Thrita. 2014 September; 3(3): e20905. DOI: 10.5812/thrita.20905
Published online 2014 August 30. **Research Article**

Effect of Early Enteral Nutrition on Clinical Outcomes in an Intensive Care Unit

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Received: June 4, 2014; **Revised:** July 8, 2014; **Accepted:** July 25, 2014

Background: There is evidence that early enteral nutrition can improve clinical outcomes in patients hospitalized in the intensive care unit.
Objectives: The purpose of this study was to evaluate the effect of early enteral nutrition on clinical outcomes in medical patients admitted to the intensive care unit.
Materials and Methods: This prospective study was performed on 94 patients admitted to the medical intensive care unit (ICU). The patients were divided into two groups according to nutrition onset. Enteral nutrition for group one was started within the first 48 hours of admission to the ICU and group two received enteral nutrition after the third day of admission to the ICU. Patients were monitored for ICU length of stay, organ failure (SOFA score), aspiration pneumonia, duration of mechanical ventilation and mortality.
Results: The average daily caloric intake between the two groups did not differ significantly ($P = 0.4$). Both groups received more than 75% of the calculated required calorie. The mean duration of hospitalization, occurrences of organ failure and mortality were lower in patients who received their calculated daily nutrition during the first 48 hours of admission ($P < 0.05$). Regarding ventilator-associated pneumonia, there was no significant difference between the two groups of early and late enteral nutrition. There was no significant difference between the two groups of early and late nutrition in the duration of mechanical ventilation. Logistic regression analysis showed that late nutrition causes a 3.3 times increase in mortality rate, 1.3 times in the length of ICU stay and 1.8 times in organ failure ($P < 0.05$).
Conclusions: Early enteral nutrition within 24 to 48 hours of admission to ICU reduces the duration of hospitalization, organ failure and mortality of the medical patients.

*Keywords:*Enteral Nutrition; Critical Ill Patients; Mortality; SOFA Score

1. Background

Patients admitted to the intensive care unit are prone to malnutrition due to increased metabolism which increases nutritional needs (1, 2). The incidence of malnutrition has been reported to be 20-69% in hospitalized patients (3). However, the prevalence of malnutrition in hospitalized patients in the intensive care unit is 40-100% (4). Severe malnutrition is highly associated with an increased risk of infection and length of hospital stay (LOS) in critically ill patients. Enteral nutrition can reduce morbidity and mortality of critically ill patients suffering from malnutrition. Nutrition is often overlooked in the intensive care unit, and this neglect can have negative effects on the patients (5, 6). On the other hand nutrition onset in critically ill patients is also an important and debatable issue. According to the American Society for Parenteral and Enteral Nutrition (ASPEN) and European Society for Parenteral and Enteral Nutrition (ESPEN), early enteral nutrition refers to enteral nutrition within 24-48 hours of admission and late enteral nutrition refers to enteral nutrition after the first three days of admission. The guidance these associations offer, regarding early enteral nutrition, has a grade C score (7). Thus, more research is required to provide stronger guidelines. One of the problems with patients hospitalized in the intensive care unit is ileus, which sets a limit for early enteral nutrition. The risk of aspiration and the following pneumonia is another concern for early enteral nutrition. It has been shown that despite the absence of bowel sounds in critically ill patients, the bowel has the ability to absorb nutrients and there is no prohibition to delay enteral nutrition (7). Although the benefits of early enteral nutrition is known at the cellular and tissue level, its effect on mortality and morbidity is still unknown. Some studies have shown an improvement in one or a number of the outcomes (8-11). These studies have shown that early enteral nutrition improves nitrogen balance, wound healing and host immune function. It also strengthens augment cellular antioxidant systems, reduces the hyper-metabolic response to tissue injury and preserves intestinal mucosal integrity. Due to these reasons, there is an attempt to provide enteral nutrition as soon as possible. However, in a number of studies there has not been a significant difference between early and late nutrition and its effect on the patient's condition.

2. Objectives

Since a few studies have been carried out on adult medical patients admitted to the intensive care unit (11-13), and most of them were done on trauma, surgery and burn patients, while, no researches were done in this field in Iran, we decided to examine the effects of early enteral nutrition against late enteral nutrition on clinical outcomes in medical patients admitted to the intensive care unit.

