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Nutrition as a Predictor of Outcome in Patients with Severe Traumatic Brain Injury

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Abstract

Background: Traumatic Brain Injury (TBI) is a critical socio-economic problem throughout the world. Immediately after TBI, there is an increase in catabolic and counter-regulatory hormones, leading to a hypermetabolic state which causes specific nutritional needs and multiple metabolic and electrolytic abnormalities. Nutritional intervention is likely to limit the patient's inflammatory response and thereby improve the ultimate health outcome.

Aim of Study: This study aimed to assess the effect of early nutrition on the rate of mortality in patients with severe traumatic brain injury.

Methods: The current work is a prospective randomized study that was conducted on 60 patients with severe traumatic brain injury. Patients were randomly classified into three groups (each was of 20 patients). Group I received enteral nutrition after 48 hours of TBI. Group II received early enteral nutrition within 1 st 24 hours after TBI. Group III received early parenteral nutrition within 1 st 24 hours after TBI.

Results: The three groups showed no statistically significant differences as regard age, sex, mode of trauma, and presence of co-morbidities. As regard vital signs, laboratory investigations, finding of Computed Tomography (CT) of brain and surgical intervention, there was no statistically significant difference between both groups at baseline. There was significant improvement in GCS in groups II and III compared to group I despite there was no significant difference between the three groups at admission. As regard duration of mechanical ventilation, there was significant decrease in the duration of mechanical ventilation in group II compared to groups I and III. There was significant increase in infection in groups I (70%) and III (60%) compared to Group I (20%). There was significant difference in mortality rate between the three studied groups and between Group I and II. At 30 days of the study, 65% of patients in Group I died. While in Group II and III the percentage decreased to 20% and 45% respectively.

Conclusion: Administration of early enteral nutrition in this study has been associated with decreased mortality, decreased duration of mechanical ventilation, less incidence of infection and improved GCS patients with severe TBI.

Key Words: *Traumatic brain injury – Nutrition – Outcome.*

Introduction

TRAUMATIC Brain Injury (TBI) is a damage to the brain from an external mechanical force. TBI can lead to temporary or permanent impairment of cognitive, physical, and psychosocial functions, with an associated diminished or altered state of consciousness [1,2].

Head trauma is characterized by a hypermetabolic state which is associated with intensive catabolism, leading to specific nutritional needs. It also causes multiple metabolic and electrolytic abnormalities [3].

Early physiological changes are thought to act as mediators of the complex systemic metabolic responses after Traumatic Brain Injury (TBI). Immediately after TBI, there is an increase in catabolic and counter-regulatory hormones such as glucagon and cortisol [4].

Systemic metabolic responses to brain injury include hypermetabolism, hypercatabolism, hyperglycemia, acute-phase response, altered gastric function, diminished immunecompetence, and increased endothelial permeability [4].

Nutrition therapy as part of TBI management might be beneficial as nutrients have the ability to interact with a variety of physiological processes. Nutrition therapy should be used as complementary to or supportive of other therapies [5].

Feeding protocols should be standardized to ensure the delivery of adequate levels of energy

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and protein to patients with severe TBI. Hospital intensive care units should include these protocols in their critical care guidelines [5].

Nutritional intervention is likely to limit the person's inflammatory response, which typically is at its peak during the first two weeks after an injury, and thereby improve the ultimate health outcome [6].

Patients and Methods

This prospective randomized controlled study was conducted in the Critical Care Unit of Emergency Medicine and Traumatology Department, Tanta University Hospitals in a duration of one year from November 2016 to November 2017. All patients underwent the standard procedures of the protocol.

The Research Ethical Committee, Faculty of Medicine, Tanta University approved the design of the study. An informed written consent was obtained from close relatives after full explanation of benefits and risks. Privacy of all patient data was granted and there was code number for every patient file that includes all investigations.

This study was conducted on 60 patients of both sexes, who had severe traumatic brain injury (GCS $\leq$8). Patients were randomly classified into three groups each group of 20 patients: Group I received enteral nutrition after 48 hours of TBI, Group II received early enteral nutrition within 1st 24 hours after TBI and Group III received early parenteral nutrition within 1st 24 hours after TBI.

Patients aged 18 or more with history of head trauma and Glasgow Coma Scale (GCS) $<$8 were included in the study. patients with brain death, hemodynamically unstable patients and pregnant patients were excluded from the study.

Methods of the study:

Prior to ICU arrival, patients in our study were managed initially, resuscitated, and stabilized in the emergency department. Patients who needed an operative intervention were transferred to the Operating Room before being admitted to the ICU. At admission to the ICU, all patients included in our study were intubated and mechanically ventilated.

