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Comparison of Different Early Enteral Feeding Formulas on Critically Ill Patients

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Summary Critically ill patients are physiologically unstable, often have complex hypermetabolic responses to trauma. These patients are facing a high risk of death, multi-organ failure, and prolonged ventilator use. Nutrition is one of therapy for critical illness, however, patients often experience malnutrition caused by disease severity, delays in feeding, and miscalculation of calorie needs. The study aims to evaluate clinical improvement in critically ill participants that were given 3 kinds of early enteral feeding formulas, which were control (5% Dextrose), high-protein polymeric, or oligomeric formulas. A total of 55 critically ill participants admitted to the intensive care unit (ICU) between October 2017–March 2018 and assigned in this controlled trial. Early enteral feeding was initiated within 24–48 h after ICU admission. Each enteral feeding group were categorized to traumatic brain injury (TBI) or non-TBI. The primary endpoints were changes in white blood cell count, Acute Physiologic and Chronic Health Evaluation (APACHE) II score, and Nutrition Risk in the Critically Ill (NUTRIC) score from baseline to day 3. Baseline characteristics were similar between control (n=22), high-protein polymeric (n=19) and oligomeric (n=14) groups. There were significant decreases for white blood cell count (13,262.5±6,963.51 to 11,687.5±7,420.92; p=0.041), APACHE II score (17.33±3.31 to 13.83±1.95; p=0.007), and NUTRIC scores changes (3.08±1.44 to 1.92±1.00; p=0.022) in non-TBI participants receiving highprotein polymeric compared those in control or oligomeric participants. But there is no significant clinical improvement in TBI patients. In conclusion, non-TBI patients benefit from early enteral feeding with high-protein polymeric formula.

Key Words critical ill, early enteral feeding, high-protein formula

Notwithstanding under "proper" hospital care, approximately 40% of patients admitted to the hospital are malnourished at admission. Malnutrition is associated with many adverse outcomes, such as immune system depression, diminished healing process, muscle wasting, prolonged length of stays, increased morbidity and mortality which lead to higher early re-admission rates and healthcare expenses Critically ill patients often have various degrees of inflammation which result in an increased in energy expenditure and protein catabolism, but reduced energy and protein intake. Regardless of the patient's pre-existing malnutrition, every patient has a highly variable metabolic and immune response to injury or illness which might be attenuated by proper nutrition therapy (*1–8*).

Enteral nutrition (EN) is one approach to modulating inflammation and coagulation in critically ill patients, which has been correlated with beneficial outcomes such as reduced infectious complications, fewer organ failures and reduced mortality. Although there is a general acceptance of early EN, only a few studies have approached the specific timing, volume, and formula type of tube feeds in critically ill patient population and fewer still have studied the effects on inflammation (*8–10*).

The expert committee of European Society for Clinical Nutrition and Metabolism (ESPEN) recommended that haemodynamically stable critically ill patients should be fed early within 24–48 h of patient's admission using an appropriate amount of feed, but there are no data showing improvement in relevant outcome parameters using early EN in these patients. This means a better understanding of managing inflammation in ICU patients could provide better targeted care to help prevent malnutrition, morbidity and mortality (*3*, *11*).

Compromised GI tract is one of inhibiting factors in critically ill patients which makes them generally susceptible to over-feeding and under-feeding. Such conditions made the patients to be fasted or given 5% dextrose for quite long period of time, hence leading to

