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Clinical evaluation of the effectiveness of different nutritional support techniques in the intensive care unit

Ömer Arda Çetinkaya[1], Süleyman Utku Çelik[2], Pınar Sonyürek Arı[3], Seher Demirer[1,3]

ABSTRACT

Objective: Malnutrition is a common condition in patients admitted to intensive care units (ICUs). Proper nutritional support is essential to reduce malnutrition-associated morbidity and mortality. The aim of this study was to evaluate the effectiveness of different nutritional support techniques in ICUs on some nutritional and inflammatory biochemical parameters.

Methods: In this retrospective study, 143 patients with a history of admission to ICUs were divided into three groups according to form of nutritional therapy: oral nutritional supplementation (ONS), enteral tube feeding (ETF), and parenteral nutrition (PN). Patients' demographic characteristics, length of stay in the ICU, length of nutritional support, serum prealbumin levels, C-reactive protein (CRP) levels, and transferrin levels at the time of nutritional supplementation initiation and treatment discontinuation were evaluated.

Results: The change in median serum prealbumin, CRP, and transferrin levels measured on days when nutritional therapy was initiated and terminated was not statistically significant (p=0.537, p=0.635, and p=0.073; respectively) in patients with ONS. Median prealbumin (0.14 vs. 0.21 mg/dL; p<0.001) and transferrin saturation (1.55% vs. 1.87%; p=0.001) levels significantly increased in patients who received ETF. In addition, median CRP (85.5 vs. 30.8 mg/L; p=0.001) levels significantly decreased. In patients with PN, only a significant increase in prealbumin level (0.10 vs. 0.13 mg/dL; p=0.003) was observed. The increases in CRP and transferrin saturation levels were not statistically significant (p=0.730 and p=0.243; respectively).

Conclusion: In the present study, a significant improvement was observed in the prealbumin, CRP, and transferrin levels in patients supported with ETF. However, similar improvement was not observed in patients with ONS.

Keywords: Enteral nutrition, intensive care units, nutritional support, parenteral nutrition

ORCID ID of the author:
Ö.A.Ç. 0000-0001-9135-8224;
S.U.Ç. 0000-0002-1570-6327;
P.S.A. 0000-0001-9717-9788;
S.D. 0000-0002-7051-7158

[1]Department of General Surgery, Ankara University School of Medicine, Ankara, Turkey
[2]Department of General Surgery, Gülhane Training and Research Hospital, Ankara, Turkey
[3]Clinical Nutrition Commission, Ankara University School of Medicine, Ankara, Turkey

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Corresponding Author:
Ömer Arda Çetinkaya

E-mail:
omerardacetinkaya@yahoo.com

Introduction

Malnutrition is an extremely common condition observed in critically ill patients treated in intensive care units (ICUs). Studies have shown that the prevalence of malnutrition among patients in ICU is between 13% and 78% (1, 2). Moreover, malnutrition associated with an increased risk of infection, prolonged mechanical ventilation requirement, and delayed recovery period in these patients (3). Therefore, several studies investigating the factors causing malnutrition and the prevention of this condition are ongoing.

Nutritional support is the most important step in the prevention of malnutrition. Most patients in ICU are unable to receive sufficient energy and protein via oral intake; therefore, enteral (EN) or parenteral nutrition (PN) support is necessary in these patients (1-5). For conducting the meta-analysis of studies to compare the enteral and parenteral approaches in these patients, interpretation of the results is challenging because of the small and heterogeneous patient groups (4, 5). However, it is always recommended that the use of EN over PN in patients with an intact gastrointestinal tract. PN also should not be started until all strategies to maximize EN tolerance have been attempted; and lastly, PN could be considered as the primary approach for special situations wherein enteral nutrition cannot be applied (5).

Appropriate parameters are required for assessing nutritional status, determining the presence of malnutrition, and assessing the effectiveness of the nutritional support. Albumin, transferrin, prealbumin, and retinol-binding protein plasma levels are the biochemical parameters frequently used for the evaluation of nutrition and

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monitoring the response to this support. However, the fact that these parameters could be affected by factors other than nutrition, such as infection, excess hydration, corticosteroid consumption, liver and renal failure, or inflammatory conditions, should be considered (6, 7).