All patients were subjected to full history taking from the relatives (included age, sex, medical history, allergies and events related to the injury) and clinical examination (included general and local chest, cardiac, abdominal and neurological examination). Routine laboratory investigations were done including random blood sugar, serum electrolytes, kidney and liver function tests, and complete blood picture.

For patients in all groups, Total daily Energy Expenditure (TEE) of each patient was calculated by a simple bedside pocket formula (30kcal/kg “desired weight”/day) [7].

In Group I, patients received enteral nutrition at 50% of caloric requirements after 48 hours of trauma. Nutrition increased gradually to achieve full caloric requirements by the sixth day after injury.

In Group II, patients received early enteral nutrition after TBI. Enteral nutrition was started at 50% of caloric requirements within 24 hours after TBI. Full caloric requirements were achieved by the second day.

Enteral nutrition formula used in this study was Fresubin® original. Each 100ml of Fresubin® provides 100kcal in the form of 13.8gm carbohydrates, 3.4gm fat, and 3.8gm protein. It also has minerals, trace elements, and vitamins. It was administered in the form of boluses every 2 hours through nasogastric tube.

In Group III, patients received early parenteral nutrition supplementation with enteral nutrition after TBI. Parenteral nutrition was started within 24 hours at 50% of caloric requirements and continued till enteral nutrition reach full caloric requirements on the sixth day after TBI.

About 70% of the total daily caloric intake was supplied by carbohydrates in the form of dextrose 25% infused over 24 hours. The other 30% was supplied by lipid in the form of Intralipid 10% infused over 16 hours. Protein was added in the form of Aminoven 10% infused over 24 hours (Dose of 1.5-2gm/kg/day).

All of the following measures were done daily and recorded at admission, on day 1, day 2, at the end of the 1st and the 2nd week: Glasgow coma score, Random Blood Sugar (RBS), albumin, prealbumin, Hemoglobin (HB), Total Leukocytic Count (TLC), C-Reactive Protein (CRP) and serum electrolytes (Na, K). Outcome of the study included: Duration of mechanical ventilation, incidence of infection and 30-day mortality.

Statistical analysis:

All statistical calculations were done using SPSS (Statistical Package for Social Science, SPSS for IBM, USA) Version 23 for Microsoft Windows. Data was presented according its type. Parametric quantitative data was presented in terms of mean and Standard deviation (SD). A probability value (p-value) less than 0.05 was considered statistically significant.

Results

There was no statistically significant difference between the three groups as regards age, sex, medical history, mode of trauma, radiological findings and surgical intervention. There was no statistically significant difference between the three studied groups regarding the vital signs at admission including mean blood pressure, respiratory rate, pulse and temperature.

There was no statistically significant difference between the three groups regarding GCS at day 2, week 1 and week 2 intervals. In Groups II and III, there was significant improvement in GCS compared to initial GCS at admission (Table 2).

There was no significant difference in RBS between the three studied groups during day 1 and week 2. While during day 2 and week 1, RBS was slightly higher in group III than groups I and II but still within normal range.

In this study, there was significant increase in TLC in Group I. At week 1 and 2, TLC was a significantly lower in Group II compared to Group I and III Fig. (1).

In Group I and III, there was significant increase in CRP levels at week 1 and week 2 compared to initial CRP levels at day 1. While in Group II, there was no statistically significant change in CRP level. There was no significant difference in CRP levels between the three studied groups at day 1, day 2, week 1 and week 2.

Serum albumin levels showed gradual decrease in all groups, but there was no statistically significant difference between the three groups. Serum pre-albumin levels showed significant decrease in all groups while in week 2, there was significant decrease in pre-albumin levels in delayed enteral compared to early enteral and early parenteral groups.

In this study, infection occurred in 70% of patients in the group who received delayed enteral nutrition and in 60% of patients in the group who received early parenteral nutrition. Incidence of infection was significantly lower (20%) in the group received early enteral nutrition Fig. (2).

In Group I, the duration of mechanical ventilation ranged from 7-24 days with mean value of 14.4±5.4. In Group II, the duration of mechanical ventilation ranged from 5-20 days with mean value of 10.5±5. In Group III, the duration of mechanical ventilation ranged from 7-26 days with mean value of 14.7±6.6.

There was significant decrease in the duration of mechanical ventilation in group II compared to group I and III Fig. (3).

At 30 days of the study, 65% of patients in Group I died. While in Group II, and III, the percentage decreased to 20%, and 45% respectively. There was statistically significant difference in mortality rate between the three studied groups, and between Group I and II (Table 3).

