Education Section

The Effect of Continuous Enteral Nutrition on Nutrition Indices, Compared to the Intermittent and Combination Enteral Nutrition in Traumatic Brain Injury Patients

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ABSTRACT

Introduction: Nutrition support is one of the most common care, which is undertaken for patients who suffered from Traumatic Brain Injury (TBI) and are admitted in intensive care units. Literature indicates some controversies regarding the appropriate method of nutrition support in these patients.

Aim: This study was conducted for determining the effect of continuous enteral nutrition on nutrition indices, compared to the intermittent enteral and combination nutrition in TBI patients.

Materials and Methods: In a randomized clinical trial, 60 TBI patients who were admitted to critical care units of Taleghani Hospital of Kermanshah-Iran in 2010 recruited to the study. The samples were allocated to three groups of continuous enteral nutrition, intermittent enteral nutrition and combination nutrition supports by random sampling. The tool was a researchermade checklist. The three methods of nutrition support were performed to the participants, then nutrition indices of patients

were measured before and during three weeks. Data were analysed using SPSS software, descriptive, and inferential statistics.

Results: The mean of received energy in the combination group $(53.1\pm 18.3\%)$ was higher than continuous $(38.5\pm 19.7\%)$ and intermittent $(32.2\pm 14.7\%)$ groups, significantly (p<0.001). The received protein was also greater in combination method (67.7±16.9%) than continuous (31.8±15.1%) and intermittent groups (17.2±10.1%), (p=0.001). The mean of nitrogen balance was improved in continuous method from -4.7± -1.6 to 7.2±5.2, (p<0.001) significantly.

Conclusion: In this study, received energy of patients was not enough by three methods. However, the continuous method, having a positive effect on nitrogen balance, reducing hypercatabolism and maintaining the total body protein, was preferred to brain injury patients compared with intermittent enteral and parenteral methods that demand more studies.

INTRODUCTION

Injuries are the leading cause of death between the ages of 15 to 44 years [1] and Traumatic Brain Injury (TBI) is the major cause of disability, morbidity and mortality among this group, which is responsible for a significant proportion of all traumatic deaths [2]. Most TBI cases were as a result of falls, mechanical forces, transport accidents and assaults that impose many related health care costs to patients and their families [3]. The incidence of TBI is rising worldwide, mainly owing to injuries associated with the increased use of motor vehicles [4]. Accordingly, the results of a meta-analysis on 23 European countries revealed a hospital admission incidence of 235 TBI patients per 100,000 people [5]. In the USA also, there are around 275,000 hospitalizations and 52,000 fatalities [6]. In Iran, more than 40% of TBI patients have been hospitalized and about 20% of them are admitted with severe symptoms [7].

For improving the prognoses in TBI patients who have severe symptoms and admitted in Intensive Care Units (ICU), some supportive cares are essential; one of them is nutritional support. Nutritional support is imperative to the recovery of head-injury patients because following TBI, systemic response to stress causes hypermetabolism and hypercatabolism, which place the patient population at increased risk for weight loss, muscle wasting, tissue atrophy, negative nitrogen balance and malnutrition [8,9]. The studies indicate that there is an increase in the incidence and progression of malnutrition and its consequent infectious

Keywords: Intensive care units, Mortality, Nutritional support

complications, the duration of ventilator dependency, the length of stay in the ICU and hospital, morbidity and eventually mortality rate in the hospitalized patients [10-14].

