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Route of nutrition and risk of blood stream infections in critically ill patients; a comparative study☆

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SUMMARY

Background and aims: The association of nutritional support practices with intensive care unit (ICU) – acquired infections is a current field of interest. The objective of this study was to determine whether different routes of delivery of nutritional support are associated with a different risk of bloodstream infection (BSI) in critically ill patients.

Methods: An observational study in a multidisciplinary ICU. Adult ICU patients, with ICU stay ≥96 h who were fed artificially were included. Patients were grouped into three categories of nutrition support routes: those on enteral nutrition alone (EN group), on parenteral nutrition alone (PN group) or on both EN and PN (EN+PN group). Illness severity, co-morbidities and routine laboratory values were recorded on ICU admission. Route of feeding, caloric, protein and immunonutrient intake was recorded daily for each patient. Nosocomial BSIs were identified by infection control surveillance methods. The incidence of BSI among the three groups was compared with Kaplan–Meier plots and Cox proportional-hazards models.

Results: A total of 249 patients were included in the analysis. There were no significant differences between groups in illness severity scores and in the time to nutritional support initiation (median time 48 [24–48] hours). The median daily caloric intake was significantly lower for the EN group than for patients of PN and EN+PN group (415 [157–687] kcal vs. 1077 [297–2087] kcal and 1292 [890–1819] kcal respectively, $p < 0.001$). BSI occurred in 69 (27.7%) patients. Bivariate Cox analysis revealed that APACHE II score and admission category were significantly associated to BSI development [hazard ratio (HR), 1.05; 95% confidence interval (CI), 1.01–1.09 and HR 0.45; 95% CI 0.18–1.15, respectively]. Presence of co-morbidities, SOFA score, hospital length of stay (LOS) before ICU admission, late initial feeding, serum albumin at admission, average daily maximum concentration of serum glucose, caloric, protein and immunonutrient intake did not affect the hazard of BSI development. After adjustment for the confounding variables, in a multivariate analysis, patients of the EN + PN group had lower incidence of BSI than the other two groups (HR 0.30; 95% CI 0.17–0.53), irrespective of the number of days of PN intake and the percentage of calories received from PN. There was no difference in the hazard for BSI development between the EN and PN group. Patients with EN + PN had a significantly longer ICU-LOS whereas mortality was not different among the three groups.

Conclusions: In this retrospective analysis of 249 consecutively enrolled ICU patients, we found that in critically ill patients EN + PN feeding strategy was associated with a significantly reduced hazard of BSI development, compared to EN or PN route of nutritional support.

Abbreviations: ICU, intensive care unit; BSI, bloodstream infection; EN, enteral nutrition; PN, parenteral nutrition; LOS, length of stay; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment.

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1. Introduction

Infections are commonly acquired in intensive care unit (ICU) patients worldwide and constitute a major cause of morbidity and mortality [1]. In these critically ill patients, providing artificial nutritional support through the enteral and/or the parenteral route (for those with contraindications or intolerant to enteral feeding) is considered a standard of care [2,3]. The relationship between different routes of nutritional support and ICU-acquired infections, including blood-stream infections (BSIs) has been an issue of concern [4–6].

According to current clinical guidelines, the gastrointestinal tract remains the preferable route of nutrition administration suggesting an association with fewer infections, compared to parenteral nutrition (PN) [2,3,6]. However, it often fails to provide more than 50% of caloric needs in the critically ill patients [7]. As a strategy for preventing nutritional deficit, initiation of supplemental PN is recommended either within 2 days after ICU admission for patients who cannot be adequately fed enterally, according to European guidelines [2] or after 7 days, according to American guidelines [3], if enteral nutrition (EN) cannot be commenced, provided that the patient is not malnourished at baseline.

Complementing the energy delivery of insufficient EN with supplemental PN and the impact of different feeding strategies on outcomes such as morbidity and mortality in the ICU have been investigated in several studies including recent prospective randomized controlled trials [8–14]. A number of them have examined the relationship between different nutritional support practices and the incidence of ICU-acquired infections [8–11,14], however, none of them has focused on BSI incidence. In some of these studies early [8] or late [10] initiation of supplemental PN was associated with reduced risk of nosocomial infections, whereas others did not find any difference [9,11].