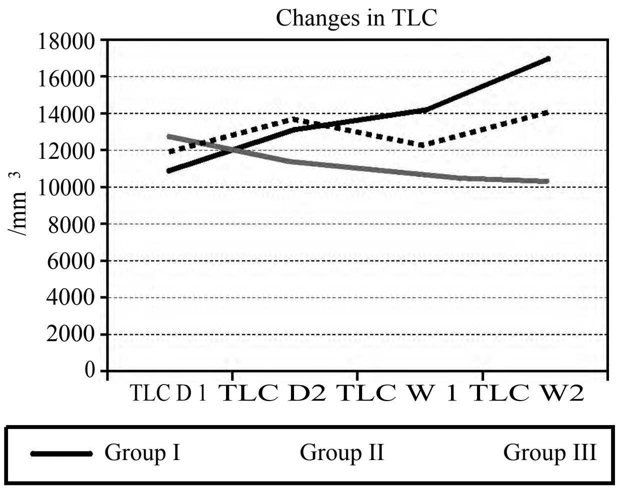

Fig. (1): TLC changes among studied groups.

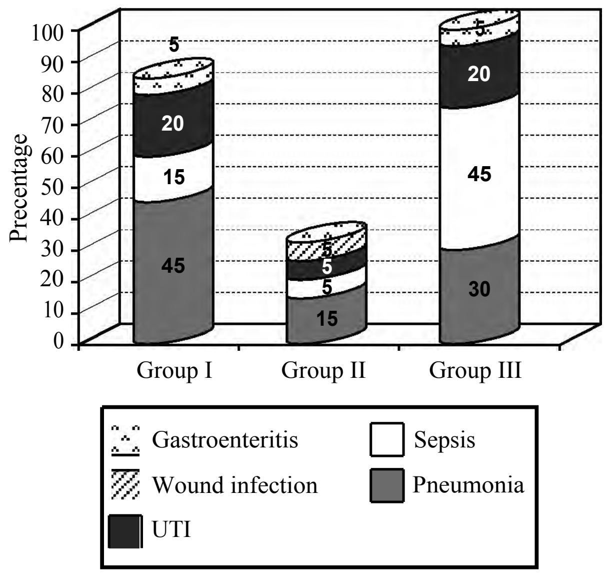

Fig. (2): Types of infection in studied patients.

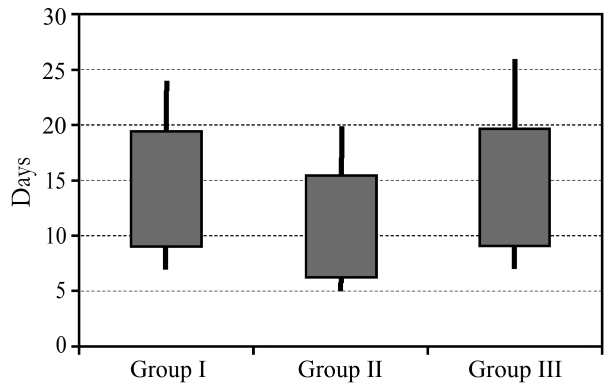

Fig. (3): Duration of ventilation among studied groups.

Table (1): Socio-demographic characteristics, medical, and smoking history of studied groups.

Variables	Group I (n=20) n (%)	Group II (n=20) n (%)	Group III (n=20) n (%)	Statistic	*p*-value
Age in years:					
Mean ± SD	28.4±10.7	26.2±8.1	28.3±10.3	F= 0.317	0.730
(Median)	(25.5)	(23.5)	(25.5)		
Range	18-57	18-50	18-54		
Gender:					
Male	13 (65)	15 (75)	14 (70)	χ^2= 0.476	0.788
Female	7 (35)	5 (25)	6 (30)		
Medical history:					
None	18 (90)	19 (95)	17 (85)	χ^2= 3.111	0.795
Hypertension	1 (5)	1 (5)	1 (5)		
Diabetes	0 (0)	0 (0)	1 (5)		
Chest disease	1 (5)	0 (0)	1 (5)		
Smoking history:					
Non-smoker	16 (80)	18 (90)	16 (80)	χ^2= 0.960	0.619
Smoker	4 (20)	2 (10)	4 (20)		

SD: Standard Deviation.
F : F test for one-way ANOVA.
$\chi 2$: Chi-square test.

Table (2): GCS changes in studied patients.