Nutritional support in TBI patients is performed in two whole procedures; Parenteral Nutrition (PN) and Enteral Nutrition (EN) [15], there are some controversies about the priority of one method over other; some studies documented the superiority of EN over PN [16,17]. But Rapp et al., study support the favorable effect of early PN on survival from a head injury [15]. Simpson & Doig indicated, use of PN should be limited to contraindications of EN [17]. Haddad & Arabi concluded, early EN is optimized in patients with severe TBI, as it is safe, cheap, cost-effective, and physiologic. Also, other potential advantages of EN include stimulation of all gastro-intestinal tract functions, preservation of the immunological gut barrier function and intestinal mucosal integrity, and reduction of infections and septic complications [18,19]. However, Wang et al., recommended the PN as the preferred method of feeding for patients with TBI in a meta-analysis [20]. In Doig et al., there was no difference between EN and PN in term of invasive ventilation and hospital stay in ICU patients [21]. Nagata et al., study results showed that a combination of parenteral and enteral nutrition feeding for patients after pancreatic surgery was better than enteral nutrition alone [22]. Other studies assessed the effect of continuous versus intermittent EN; given the side effects of both in similar, selecting one of them is dependent to much investigations [23,24], the nutritional indexes also investigated by Maurya et al.

that results showed no difference between two approaches [25]. However, some researchers believe the continuous EN is more tolerable and appropriate method [26,27] and other have opposite views [28]. Perhaps, due to simplicity and ease of doing, the current guideline that performed to feed TBI patients in Iranian hospitals is intermittent and physicians would prefer to undertake this EN type [27]. Therefore, with regard to the controversial reports about the appropriate method of nutrition support for ICU patients [21-28] and a paucity of information about TBI clients, this study was conducted to investigate the effects of continuous EN on nutrition indices TBI patients and compare with intermittent EN and a combination of enteral and PN.

MATERIALS AND METHODS

In a single-blind randomized clinical trial, 60 patients with TBI who were admitted to the ICUs of Taleghani Hospital of Kermanshah-Iran during March to August 2010 were investigated in terms of nutritional indices. The study was conducted after receiving permission from research council and ethics committee of Kermanshah University of Medical Sciences (KUMS). Patients' information remained confidential throughout the study. An informed consent was obtained from patient's immediate family before enrollment. This location as a trauma center has two ICUs with 22 active beds. Sample size was calculated with using the Villet et al., study [29], special formula for measuring the difference between two means [30] and considering confidence level 95% and 90% power of test, 17 cases for each group were obtained, but due to attrition probability, 20 people in each group were recruited. Sampling lasted about 6 months, from March to August. Eligible patients were randomly assigned into three groups (n=20 people in each group); continuous group as case and, intermittent and combination groups as a control.

Inclusion criteria were a diagnosis of severe TBI based on Glasgow Coma Scale (GCS) between 3-8, Injury Severity Score (ISS) (using the patient's brain CT scan results according to neurosurgeon), Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score on admission; at least 40% probability of survival on admission based on Revised Trauma Score (RTS) criteria; being older than 18 years and less than 65-year-old; Body Mass Index (BMI) between 18.5 to 29.9; no special diets (diabetes, hypertension, hyper lipidemia, etc.,); not receiving food orally or total PN at the beginning of the feeding time or at admission time to the ICU; and receiving informed consent from patients' relatives for their participation in the study. Exclusion criteria included patient's discharge or death prior to the 7th day after enrollment, beginning oral nutrition during the study, beginning parenteral feeding during the study period in patients of intermittent or continuous EN groups.

To collect the data, two checklists, demographic information and nutrition index (daily and weekly), were used. Demographic information checklist included information such as age, sex, height, weight, BMI, type of nutrition support on admission to the ICU, underlying diseases, GCS, ISS, APACHE-II, RTS and drugs used. In nutrition checklist, information such as time, amount, and type of nutrition support, amount, and type of enteral and parenteral nutrition, the gastric residual content at the time of each aspiration, the percentage of daily energy and protein intake and the daily GCS were recorded.

Interventions including the continuous EN, intermittent EN and combination method (enteral intermittent and parenteral methods), also data collection were performed by the researcher and the nurses working in the study setting (ICU units) assisted to perform the procedures, the nurses had been instructed by the researcher for about 2 weeks before commencing the study in term of the procedures, examinations and completing the checklists. The individuals who participated in the study were unaware of the sample categorization during completing the checklists.

