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A Proper Enteral Nutrition Support Improves Sequential Organ Failure Score and Decreases Length of Stay in Hospital in Burned Patients

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Abstract

Background: Severe burned patients developed metabolic imbalances and systemic inflammatory response syndrome (SIRS), which can lead to malnutrition, impaired immunologic response, multiple organ failure and death. Studies have shown that providing an early and adequate nutrition support can lower hypermetabolic response and improve the outcome. Unfortunately, little emphasis has been given to the role of nutritional support, especially for demonstrating the importance of a proper nutritional support in determining the outcome of critically burned patients.

Objectives: This study was designed to determine the possible protective effect of early and adequate nutrition support on sequential organ failure assessment (SOFA) score and length of stay (LOS) in hospital, in thermal burn victims.

Patients and Methods: Thirty patients with severe thermal burn (More than 20% of total body surface area [TBSA] burn), on the first day in the intensive care unit, joined this double-blinded randomized controlled clinical trial. Patients were randomly divided into two groups: control group (group C, 15 patients) received hospital routine diet (liquid and chow diet, ad libitum) while intervention group (group I, 15 patients) received commercially prepared solution, with oral or tube feeding. The caloric requirement for these patients was calculated, according to the Harris-Benedict formula. The SOFA score was also measured on admission (SOFA0), day 2 (SOFA1), day 5 (SOFA2) and day 9 (SOFA3), consequently. The difference between the last measurement (SOFA3) and day 2 (SOFA1) was calculated.

Results: The results showed that there was a significant change between SOFA3 and SOFA1, {-1[(-1) - 0], P = 0.013 vs. -1 [(-2) - 0], P = 0.109}. Mean LOS in hospital, for patients consuming commercial standard food, also proved to be shorter than those consuming hospital routine foods (17.64 ± 8.2 vs. 23.07 ± 11.89).

Conclusions: This study shows that an adequate nutritional support, in patients with severe burn injury, can improve SOFA score. It is also more cost-effective, resulting in a shorter LOS in hospital.

Keywords: Burns, Enteral Nutrition, Systemic Inflammatory Response Syndrome, Multiple Organ Failure, Sequential Organ Failure Assessment Scores, Length of Stay

1. Background

Burn injury may result in severe metabolic disturbances. Burned patients have the highest metabolic rate among all critically ill patients (1, 2). Increased energy expenditure can cause malnutrition, with sever body weight loss and, also, negative nitrogen balance (3, 4). After burn injury, a broad systemic response starts immediately, which may adversely affect immune function (5). On the other hand, gut-derived bacteria or endotoxemia are potent signals that trigger or exacerbate the hyper metabolic and immune inflammatory responses (6). Prolonged and persistent hypercatabolism is characterized by the loss of lean body mass (7, 8), as well as progressive decrease of host defenses (9, 10) that can lead to a late form of multiple organ dysfunction syndrome (11, 12).

Protein-energy malnutrition (PEM) can also cause impaired immunologic response (13). A number of factors, such as protein-calorie nutritional status, recent immunologic events and the intensity, repetitiveness and the duration of the inciting insult seem to affect the magnitude of the stress response and its consequences (14, 15). Studies have shown that an aggressive and immediate administration of enteral nutrition support can extenuate the stress response, attenuate hypermetabolism, reduce devastating catabolism (7, 8, 16, 17) and, therefore, improve the outcome (9). The right balance of nutrition support is essential for reducing the hypermetabolic and hypercatabolic responses, induced by burn injury (1).

Despite increasing experimental evidence, supporting the concept of nutritional support role in the outcome of burn patients, unfortunately, little emphasis has been giv-

en to the role of nutritional support. In most of developing countries, especially in our hospitals, low priority and unclear assignment are among the most common reasons for poor nutrition. The purpose of this study is to demonstrate the importance of a proper nutritional support in determining the outcome of critically burned patients.

Therefore, we decided to use commercial enteral feeding, as well as daily assessment of required calorie intake, to show the importance of nutrition therapy on clinical recovery of burned patient and compare it with the hospital's routine nutrition, which involves free nutrition. For this purpose, Sequential Organ Failure Assessment (SOFA) score and duration of hospital stay have been measured.