GCS	Group I (n=20) n (%)	Group II (n=20) n (%)	Group III (n=20) n (%)	Statistic	*p*-value
• *GCS D1:*					
3-8	20 (100)	20 (100)	20 (100)		NA
• *GCS D2:*					
3-8	20 (100)	17 (85)	18 (90)	MCET	0.350
9-12	0 (0)	3 (15)	2 (10)		
• *GCS W1:*					
3-8	12 (60)	9 (45)	9 (45)	MCET	0.653
9-12	8 (40)	10 (50)	11 (55)		
13-15	0 (0)	1 (5)	0 (0)		
• *GCS W2:*					
3-8	11 (55)	6 (30)	9 (45)	χ^2= 4.167	0.384
9-12	6 (30)	7 (35)	4 (20)		
13-15	3 (15)	7 (35)	7 (35)		
• Friedman chi-square	7.152	33.603	13.196		
• *p*-value	0.067	<0.001*	0.004*		

* : Indicates statistical significance (p<0.05).
NA: Not Applicable.

Table (3): Outcome of the study.

Outcome	Group I (n=20) n (%)	Group II (n=20) n (%)	Group III (n=20) n (%)	Statistic	*p*-value
Survivors	7 (35)	16 (80)	11 (55)	χ^2= 8.281	0.016*
Non-survivors	13 (65)	4 (20)	9 (45)		

	Group I & II	Group I & III	Group II & III
χ^2	8.286	1.616	2.849
p-value	0.004*	0.204	0.091

*: Indicates statistical significance (p<0.05).

Discussion

Traumatic Brain Injury (TBI) is a major cause of mortality and morbidity all over the world. Patients with head trauma have a hypermetabolic state that increases systemic and cerebral energy requirements.

After TBI, adequate and appropriate nutrition is recommended to meet these metabolic needs. The optimal timing and route of nutritional support has been a clinical challenge for several years.

A better clinical outcome of TBI patients receiving early enteral nutrition can be explained by:

- Early enteral nutrition may reduce TBI-evoked changes in the hormonal system and may reduce catabolic and inflammatory processes induced by TBI **[8]**.
- Use of nutrient additives (e.g. glutamine, choline, zinc) may aid recovery after TBI **[9]**.

In the present study, there was significance difference in mortality rate between the three studied groups. Mortality rate was significantly lower in the group received early enteral nutrition (Group II) compared to the group received delayed enteral nutrition (Group I). While there was no significant difference between early enteral (Group II) and early parenteral groups (Group III).

The effect of early nutrition on mortality can be due to provision of important nutrients during a critical time period when demand exceeds available resources as a result of the rise in energy expenditure after TBI, even in paralyzed patients **[10]**.

The lower mortality in patients received early nutrition in our study can be explained by the lower infection rate in these patients **[10]**.

In agreement with our results, Chiang et al., **[8]** who examined the effect of early enteral nutrition support on survival rate, and clinical outcome of sever TBI patients. Their study showed that the clinical outcome was significantly better in the early enteral group (started within 48h after TBI) with p-value <0.001. The mortality rate (at one month) was significantly lower in the early enteral group (26.9%) compared to the non-early enteral group (92.1%).

A meta-analysis of three randomized controlled trials by Doig et al., [9] revealed a statistically significant reduction in mortality in favor of early enteral nutrition provided within 24 hours of injury. This is in agreement with our results.

Meirelles et al., [11] compared enteral and parenteral nutrition in traumatic brain injury and was in line with our results and showed that there was no significant difference in mortality between the early enteral and parenteral groups.

Härtl et al., [12] study examining the effect of timing and quantity of nutritional support on early mortality was in line with our study, two-week mortality was significantly higher (2-fold increase with a p-value <0.001) in the patients who didn't receive early nutrition within 5 days.

Yanagawa et al., [13] in a meta-analysis noted that early feeding (either enteral or parenteral) was associated with a trend toward better outcome in terms of survival and disability.

In the present study, infection occurred in 70% of patients in the group who received delayed enteral nutrition and in 60% of patients in the group who received early parenteral nutrition. Incidence of infection was significantly lower in the group received early enteral nutrition (20%).

Low incidence of infection in patients received early nutrition may be explained by its attenuation of the post-traumatic stress response and by improvement of early immunological function. This could result in an indirect effect on outcome mediated by a lower infection rate.

In a study by Chourdakis et al., [6] Ventilation Associated Pneumonia (VAP) and non VAP occurred in about 80%, and 58.7% of patients received delayed, early enteral feeding respectively.

In a meta-analysis of randomized controlled trials by Doig et al., [9], one included trial reported the incidence of pneumonia was significantly lower in patients receiving EN within 24h of injury. This is in agreement with our results.

A study by Meirelles et al., [11] found that pneumonia and sepsis occurred in 40% of patients receiving early parenteral nutrition while patients receiving early enteral nutrition no sepsis but pneumonia occurred in only about 16.7% of patients.

