NITROGEN BALANCE AND ITS RELATION WITH ENERGY AND PROTEIN INTAKE IN CRITICALLY ILL ELDERLY PATIENTS

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Abstract—**Introduction:**Nitrogen balance in criticaly ill patients has the tendency to be negative due to stress response. In the elderly patients, the metabolic changes risk to worsening nitrogen balance. The aim of this study was to determine nitrogen balance and its correlation with energy and protein intake in critically ill elderly patients within 48 hours in ICU.

Methods: The method was cross sectional, consecutive sampling on 26 critically ill elderly subjects. Inclusion criteria were patients admitted to ICU, age ≥60 years old, male/female, whose family/relatives agreed to join this study. Patients who had urine output <0,5 mL/kg/hours were excluded. Data collected were energy and protein intake, urinary urea nitrogen (UUN), and nitrogen balance during 24 hours I and II of admission.

Results: The median age was 70 (61 – 85) years old, body mass index was 22. 9 ± 2.7 kg/m^2, most of the subjects were surgical patients. In 24 hours I and II, the nitrogen balances were -5.2 (-31.2 − -4.1) and -4.5 ± 4.6 respectively, energy intakes were not significantly different; 78.8 ± 45.0% and 91.1 ± 50.2% respectively, and protein intakes were significantly different; 34.1 + 19.3 g/d and 41.2 + 21.3 g/d respectively. There was positive correlation between nitrogen balance and energy intake; r=0.6 and r=0.5, and also between protein intake; r=0.5 and r=0.4, in 24 hours I and II respectively.

Conclusion: There were significantly positive correlation between nitrogen balance with energy and protein intake.

Keywords: elderly, critically ill, nitrogen balance, energy intake, protein intake

INTRODUCTION

Population of elderly people in the world is growing.[1] In America, half of ICU patients are elderly.[2] In Australia and New Zealand, the proportion of critically ill elderly patients in ICU had been increased 5.6% per year.[3] The prevalence of critically ill elderly patients in ICU of Cipto Mangunkusumo General Hospital in 2011 and 2013 was 19.6% and 21.2% respectively.[4] Morbidity and mortality of critically ill elderly patients are higher than young adult critically ill patients.[3,5,6]

Critically ill is a condition caused by physiologically unstable condition and organ failure that may cause death in several minutes or hours.[7] Nitrogen balance tend to be negative due to stress response. Critically ill elderly patients relatively have low muscle mass[8,9] in conjunction with higher muscle degradation.[10,11]

Energy and protein intake[12] may increase denomination of nitrogen balance in critical illness,[13-16] including elderly patients.[16] Therefore critically ill patients need an adequate nutrition intake in early handling. The ICU of RSUPNCM applies evidence-based nutrition protocol,[17-19] to restore nitrogen balance. A research by Sinaga[14] in 2013 which was done to both young adults and critically ill elderly patients in the first 24 hours of admission in ICU, concluded that patients who had energy and protein intake closer to the protocol target had better nitrogen balance.

Therefore, this study of nitrogen balance and its relationship to energy and protein intake in critically ill elderly patients was conducted in ICU of RSUPNCM. It was expected that the results of this study can be used as an evaluation for the development of nutrition management in ICU of RSUPNCM, and most other ICU. This study was done in 2 days to observe the difference of energy and protein intake between day 1 and 2. Since patients were tend to be more stable in day 2, it was expected that the energy and protein intake would be higher on day 2 compared to day 1.

METHODS

The research was held on December 2013 to June 2014, and had been approved by The Ethics Committee of the Faculty of Medicine, University of Indonesia. The inclusion criteria were male/female critically ill elderly patients, age $\geq$60 years old, and gained permission by his/her family. The exclusion criteria was urine output <0.5 mL/kg/hour. The patient will be dropped out if being unable to complete the study or had incomplete data.

The research was carried out for eight weeks with 26 subjects were analyzed. There were 33 patients admitted to ICU and approved to participate in the study by patients family. Two subjects did not complete the study, and five subjects had incomplete data.

Characteristic data such as age, gender, BMI, and nutrition intakes were taken from the medical records. Energy intake data was compared to ESPEN guideline (%).[17] Anthropometric measurements of weight and body length were done. Body weights were measured by using bed scale (Seca 984 series, with precision 0.1 kg). Body lengths were measured by using measuring tape, with precision of 0.1 cm. From anthropometric data, body mass index (BMI) and nutrition intakes were calculated. Urinary urea nitrogen (UUN) was measured from 24 hours collected urine. Nitrogen balance was calculated from nitrogen intake (protein intake in gram divided by 6.25) and UUN.