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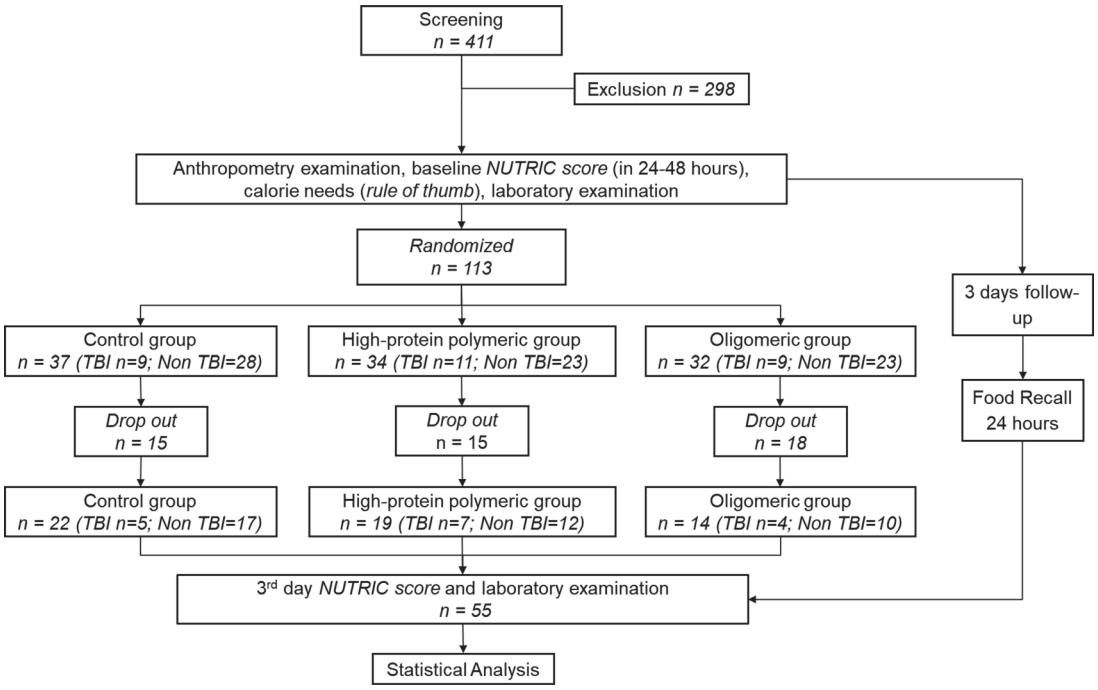

Fig. 1. Flow chart of the study population.

energy deficiency in these patients.

Many enteral formulations exist for the nourishment of the malnourished or at-risk patients, but most studies have failed to recognize their benefits. Nutritional guidelines suggest using polymeric formula when initiating enteral feeding in critically ill patients. In most cases, the given amount of protein is not adequate, although several studies have shown that low protein intakes can be related to adverse clinical outcomes (*11–15*).

There is limited evidence for applying oligomeric formulas in the ICU. This formula is slightly more expensive than polymeric formula, but data indicated that they are better tolerated by compromised GI tract patients because these peptides are water-soluble and readily absorbed by the intestine and metabolized by the liver. Because it is partially digested, greater nutrient delivery may be obtained and reduced the degree of regurgitation, gastric emptying times, and gagging while improving tolerance. As a result, they have fewer gastrointestinal complications, improved visceral protein levels, and decreased rates of mortality (*15–17*).

There is no specific ICU nutritional score has been validated thus far. NUTRIC score was assicoated with mortality and nutritional support might lower mortality in patients with a high NUTRIC score (>5). (*15*, *18*, *19*).

We conducted this trial to compare the effects of different early enteral feeding formulas on inflammatory markers, NUTRIC score, length of stay, and mortality in critically ill patients.

MATERIALS AND METHODS

Study population and design. This was a controlled clinical trial, conducted among adult ICU patients of Wahidin Sudirohusodo Hospital, Makassar, Indonesia, from October 2017 to March 2018. This study included 55 participants who aged older than 18 y and with stable hemodynamic values. The exclusion criteria were gastrointestinal resection, contraindications for enteral feeding, history of diabetes or chronic kidney disease, receiving parenteral nutrition, severe intolerance for enteral nutrition or formula, gastric residual volume >250 mL/4 h. Informed consent was obtained from participants family members.

Participants were consecutively assigned to either the control group receiving dextrose 5%, high-protein polymeric formula (Peptisol®) group (22.4% protein from total calorie), or the oligomeric (Peptamen®) formula group (16.2% protein from total calorie). All participants were initiated on enteral feeding, as early as possible (within 24–48 h) after intensive care unit (ICU) admission. Participants in the control group were given 5% dextrose as a starting regimen and were continued with other types of feeding regimen based on anesthesiologist instruction. Participants in the high-protein polymeric diet group or oligomeric enteral nutrition group were given a feeding regimen which was administered as boluses via a nasogastric tube. A total of 5 aliquots were administered at 4-hourly intervals in a daily feeding period of 24 h, with the patient positioned 30° head-up.

Critically ill participants who completed the intervention period were analyzed based on the diagnoses categories of traumatic brain injury (TBI) and non-TBI.

Anthropometry and laboratory measurements. Upon first 24 h ICU admission, demographic data were collected; this included age, gender, height (patient in the supine position), ideal body weight (IBW), mid-upper-

Table 1. Anthropometric profile.

