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Original article

Supplemental parenteral nutrition in intensive care patients: A cost saving strategy

Lorenzo Pradelli [a, *], Séverine Graf [b, c], Claude Pichard [c], Mette M. Berger [d]

[a] AdRes Health Economics and Outcomes Research, Via Vittorio Alfieri, 17, 10121 Turin, Italy
[b] Service des Soins Intensifs, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, 1205 Geneva, Switzerland
[c] Nutrition Unit, Division of Intensive Care, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, 1205 Genève Switzerland
[d] Service of Adult Intensive Care, Lausanne University Hospital, Rue du Bugnon 46, 1011 Lausanne Switzerland

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SUMMARY

Background & aims: The Swiss supplemental parenteral nutrition (SPN) study demonstrated that optimised energy provision combining enteral nutrition (EN) and SPN reduces nosocomial infections in critically ill adults who fail to achieve targeted energy delivery with EN alone. To assess the economic impact of this strategy, we performed a cost-effectiveness analysis using data from the SPN study.
Methods: Multivariable regression analyses were performed to characterise the relationships between SPN, cumulative energy deficit, nosocomial infection, and resource consumption. The results were used as inputs for a deterministic simulation model evaluating the cost-effectiveness of SPN administered on days 4–8 in patients who fail to achieve ≥60% of targeted energy delivery with EN by day 3. Cost data were derived primarily from Swiss diagnosis-related case costs and official labour statistics.
Results: Provision of SPN on days 4–8 was associated with a mean decrease of 2320 ± 338 kcal in cumulative energy deficit compared with EN alone ($p < 0.001$). Logistic regression analysis showed that each 1000 kcal decrease in cumulative energy deficit was associated with a 10% reduction in the risk of nosocomial infection (odds ratio 0.90; 95% confidence interval 0.83–0.99; $p < 0.05$). The incremental cost per avoided infection was −63,048 CHF, indicating that the reduction in infection was achieved at a lower cost.
Conclusion: Optimisation of energy provision using SPN is a cost-saving strategy in critically ill adults for whom EN is insufficient to meet energy requirements.

1. Introduction

Adequate nutrition support is vitally important in the management of patients in the intensive care unit (ICU) [1–3]. Due to the persistent metabolic demands and the difficulty of initiating feeding in ICU patients, energy deficits accumulate rapidly during the first week following admission to the ICU [4], leading to an increased risk of infection, prolonged duration on mechanical ventilation, longer stay in the ICU, and increased mortality [5–9]. To prevent such complications, clinical practice guidelines recommend early initiation of enteral nutrition (EN) in haemodynamically stable critically ill patients who are unable to maintain volitional intake [1–4]. However, EN alone is often insufficient to meet energy and protein requirements [10–15]. As a result, a significant proportion of critically ill patients fail to achieve adequate nutritional intake [12].

Supplemental parenteral nutrition (SPN) has been shown to improve the cumulative energy balance and reduce infectious morbidity in ICU patients who fail to achieve energy and protein goals with EN alone [16]. Nonetheless, parenteral nutrition (PN) is often withheld in practice due to cost and perceived risks [17–21]. In the Swiss SPN study, we tested the hypothesis that individually optimised energy provision using EN plus SPN would improve clinical outcomes in critically ill patients who fail to achieve ≥60% of energy goals with EN alone by day 3. The findings showed that supplemental administration of PN on days 4–8 resulted in a 35% reduction in the adjusted risk of nosocomial infection compared with continued administration of EN alone (hazard ratio 0.65; 95% confidence interval [CI] 0.43–0.97; $p = 0.03$) [16]. To assess the economic impact of this strategy, we performed a cost-effectiveness analysis using modelled outcomes derived from the Swiss SPN study.

* Corresponding author.
E-mail address: l.pradelli@adreshe.com (L. Pradelli).

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2. Materials and methods

The primary objective of the study was to evaluate the cost-effectiveness of SPN in critically ill adult ICU patients who fail to achieve ≥60% of calculated energy targets with EN alone. A deterministic model-based analysis integrated clinical data from the SPN trial with cost data derived from other sources to simulate clinical outcomes and resource utilisation in the target population. Data from the SPN study were analysed using multivariable regression models to sequentially characterise the relationships between nutritional intervention, cumulative energy deficit, and nosocomial infection. Linear multiple regression analysis was then used to estimate the effect of nosocomial infection on resource consumption parameters such as antibiotic use, duration of mechanical ventilation, and length of stay in the ICU and hospital. Finally, effect size estimates from the multivariable analyses and cost estimates derived primarily from Swiss diagnosis-related case costs were used as model inputs for a pharmacoeconomic analysis to evaluate the cost-effectiveness of SPN.

