The effect of high protein enteral nutrition on protein status in acute stroke patients

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Abstrak

*Penelitian ini dilakukan untuk mengetahui pengaruh pemberian nutrisi enteral tinggi protein pada status protein penderita stroke akut. Subjek penelitian dibagi 2 kelompok secara randomisasi blok, yaitu kelompok perlakuan mendapat nutrisi enteral tinggi protein (NETP) dan kelompok kontrol mendapat nutrisi enteral standar rumah sakit (NERS). Tiga puluh enam subjek dari 60 penderita stroke akut berhasil menjalani 7 hari penelitian ini. Hasil penelitian menunjukkan bahwa pemberian NETP dapat meningkatkan kadar prealbumin serum, menurunkan ekskresi kreatinin urin, dan memperkecil penurunan kadar albumin serum dibandingkan kelompok kontrol. (**Med J Indones 2005; 14: 37-43**)*

Abstract

*The objective of this study was to determine the effect of high protein enteral nutrition on protein status in acute stroke patients. The subjects were divided into two groups using block randomisation, i.e. the intervention group that received high protein enteral nutrition (HPEN), and the control group that received enteral hospital diet. Thirty six out of 60 acute stroke patients had completed 7 days of follow-up. The results showed that HPEN have increased prealbumin level, decreased urinary creatinine excretion, and decreased the decline of albumin serum compared to the control group. (**Med J Indones 2005; 14: 37-43**)*

Keywords: albumin, prealbumin, urinary urea nitrogen, urinary creatinine, nitrogen balance

The identification of undernutrition may have important clinical implications on a hospital patient's outcome. Numerous studies have demonstrated positive associations between specific clinical markers of undernutrition and morbidity or mortality in acute clinical care environment. Stroke patients are particulary at risk of undernutrition because the majority are old and have premorbid fraility. Up to 16% of stroke patients may be undernourished on admission to hospital and undernutrition tends to worsen during the hospital stay, especially in the more dependent patients.[1]

In stroke patients, neurologic defect after stroke such as swallowing difficulty, reduced consciousness, motor and sensory dysfunction, and communication difficulties also lead to poor nutritional intake. Furthermore, stress response in acute stroke may lead to undernutrition by hypercatabolism and hypermetabolism. Both stress and undernutrition can worsen the prognosis by decreasing protein synthesis and increasing protein degradation, thus reducing the circulating levels of proteins such as albumin and prealbumin.[1,2] Hypoproteinemia may complicate an illness and its treatment and has been associated with reduced wound healing, wound dehiscence, decubitus ulcer formation, reduced immune responsiveness, and reduced small intestinal mobility and absorbtion.[3]

There is evidence that nutritional supplementation improves nutritional status and can reduce morbidity and mortality.[3] Adequate nutritional support in stroke patients has been found to decrease complication rate, shorten the length of hospital stay, improve functional outcome and lower mortality.[1,4]

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The aim of this study was to determine the effect of high protein enteral nutrition on protein status in acute stroke patients.

METHODS

This study was conducted from September 2002 through March 2003, at IRNA B, Department of Neurology, Cipto Mangunkusumo General Hospital, Jakarta. Inclusion criteria for subjects enrolled in this study were (1) had hemorrhage or ischaemic stroke diagnosed by CT scan or clinical examination; (2) admission delay of less than 48 hours from onset of stroke; (3) had swallowing problem. Exclusion criteria were (1) hepatic or renal impairment; (2) blood glucose level at admission $\geq$ 200mg %; and (3) were receiving ongoing corticosteroid treatment for more than 2 weeks. The subjects were allocated to the intervention or control group using block randomization.

Nutritional status was assessed on admission. The anthropometric measurements done were body weight, height, and body mass index. Laboratory assessments were (1) albumin and prealbumin level on the 1st and 7th day; (2) urinary urea nitrogen (UUN) and urinary creatinine on the 1st, 4th, and 7th day using a 24-hour urine collection. Nitrogen balance was calculated by substracting nitrogen intake with urinary urea nitrogen.