3. Patients and Methods

Overall, 94 patients, who had admitted to the medical intensive care unit of a tertiary care university hospital from February to October 2013, participated in this prospective study. Inclusion criteria included age being over 18 years and having only gastric enteral nutrition. Patients were divided into two groups based on the physician’s judgment for nutrition onset: the first group included patients who received enteral nutrition within the first two days of entering the intensive care unit (early enteral nutrition) and the second group received enteral nutrition after three days of entering the intensive care unit (late enteral nutrition). Patients, who were discharged before the third day, were excluded from the study. This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and written informed consent was obtained from each participant or their relatives. The duration of study was at least three days and the patients were monitored until the end of the hospitalization period in the intensive care unit. The patients’ baseline medical history, physical examination, acute physiology, chronic health evaluation II score (APACHE II) and primary diagnosis were recorded. Patients were followed for the duration of mechanical ventilation, length of stay in the ICU, organ failure, the incidence of ventilator associated pneumonia (VAP) and mortality. Sequential organ failure assessment score (SOFA score) was used to determine the extent of an individual’s organ function. Each patient was evaluated for cardiovascular failure (systolic blood pressure being $\leq$ 90 mm Hg or requiring vasopressor support), central nervous system failure (Glasgow coma score $\leq$ 12), coagulation failure (platelet count $\leq 80 \times 109/L$), hepatic failure (bilirubin $\geq$ 2 mg/dL), and renal failure (serum creatinine $\geq$ 2 mg/dL or 25% rise from the baseline). All patients were fed via a nasogastric tube with a high-protein standard kitchen formula prepared at the hospital in an intermittent fashion. The distribution of macronutrients was as follows: 20% protein, 30% lipids, and 50% carbohydrates. Caloric intake was calculated based on 20 kcal per kg of body weight for patients in the catabolic phase and 30 kcal per kg of adjusted body weight for patients in the anabolic phase (7). For assessment of calorie intake of each patient, the daily energy intake from tube feeding during the study period was recorded.

3.1. Statistical Analysis

Data analysis was performed using SPSS version 16. We used the t-test for normally distributed variables, Mann-Whitney test for non-normally distributed variables and the chi-square test for qualitative variables to compare the baseline characteristics of patients in both groups. Logistic regression analysis was used to determine the risk of outcomes. Odds ratio was calculated with 95% confidence interval. To assess the independent effect of early enteral nutrition on the outcomes, confounding variables of age, gender, reasons for hospitalization and APACHE II score were adjusted. $P < 0.05$ was considered significant.

4. Results

In total, 94 patients with underlying medical conditions were studied. Enteral nutrition was started before the third day for 48 patients and after the third day for 46 patients. The mean age of these patients was 53.9 ± 20.3. Demographic characteristics of patients are shown in Table 1. There was no significant difference in the average daily caloric intake between the early enteral nutrition group and late enteral nutrition group (1701 ± 151 versus 1688 ± 176, P = 0.4) and both groups received more than 75% of the calculated calories required. The mean duration of hospitalization for the early enteral nutrition group was less than the late enteral nutrition group (14.91 ± 9 versus 18.96 ± 9.4, P = 0.02). The mean SOFA score for the early enteral nutrition group was less than the late enteral nutrition group (5.83 ± 1.63 versus 6.83 ± 1.93, P = 0.03). Mortality rate was 24% for patients who had received enteral nutrition after the third day of admission and 18.1% for patients who had received enteral nutrition within the first 48 hours (P = 0.05). In ventilator-dependent patients there was no significant difference in getting VAP between the two groups of early and late enteral nutrition (22.8% versus 25%, P = 0.3). There was no significant difference between the two groups of early and late enteral nutrition in duration of mechanical ventilation (10.6 ± 3.5 versus 11.2 ± 4.1, P = 0.2). Multivariate logistic regression analysis showed a significant relationship between late enteral nutrition and length of ICU stay, SOFA score and mortality (Table 2). This analysis showed that late enteral nutrition increases mortality rate 3.3 times, the length of ICU stay 1.3 times and the risk of organ involvement 1.8 times.