	TBI							NON TBI						
	Control		High-protein polymeric		Oligomeric		*p*-value	Control		High-protein polymeric		Oligomeric		*p*-value
	mean	SD	mean	SD	mean	SD		mean	SD	mean	SD	mean	SD	
Age (y)	29.4	5.73	38.29	18.35	41.6	20.11	0.490	55.41	15.47	50.25	15.92	42.44	20.27	0.249
Height (cm)	159.4	7.50	163.29	9.83	161.2	5.22	0.715	157.35	4.89	156.08	8.15	160.06	7.54	0.406
IBW (kg)	56.76	5.07	59.27	6.87	56.2	3.90	0.371	52.55	4.09	52.48	5.44	55.26	6.26	0.528
MUAC (cm)	23.7	5.67	24.86	5.18	28.06	5.33	0.429	25.62	3.25	25.53	2.83	26.28	6.10	0.900

TBI: traumatic brain injury; IBW: ideal body weight; MUAC: mid upper arm circumference. Data presented as mean (standard deviation).

Table 2. Baseline characteristics.

		TBI						NON TBI					
		Control		High-protein polymeric		Oligomeric		Control		High-protein polymeric		Oligomeric	
		n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
TLC (cells/ЧL)	<900	2	40.0	2	28.6	2	40.0	10	58.8	4	33.3	5	55.6
	<1,500	3	60.0	5	71.4	3	60.0	7	41.2	8	66.7	4	44.4
MUAC (cm)	<19	1	20.0	1	14.3	0	0.0	0	0.0	0	0.0	1	11.1
	19–21.9	0	0.0	1	14.3	0	0.0	1	5.9	0	0.0	1	11.1
	22–23	2	40.0	1	14.3	1	20.0	4	23.5	3	25.0	0	0.0
	>23	2	40.0	4	57.1	4	80.0	12	70.6	9	75.0	7	77.8
NUTRIC Score	0–4	5	100.0	7	100.0	4	80.0	16	94.1	12	100.0	9	100.0
	≥5	0	0.0	0	0.0	1	20.0	1	5.9	0	0.0	0	0.0
Albumin (g/dL)	≥3.5	1	20.0	1	14.3	1	20.0	5	29.4	3	25.0	3	33.3
	<3.5	4	80.0	6	85.7	4	80.0	12	70.6	9	75.0	6	66.7
Comorbid	0–1	5	100.0	6	85.7	4	100.0	16	94.1	11	91.7	10	100.0
	>1	0	0.0	1	14.3	0	0.0	1	5.9	1	8.3	0	0.0

TBI: traumatic brain injury; TLC: total lymphocyte count; MUAC: mid upper arm circumference; NUTRIC Score: nutrition risk in critically ill score; *n*: number of patients included in analysis. Data presented as mean (standard deviation).

arm circumference, and primary admission diagnosis (TBI or non-TBI). Severity-of-illness scores and laboratory assessment was conducted on 24 h from admission and on day 3, which included:. biochemical variables such as platelets, white blood cells, lymphocytes, serum creatinine levels, blood urea nitrogen (BUN) levels, albumin, serum potassium levels, serum sodium levels, serum pH, partial pressure of carbon dioxide, and partial pressure of oxygen (PO2), Acute Physiology and Chronic Health Evaluation II score (APACHE II score), Sequential Organ Failure Assessment score (SOFA score), Nutrition Risk in the Critically Ill score (NUTRIC score).

Calculation of nutritional goals and protein intake. The daily calorie and protein prescriptions were calculated from standard recommendations (calories 25–30 kcal/kg/d, proteins 1.2–2 g/kg/d). A meticulous record of the calories and protein of intake was maintained for 3 d follow up.

Study end points. Our primary outcome was changes in laboratory values and nutritional indicators from baseline to day 3.

Statistical analysis. The statistical package SPSS version 24 was used for the statistical analysis. All values were expressed as the means±standard deviation. The changes between pre and post intervention were assessed using paired *t*-test or Wilcoxon signed-rank test. Differences of mean values between the 3 groups were compared using the Anova or Kruskal-Wallis test. A *p*-value <0.05 was considered statistically significant. To interpret the magnitude of effect, Cohen's d effect sizes (±95% confidence limits) were estimated using a purpose-built spreadsheet, with effect size thresholds set at <0.20, >0.50, >0.80, >1.20, >2.0 for trivial small, moderate, large, very large, huge, respectively.

Ethical approval. The study was approved by the Faculty of Medicine, Hasanuddin University Ethics Committee.