On the 1st and 2nd day, both groups received the hospital enteral nutrition appropiate to basal energy expenditure (BEE) which were calculated using Harris Bennedict equations.[4,5] On the 3rd until the 7th day, the intervention group were given high protein enteral nutrition (HPEN), which was equal to total energy expenditure (BEE + thermic effect of food + physical activity + stres factors),[5] whereas the control group was given enteral hospital diet (Table 1).

Statistical analysis

Statistical program for social science (SPSS) version 10 was used for data analyses. Descriptive data are presented in mean $\pm$ SD, median, and minimum-maximum values. Comparison between intervention and control groups were analyzed using t-test if the distribution of the data was normal, and using Mann-Whitney test if the distribution of the data wasn't normal.

Comparison between pre and post intervention measurements were analyzed using dependent t-test if the distribution of the data was normal, and using Wilcoxon test if the distribution was not normal.

RESULTS

There were 342 patients admitted to IRNA B, and sixty subjects were recruited into the study. On the follow up, 24 patients were droped out due to death (12 patients), stress ulcer (5 patients), discharged without permission (5 patients), and transfer to another place (2 patients). Overall, there were 36 patients, 18 patients in each group who had completed the study.

Characteristics of the subjects are shown in table 2. Anthropometric and laboratory indices in the two study groups were similar. Baseline serum albumin and prealbumin level tended to be higher in the control group compared to the intervention group, but it was not significant. On the 1st day, in both groups, UUN was above the normal range, nitrogen balance was negative, and the urinary creatinine was in the normal range.

Table 1. Ingredients and nutrition value of enteral nutrition

	Hospital enteral nutrition	High protein enteral nutrition (Peptisol)®
Ingredients :	Dancow full cream®, skim milk powder (Tropicana Slim)®, low lactose milk (LLM), egg, sugar, peanut oil, rice powder, orange juice	Maltodextrine, sugar, vegetable oil, soy lesitin, mineral and vitamins
Nutrition value / 1000 ml :	Carbohydrate = 125 g (51%)[*] Protein = 43.4 g (18%)[*] Fat = 34.25g (31%)[*]	Carbohydrate = 140.4 g (56%)[*] Protein = 56 g (22.4%)[*] Fat = 24 g (21.6%)[*]

[*] = percentage of energy intake

Table 2. Baseline characteristics of the intervention and control group

	Intervention group (n = 18)	Control group (n = 18)	Difference
Age (years)	54.44 (31-72)[**]	58.44 (43-82)[**]	NS[m]
Body weight (kg)	60 ± 10.08[*]	61.89 ± 12.76[*]	NS[t]
Height (cm)	158.72 ± 7.06[*]	161 ± 10.23[*]	NS[t]
BMI (kg/m^2)	23.75 ± 3.09[*]	23.64 ± 3.29[*]	NS[t]
Albumin (g/dL)	3.77 ± 0.51[*]	3.80 ± 0.17[*]	NS[t]
Prealbumin (g/L)	0.16 (0.10-0.30)[**]	0.18 (0.09-0.27)[**]	NS[m]
UUN (g/24 hours)	7.50 (2-13)[**]	7.50 (2-12)[**]	NS[m]
Nitrogen balance (g/24 hours)	-2.20 (-7.85-2.91)[**]	-2.47 (-6.40-3.60)[**]	NS[m]
Urinary creatinine (mg/24 hours)	1019 (307-1530)[**]	1176 (311-2372)[**]	NS[m]

BMI= body mass index, UUN= urinary urea nitrogen, [*] = mean ± SD, [**] = median (minimum-maximum),
NS= not significant (p > 0.05), [t] = independent t test, [m]= Mann-Whitney test

Energy intake in both groups on the 1st and 2nd day were similar, while starting on the 3rd day the intervention group received more protein and carbohydrate than the control group (table 3). Protein intake in intervention and control group was 1.6 and 0.9 g/kg per day, respectively.