Enteral assists the continuation of the barrier function of the gastrointestinal system, prevention of mucosal atrophy, and inhibition of bacterial translocation (8). However, it has been reported that achieving desired nutrition levels via EN, particularly at the early stages of ICU, is difficult; there is a definite increase in morbidity and mortality due to energy deficit occurring at the long term (9). It is also considered to increase the risk of bacterial colonization and aspiration pneumonia in patients with high gastric residual volume (8, 10, 11). Meanwhile, PN is a nutritional support method that enables the nourishment of patients who have limited absorption capacity or nonfunctional gastrointestinal system or an issue causing an obstacle for EN. However, the time and the conditions for initiation, the duration of the support, and the timepoint of switching to EN are being discussed in patients in ICU receiving PN because in this patient group, although positive effect could be observed on the clinical course when appropriately applied, inappropriate use could result in metabolic or infectious complications, such as overnutrition, hyperglycemia, fatty liver, or sepsis (12, 13). Although it is recommended to meet the energy requirements during the early and late period, large prospective randomized controlled studies are warranted in this field (14, 15).

In the present study, we aimed to determine the effectiveness of different approaches used on patients in ICU receiving nutritional support via some biochemical markers and investigate the severity of the inflammatory response in patients.

Methods

The study was performed in accordance with the principles of the Helsinki Declaration, and written informed consents were obtained from the patients and/or their relatives. This study included patients aged ≥18 years who were supported with nutritional support for ≥3 days in the surgical ICU between March 2015 and June 2015. Patients from whom informed consents could not be obtained; those who were connected to mechanical ventilators for >48 hours or those with enteral or parenteral support for <3 days; hemodynamically instable patients who were treated with inotropic or vasopressor agents due to long-term uncontrollable sepsis; and patients with renal or kidney failure were excluded from this study. The calorie needs of a patient was calculated as 25-35 kcal/kg/day, and the protein support target was determined to be 1.2-1.5 g/kg/day depending on state of catabolism.

Within the indicated time interval, data of 143 patients who were followed at the "Nutrition Department" were obtained from the hospital database, ICU database, and patient files. The patients were divided and analyzed in three groups: those under oral nutrition supplementation (ONS), enteral tube feeding (ETF), and parenteral nutrition (PN). The demographic characteristics of the patients; diagnoses; length of stay in the ICU; nutritional support durations; and serum prealbumin, C-reactive protein (CRP), and transferrin levels at the time of initiation and termination of the nutritional support were recorded.

Statistical analysis

Statistical Package for the Social Sciences programme 15.0 version (SPSS Inc.; Chicago, IL, USA) was used for the evaluation of the data obtained from this study. Continuous variables were expressed as mean ± standard deviation or median (minimum-maximum), where appropriate. Categorical variables were expressed as a percentage (%). The Chi-square test was used to compare categorical variables, whereas the Kruskal-Wallis test was used for the parameters not distributed normally in triple-group analyzes, and the Wilcoxon test was used for the evaluation of the differences among dependent groups. The significance level was accepted as $p<0.05$ in all statistical analyses.

Results

This study included a total of 143 patients. Of the 34 patients who underwent ONS, 9 (26.5%) were followed up for benign reasons and 25 (73.5%) for malignant reasons. Of the 54 patients who underwent ETF, 16 (29.6%) were benign and 38 (70.4%) were malignant. Additionally, of 55 patients who were treated with PN, 20 (36.4%) were followed up for benign and 35 (63.6%) for malignant reasons. No statistically significant difference was detected between patient groups in terms of age, gender, diagnosis, and length of stay in the ICU ($p>0.05$). However, nutritional support duration was significantly higher in patients under ETF support compared with others (8.01 days; $p=0.026$). The demographic and clinical features of the patients are presented in Table 1.