2. Objectives

This study was designed to determine the possible protective effect of early and adequate nutrition support on SOFA score and length of stay (LOS) in hospital, in thermal burn victims.

3. Patients and Methods

This study is a prospective, interventional, single-center, concealed blocked randomization, double-blinded (subject, outcome assessor) clinical trial. The study was carried out in the Burn Center of Sina hospital, in Tabriz, Iran. The ethics committee of Tabriz university of medical sciences, Tabriz, Iran, approved the study protocol. This study protocol was submitted to Iranian registry of clinical trials (IRCT) and approved under number 201307082017N13. Informed consent was obtained for each subject or his family members.

3.1. Patients and Groups

For sample size determination, primary information on SOFA score was attained via a pilot sample of five, in size. Considering 95%CI, 90% power, two tailed test and utilizing Pocock's formula, at least 14 samples per group were determined, while taking into accurate 30% drop-out rate, the sample size increased to 19 cases, per group.

The participants in this study were composed of 41 patients, in total. They were admitted to the hospital between March and December 2013. These patients were admitted in the first day of burn injury, with 20% - 90% burn of the total body surface area (TBSA), with plausible indication for enteral nutrition for > 48 hours. Patients having cardiogenic shock, serious inhalation injury, hepatic failure, renal failure, enteral feeding contraindication and pregnant women were excluded.

From those 41 patients initially selected, during the first 2 days, seven patients died, because of severity of burn, and four were excluded (two as a result of intolerance to enteral feeding and two because of severe diarrhea). As a consequence, only 30 patients with 20% - 70% TBSA were considered in this study. Total burned surface area was calculated on admission by using the rule of nines diagram.

The participants were randomly allocated in intervention and control groups, using randomized block procedure, stratifying on TBSA burned percentage (20% - 30%, 31% - 50% and 51% - 70%), age and sex (Figure 1).

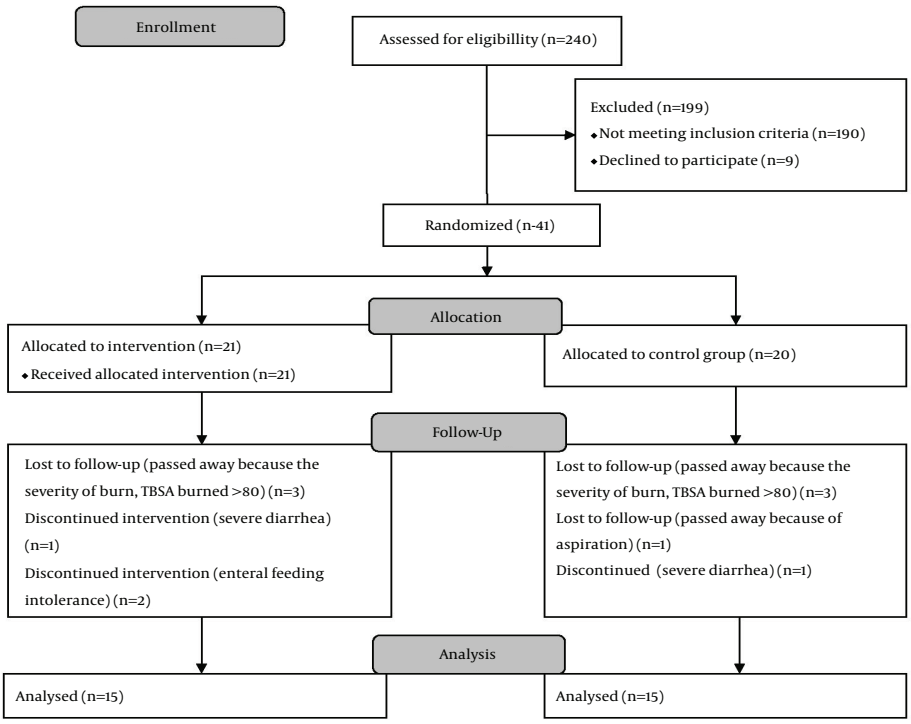

Figure 1. Flowchart Showing Initial Patient Eligibility, Application of Exclusion Criteria and Final Analysis of Patients Investigated in the Study