2.1. Source data—clinical outcomes

The source population for the analysis of clinical outcomes included all patients enrolled in the Swiss SPN Study (N = 305; ClinicalTrials.gov registration number, NCT00802503) [16]. Study design and enrolment criteria have been previously described [16]. Briefly, eligible patients were critically ill adults with a functional gastrointestinal tract who failed to achieve ≥60% of targeted energy delivery with EN by day 3 following ICU admission. Patients were randomised to receive continued EN alone or EN plus SPN on days 4–8 with the aim of delivering 100 percent of the energy expenditure measured by indirect calorimetry. There was no catch-up feeding of the previous deficit. The primary study endpoint was the occurrence of nosocomial infections between days 9 and 28, defined according to the Centers for Disease Control and Prevention [22].

2.2. Source data—cost analysis

Unit costs for medical resources were derived primarily from the Swiss Federal Statistical Office 2013 diagnosis-related case costs for a sample population of 7614 mechanically ventilated adult ICU patients with a Simplified Acute Physiology II (SAPS II) score >30 and an ICU stay ≥3 days. The cost of SPN was calculated as the acquisition cost of a representative PN product (StructoKabiven®, Fresenius Kabi GmbH; 1 bag per day administered for 4 days) plus the cost of medical staff to prescribe and administer PN. The latter was estimated based on gross wages for medical and nursing staff obtained from the Swiss Federal Statistical Office and the mean PN administration times reported in a previous time-and-motion study [23]. Daily costs for standard doses of antimicrobial therapy for nosocomial infection were obtained via interviews with experts from two Swiss university hospitals (interviews conducted by Polynomics AG, Olten, Switzerland, August 2015).

2.3. Statistical analysis—clinical outcomes and resource utilisation

Linear multivariable regression analysis was used to characterise the relationship between potential explanatory variables and cumulative energy deficit during days 1–8 in the SPN trial. Logistic multivariable analysis was used to examine the relationship between potential explanatory variables and nosocomial infection from day 9 to day 28. Additionally, the effect of nosocomial infection on medical resource consumption (antibiotic days, hours on mechanical ventilation, length of stay in the ICU, and length of stay in the ward) was estimated using linear multivariable regression analysis. Potential explanatory variables included age, gender, height, weight, body mass index (BMI), diagnosis, institution, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, baseline infection status, duration of prophylactic antibiotic therapy, cumulative energy deficit during days 1–8, mean percentage of energy target achievement on days 1–8, and mean energy delivery on days 1–8. Independent variables were selected for the initial models based on the strength of associations in unadjusted univariable analyses. Multi-collinearity was evaluated using the variance inflation factor (VIF). Among coupled variables with a VIF >2.50, the variable with the weaker association was eliminated from the model. Parameter estimates for the linear regression analyses were evaluated using the Student t-test. The fully specified multivariable model was evaluated using Fisher's exact test. The logistic regression model was evaluated using the z-test. All analyses were performed using R statistical software, version 3.1.2 (R Foundation, Vienna, Austria).

Analyses evaluating resource consumption parameters as the response variable were based on the full dataset from the intent-to-treat population in the Swiss SPN study (N = 305). Analyses evaluating cumulative energy deficit and nosocomial infection as the response variable were based on the per protocol population (N = 275) due to missing data for cumulative energy deficit (N = 30).

2.4. Cost-effectiveness analysis

The cost-effectiveness analysis was conducted from the perspective of Swiss hospitals. Effect size estimates derived from the Swiss SPN study were used as model inputs for a pharmacoeconomic model evaluating the cost-effectiveness of SPN compared with continued EN in critically ill patients who fail to achieve targeted energy delivery with EN. Discrete event simulation was used to model patient outcomes following ICU admission in two cohorts (Fig. 1) [24]. The time horizon of the model corresponds with the observation period in the clinical trial. The initial step in the model was the decision to either continue EN therapy alone or add SPN. Patients receiving EN alone were assigned a cumulative energy deficit based on the observed cumulative energy deficit for days 1–8 in the corresponding treatment group in the SPN trial. For those receiving SPN, the cumulative energy deficit was determined by applying the estimated nutritional advantage attributed to SPN in the multivariable analysis to the observed cumulative energy deficit in the EN group. The occurrence of infection in patients receiving EN was determined based on the observed probability of nosocomial infection between days 9 and 28 in the EN group during the SPN study. In patients receiving SPN, the occurrence of infection was based on the adjusted odds ratio (OR) for nosocomial infection in the logistic regression analysis. For patients without infection, values for resource utilisation parameters were based on the observed mean values for non-infected patients in the SPN trial; for patients with infection, adjusted estimates from the multivariable analyses were used.

The primary outcome of the pharmacoeconomic analysis was the incremental cost per infection avoided, reported in Swiss francs (CHF). All direct hospital costs from the time of admission until discharge were included in the model and assigned to one of the following categories: ICU stay, ward stay, mechanical ventilation, antimicrobial therapy, and SPN administration. Because the time horizon was limited to the hospital stay, future costs and outcomes were not discounted.

A probabilistic sensitivity analysis was conducted to assess the effect of uncertainty surrounding parameter estimates. Additionally, a one-way deterministic sensitivity analysis was performed to

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