Vitaz et al., [14] study evaluating the outcome of patients suffering moderate TBI was in concordance with our results and showed that incidence of pneumonia was higher in patients receiving delayed enteral nutrition (45% of patients). While in patients receiving early enteral nutrition, pneumonia occurred in about 29% of patients.

In the present study, the mean value of duration of mechanical ventilation in the early enteral group (10.5 days) was significantly lower than the delayed enteral (14.4 days) and the early parenteral (14.7 days) groups.

In a study by De Arruda et al., [15] on the benefits of early enteral nutrition with glutamine and probiotics in brain injury patients, two groups both received early enteral nutrition one of them with glutamine and probiotics. The mean value of the duration of mechanical ventilation in the control group was 14 days while in the group received enteral nutrition with glutamine and probiotics was 7 days.

In line with our results, Vitaz et al., [14] study found that there was a significant difference between patients receiving early and patients received late enteral nutrition as regard duration of mechanical ventilation (4.9±4.6 and 7.2±3.4 respectively). Mean duration of ventilation was lower than our study as the study conducted on patients with moderate TBI.

Limitation of the study:

- Small sample size in each group.
- This study included only patients with severe TBI.

Conclusion:

After exclusion of other causes known to affect mortality as age, GCS, CT of the brain and hemodynamic instability, early nutrition has better outcome, better neurologic recovery and associated with less mortality and complications in patients with severe traumatic brain injury.

Furthermore, the route of nutrition is related to mortality. Enteral nutrition compared to parenteral nutrition was associated with less mortality and complications.

Recommendation:

Early nutritional support in patients with severe traumatic brain injury is recommended as it can decrease both rate of infection and mortality. Early enteral nutrition administration has been found as the preferred route over parenteral nutrition with a lower incidence of mortality.

However, more studies to record the mortality beyond 90 days in patients with severe traumatic brain injury receiving early nutrition (enteral or parenteral) are required.

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التغذية كمؤشر للناتج الإكلينيكى
فى مرضى إصابات المخ الشديدة

إصابات الدماغ الشديدة تتسم بدرجة من زيادة التمثيل الغذائى وزيادة الآيض الهدمى مما يؤدى إلى زيادة متطلبات الطاقة النظامية والدماغية.

قارنت الدراسة الحالية تأثير التغذية المبكرة سواء المعوية أو الوريدية على الوفيات والنتائج السريرية لمرضى إصابات الدماغ الشديدة. أجريت الدراسة على ٦٠ مريضا من كلا الجنسين. تم تصنيف المرضى عشوائيا إلى ثلاث مجموعات كل مجموعة من ٢٠ مريضا. معايير التضمين هى السن ١٨ سنة أو أكثر، وصدمة بالرأس ومقياس غلاسكو للغيبوبة ≥٨. تم إستبعاد المرضى الذين يعانون من الموت الدماغى، والمرضى ذوى الدورة الدموية غير المستقرة والمرضى الحوامل من الدراسة.

كشفت الدراسة الحالية عن عدم وجود فروق ذات دلالة إحصائية عند بداية الدراسة بين المجموعات الثلاث المدروسة من ناحية البيانات الإجتماعية الديموجرافية، والعلامات الحيوية، والتحاليل المختبرية والآشعة المقطعية على المخ.

لقد كان هناك تحسن واضح فى مقياس جلاسكو للغيبوبة فى المجموعتين (٢) و (٣) بالمقارنة مع المجموعة (١) على الرغم من عدم وجود فرق كبير بين المجموعات الثلاث عند الدخول. وفيما يتعلق بفترة التنفس الصناعى، كان هناك إنخفاض كبير فى بفترة التنفس الصناعى فى المجموعة (٢) مقارنة بالمجموعات (١) و (٣). كانت هناك زيادة واضحة فى نسبة العدوى فى المجموعات ١ (٧٠٪) والمجموعة ٣ (٦٠٪) مقارنة مع المجموعة ٢ (٢٠٪).

كان هناك فرق كبير فى معدل الوفيات بين المجموعات الثلاث المدروسة وأيضا بين المجموعة (١) و (٢). فى ٣٠ يوما من الدراسة، توفى ٦٥٪ من المرضى فى المجموعة الأولى. بينما فى المجموعة (٢) و(٣) إنخفضت النسبة إلى ٢٠٪ و٤٥٪ على التوالى. فى هذه الدراسة إرتبط الحصول على التغذية المعوية فى وقت مبكر مع إنخفاض معدل الوفيات والإعتلال للمرضى الذين يعانون من إصابات المخ الشديدة.