The mean age was 43.7 (+/-3.8) years in the gln group and...
40.0 (+/- 4.3) years in the control group. The body weights were 73.2 (+/- 3.3) kg (gln group) and 69.8 (+/- 4.0) kg (control), respectively. The patients in the gln group had 70.4% (+/- 8.1) total body surface burn and 32.3% (+/- 7.1) third-degree burns. The patients in the control group had 65.2% (+/- 9.6) total body surface burn and 33.8% (+/- 6.6) third-degree burns.

**Study design**
This was a prospective, double-blind, randomised controlled trial that was performed in a single centre. A pharmacist prepared the gln-enriched and standard enteral nutrition solutions according to randomisation numbers for each participant of the study. All care providers and laboratory workers were blinded to the group allocation, and the two feeding solution were identical in colour, smell, texture and taste. The patients were followed up for 30 post-burn days (PBD). No loss to follow-up was reported.

**Analysis of effectiveness**
The basis of the clinical study was treatment completers only. The primary health outcomes used in the analysis were:

- the plasma gln concentration at PBDs 1 and 12 (PBD +1, PBD +12);
- the intestinal permeability, measured as the lactulose-mannitol ratio (L/M ratio), at PBDs +1, +3, +6 and +12; and
- the endotoxin concentration, measured as EU/mL, at PBDs +1, +3, +6 and +12.

In addition, wounds healed, body weight, body weight loss and hospital length of stay were estimated at PBD +30. The two groups were comparable at baseline in terms of their age, body weight, total body surface burn, third-degree burns, body mass index, and acute physiology and chronic health evaluation.

**Effectiveness results**
The plasma gln concentration was below the reference value for Chinese healthy individuals in both groups at PBD +1. However, at PBD +12 it increased in the gln group but remained unchanged in the control group. The difference in the two groups at PBD +12 was statistically significant, (p=0.048).

Compared with the control group, the L/M ratio fell significantly at PBD +3 and PBD +6 in the gln group, (p=0.001 and p=0.034), showing attenuated intestinal permeability. At PBD +12, the L/M ratio was still lower for the gln group, although the difference was no longer significant, (p=0.23).

In terms of endotoxin concentration, there was a statistically significant difference in favour of the gln group (reduction in EU/mL) at PBD + 3. However, the two groups were comparable at PBD +1, +6 and +12, (p non significant).

At PBD +30, wound healing was significantly higher in the gln group (86% +/- 2) than in the control group (72% +/- 3), (p=0.041). The gln group also demonstrated better results than the control in terms of body weight (61.1 +/- 8.9 kg versus 52.4 +/- 11.0 kg; p=0.042) and body weight loss (-12.1 +/- 5.4 kg versus -17.4 +/- 7.2 kg; p=0.028) at PBD +30.

The average hospital length of stay was significantly lower for patients in the gln group (67 +/-4 days) than for patients in the control group (73 +/-6 days), (p=0.026).

**Clinical conclusions**
The authors concluded that gln supplementation supported the plasma gln concentration, attenuated intestinal permeability, reduced early increase in plasma endotoxin level, improved wound healing and reduced hospital length of stay.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used. A cost-consequences analysis was therefore carried out.
Direct costs
Discounting was not conducted, which was appropriate given the short time in which the costing was undertaken. The unit costs and the quantities of resources were not reported separately. The quantity/cost boundary appears to have been that of the hospital. The categories of costs included were hospitalisations and enteral nutrition (with and without gln). The resource use quantities were gathered from actual data obtained from the patients enrolled in the clinical study. The unit costs were obtained from the hospital's finance office. The dates during which the quantities of resources used were measured were not reported. The price year was also not stated.

Statistical analysis of costs
Standard statistical tests were carried out to estimate the significance of differences in the total costs between the groups. The total costs were presented as mean values plus standard deviations.

Indirect Costs
The indirect costs were not included in the analysis

Currency
Chinese Renminbi (RMB). The total costs were also converted to US dollars ($). The exchange rate was 1$ = 8.27 RMB.

Sensitivity analysis
No sensitivity analyses were carried out

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

Cost results
The total enteral nutrition costs were RMB4,072 +/- 629 ($492 +/- 76) in the gln group versus RMB2,233 +/- 616 ($270 +/- 50) in the control group. This difference was statistically significant, (p=0.024). However, the total hospitalisation costs were significantly lower, (p=0.031), in the intervention group (RMB62,794 +/- 6,178; $7,593 +/- 747) than in the control group (RMB68,996 +/- 8,620; $8,343 +/- 1,042).

Synthesis of costs and benefits
Not relevant because a cost-consequences analysis was performed.

Authors' conclusions
Glutamine (gln) supplementation was more effective and less costly than standard enteral nutrition for patients suffering from severe burn injuries.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The addition of a gln dipeptide to standard enteral nutrition had shown favourable results in preliminary studies, and the authors wished to compare the two alternatives in terms of their effectiveness and costs. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a randomised controlled trial that was appropriate for the study question. The health care providers were blinded from the group allocation and there were no differences between the two groups at baseline. Therefore, the internal validity of the study appears to have been assured. However, no power calculations were performed and the sample size seems to have been relatively small. The authors accurately described the feeding formulas, sampling and analytical methods. The study sample was representative of the study population. The effectiveness results were based on treatment completers only, but only one patient discontinued the assigned diet due to early death. These issues tend to limit the internal validity of the analysis.

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

**Validity of estimate of costs**
The perspective of the cost analysis appears to have been that of the hospital, therefore the categories of costs included were appropriate. However, only the total costs were presented and a breakdown of the cost categories was not given. Also, the resource use quantities were not presented separately from the unit costs, thus limiting the reproducibility of the analysis. No sensitivity analyses were carried out and no details of when the resource use data were collected were reported. Appropriate currency conversions were conducted, but the price year for the unit costs (and therefore the currency conversion) was not included. Thus, the cost analysis was not conducted satisfactorily.

**Other issues**
The authors compared their findings with those of other published studies, showing consistency among the trials' results. However, the issue of generalisability of the cost-effectiveness results to other settings was not addressed because of the lack of a sensitivity analysis and the lack of cost information (resource use and unit costs). In general, the clinical study was presented in more detail than the cost analysis, in which little information was provided. The authors did not explicitly discuss any limitations of their study.

**Implications of the study**
The results of this study confirmed the favourable effect of gln supplementation to enteral nutrition on the preservation of intestinal structure in patients severely burned, which had been found in other studies, and showed an additional advantage in terms of a reduction in the hospitalisation costs.

**Source of funding**
Supported by the Ministry of Health Project Grant 97010204, the Ministry of Health Key Project Grant 2001-Surgical-1-8A, and an International Education Grant from Ajinomoto, Japan.

**Bibliographic details**

**PubMedID**
12903886

**Other publications of related interest**
Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Burns /microbiology /physiopathology /therapy; China; Dietary Supplements; Digestive System /physiopathology; Double-Blind Method; Endotoxins /blood; Enteral Nutrition; Escherichia coli Infections /epidemiology; Food, Formulated; Glutamine /administration & dosage /blood; Humans; Middle Aged; Pseudomonas Infections /epidemiology; Staphylococcal Infections /epidemiology; Time Factors; Treatment Outcome; Weight Loss; Wound Healing; Wound Infection /epidemiology /microbiology /prevention & control

AccessionNumber
22003009764

Date bibliographic record published
30/04/2004

Date abstract record published
30/04/2004