When the measurements were performed at the initiation and termination of the nutritional support in patients with ONS, the median prealbumin levels were 0.15 (0.03-0.41) and 0.16 (0.05-0.38) mg/dL, CRP values were 40.0 (0.8-166.0) and 23.1 (0.8-176.0) mg/L, and transferrin saturation levels were 1.65% (0.59-3.69) and 1.82% (0.61-3.17),

Table 1. Demographic and clinical features of the patients

	ONS (n=34)	ETF (n=54)	PN (n=55)	p
Age	61.7±15.1	56.0±13.6	56.7±15.8	0.181
Gender (F/M)	9/25	12/42	21/34	0.169
Primary disease				
Benign	9 (26.5%)	16 (29.6%)	20 (36.4%)	0.216
Malignant	25 (73.5%)	38 (70.4%)	35 (63.6%)	
Nutritional support duration (day)	6.38±3.11	8.01±3.26	7.32±3.06	0.026*
Length of stay in the ICU (day)	7.76±3.37	8.68±3.50	9.38±3.33	0.062

* The statistical significance was obtained from the comparison of ONS and ETF. ONS: oral nutritional supplementation; ETF: enteral tube feeding; PN: parenteral nutrition; F: female; M: male; ICU: intensive care unit

Table 2. Median prealbumin, CRP, and transferrin saturation levels of the patients at the initiation and termination of the nutritional support

	ONS (n=34)	ETF (n=54)	PN (n=55)	p^1	p^2	p^3
Prealbumin (mg/dL)						
Initiation	0.15 (0.03-0.41)	0.14 (0.03-0.31)	0.10 (0.02-0.29)	0.537	<0.001	0.003
Termination	0.16 (0.05-0.38)	0.21 (0.03-0.37)	0.13 (0.02-0.32)			
CRP (mg/L)						
Initiation	40.0 (0.8-166.0)	85.5 (4.5-296.0)	74.1 (1.5-323.0)	0.635	0.001	0.730
Termination	23.1 (0.8-176.0)	30.8 (0.9-321.0)	66.3 (2.0-209.0)			
Transferrin (%)						
Initiation	1.65 (0.59-3.69)	1.55 (0.63-2.43)	1.26 (0.47-2.48)	0.073	0.001	0.243
Termination	1.82 (0.61-3.17)	1.87 (0.60-3.25)	1.30 (0.11-2.06)			

p^1, The comparison of laboratory values of ONS measured at the initiation and termination, p^2, The comparison of laboratory values of ETF measured at the initiation and termination, p^3, The comparison of laboratory values of PN measured at the initiation and termination. ONS: oral nutritional supplementation; ETF: enteral tube feeding; PN: parenteral nutrition; CRP: C-reactive protein

respectively. However, there was no significant difference between the laboratory parameters of these patients on the days the nutritional support was initiated and terminated (p=0.537, p=0.635, and p=0.073 for prealbumin, CRP, and transferrin, respectively). Patients with ETF support had significantly increased levels of median prealbumin (0.14 vs. 0.21 mg/dL; p<0.001) and transferrin saturation (1.55% vs. 1.87%; p=0.001) at termination of nutritional support when compared with baseline levels; there was a definite decrease in CRP levels (85.5 vs. 30.8 mg/L; p=0.001). However, decrease in CRP levels (74.1 vs. 66.3 mg/L; p=0.730) and increase in transferrin saturation levels (1.26% vs. 1.30%; p=0.243) were not found to be significant (Table 2).

Discussion

Today, supplemental nutritional support for ICU patients is an integral part of routine treatment (1, 4, 16). Although a pragmatic approach remains to consider EN as the first choice for nutrition support, parenteral approach stands out at some special conditions where EN cannot be performed. In a recent multicenter randomized controlled study, it was reported that there is no difference in terms of the clinical results (30-day mortality, complications, hospitalization duration) between patients supported with EN or PN (1). Although the combined use of enteral and parenteral nutrition is the most commonly used method in clinical practice, the benefits of supplementary PN use are still controversial in patients who are well tolerated and can be nourished to the targeted dose at a good level (5).