To calculate the amount of energy and protein requirements, Harris-Benedict formula [31] was used, in this formula sex, age, height and weight are considered, so, once the basic energy is calculated and multiply in activity and stress factors. Moreover, the nutritional status of patients was evaluated on admission and then weekly through nutrition indexes of laboratory findings (serum albumin and total protein), anthropometric indices (weight and percentage of ideal body weight) and nitrogen balance.

The intervention group received continuous EN using the infusion pump (Kangaroo nutrition feeding pump, the e-Pump TM, Rasoolzadeh Va Shoraka Co.), and the control groups were fed by enteral intermittent or combination method (enteral intermittent and parenteral methods). Continuous EN feeding started at 6 am at a rate of 20ml per hour and continued until 12 MN every day. If tolerated, the amount of nutrition was increased 10 to 15 ml until the target energy requirement was achieved. In the intermittent enteral group, nutrition started with 50ml every 3 hours. If patients could tolerate according to physician's instructions, this amount increased to a maximum of 400ml. In EN, the tolerance was investigated based on remaining contents of the stomach and gastrointestinal symptoms such as nausea, vomiting and abdominal distention. In PN of patients, hypertonic solutions such as intralipid 10%, aminoacid 10-15% and sometimes glucose 10-20% were used according to the physician's order.

The content of the EN solution was the same for all the patients in the study and the reported energy was 0.7 kcal/ml. The amount of energy from carbohydrates, protein and fat in the gavage liquids and hypertonic solutions were recorded based on existing documents [32]. It should be mentioned that all the study patients underwent mechanical ventilation with SIMV mode and received a tidal volume of 500 to 700ml on admission to the ICU, and changed to spontaneous breathing/pressure support after the patient's condition improved.

STATISTICAL ANALYSIS

The data were analysed using the 16th version of the Statistical Package for Social Sciences (SPSS v.16.0; SPSS Inc., Chicago, IL, USA), descriptive statistical tests (frequency, mean and standard deviation) and the analytical tests (ANOVA, Kruskal-Wallis H-Test, independent t-test and paired t-test).

RESULTS

From 60 patients who participated in the study, 76.7% (n=46) were male, the mean and standard deviation (SD) of age were 34.6 ± 12.4 years, and 36.7% (n=22) were in 20-29 years. In 81.7% of patients (n=49) BMI was in range of 18.5-24.9kg/m², the survival rate of 41.7% of patients (n=25) was more than 90% on admission. Mean and SD of survival percent in three groups estimated about 83.5 ± 11.6 . Parenteral albumin was ordered for 80% of patients (n=48) by the neurosurgeon. [Table/Fig-1] shows the demographic characteristics of the three groups in detail.

The mean percentage of total energy was $38.5\pm19.7\%$ in the continuous group, $32.2\pm14.7\%$ in the intermittent group, and $53.1\pm18.3\%$ in the combination group. The mean percentage of received protein was calculated $31.8\pm15.1\%$ in the continuous group, $17.2\pm10.1\%$ in the intermittent group, and $67.7\pm16.9\%$ in the combination group. The mean percentage of total energy in patients during hospital stay was significantly higher in the combination group than in the intermittent and continuous enteral groups by ANOVA test (p<0.001) [Table/Fig-2], but there was no significant difference between the intermittent and continuous groups (p=0.06). The paired t-test indicated that the mean percentage of energy intake increased significantly in patients who were in the intermittent and continuous enteral groups (p=0.003 and p=0.01, respectively).