Table 3. Energy intake, basal energy expenditure and total energy expenditure in the intervention and control groups during the study

	Intervention group (n = 18)	Control group (n = 18)	Difference
On 1st and 2nd day			
BEE (kcals)	1287.56 ± 150.87[*]	1323.41 ± 245.82[*]	NS[t]
Energy intake (kcals):	1303.82 ± 176.47[*]	1313.47 ± 260.11[*]	NS[t]
Protein (g)	55.50 ± 9.64[*]	57.13 ± 12.18[*]	NS[t]
Fat (g)	47.50 (19.80 – 60.23)[**]	50.82 (27.55 – 72.40)[**]	NS[m]
Carbohydrate (g)	168,46 ± 22,78[*]	164.75 ± 30.61[*]	NS[t]
On 3rd until 7th day			
TEE (kcals)	1759.92 ± 216.69[*]	1789.02 ± 325.86[*]	NS[t]
Energy intake (kcals):	1763.97 ± 213.02[*]	1760.55 ± 308.21[*]	NS[t]
Protein (g)	97.56 ± 11.86[*]	75.29 ± 13.75[*]	S[t]
Fat (g)	42.07 ± 5.08[*]	65.06 ± (32.45 – 84.7)[**]	S[m]
Carbohydrate (g)	249.74 ± 30.88[*]	224.66 ± 43.35	S[t]

BEE= basal energy expenditure, TEE= total energy expenditure, [*]= mean ± SD, [**]= median (minimum-maximum),
S= significant (p < 0.05), NS= not significant (p > 0.05), [t]= independent t test, [m]= Mann-Whitney test
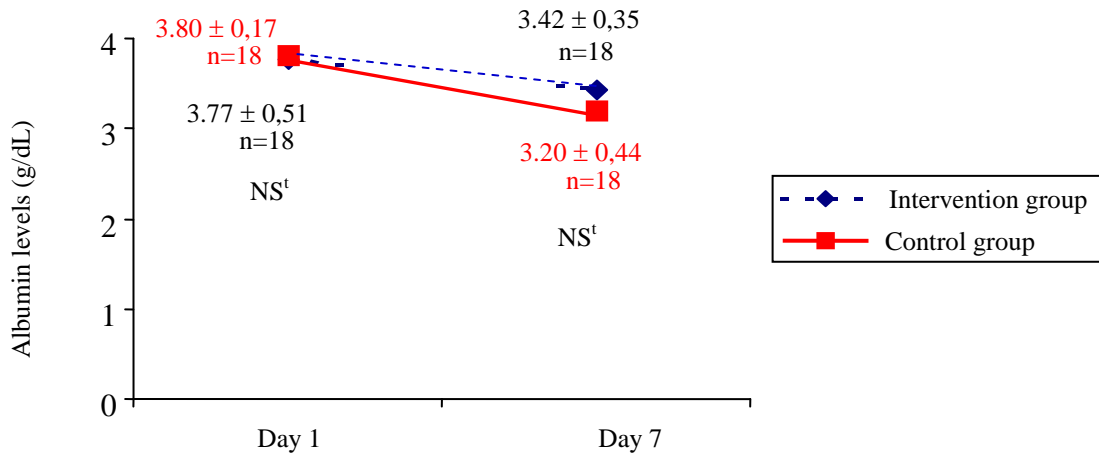
Figure 1. Albumin levels in the intervention and control goups

Value= mean ± SD, NS= not significant (p > 0.05), ^{t}= t test

Figure 1 shows the change in albumin level in both groups at admission and the 7th day. There was no significant difference in albumin level between the two groups, although in the control group, there was a higher decrease compared to the intervention group.