Data were analyzed using Statistical Package for Social Science (SPSS) version 20. The Shapiro-Wills normality test was used to analyze data distribution. Body mass index, energy and protein intake were presented in mean and standard deviation. Age, UUN and nitrogen balance were presented in median (minimum− maximum). T-pair test was used to analyzed the difference between energy and protein intake in 24 hours I and II. The Wilcoxon test was used to analyzed the difference of UNN and nitrogen balance in 24 hours I and II. The Man Whitney test was used to assess nitrogen balance in <50% and >50% target energy intake in 24 hours I and independent t-test in 24 hours II.

RESULTS

Characteristic data is shown in Table 1. Most subjects were digestive surgical patients, who could not receive nutrition therapy aggressively.

Energy and protein intake, UUN, and Nitrogen Balance

The target of energy intake from oral, enteral, and parenteral was referring to ESPEN guidelines for critically ill patients (20 kcal/kgBW/day). As seen in Table 2, the energy intake of subjects in 24 hours I and II was not significantly different. There was significant difference of protein intake between 24 hours I (34.1 $\pm$ 19.3 g/d) and II (41.2 $\pm$ 21.3g/d), however there were no differences of UUN and nitrogen balance between 24 hours I and II. Carbohydrate, mostly had been given in 24 hours I. Although protein intake was increased significantly in 24 hours II compared to I, UUN was not significantly different between both days. Nitrogen balance was also not significantly different.

Subject's energy intake and nitrogen balance are shown in Table 3. The number of subjects who had target energy intake $\leq$50% decreased from 8 subjects in day I to 4 subjects in day II. We then divided the subjects into group A (who had received energy intake $\leq$50% target) and group B (who had received energy intake >50% target). In group A, UUN excretion in 24 hours II was less than 24 hours I, resulting a better nitrogen balance in 24 hours II. In 24 hours II there were extreme values in group B which made nitrogen balance did not differ significantly compared to group A. There was no subject suffered from overfeeding even though their energy intake exceed 110% in group B during 24 hours II. Excessive energy intake was due to the target used for analysis was lower than target of energy intake in clinical usage.

The Correlation between Nitrogen Balance with Energy and Protein Intake

Spearman correlation test was used to analyzed the correlation between nitrogen balance with energy and protein intake in 24 hours I, and Pearson correlation test was used in 24 hours II. The correlation between nitrogen balance with energy intake in 24 hours I and II were significantly positive; r=0.6 and r=0.5. The correlation between nitrogen balance with protein intake in 24 hours I and II were significantly positive; r=0.5 and r=0.4. These results can be seen in Figure 1 to 4.

Table 1 Characteristic of the Subjects

Variable	Results
Gender	
- Male, n(%)	11 (42)
- Female, n(%)	15 (58)
Age (years)	70 (61−85)
BMI* (kg/m2)	22.9 ± 2.7
Diagnosis	
- Nonsurgical, n(%)	6 (23)
- Surgical, n(%)	20 (77)
Nutrition delivery method in 24 hours I	
- Total Enteral, n(%)	18 (69)
- Total parenteral, n(%)	0 (0)
- Enteral and parenteral, n(%)	8 (31)
Nutrition delivery method in 24hours II	
- Total enteral, n(%)	13 (50)
- Total parenteral, n(%)	0 (0)
- Enteral and parenteral, n(%)	8 (31)
- Oral and enteral,n(%)	4 (15)
- Oral	1 (4)

Table 2 Energy, protein intake, and nitrogen balance 24 hours

Variable	24 hours I	24 hours II	δ	p
Energy intake (%)	78.8 ± 45.0	91.1 ± 50.2	12.3 ± 5.1	>0,05
Protein intake (g/d)	34.1 ± 19.3	41.2 ± 21.3	7.1 ± 2	<0.05
UUN *(g/d)	6.3 (1.7−27.2)	6.75 (2.1−23.3)	0.45 (0.4−3.9)	>0.05
Nitrogen balance	-5.2 (-31,2− -4,1)	-4.5 ± 4.6	1.3 ± 1.2	>0.05

Table 3 Energi Intake and Nitrogen Balance in 24 Hours I dan II

Group	Energy Target	n (26)	Energy Intake (%)	p	UUN* (g)	p	Nitrogen Balance (g)	p
24 hours I								
A	≤50%	8	31.9 ± 15.1	<0.001	7.7 ± 8.2	>0.05	-9.7 ± 8.9	<0.05
B	>50%	18	99.6 ± 37.5		7.1 ± 3.3		-4.1 ± 3.4	
24 hours II								
A	≤50%	4	26.7 ± 10.3	<0.005	4.5 ± 2.1	>0.05	-6.9 ± 2.2	>0.05
B	>50%	22	102.8 ± 45.2		7.7 ± 4.4		-4.1 ± 4.8	

*UUN: Urinary urea nitrogen

The correlation was weaker in 24 hours II because there was an extreme values, in which higher energy and protein intakes brought a more negative nitrogen balance. By excluding the extreme values from analysis, the correlation will be much stronger, with r=0.7 for the correlation between nitrogen balance with energy intake in both 24 hours I and II. The correlation between nitrogen balance with protein intake in 24 hours I and II were r=0.5 and r=0.7. The extreme values was probably due to patient who had second digestive surgical within 14 days who possibly has more severe catabolism.