Variables\Groups	Intermittent (n=20)	Continuous (n=20)	Combination (n=20)	Mean (n=60)		
Age (year)	34.2± 11.3	32± 8.7	37.8±16	34.6± 12.4		
Sex (male/female)	4/16	7/13	3/17	46/14		
BMI (kg/m²)	22.5±3.6	21.9±2.8	20.8± 3.4	21.7±3.3		
Survival rate (%)	84.3± 10.4	85± 10.7	82.2± 13.8	83.5± 11.6		
ISS	8.3± 7.6	14.5± 8.9	11.6± 8.2	11.4± 8.5		
APACHE-II	18.7±5.3	18.6±4.6	17.6±5.8	18.3±5.2		
GCS	6± 2.6	6.6± 2.6	6.5± 2.9	6.3± 2.7		
Using of Albumin during hospitalization (%)	85± 0.36	79± 0.41	78± 0.42	81± 0.39		
Starting time of EN (day)	5.2± 3.9	4.1± 1.9	4.6± 4.8	4.7± 3.6		
Starting time of PN (day)	0	0	15.1±13.5	4.8± 10.3		
Dependency duration to mechanical ventilation (day)	10.1±6	9.9± 8.9	11.3± 8.9	10.4± 7.9		
[Table/Fig-1]: Demographic characteristics in three nutrition support groups at the beginning of admission.						

Nutritional indexes/ Groups		Intermittent	Continuous	Combination	Mean	test
Received energy (%)	W1	16.1± 12.2	21.1 ± 13.2	48.4 ± 15.4	28.4 ± 19.6	p< 0.001*
	W2	25.9± 17.9	39.2 ± 24.9	57.2 ± 22.9	39.9 ± 24.9	p= 0.006*
	W3	49.9± 29.6	57.1 ± 28	63.6 ± 25.4	55.5 ± 27.6	p= 0.366
	Mean	32.2 ± 14.7	38.5 ± 19.7	53.1 ± 18.3	37.5 ± 21.5	p< 0.001*
Received protein (%)	W1	11.8 ± 6.4	15.6 ± 8.4	64.5 ± 17.7	30.5 ± 26.9	p< 0.001*
	W2	22.1 ± 12.9	33.8 ± 17.9	68.8 ± 18.9	40.5 ± 25.7	p< 0.001*
	W3	35.7 ± 24.3	49.1 ± 25.8	75.6 ± 35	55.4 ±32	p=0.057
	Mean	17.2 ± 10.1	31.8 ± 15.1	67.7 ± 16.9	38.5 ± 25.7	p< 0.001*
Serum albumin (mg/dl)	W1	4.2 ± 0.5	4.7 ± 0.8	4.1 ± 0.6	4.3 ± 0.7	p= 0.06
	W2	4.7 ± 0.7	4.3 ± 0.6	4.2 ± 0.7	4.3 ± 0.6	p= 0.5
	W3	5.6 ± 0.1	4.8 ± 0.7	5.1 ± 0.07	4.9 ±0.6	p= 0.6
	Mean	4.3 ± 0.6	4.5 ± 0.5	4.1 ± 0.4	4.3 ±0.5	p= 0.09
Total serum protein (mg/dl)	W1	6.3 ± 0.5	6.4 ±0.6	6.1 ± 0.7	6.2 ± 0.6	p= 0.4
	W2	6.3 ± 0.6	6.1 ± 0.5	6.3 ±0.9	6.2 ± 0.7	p= 0.8
	W3	7.7 ± 0.1	6.8 ± 0.4	6.1 ± 0.2	6.8 ± 0.5	p= 0.05
	Mean	6.3 ± 0.4	6.2 ± 0.4	6.2 ± 0.5	6.2 ±0.4	p= 0.6
Nitrogen balance	W1	-1.08 ± 3.7	- 1.51 ± 2.5	5.18 ± 5.5	0.92 ± 5.1	p= 0.001*
	W2	0.75 ± 5.4	4.38 ± 3.1	6.34 ± 5.6	4.44 ± 4.9	p= 0.1
	W3	0.6 ± 1.1	7.25 ± 5.2	6.77 ± 5.1	6.35 ± 5.1	p= 0.5
	Mean	-2.49 ± 2.7	-0.41 ± 2.5	4.24 ± 4.8	0.46 ± 4.5	p< 0.001*

The mean of total protein intake in the combination group was reported higher than that in the intermittent and continuous enteral groups (p=0.001). The mean of daily protein intake in the continuous group was higher than that in the intermittent group by independent t-test (p=0.03). The mean of daily protein intake of the intermittent and continuous enteral groups increased significantly during the hospital stay (p=0.003 and p<0.001, respectively). In the combination group, there was no significant difference between the mean percentage of daily protein intake at the end of the first week and at the end of the study.