Table 1. Sequential Organ Failure Assessment Scores[a,b]

Variables	SOFA Score				
	0	1	2	3	4
Respiratory PaO_2:FiO_2, mmHg	> 400	≤ 400	≤ 300	≤ 200 [c]	≤ 100 [c]
Coagulation Platelets, $\times 10^3$ μL^{-1}	> 150	≤ 100	≤ 100	≤ 50	≤ 20
Liver Bilirubin, mg dL^{-1}	< 1.2	1.2 - 1.9	2.0 - 5.9	6.0 - 11.9	> 12.0
Cardio Vascular Hypotension	No Hypotension	MAP < 70 mmHg	Dopamine ≤ 5 or Dobutamine (any dose)	Dopamine > 5, Epinephrine ≤ 0.1, or Norepinephrine ≤ 0.1	Dopamine > 15, Epinephrine > 0, or Norepinephrine > 0.1
CNS GCS	15	13 - 14	10 - 12	6 - 9	< 6
Renal Creatinine, mg/ dL^{-1} or UO mg dL^{-1}	< 1.2	1.2 - 1.9	2.0 - 3.4	3.5 - 4.9 or < 500	> 5.0 or < 200

Abbreviations: CNS, central nervous system; FiO2, fraction of inspired oxygen; GCS, Glasgow coma scale; MAP, mean arterial pressure; PaO2, partial pressure of oxygen; SOFA, sequential organ failure assessment.
[a]Adrenergic agents were administered for at least 1 hour.
[b]Doses are given in μg/kg per min.
[c]Values are with respiratory support.

3.2. Nutrients

One group of patients (Group I) started enteral feeding in the first hour of admission. Commercial enteral formula –ENTERA Meal (Karen pharma and food supplement co, Tehran, Iran) (54.6% carbohydrate, 14% protein, 31.6% fat), 1 Kcal/mL- began at 25 mL/h and rose to calculated energy requirement, within 3 days. After 3 days of burn and onwards, the volume of tube feeding administered varied on the basis of the patients' calculated needs and their ability to absorb the administered tube feeding (The patients with > 30% TBSA burns had additional protein, reaching to 1.5 - 2 g/kg total protein/day).

Several patients did not require tube feeding, since they could resume normal feeding. These patients were excluded from the study on the day they stopped tube feeding. We evaluated periodically the energy requirement of these patients, using the Harris–Benedict equation × 1.5. The second group of patients (Group C) was given hospital routine diet ad libitum (liquid food for 2 days after injury, followed by chow diet).

3.3. Sequential Organ Failure Assessment Score Measurement

We collected all necessary information to calculate the SOFA score on days 0, 2, 5 and 9 of post-burn (Table 1). The arterial oxygen partial pressure (PaO_2)/ fraction of inspired oxygen (FiO_2) was recorded on the blood gas system (TechnoMedica Gastat602I, Blood Gas System, Japan), serum creatinine level was measured by Jaffe's laboratory method, serum bilirubin by DCA laboratory method, while the complete blood count (platelet count) by Sysmex KX-21N (Sysmex Corp., Kobe, Japan) cell counter. Data were measured in the main laboratory of Sina Hospital, Tabriz university of medical sciences, Tabriz, Iran, and Glasgow Coma Scale (GCS) was measured by a medical doctor. The SOFA0 was based on data obtained at the time of burn intensive care unit (BICU admission, SOFA - 48 hours, SOFA2 - day 5, and SOFA3 - day 9.

The neurological part of the SOFA score was calculated according to the GCS after admission in the ICU. In sedated patients, the score was given based on the previous available assessment, before sedation.

3.4. Length of Stay

To measure the LOS in hospital, the numbers of days, from admission to the ICU to final discharge from the hospital, were considered.