RESULTS

The anthropometric profile and baseline characteristics of the study population are depicted in Table 1 and Table 2. During the study period, we screened 411 participants who were admitted to the ICU, 298 participants was excluded from our trial mostly due patient's mortality. A total of 113 participants included in our trial were randomly assigned to either the control (5% dextrose), high-protein polymeric or oligomeric groups. We also separated our participants based on their diagnosis, which were Traumatic Brain Injury (TBI) and non-TBI participants. Participants in the control group were given 5% dextrose as a starting feeding regimen and were continued with other types of feeding regimen based on anesthesiologist's instruction. Whereas participants in the high-protein polymeric group or oligomeric group were given a total of 5 aliquots feeding regimen via a nasogastric tube, which were administered at 4-hourly intervals. We had 48 drop-out participants during our 3 d follow-up and a total of 55 participants were included in our statistical analysis comprising both male (53%) and female (47%) subjects. Twenty-two participants were included in the control group (5 participants were diagnosed with TBI and 17 participants were diagnosed with non-TBI), 19 participants in the high-protein polymeric formula group (7 participants were diagnosed with TBI and 12 participants were diagnosed with non-TBI), and 14 participants in the oligomeric formula group (4 participants were diagnosed with TBI and 10 participants were diagnosed with non-TBI) (Fig. 1).

At the time of ICU admission, the participants which were in the condition of malnutrition based on the TLC examination (*19*). In the TBI group were 6 participants in the category of severe malnutrition and 11 participants in the category of mild malnutrition. Whereas in the non-TBI group, 19 participants were included in the category of severe malnutrition and 19 participants were included in the category of mild malnutrition. Based on patient's MUAC examination, we divided our participants in the TBI group as 2 participants were included in the category of severe malnutrition, 1 patient was included in the category of moderate malnutrition, 4 participants were included in the category of mild malnutrition, and 10 participants were included in the category of good nutrition. In the group diagnosed with non-TBI 1 participant was in the category of severe malnutrition, 2 participants were in the category of moderate malnutrition, 7 participants were in the category of mild malnutrition, and 28 participants were included in the category of good nutrition.

Before we began the intervention, a risk assessment for malnutrition was conducted to our participants based on the NUTRIC score for each participant in the TBI or non-TBI groups. The participants in this study were more dominated by participants with NUTRIC score 0–5, and hence it was included in the category of mild risk of malnutrition. Whereas for the result for serum albumin levels before the intervention, we found that the majority of our patients were in hypoalbuminemia state. Most of the participants did not have any comorbid or only had 1 comorbid, both in the TBI and non-TBI groups.

There were several variations in the duration of administration of 5% dextrose that we observed in our study's participants. In the TBI group, there were 2 participants who were given 5% dextrose for 1 d, 1 participant who was given 5% Dextrose for 2 d, and 2 participants who were given 5% Dextrose during the 3 d of our observation in the ICU. Whereas in the non-TBI group there were 2 participants who were given regular food from the beginning of entry into the ICU, 10 participants were given 5% dextrose for 1 d, 2 participants were given 5% dextrose for 2 d, and 3 participants were given 5% dextrose for 3 d.

Both of TBI and non-TBI groups who were given early enteral feeding with 5% Dextrose obtained significantly lowest amount of energy and protein intake compared to the high-protein polymeric formula group and the oligomeric formula group (Table 3, Fig. 2). In contrast, there was no significant different in energy intake between the high-protein polymeric and the oligomeric formula groups. However, protein intake was higher in high-protein polymeric formula group than those in oligomeric and control groups (Table 3, Fig. 3).

There was no difference in mean white blood cells count between pre and post-intervention for each TBI group (Table 4). Whereas for the non-TBI group, the result showed that there was a significant decrease (1,575±10,320.86) in white blood cells count between the pre and post intervention in the non-TBI group who received the intervention of high-protein polymeric formulas with Cohen's d effect sizes=3.40 (huge).

The effect of early enteral feeding on the changes in APACHE II score showed that there was no significant difference between the pre and post-intervention in the TBI group that was given 5% Dextrose (1.2±3.90) and high-protein polymeric formula (0.14±4.49), but there was a significant increase in the group given an oligomeric formula (3.2±2.49) with Cohen's d effect sizes=1.4 (very large). In the non-TBI group, it can be interpreted that there was no significant difference in mean APACHE II score between the pre and post intervention in the control (0.59±6.61) and the oligomeric formula (1.67±3.57) group, but there was a significant decrease (3.5±3.66) in the APACHE II score in the group given high-polymeric protein formula with Cohen's d effect sizes=2.5 (huge) (Table 4).

