Effectiveness and cost-effectiveness of supplemental glutamine dipeptide in total parenteral nutrition therapy for critically ill patients: a discrete event simulation model based on Italian data

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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.

CRD summary
This study examined the cost-effectiveness of adding alanyl-glutamine, a dipeptide, to the usual total parenteral nutrition, for critically ill patients, who were admitted to an intensive care unit. The authors concluded that the addition of alanyl-glutamine could produce health benefits and cost savings, for Italian hospitals. The data sources were clearly stated and the uncertainty was satisfactorily investigated. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of adding alanyl-glutamine, a dipeptide, to conventional total parenteral nutrition, for critically ill patients, who were admitted to an intensive care unit (ICU).

Interventions
Alanyl-glutamine, added to the usual parenteral nutrition, was compared with the usual parenteral nutrition alone.

Location/setting
Italy/tertiary care (ICU).

Methods
Analytical approach:
The analysis was based on a discrete event simulation, covering the time in hospital. The authors stated that they took the perspective of the hospital.

Effectiveness data:
The initial clinical event rates were from a prospective database of ICU outcomes and activities, from 200 Italian centres, with over 60,000 patients. The treatment effect and death rates before, during, and after ICU stay, which were the primary endpoints of the analysis, were identified by a systematic search of EMBASE and MEDLINE. Fifteen clinical trials were selected and a random-effects meta-analysis was conducted to obtain the initial inputs for the decision model.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The number of deaths and the number of infections, were the benefit measures.

Cost data:
The economic analysis included the costs of alanyl-glutamine, ICU and general ward stays, and new infections acquired in the ICU. Most of the quantities of resources were from the clinical trials. The costs of the dipeptide and parenteral nutrition were based on the maximum price paid by Italian hospitals. The costs of ICU stay were from an Italian study that included variable costs (disposable materials, drugs, blood and its derivatives, diagnostics, and physiotherapy),
fixed ICU costs (staff and equipment), and ancillary costs (electricity, water, heating, laundry, etc.). The costs of
general ward stay were from the National Agency for Regional Health Services. The cost of treating infections was
based on a published Italian study. All costs were in Euros (EUR) and the price year was 2008.

**Analysis of uncertainty:**
A two-level Monte Carlo simulation was carried out to consider the variability in the population and the uncertainty in
the key model parameters. One-way and scenario analyses were carried out, using published ranges of values or
alternative sources of evidence.

**Results**
The expected deaths per 10,000 patients were 3,446 (SD 208) with parenteral nutrition alone, and 2,460 (SD 159) with
alanyl-glutamine. The expected infections were 1,878 (SD 391) with parenteral nutrition alone, and 1,377 (SD 287)
with alanyl-glutamine.

The total cost per patient was EUR 24,161 (SD 3,523) with parenteral nutrition alone, and EUR 23,409 (SD 3,345) with
alanyl-glutamine. The additional cost of alanyl-glutamine was more than offset by the reduced costs of the shorter
hospital stay and fewer antibiotics to treat infections.

Alanyl-glutamine was dominant as it was more effective and less expensive than parenteral nutrition alone. It was
clinically superior to parenteral nutrition in all simulations and cheaper in 99% of them.

The most influential inputs were the daily cost of the ICU, the cost of alanyl-glutamine, mortality, and the average
survival time, but in all scenarios alanyl-glutamine was the preferred option.

**Authors’ conclusions**
The authors concluded that the addition of alanyl-glutamine could provide health benefits and cost savings, for Italian
hospitals.

**CRD commentary**
**Interventions:**
The selection of the comparators was appropriate as the addition of the dipeptide was compared with the usual nutrition
in an ICU.

**Effectiveness/benefits:**
The clinical data were generally from valid sources. A Bayesian random-effects model was used for the treatment
effect, and this was a reliable method. Only clinical trials were selected and the results for each of these were accurately
reported. Other clinical data were from a large Italian study, which was representative of the authors’ setting and
provided data on clinical practice and the initial risk for critically ill patients. Extensive sensitivity analysis was
conducted on all the model parameters. The benefits measures were specific to patients in intensive care, but mortality
allows comparisons with other diseases.

**Costs:**
The economic analysis was consistent with the stated perspective of the hospital. The sources were appropriate for
hospital reimbursements in Italy. Some unit costs were reported separately from their quantities of resources, but most
were presented as combined totals. The total costs for the two treatments were presented for each cost category,
allowing the comparison of the impact of alanyl-glutamine between the phases of hospitalisation. The price year was
given, allowing reflation exercises. Variations in the economic inputs were appropriately assessed in the sensitivity
analyses.

**Analysis and results:**
The results were extensively presented, with average and incremental findings. A number of additional model outcomes
were given. Various appropriate statistical approaches were used to assess uncertainty. Probabilistic and deterministic
analyses were conducted, and their methods and results were clearly reported. The main strength of the analysis was the
use of a Bayesian meta-analysis for the clinical inputs, as highlighted by the authors. The results appear to be specific to
Italy, and it is unclear whether they could be applied to other countries.
Concluding remarks:
The data sources were clearly stated and the uncertainty was satisfactorily investigated. The authors' conclusions appear to be robust.

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