The mean of serum albumin in all three groups was normal during the study period. There was no significant difference between the mean albumin and total protein levels in three groups from the admission time to the end of the study. The mean total serum protein in the intermittent and continuous enteral groups was in normal range only at the end of the study [Table/Fig-2].

The mean of nitrogen balance in the combination group was more than that in the intermittent group (p<0.001) and continuous

group (p=0.01) significantly. The mean of nitrogen balance in the continuous group during the study period increased from $-4.7\pm$ 1.6 to $7.2\pm$ 5.2 (p<0.001). There was no significant relationship between the mean of nitrogen balance in the intermittent nutrition group and the combination group during admission and at the end of the study.

There was no significant difference in term of anthropometric indicators between three nutrition support groups. The mean of weight in the intermittent and continuous groups decreased during the hospital stay significantly from 65.3 ± 11.6 kg before intervention to 54.7 ± 16.8 kg at the end of the study in the intermittent group (p<0.001), and 66.4 ± 13.1 kg to 60.7 ± 11.2 kg in the continuous group, (p=0.04). The percent mean of Ideal Body Weight (IBW) decreased in patients in the intermittent group (p=0.003), and from $88.4\pm76.6\%$ to $80.5\pm11.7\%$ in the continuous group (p=0.03). There were no significant changes in mean body weight and percentage of ideal body weight in the combination group during the hospital stay [Table/Fig-3].

Anthropometric indexes/ Groups		Intermittent EN	Continuous EN	Combination	p-value
Weight (Kg)	admission	65.3±11.6	66.4± 13.1	67.6± 2.2	p=0.9
	W1	64.7± 16.8	66.1± 11.7	66.9±10.5	p=0.8
	W2	63.2±13.9	65.2± 10.2	71.2± 14.4	p= 0.3
	W3	54.7±16.8	60.7± 11.2	67.3± 11.7	p= 0.8
	p-value	p<0.001	p=0.04	p=0.7	
IBW (%)	admission	91.5±11.4	88.4± 76.6	90.6± 16.8	p=0.5
	W1	86.6± 14.1	86.1± 16.3	86.8± 14.3	p=0.4
	W2	83.1± 16.7	82.2± 9.4	92.8± 18.6	p=0.3
	W3	76.6± 14.0	80.5± 11.7	91.5± 7.7	p=0.3
	p-value	p=0.003	p=0.03	p=0.8	

DISCUSSION

In this study, none of the three nutrition support groups received adequate energy and protein (100% of required energy and protein) during the study. In Waele E De et al., and De Jonghe et al., studies, were consistent with our findings, patients did not receive the required energy during hospitalization [33,34]. Possible causes of this problem include the absence of nutritionist in the ICU, inadequate knowledge of other health care providers regarding the principles of nutrition and nutrition therapy in the ICU which is proved in previous studies [35-37]. Moreover, other causes can be food intolerance in trauma patients as a result of acute inflammatory reaction of the body against injury, failure to calculate the amount of energy and protein needs of patients, and failure to consider the high-protein diet for trauma patients under study with respect to their needs and insufficient gavage solution provided for patients hospitalized in the ICU. In addition to the mentioned causes, given the intermittent EN approach was the general procedure to feed the ICU patients, the following factors were presented concerning the continuous group: inadequate familiarity of nurses with the new nutrition procedures thus failure to completely implement continuous EN guide despite the short term training at the beginning of the study and continued training by the researcher in various work shifts. It should be noted that due to the following: conducting most of diagnostic and treatment measures for patients namely; radiography and some minor surgeries in the ICU and nurses' coordination with the relevant wards, if there was a need to transfer a patient from the ICU to perform other procedures such as CT scan and surgery; gavage disconnection was minimum. In De Jonghe et al., study, due to the "under prescription" and "under delivery" reasons, only 71% of required caloric had been delivered, so they suggested a specific