The results of statistical tests for the TBI group conducted to assess the effect of early enteral feeding on changes in NUTRIC score revealed no significant difference in NUTRIC scores between pre and post intervention for all groups. On the other hand, there was no significant difference in NUTRIC score between pre

Table 3. Feeding profile.

		TBI							NON TBI						
		Control		High-protein polymeric		Oligomeric		*p*-value	Control		High-protein polymeric		Oligomeric		*p*-value
		mean	SD	mean	SD	mean	SD		mean	SD	mean	SD	mean	SD	
Energy (kcal)	Day 1	15.41	21.16	447.43	283.51	448.00	422.52	0.017*	98.02	160.82	310.00	217.28	313.18	240.15	0.039*
	Day 2	377	324.65	710.71	284.26	842.60	369.48	0.094	336.42	260.21	634.33	212.21	672.78	214.17	0.001*
	Day 3	595.65	498.70	1200.51	259.37	1046.34	143.99	0.020*	569.04	333.14	1054.63	387.42	901.17	251.13	0.001*
	Total	988.06	765.33	2358.65	714.57	2336.94	891.93	0.019*	1003.48	583.08	1998.96	684.16	1887.12	598.72	0.000*
Protein (g)	Day 1	0	0	22.91	15.96	16.96	14.35	0.023*	2.78	8.60	15.78	12.88	11.71	9.30	0.003**
	Day 2	20.72	19.56	39.76	15.86	32.92	13.49	0.176	19.56	15.02	32.16	11.79	27.59	11.28	0.048*
	Day 3	36.40	29.23	71.36	16.91	43.91	5.64	0.017*	32.94	23.06	54.94	18.60	40.99	16.24	0.041*
	Total	57.12	44.65	134.03	42.58	93.79	26.65	0.016*	55.28	35.87	102.88	37.47	80.29	29.38	0.004*

TBI: traumatic brain injury. Data presented as mean (standard deviation).

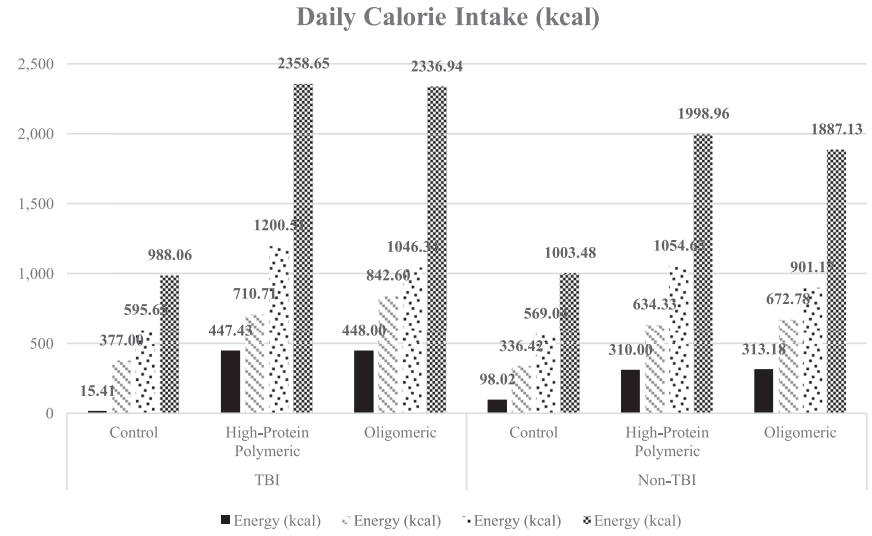

Fig. 2. Daily Calorie Intake (kcal).