The primary objective of this study was to examine the relationship among three different routes of nutrition delivery (EN, PN, EN + PN) and the development of BSI in our multidisciplinary ICU. Secondary objectives included any association between routes of feeding and ICU–length of stay (LOS), and also mortality.

2. Materials and methods

2.1. Study design and setting

We conducted a single-center, observational study from May 2010 through May 2011 in the ICU of “Evangelismos” Hospital, Athens, Greece, a 25-bed, multidisciplinary, university ICU in a 1000-bed, tertiary-care hospital. This is a retrospective analysis of prospectively collected data from patient charts during their hospitalization in the ICU. The Hospital Ethics Committee approved the study protocol; since it was of observational nature and privacy and anonymity of patients were protected, the need for written informed consent was waived.

All patients who were admitted to the ICU during the study period and were expected to remain in the ICU more than 96 h, were eligible to be included in the study. Exclusion criteria were: *(i)* ICU-LOS < 96 h; *(ii)* readmission to the ICU or transfer from other ICU; *(iii)* patients having a do-not-resuscitate order; *(iv)* pregnancy, *(v)* patients with BSI within the first 96 h of ICU stay and *(vi)* patients with oral food intake. Patients were studied for the first 20 days of ICU stay or until they *(i)* died in the ICU; *(ii)* were discharged; *(iii)* developed a BSI. The 20-day-time period was selected since in a previous study in our ICU, the median time of the first BSI development was found to be 11 [IQR: 4–19] days after ICU admission [15].

Demographic characteristics, admission diagnosis, pre-existing co-morbidities, illness severity, hospital LOS prior to ICU admission, ICU-LOS, days on mechanical ventilation and ICU mortality were recorded. Illness severity was assessed by the Acute Physiology and Chronic Health Evaluation (APACHE) II [16] and the Sequential Organ Failure Assessment (SOFA) [17] scoring systems, calculated on ICU admission. Laboratory values were recorded for serum albumin, C-reactive protein (CRP) and total lymphocyte count, on ICU admission. The daily maximum measured blood glucose and the average maximum blood glucose concentration were recorded.

An episode of BSI was defined as a positive blood culture in a patient with clinical signs of infection [18]. The onset of BSI was defined as the date of blood sampling. Blood cultures were obtained via peripheral venous puncture using a standard sterile technique or from a new central venous catheter immediately after placement and prior to breaking the sterile field that was used for the catheterization. Only the patients' first BSI during ICU stay was included in the study.

2.2. Nutritional data

Decisions regarding nutritional support, route of administration and formula type and volume, were made by the attending physicians according to clinical judgment. All patients on PN received ready-to-use, multi-chamber bags either of 3 (carbohydrates, protein and fat) or 2-chambers (carbohydrates and protein) through a central venous catheter. Ready-to-use enteral formulas through a naso-gastric or a naso-jejunal tube were used for EN. Daily caloric and protein intake as well as any immunonutrient (glutamine, arginine or n-3 polyunsaturated fatty acids) intake were recorded. The time point at which nutrition was commenced was also recorded. Initiation of feeding within 48 h after ICU admission was defined as early.

Patients who met the inclusion criteria were divided into those who received EN alone (EN group), those who received exclusively PN (PN group) and those who received both EN and PN (EN + PN group). The latest group included patients that received EN and PN irrespective of the time they started and the duration they received each type of feeding.

In the context of a sensitivity analysis in order to further investigate the contribution of the PN component to EN + PN (reflected by the amount of calories and the duration of administration of PN in the EN + PN group), two variables were alternatively constructed to reflect route of feeding: (i) EN + PN group was subdivided into two subgroups, according to the percentage of time during which they received PN, that is, a subgroup of patients receiving PN for more than 50% of the time during which they received EN + PN and another subgroup receiving PN for less than 50% of the time during which they received EN + PN, regardless of the daily or total amount of PN; and (ii) EN + PN group was subdivided into quartiles of daily calories received from PN based on the average daily percent of EN + PN calories (<25%, 25–49%, 50–74%, and ≥75%).

2.3. Statistical analysis

Continuous variables are presented as median and inter-quartile range [IQR] and categorical variables as percentages. Chi-square tests for categorical variables and Kruskal–Wallis tests for continuous variables were applied to examine the differences between patients among the three different feeding group categories. Comparisons by two groups for categorical variables were made by the chi-square test and for continuous variables by Mann–Whitney