3.5. Statistical Analysis

The SPSS version 21 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis and Kolmogorov-Smirnov test was used to assess the normality of data. Normally distributed variables were shown as means ± standard deviation (SD) and an independent t-test was applied for between-groups comparison. Median and interquartile range (IQR) (standard 25^{th} - 75th percentiles) showed non-normally distributed variables. Wilcoxon signed-ranks test was carried out for within group comparison and Mann-Whitney U test for between group comparisons. A $P < 0.05$ was considered significant (18).

4. Results

Thirty patients were included in the present study, of which 22 were male (73.3%) and eight were female (26.7%).

The patients' age ranged from 18 to 60 years old. Patients had 20% - 70% TBSA of burn, averaging at 32.26 ± 12.83. There were no significant differences between the groups in burn percentage, age, gender or anthropometric measurements (Table 2).

We selected SOFA 1 (48 hours), since previous studies showed that organ dysfunction should not be assessed in the first 48 hours, until the acute resuscitation period is finished (Table 3). Because acute and reversible changes in organ function might be reflected by dysfunction due to massive fluid shift in the vascular and extravascular space, or incomplete resuscitation (13). There was a significant difference (P = 0.039) in SOFA3 between two groups (Table 3). No significant difference was observed between two groups in SOFA 0, 1, 2 (Table 3). There was a significant decrease (P = 0.013) in SOFA score in I group, whilst it didn't change significantly (P = 0.109) in C group (Table 4). A significant difference was observed between SOFA 3 and 1 in I group {-1 [(-1) - 0], P = 0.013 vs. -1 [(-2) - 0]} (Table 3). In comparison to baseline, There was no significant difference in SOFA 0 between two groups (P = 0.317), SOFA score decreased significantly (P = 0.013) in I group whilst it didn't change significantly (P = 0.712) in control group (Table 5). It seems that intervention in nutrition led to the more and significant improvement in SOFA score, compared with hospital diet ad libitum. Patients in group I had a lower LOS than control group (17.64 ± 8.2 vs. 23.07 ± 11.89, P = not statistically significant).

Table 2. Patient Characteristics[a]

Characteristics	Control Group C	Intervention Group I	P Value[b]
Age, y	33.14 ± 8.08	36.26 ± 14.85	.728
Male/Female ratio	11/4	11/4	NA
Weight, kg	66.81 ± 13.81	72.86 ± 17.85	.750
Height, cm	164.93 ± 10.43	168.26 ± 11.19	.658
TBSA burned, %	32.73 ± 11.84	31.80 ± 14.16	.980
LOS	23.07 ± 11.89	17.64 ± 8.2	.375

Abbreviations: NA, not available; LOS, Length of Stay; TBSA, Total Body Surface Area.
[a]Data are presented as mean ± SD and N = 15.
[b]P value indicates the difference between groups (independent t-test).

Table 3. Sequential Organ Failure Assessment Scores Measurements During Four Intervals, Group C vs. Group I[a]

	SOFA0	SOFA1	SOFA2	SOFA3
Control Group C	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	2.0 (1.0 - 3.0)
Intervention Group I	2.0 (1.0 - 2.0)	2.0 (1.0 - 3.0)	2.0 (1.0 - 2.0)	1.0 (0.0 - 2.0)
P[b]	0.317	0.317	0.222	0.039

Abbreviations: SOFA, Sequential Organ Failure Assessment.
[a]Data are presented as median (IQR).
[b]P indicates difference between groups (Mann-Whitney test).

Table 4. A Between- and Within- Group Comparison - SOFA1 and SOFA3[a]

	SOFA1	SOFA3	P[b]
Control Group C	2.0 (2.0 - 3.0)	2.0 (1.0 - 3.0)	.109
Intervention Group I	2.0 (1.0 - 3.0)	1.0 (0.0 - 2.0)	.013
P[c]	0.222	0.039	NA

Abbreviations: NA, not available; SOFA, Sequential Organ Failure Assessment.
[a]Data are presented as median (IQR).
[b]P indicates difference within groups (Wilcoxon signed-ranks test).
[c]P indicates difference between groups (Mann-Whitney test).