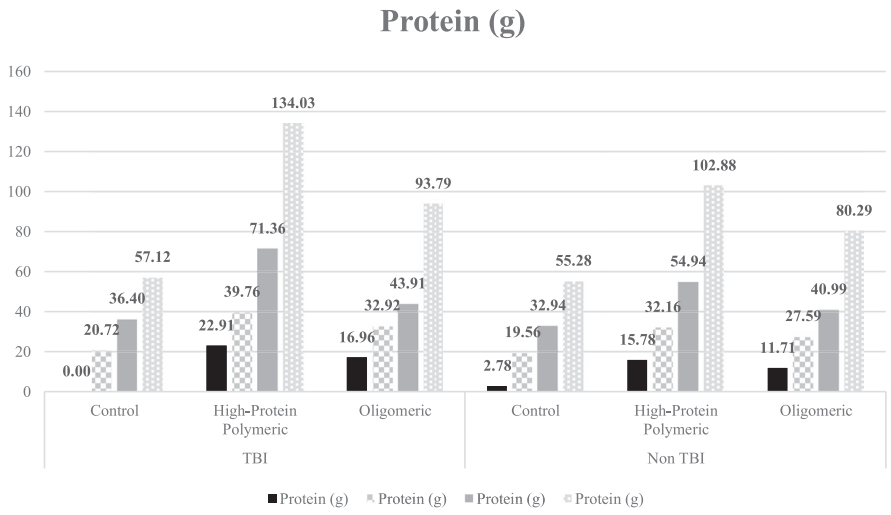

Fig. 3. Daily Protein intake (g).

Table 4. Laboratory and scoring system results at baseline and at day 3 after initiating enteral nutrition.

Parameter		TBI						NON TBI					
		Control		High-protein polymeric		Oligomeric		Control		High-protein polymeric		Oligomeric	
		mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
TLC (cells/ΨL)	Baseline	982.40	378.17	1.071.43	554.93	914.00	415.66	815.94	513.67	1,228.25	695.28	838.00	337.40
	Day 3	1.208.80	639.47	1.203.86	675.36	1.232.2	583.16	970.41	591.28	973.17	542.60	762.00	577.08
Serum Albumin (g/dL)	(Baseline	3.14	0.83	2.81	0.62	2.98	0.61	2.80	0.84	2.95	0.84	3.33	0.53
	Day 3	2.96	0.47	2.76	0.50	2.9	0.32	2.96	0.59	3.13	0.65	3.09	0.55
PLR	Baseline	167.19	82.27	151.97	51.24	279.21	211.39	482.83	454.46	296.84	270.54	351.72	271.04
	Day 3	185.95	77.70	166.52	77.4	196.33	95.70	280.00	238.60	291.89	173.74	399.32	218.10
WBC (cells/ΨL)	Baseline	10.320.00	2.107.61	11.671.43	4.530.16	15.080.00	5.987.24	16.323.53	8.069.20	13.262.50	6.963.51	1.1313.33	4.061.60
	Day 3	12.060.00	2.364.95	11.000.00	4.105.69	13.300.00	5.257.38	12,511.76	6.058.35	11.687.50	7.420.92	9.655.56	3.022.05
IL-6 (ng/mL)	Baseline	55.0	31.12	159.71	168.62	29.5	11.44	170.29	227.84	120.25	203.60	59.34	97.50
	Day 3	121.48	184.65	171.93	193.75	107.58	169.94	121.44	149.76	67.16	99.34	177.28	270.04
APACHE II Score	Baseline	19.2	8.44	21.0	4.32	23.2	5.40	16.12	6.30	17.33	3.31	17.33	3.24
	Day 3	18.0	8.63	20.86	6.15	26.4	3.13	16.71	7.30	13.83	1.95	15.67	4.80
SOFA Score	Baseline	4.6	2.19	4.43	0.79	4.2	1.10	3.18	2.01	4.00	2.66	3.44	2.46
	Day 3	4.2	2.17	5.29	2.36	4.2	1.92	3.82	3.15	2.50	1.98	3.56	2.46
NUTRIC Score	Baseline	2.0	2.12	2.57	1.40	4.0	1.87	2.88	1.80	3.08	1.44	3.22	1.48
	Day 3	2.4	2.3	2.86	2.27	4.4	1.52	3.18	2.04	1.92	1.00	3.00	1.87

Parameter		TBI				NON TBI	
		Control	High-protein polymeric	Oligomeric		Control	High-protein polymeric	Oligomeric	
		p-value	*p-value*	*p-value*		*p-value*	*p-value*	*p-value*	
TLC (cells/ΨL)	Baseline	0.596	0.514	0.345		0.389	0.113	0.314	
	Day 3								
Serum Albumin (g/dL)	(Baseline	0.709	0.827	0.700		0.452	0.548	0.212	
	Day 3								
PLR	Baseline	0.586	0.716	0.405		0.163	0.814	0.515	
	Day 3								
WBC (cells/ΨL)	Baseline	0.684	0.760	0.411		0.122	0.041*	0.094	
	Day 3								
IL-6 (ng/mL)	Baseline	0.686	0.499	0.500		0.277	0.071	0.374	
	Day 3								
APACHE II Score	Baseline	0.529	0.731	0.045*		0.718	0.007*	0.205	
	Day 3								
SOFA Score	Baseline	0.670	0.34	1.000		0.405	0.075	0.907	
	Day 3								
NUTRIC Score	Baseline	0.178	0.655	0.477		0.483	0.022*	0.645	
	Day 3								