There was a significant difference in the change of prealbumin level (between the 1st and the 7th day) between the two groups. In the intervention group, there was a slight increase in prealbumin level, while in the control group, there was a decline in prealbumin level (Figure 2).
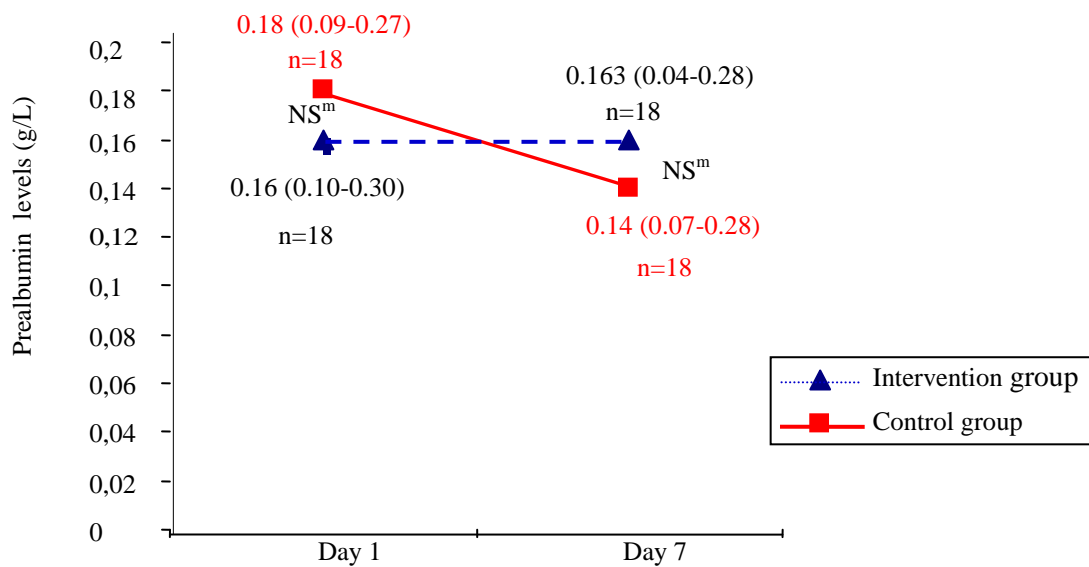
Figure 2. Prealbumin levels in the intervention and control group

Values= median (minimum - maximum), NS= not significant (p > 0.05), ^{m}= Mann Whitney test
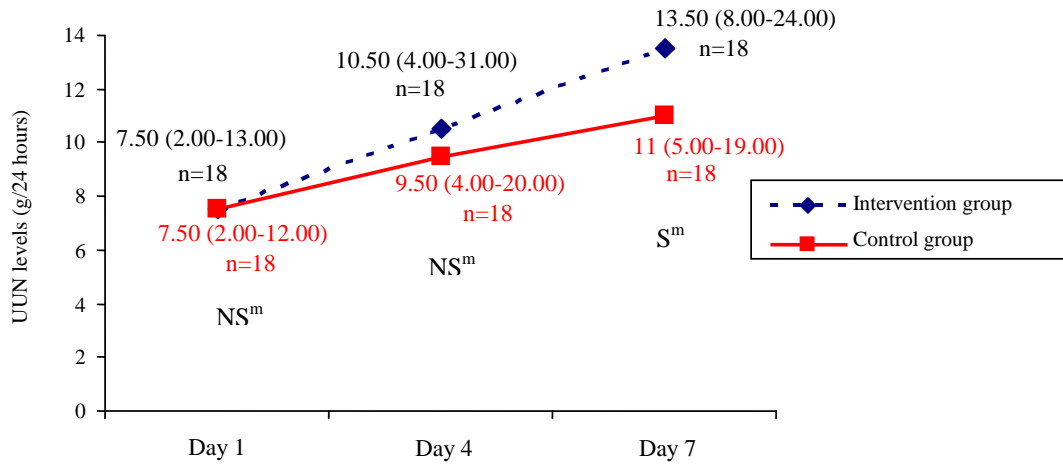
Figure 3. Urinary urea nitrogen on day 1, 4, and 7 in the intervention on and control groups