Table 5. A Between- and Within- Group Comparison - SOFA0 and SOFA3[a]

	SOFA0	SOFA3	P[b]
Control Group C	2.0 (2.0 - 3.0)	2.0 (1.0 - 3.0)	.712
Intervention Group I	2.0 (1.0 - 2.0)	1.0 (0.0 - 2.0)	.013
P Value[c]	0.317	0.039	NA

Abbreviations: NA, not available; SOFA, Sequential Organ Failure Assessment.
[a]Data are presented as median (IQR).
[b]P indicates difference within groups (Wilcoxon signed-rank test).
[c]P indicates difference between groups (Mann-Whitney test).

5. Discussion

Burn is considered as one of the most hypermetabolic states, which might persists up to 2 years after occurrence (19). Nutritional therapy is a crucial part of burn care (3, 9, 12, 20). Multiple studies have pointed out that malnourished patients undergo worse outcomes, including prolonged LOS in hospital, increased readmission and mortality, in comparison to well-nourished patients (21, 22).

An effective provision of the required amount of calories can be ensured via oral, enteral, or parenteral route. However, enteral nutrition seems to be the preferred supplementary route, in acutely injured burn patient cases.

In human studies, it has been shown that an early and continuous enteral nutrition, influentially delivering caloric requirements, would decrease the hypermetabolic response. At the same time, it would decline circulating levels of catecholamines, cortisol, and glucagon (23, 24). Early initiation of enteral nutrition also helps support the mucosal integrity, motility and intestinal blood flow, where all play a vital role in intestinal hypoperfusion prevention or ileus, caused by delays in resuscitation or reperfusion (25). In animal studies, Mochizuki et al. showed that post-burn hypercatabolism and hypermetabolic response are decreased when adequate calories are administered, via intra gastric route, to fulfill required energy consumption (26). The nutritional state and gut integrity is maintained, as well (12).

The result of the current study showed that SOFA score decreased significantly in the group that used nutrition support, {-1 [(-1) - 0], P = 0.013 vs. -1 [(-2) - 0], P = 0.109}, which can be related to lower hypermetabolic response (1, 2, 23, 24), negative nitrogen balance and improved immunity, causing the infection incidence to decrease (27). Length of hospital stay was also decreased, in this group (17.64 ± 8.2 vs. 23.07 ± 11.89), as result of improved immunity and better wound healing, causing a decrease in infection rate (28).

Consistent with the present study, Rimdeika et al. have also reported that burned patients receiving 30 kcal/kg during 24 hours more had lower sepsis, pneumonia and mortality rate, with shorter duration of treatment (29). In a different study, Suri et al. also showed a reduction in mortality and LOS, in burned patients, nourished aggressively (27).

Khorasani et al. obtained similar results in a study conducted on burned children. The ones who were administered an early enteral nutrition, had a short LOS and decreased mortality rate (30).

The use of nutrition therapy, in burn patients, plays a key role, especially when an aggressive approach is implied (20). Proper nutrition is essential for wound healing, mediation of inflammation, suppression of the hypermetabolic response and reduction of sepsis-related morbidity and mortality (31).

Our study has several limitations, accounting for short study period, small sample size and, also, > 50% of our patients were allocated in the range of 20% - 30% TBSA burn.

This trial is the first to investigate the effects of proper nutrition on critical burned patients and the accuracy of this study is high, as it was performed by one single observer.

5.1. Conclusions

The results of this study demonstrated that a proper nutritional therapy, after thermal injury, reduced the post-burn organ damage, as evidenced by changes in SOFA score. It also reduced the LOS in hospital. We conclude that a proper nutrition support is an important factor and, therefore, it should be considered as a critical aspect of care given to burn patients in hospitals. Adopting such a practice will be beneficial for the patients, as well as for reducing the overall costs.

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Footnotes

Authors' Contribution: Conception and design: Sima Lak, Alireza Ostadrahimi; analysis and interpretation: Mohammad Asghari-Jafarabadi; data collection: Sima Lak, Hossein Zalouli, Sanaz beigzali; writing the article: Sima Lak, Sanaz Beigzali; critical revision of the article: Alireza Ostadrahimi, Behrooz Nagili; final approval of the article: Alireza Ostadrahimi.

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