TBI: traumatic brain injury; TLC: total lymphocyte count; PLR: platelet to lymphocyte ratio; WBC: white blood cell; IL-6: interleukine-6; APACHE II Score: acute physiology and chronic health evaluation II score; SOFA Score: sequential organ failure assessment score; NUTRIC Score: nutrition risk in critically ill score. Data presented as mean (standard deviation).

and post-intervention in the non-TBI group who received 5% Dextrose (0.29±1.69) intervention and oligomeric formula (0.22±1.39) intervention, but there was a significant decrease (1.17±1.40) in NUTRIC scores between pre and post in the non-TBI group who received high-protein polymeric formula interventions with Cohen's d effect sizes=2.6 (huge) (Table 4).TBI participants who received high-protein polymeric formula and control group's in the non-TBI patients had the shortest ICU length of stay and hospital length of stay (Table 5). There was no significant difference in mortality percentage between TBI and non-TBI groups (Table 6)

DISCUSSION

Our study was comparing the effect of 5% dextrose, high-protein polymeric formula, and oligomeric effects on critically ill patients. It revealed that early enteral feeding with high-protein polymeric formula in the treatment of non-TBI critically ill patients appears to improve patient's clinical outcomes.

The definition of energy requirements is the amount of macronutrients and micronutrients which are needed to balance energy expenditure. It is used to maintain reserve, normal metabolic, and physiological functions. Nutritional care in the intensive care unit (ICU) poses a challenge to the clinicians because the patients manifest hypermetabolism, proteolysis with nitrogen loss and accelerated gluconeogenesis and glucose utilization. The degree of metabolic response to assault depends on the length and severity of insult and is mediated through the release of cytokines and counterregulatory hormones. Other factors that influence metabolic needs during acute illness are mechanical ventilation, administration of vasoactive or sedative agents, type of the disease, the severity of illness, nutritional state before ICU admission, and comorbidities of the patient (*20*).

Guidelines recommend to give 20–25 kcal/kg/d in the acute phase and 25–30 kcal/kg/d in the recovery phase for most critically ill patients. Protein requirements are higher than normal Due to loss of total body protein, which is inevitable in the first days of ICU, even with an aggressive nutritional approach, primarily due to the catabolism of muscle. For non-previously malnourished patients, it is recommended to provide 0.20–0.25 g/kg/d of nitrogen (1.3–1.5 g proteins/kg ideal body weight/d or 1.2–2.0 g/kg actual body weight/d) and it can be increased to 0.35 g/kg/d (2.2 g/kg ideal body weight/d) of nitrogen in case of previous malnutrition or significant catabolism (*20, 21*). Although early enteral nutrition in critically ill patients with clear liquid diet (5% dextrose) as their initiation food has been used, more recent guidelines recommended the use of full liquid diet (*22*).

Head-injured patients frequently have increases in metabolic rate and protein catabolism that elevate nutritional needs. Energy expenditure may increase until 200% from normal values but factors such as delayed gastric emptying, interruptions to feeding due

Table 5. Length of stay (d).

	Groups		ICU length of stay		Hospital length of stay	
		n	Mean	SD	Mean	SD
TBI	Control	3	35.33	52.58	46.33	60.50
	High-Protein Polymeric	3	15.33	9.02	24.33	10.21
	Oligomeric	3	17.33	9.71	44.33	27.39
	p-value		0.837		0.494	
NON TBI	Control	14	4.93	2.82	13.21	7.17
	High-Protein Polymeric	10	7.60	6.20	16.60	9.35
	Oligomeric	8	6.00	3.51	17.38	6.95
	p-value		0.402		0.361	

TBI: traumatic brain injury; ICU: intensive care unit; *n*: number of patients included in analysis. Data presented as mean (standard deviation).

Table 6. Mortality percentage.