Table 1. Baseline Characteristics of the Study Population [a,b]

	Enteral Nutrition Group		P Value
	Early (n = 48)	Late (n = 46)	
Age, y	53.65 ± 19.1	54.25 ± 21.5	0.1
Gender			0.4
Female	28 (29.7)	24 (25.5)	
Male	20 (21.2)	22 (23.4)	
APACHE II	20.13 ± 7.5	20.67 ± 6.6	0.09
Mechanical ventilation			0.2
With	27 (29)	28 (30)	
Without	21 (22)	18 (19)	
Reason for ICU admission			0.4
Respiratory problem	20 (21)	23 (24)	
Sepsis	14 (15)	12 (13)	
Central nervous system	12 (13)	13 (14)	
Albumin, g/dL (admission)	2.9 ± 1.1	3.09 ± 1.2	0.4

[a] Abbreviation: APACHE, Acute Physiology and Chronic Health Evaluation II Score.
[b] Data are presented as Mean ± SD or No. (%).

Table 2. Outcomes Associated With Late Enteral Nutrition [a,b]

	OR	95% CI	P value
Mortality	3.3	2-5.5.8	< 0.001
LOS	1.3	1.06-1.8	0.01
SOFA score	1.8	1.1-2.9	0.02

[a] Abbreviations: OR, odd ratio; LOS, length of stay; SOFA, Sequential Organ Failure Assessment.
[b] Analysis by Logistic Regression.

5. Discussion

Results of this prospective study showed that early enteral nutrition, within 24 to 48 hours of admission to the ICU, reduces the duration of hospitalization, organ failure and mortality of medical patients. Enteral nutrition in patients admitted to the intensive care unit is often delayed due to reasons including gastrointestinal dysfunction, elective discontinuation of procedures and physicians' lack of knowledge of patients' nutritional needs (14, 15). Insufficient information about enteral nutrition and lack of firm guidelines from ASPEN and ESPEN on the subjects are causes of malnutrition in patients (16). Long-term starvation suppresses the immune system, leading to an increased risk of infection; these effects can be reversed by nutrition. However, the advantage of immediate nutrition after illness or injury over late nutrition is still a controversial issue (8). A meta-analysis which analyzed 19 trauma, surgical and burn studies showed that early enteral nutrition does not affect the length of hospital stay and morbidity while it doesn't decrease mortality, either (17). What makes our study different from the above mentioned studies is that our study was done on medical patients admitted to the intensive care unit. Studies conducted on medical patients admitted to the intensive care unit showed different effects on patients' clinical outcomes. In one of these studies, early nutrition led to a reduction in mortality and length of stay at the intensive care unit, but there was no positive impact on the other outcomes (11). In another study conducted on medical patients, the only positive impact of early nutrition was a reduction in mortality, but there was an increase in VAP in the early nutrition group (13). There was no positive impact from early nutrition on clinical outcomes of patients admitted to the intensive care unit in Doig's study (12). The reason our study results are different from other studies is that the amount of calorie intake was specified and determined by our study. In fact, we decreased caloric intake of patients and prescribed 20 kcal per kg of adjusted body weight in the catabolic phase, and then increased this amount in the anabolic phase. The higher incidence of VAP in one of the above mentioned studies could be due to higher caloric intake in the early days of hospitalization (catabolic phase). This may be the reason for the longer duration time of mechanical ventilation in mentioned studies. But in our study there was no difference in the duration of mechanical ventilation and occurrence of VAP between two groups. We found that the development of organ failure was lower in the early nutrition group. Also the duration of stay at the ICU was significantly lower in the early nutrition group versus the late nutrition group. Multiple hypotheses have been proposed to explain the development of organ failure (18). It appears that bacterial translocation due to disruption of the gut barrier function could be a critical component for the development of organ failure and therefore the duration of stay at the ICU. As late enteral nutrition disrupts this barrier, introduction of foods during the early stages of hospitalization, prevents bacterial translocation. Similar studies have not assessed organ dysfunction in their research. One of the limitations of our study was its low sample size, yet the decrease in the length ICU stay, SOFA score and the mortality that was observed in the early enteral nutrition group deserves further attention in future larger trials. Our study's strength, on the other hand, was the fact that it was performed only on medical patients and that calorie intake was calculated based on different phases of metabolic stress.

Our study is underpowered to indicate a clinically significant effect on outcome measures, yet the decrease in length of hospitalization, organ failure and mortality in critically ill medical patients receiving early enteral nutrition within 24 to 48 hours of admission deserves further attention by future larger trials.

Acknowledgements

We acknowledge the National Nutrition and Food Technology Research Institute, Tehran, Iran.

Author's Contributions

Sima Ghorabi designed the experiments and collected the data. Zahra Vahdat Shariatpanahi designed the experiments, provided the consultations and wrote the manuscript.

Funding/Support

Funding was provided by the National Nutrition and Food Technology Research Institute.

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