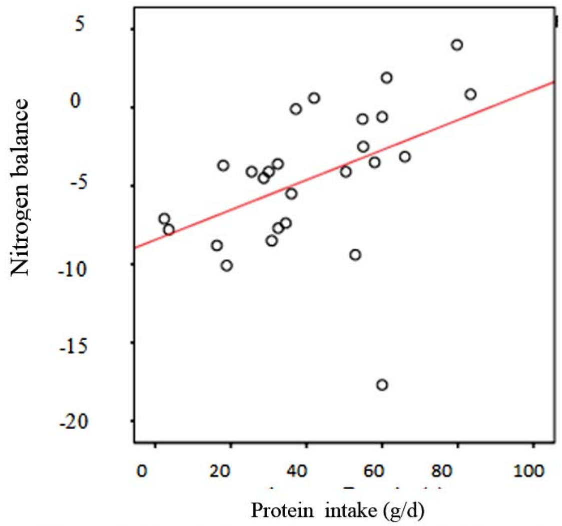

Figure 4. Correlation between protein intake and nitrogen balance in 24 hours II

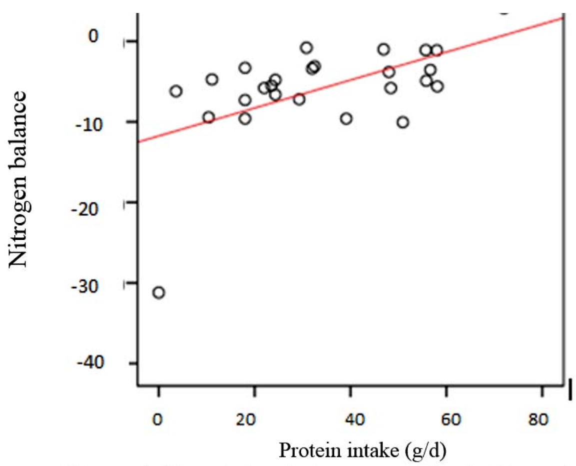

Figure 2. Correlation between protein intake and nitrogen

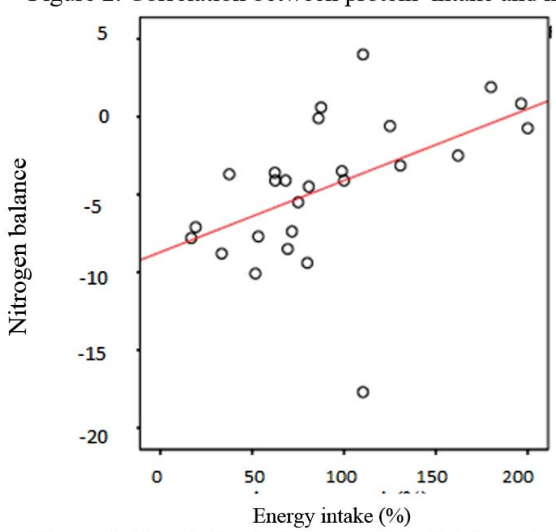

Figure 3. Correlation between energy intake and nitrogen balance in 24 hours II

DISCUSSION

The median age of the subjects was 70 (61-85) years old, UUN is lower in elderly patients which may caused by lower muscle mass.[16] The BMI in this study was in normal category.[20]

Energy Intake

Nutrition given to patients in this research is based on the guidelines: all patients who are expected not be able to receive full oral diet within three days should receive enteral nutrition.[17] Also, if nutrition needs could not be fulfilled with enteral nutrition, or if enteral nutrition is contraindicated or intolerable, then the patient should receive parenteral nutrition within 24 to 48 hours.[18] Therefore, energy intake in 24 hours I and II was similar.