Hospital Mortality			Groups			*n*	*p*-value
			Control	High-protein polymeric	Oligomeric		
TBI	Survive	*n*	3 (60.0%)	3 (42.9%)	3 (75.0%)	9 (56.3%)	0.574
	Non-survival	*n*	2 (40.0%)	4 (57.1%)	1 (25.0%)	7 (43.8%)	
NON TBI	Survive	*n*	14 (82.4%)	9 (75.0%)	8 (80.0%)	31 (79.5%)	0.889
	Non-survival	*n*	3 (17.6%)	3 (25.0%)	2 (20.0%)	8 (20.5%)	

TBI: traumatic brain injury; ICU: intensive care unit; *n*: number of patients included in analysis.

to fasting for medical procedures, and accidental removal of feeding tubes prevent the provision of adequate nutrition. This induce up to 30% loss of body weight and signs of malnutrition in about two thirds of patients two months after hospital admission (*23–25*). In TBI patients, the nutrition goals were to reach 35–45 calories/kilogram and a protein intake of 2–2.5 g/kg on day one or as soon as possible. Adequate calories are required to prevent malnutrition and to improve healing and recovery. The brain functions as the regulator for metabolic activity leads to a complex milieu of metabolic alterations in TBI consisting of hormonal changes, aberrant cellular metabolism, and a vigorous cerebral and systemic inflammatory response in an effort to liberate substrate for injured cell metabolism. The degree of the hypermetabolic state is equal to the severity of injury and motor dysfunction (*23*). In our study, there are some expected clinical effects in the non-TBI group due to the more appropriate nutritional therapy achievement which helps to decrease the inflammation process, especially in the group which was given high-protein polymeric formula. The results of this study also found that the non-TBI group that did not receive appropriate therapy (control group) had an increased risk of malnutrition.

In the ICU, complete blood count, various biochemical tests, and inflammatory markers are a routine test which performed on patient upon their admission. A follow-up test is generally coordinated based on patient's clinical characteristics and the underlying disease (*25*). Thrombocytopenia is one of the most common laboratory abnormalities in critically ill patients, with the incidence ranging from 13–60%. It can be a result of increased platelet destruction, hemodilution process, platelet sequestration, or decreased production. Many previous studies have reported that thrombocytopenia in ICU is associated with prolonged hospital stay and reduced survival. Acute Physiology and Chronic Health Evaluation (APACHE) II score which is the most commonly used prognostic score in ICU patients does not include platelet count and albumin levels (*26*). The platelet counts and lymphocyte count are parts of complete blood count (CBC) analysis. Platelet-to-lymphocyte ratio (PLR) can be used as an inflammatory marker. It has been found to be predictive of the prognoses of patient with diverse inflammatory and ischemic conditions, such as various cardiovascular diseases, chronic inflammation disease, and tumors. A positive monotonic association between a high PLR and a poor prognosis for these diseases has been reported. Significance of PLR examination has also been developed for inflammatory status in critically ill patients. It does not require additional tests or costs as they are calculated from the hemogram, which makes it cost-effective and easy to be

applied to virtually all patient (*27–31*).

In both TBI and non-TBI groups, we observed that there was a relationship between some inflammatory markers (serum albumin levels, interleukin-6, and PLR). Albumin serum level is inversely proportional to the results of IL-6 and PLR. However, due to the limited number of samples in this study, further research is needed. To our knowledge, this is the first study to examine the relationship of PLR with interventions of early enteral feeding. Therefore, further research is still needed to assess the correlation between PLR and food intake in critically ill patients.

The results of the non-TBI group study were similar to those in respiratory ICU patients conducted in India. The enteral nutrition was initiated within the first 24–48 h following admission and was advanced toward goal over the next 48–72 h. Their goals for daily basis were 25%, 50% 75%, and 100%. They used both commercial and home-based formulas. The mortality rate was improved significantly from a 25% mortality rate to a 15% mortality rate APACHE score (*32*). This finding confirms that adequate nutritional support at right time not only reduces the participant's length of stay, ventilator support days, but also improves the overall nutritional status of the patients. Proper nutrition also has proven to reduce the mortality risk of the patients (*34*).

In contrast to the non-TBI group, there was an increasing tendency of the NUTRIC score for the TBI group after feeding administration, which is different from the existing literature results (*34*). TBI group tended to have higher energy and protein need than the non-TBI group, hence calorie and protein achievement in this group was lower.

The limitations of this study is that the calculation of calorie need was based on weight estimation, and not indirect calorimetry as a gold standard. We also did not assess the adequacy of protein intake using the more precise method of urine urea nitrogen calculation. Observation time was limited due to participant's short ICU's length of stay.

In conclusion, non-TBI patients benefit from high-protein polymeric early enteral feeding than oligomeric or 5% Dextrose. By giventhis formula, the patient had decreased of white blood cells counts, APACHE II score, and NUTRIC score.

Disclosure of state of COI

There are no conflicts of interest. The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this publication.

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