Value= median (minimum - maximum), NS= not significant (p > 0.05), S= significant (p < 0.05), ^{m}= Mann Whitney test
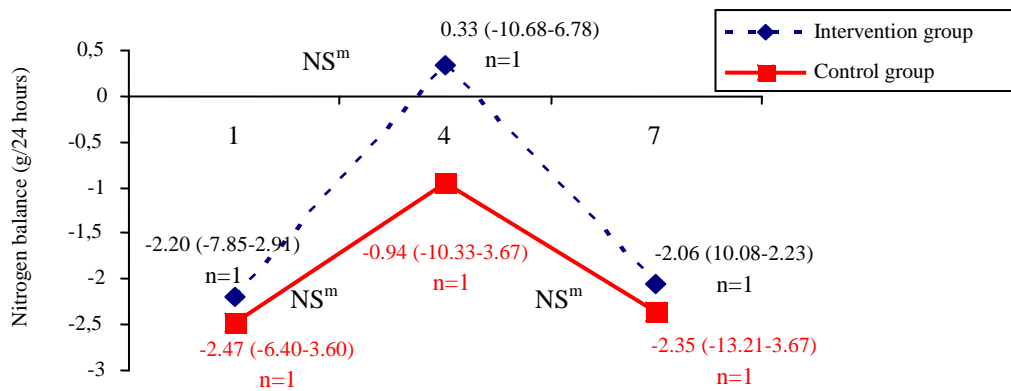

Figure 4. Nitrogen balance on day 1, 4, and 7 in the intervention and control groups

Value= median (minimum - maximum), NS= not significant (p > 0.05), ^{m} = Mann Whitney test
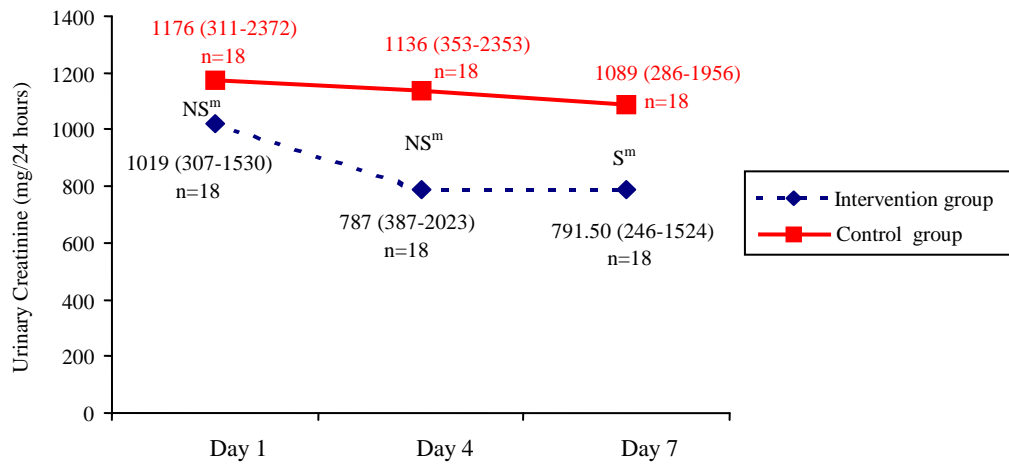

Figure 5. Urinary creatinine on day 1, 4, and 7 in the intervention and control groups

Value= median (minimum - maximum), NS= not significant (p > 0.05), S= significant (p < 0.05), ^{m}= Mann Whitney test

Figure 3, 4, and 5 showed urinary urea nitrogen, nitrogen balance, and urinary creatinine respectively, that was measured on day 1, 4, and 7, in the intervention and control groups.