Energy intake in this research was higher than research by Sinaga,[14] 2013 in ICU of RSUPNCM (56.3 $\pm$ 33.9%), which used the same guidelines. At that time, commercial enteral nutrition was not available yet in Nutrition Unit in RSUPNCM, thus complete nutrition enteral feeding could not be given as soon as patients could be fed. Energy intake in O'Meara[21] research was 56.3 $\pm$ 33.9% using Harris-Bennedict equation. Krishnan[22] study based on American College of Chest Physician (ACCP) guidelines (25−27 kcal/kgBW/d) energy intake was 50.6%. Japur[23] research using indirect calorimeter was able to meet 92% energy intake target. A multicenter research by Heyland[24] from 2007 to 2009 concluded that energy intake could only reach 40−50% from calorie target.

The guidelines formula have some variables, such as weight, age, sex, stress factors, and others into account. It is necessary to use an accurate method to calculate target of nutrition intake for critically ill elderly patients. Indirect calorimeter can be used to measure total nutritional daily needs which fluctuating in critically ill patients, and misallocation of formula-based total energy target from variable data inaccuracies can be avoided.

Protein Intake

Based on guidelines, protein needs for critically ill patients is 1.5 to 2 g/kgBW/d.[17] In this study protein intake reached 0.6 g/kgBW/d (34.1 $\pm$ 19.2 g/d) in 24 hours I, and 0.7 g/kgBW/d (41.2 $\pm$ 21.3 g/d) in 24 hours II. Protein intake in this study was higher than research by Sinaga[14] (23.75 ± 16.87 g/d), but less than Japur[23] (59.37 ± 32.5 g) and Dickerson[16] studies (1.1 g/kgBW/d in elderly and 1.3 g/kgBW/d in adult critically ill). Hoffer[15] reviewed 13 studies published from 1948 to 2012 which strongly suggest 2 to 2.5 g/kgBW/d protein intake for critically ill patients, however obviously most critically ill patients could only take less than half of the common recommendation (1.5 g/kgBW/d).

By using guidelines for nutritional management, energy intake in ICU of RSUPNCM can achieve the target of 20 kcal/kgBW/day at 24 hours I and II. However, protein intake target according to the recommendations could not be achieved, despite an increase in protein intake on 24 hours II. This was due to the low energy intake target at the beginning of critically ill. Nevertheless, if patient's critical condition can be stabled then energy intake target can be raised, thus protein intake is also expected to raise.

Urinary Urea Nitrogen (UUN)

In acute phase of critical illness, inflammation and immobilization cause great protein degradation.[10] The degradation of body protein can cause the increase of nitrogen excretion.[25]

Urinary urea nitrogen in this study was less than research by Sinaga[14] (8.3 ± 4.4 g/d), and Japur[23] studies (14.7 ± 4.8 g/d). The subjects in those studies were relatively young. According to Dickerson study,[16] aside from less lean muscle mass in elderly, less severity of illness can also lower UUN excretion in critically ill elderly patients. However, this study did not measure the severity of illness which brought a limitation of this study.

Nitrogen Balance

In acute phase of critically ill, nitrogen balance is always negative due to inflammation[26] and immobilization.[11] In Mohil[27] study, nitrogen balance did not seem to be less negative even on the fourth day post operation, eventhough protein intake was raised. It was because the amount of protein (0.2 to 0.8 g/kgBW/d) was not enough to make nitrogen balance better. It was less protein intake than in Hoffer[15] and Dickerson[16] studies. In Dickerson[16] study, nitrogen balance measurement was done on day 5 to 14 post-trauma, therefore it is possible that the influence of inflammation had been reduced at that time. Another possibility is that protein intake in this study (0.6 - 0.7 g/kgBW/d) and Mohil's (0.2 - 0.8 g/kgBW/d) [27] were less than protein intake in Dickerson's[16] study and Hoffer's[15] review.

Energy intake also had an important role to improve nitrogen balance. Kan et al[28] showed evidence that nitrogen balance would become positive on the seventh day of critical illness, if the patients had sufficient energy intake.

The Correlation between Nitrogen Balance with Energy and Protein Intake

In this study, the correlation between nitrogen balance and energy and protein intake in the 24 hours I and II were significantly positive. Dickerson[16] concluded there were no significant difference on correlation between nitrogen balance and protein intake in young adult and elderly critically ill patients. The correlation between nitrogen balance and energy intake in Sinaga's[14] study (subjects; age 48 ± 13.2 years old) had similar value with this study. According to her study the correlation between nitrogen balance and energy intake in 24 hours were not different between young adult and elderly critically ill patients.

In conclusion, there were significantly positive correlations between nitrogen balance with energy and protein intake. Further research is needed to determine nitrogen balance difference in surgical and non surgical patients, and also whether the disease severity affect the nitrogen balance. Periodic examination of nitrogen balance should be considered to assess body response to energy and protein intake, in order to evaluate nutritional intake adequacy on critical ill elderly patients.

Conflicts of Interest

Authors declared no conflict of interest regarding this study.

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