Another controversial point is the evaluation of nutritional status. Clinical evaluation, anthropometric measurements, score-based evaluation indexes, and physical functionality tests are the most common methods; however, there is no gold standard parameter. In addition, a marker which can show malnutrition precisely and definitely have not been defined in biochemical tests. In spite the fact that plasma proteins have limited validity, parameters such as prealbumin (transthyretin), retinol binding protein, fibronectin or CRP are frequently being used. The half-life of prealbumin which is among the most commonly used biochemical markers is two days. Measuring CRP at the same time is necessary since prealbumin is affected from inflammatory conditions because the decrease in prealbumin levels in cases where CRP remains constant is related to a poor nutritional status. The half-life of transferrin is eight days, but it is believed to reflect the recent nutrient intake more accurately (1, 2, 6, 14).

Despite the definite benefits of early enteral nutritional support, the use of oral nutrition in ICU patients is often limited and not effective due to mechanical ventilation, changes in patients' vital functions, and frequent surgical interventions (4, 5, 15). The guidelines recommend early initiation of enteral feeding in patients with functional gastrointestinal tract (14, 17). However, studies show that EN alone results in insufficient energy and protein intake (9).

In our study, as a result of the evaluation of 34 patients who did not need mechanical ventilation and who received ONS in ICU for various reasons, decrease in CRP and increase in the levels of prealbumin and transferrin saturation were found between the initiation and termination of nutritional support, but these changes were not statistically significant. Patients with ETF support were found to have significantly decreased serum CRP values at termination of nutritional support when compared with baseline levels, while serum prealbumin levels and transferrin saturation were significantly increased. In this study, there were significant changes in the levels of biochemical markers measured in patients with ETF which might be suggestive of positive clinical results. Although there were similar changes in the markers of ONS patients, no statistically significant difference was found. While this may be due to the patients in the ONS group having a better general clinical condition than the patients in the ETF group, it can also be due to the fact that nutritional support is administered at longer periods in the ETF group than in other groups. Another possible reason may be that the caloric requirement calculated in patients with ETF support can be reached at desired levels, while patients with ONS are not able to achieve a sufficient nutritional support for various reasons (failure to comply, inability to use the nutrition product effectively, vomiting).

The optimal energy balance in ICU patients is an important target. The inability of reaching the desired targets in enteral nutrition is common due to especially gastrointestinal dysmotility or hemodynamic conditions. In 2018, ESPEN (European Society for Clinical Nutrition and Metabolism) published a guideline on clinical nutrition in the ICU and stated that every patient staying in ICU for more than 48 hours had a risk of malnutrition. It is emphasized in the guideline that oral feeding is superior to all supportive therapies and that all patients who are not expected to receive oral nutrition should be supported early with EN (within 48 hours). The guideline also recommends that PN should be implemented within 3 to 7 days, in case of contraindications to oral and EN (14). In the present study, there was a statistically significant improvement in prealbumin level in patients with PN, but the decrease in CRP and the increase in transferrin saturation were not statistically significant.

The meta-analyzes of EN and PN performed in recent years have been shown that PN does not have a significant relationship with clinical adverse outcomes (16). Furthermore, reduced infection incidence due to a better understanding of the importance of central venous catheter care and adequate nutritional support with PN have reduced negative prejudices, regarding PN in ICU patients (1, 4, 5, 14, 16).

The main limitation of the study was that patients included in the study were not from a single ICU in the hospital but gathered from several units and the fact that the calories and protein requirements calculated for each patient were excluded from the evaluation. Another limitation is that the underlying pathologies and complications have not been evaluated. Our future studies should include nutritional assessments, risk classifications, complications during treatment, and clinical outcomes. However, the evaluation of the nutritional status of the patients by a single team and the application of the standardized nutrition plan were the strengths of this study.

In conclusion, a significant improvement was observed in the prealbumin, CRP and transferrin levels of the patients supported with ETF, in the present study. Only prealbumin level was significantly increased with PN support, while similar improvements were not observed in the biochemical markers of patients with ONS. This may be due to the inability of the ONS to reach the desired targets.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013)

Informed Consent: Written informed consent was obtained from the patients and/or their relatives who participated in this study.

Peer-review: Externally peer-reviewed.

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