nutritional protocols including a pharmacist and a nutritionist or dietitian, regular training of medical staff involved in nutritional support prescription, and routine review of practice in ICUs for achieving optimal nutrition care in critically ill patients [34]. However, despite the shortcomings, Helmy et al., in their guideline to TBI patients, argued: "enteral formulas are preferable because it is apparent that the enteral route is more physiological, less expensive, and less risky than total parenteral nutrition" [38]. It seems addition to aforementioned, more detailed assessment of patients' nutrition statuses and educating staff about this issue are effective measures for providing proper nutrition plan in TBI hospitalized patients.

The results presented, the percent mean of received energy and protein in continuous group were increased in week one to the end of the study and also were higher than the intermittent group, while this increment was not significant in the combination group, so these indices were upmost in combination group. The results of Huang et al., study showed there are no difference between the combination and EN in term of received protein and energy during 14 days [39], but due to frequent interruptions for diagnostic and therapeutic measures, the intermittent EN was more appropriate over continuous EN about protein and calorie intake in MacLeod et al., study [40]. It seems the high percent of energy and protein intake in combination group can be attributed to receiving more hypertonic solutions (Amino acid 5-10%, Intralipid 10%, and glucose serum 10%) through central vein line, also in our study most of the related constraints to continuous EN such as repeated interruptions has been limited as possible, which justify the more percent of received protein and energy compared to the intermittent EN.

The mean of total albumin and serum protein did not show a significant difference among the three groups during the hospital stay, and the mean nitrogen balance in the combination group was significantly higher than that in the intermittent and continuous groups and there was no significant relationship between the intermittent and continuous groups. In Dhandapani et al., study on TBI patients' nutrition feeding with the enteral method, only albumin serum level decreased significantly and total protein serum level had an insignificant increase in patients who started enteral feeding prior the third day of study during 3 weeks [41]. In Justo Meirelles & de Aguilar-Nascimento study, no significant difference was found in nitrogen balance of patients with trauma receiving enteral and parenteral feeding within 5 days after admission and it increased significantly during admission in both groups [42]. In Jivnani et al., study on patients with head trauma, negative nitrogen balance was reported during the study period [43]. In our study, it seems the reason for a significant increase in nitrogen balance in the continuous group was repair and rebuild of body proteins. Moreover, differences between the present study and Justo Meirelles & de Aguilar-Nascimento study can be attributed to merely parenteral feeding use during admission in the ICU and shorter period of the Justo Meirelles & de Aguilar-Nascimento study.

The mean anthropometric indicators (weight and ideal body weight percent) decreased during hospital stay in the intermittent and continuous groups, significantly, however it did not increase in the combination group. In Park et al., study, patients in the continuous enteral feeding group could faster gain their initial weight prior to sickness compared to patients that received total parenteral nutrition [44]. Probably, the reason for significant weight loss and percentage IBW in the intermittent and continuous group patients in our study was related to insufficient content of gavage solution, inadequate awareness of nurses with new continuous nutrition feeding method and other reasons that are mentioned in the first paragraph of "discussion" part.

LIMITATION

For conducting the study we had some restraints; accordingly continuous EN was a new method for staff and it needs constant checking, in this case we educated some of the employees of the ICU to collaborate with us. Furthermore, we have no control over the process of preparing the nutrient content, because it was provided in the hospital kitchen.

CONCLUSION

In this study, the percentage of received energy and protein and nitrogen balance was significantly higher in the combination group than intermittent and continuous groups, while the percentage of the received protein in the continuous group was reported significantly more than intermittent group which presented as a significant increase in nitrogen balance during hospitalization. Therefore, owing to the complications of PN method such as infection risk and the lack of normal bowel function, also ineffectiveness of intermittent EN for handling nutritional needs of ICU patients, it is suggested continuous EN be considered as a proper approach for substituting the other feeding methods in ICU patients, which demanded more related studies.

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