DISCUSSION

The average energy intake in both groups compared to the energy requirement during the study period was more than 95%, and no significant difference was found in terms of the energy intake in both groups (Table 3). Enteral feeding is effective in improving nutritional intake and status in stroke patients.[1] Enteral nutrition generally is preferred over parenteral feeding because it is more physiologic, and maintains gastrointestinal tract integrity, and acts as intestinal mucosal barrier to bacteria. Furthermore large quantities of energy can be provided enterally without fluid overload.[6]

In this study, we monitored albumin and prealbumin level. Ideally, a protein marker should readily respond to changes in nutrient intake, and is not influenced by other disease processes. The marker must have a short biologic half-life, exists in a relatively small pool, has a predictable catabolic rate, and a rapid rate of synthesis that responds only to protein intake.[7]

Albumin level is a traditional marker that has long been used in assessments of hospital patients, and it is useful in identifying long-term malnutrition. However, serum albumin is not very sensitive to short-term changes in protein status. It has a large body pool, a long half-life (20 days), and is affected by many factors other than protein energy nutritional status. A large propotion of albumin is present in extravascular compartments, and can be mobilized during periods of protein depletion. Albumin level is also sensitive to variations in hydration and liver function.[8,9]

On the other hand, prealbumin has a short half-life (2 days) and a small body pool, which makes it sensitive to fairly rapid changes in protein energy status and responds more rapidly to dietary treatment. Prealbumin level is not affected by hydration status, and is less affected by liver disease compared to other serum proteins.[7,9] In patients who are receiving nutritional support, a response in prealbumin level can be anticipated as early as four days after supplementation is started, with a definite response at the 8th day.[7]

Seven days after admission there was a decline in serum albumin level in the two groups, especially in the control group (Figure 1). In addition, serum prealbumin level was a slightly increased in the intervention group, while in the control group it was markedly decreased (Table 2). The protein intake were significantly greater in the intervention group (1.6 g/kg per day vs 0.9 g/kg per day). This fact suggested that dietary high protein could maintain albumin level, and improve prealbumin level.

The catabolic state and associated neuroendocrine response that is likely to follow acute stroke may lead to altered serum albumin concentration in the period immediately after the stroke. There was already an evidence linking high stress reaction during the first week after the stroke and undernutrition.[10] In this study, serum albumin was used to indicate the degree of stress, while serum prealbumin was used to observe response to dietary treatment. Stroke patients with hypoalbuminemia had greater risk of infective complications and poor functional outcome during hospitalization compared to those with normal or higher serum albumin concentrations.[11]

Urinary urea nitrogen excretion in the intervention group was higher than the control group. This phenomenon was caused by more substantial protein intake from HPEN. Raised UUN may come from some of ingested protein that is catabolized and converted to UUN.[3] In this study, there was negative nitrogen balance since the 1st day. Usually, metabolic response to stress is characterized by an accelerated catabolism of lean body or skeletal mass that clinically results in negative nitrogen balance. To meet the increased metabolic demands, higher levels of both calories and protein are required.[12] A report indicated that aggressive nutritional support did not prevent substantial body protein loss during severe catabolic illnesses.[10] However, aggressive nutritional support decreases negative nitrogen balance by supplying the liver with substrates for protein synthesis and subsequently reducing the need for endogenous proteins from peripheral tissue.[3]

A decreased urinary creatinine in the intervention group was consecutively followed by improvement in nitrogen balance on the 4th day, although on the 7th day there was recurrent negative nitrogen balance again with increased urinary creatinine excretion. Furthermore, this study suggests that the flow phase

of the metabolic stress occurred after the 4th day of the onset of stroke, therefore patients with acute stroke must be considered to be reevaluated for energy-protein requirement after the 4th day.

In conclusion, in the intervention group, there was a slihgt increase in prealbumin level, while in the control group the prealbumin level was markedly decreased. The albumin level was decreased in both groups, but albumin level in the intervention group decreased less than the control group. In the intervention group, urinary creatinine excretion decreased significantly, but UUN and nitrogen balance did not show any improvement. Therefore, HPEN in a certain period was able to improve the protein status of acute stroke patients.

Acknowledgment

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