Improvement of Nutritional Status in Liver Cirrhotic Patients with Adequate Dietary Feeding and High Branched-chain Amino Acids Supplementation

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ABSTRACT

***Background**: There is still a high prevalence of malnutrition among liver cirrhotic patients despite the fact that it deteriorates their prognosis. Pre-albumin can be used as a parameter to evaluate short-term nutritional status. This study was conducted to find out the overall outcome of calories and protein diet, and substitution of branched-chain amino acids (BCAA) to enhance pre-albumin serum level in cirrhotic patients with malnutrition.*

***Method**: This was a quasi-experimental study conducted in liver cirrhotic patients who visited Koja Hospital between April and September 2009. Mid-arm muscle circumference (MAMC) was used to evaluate nutritional status. Those with MAMC below the 15th percentile were considered as malnourished. Diet of adequate calories and protein with the substitution of 2 x 4 scoop (± 60 g) BCAA milk powder in 200 mL warm water twice daily (± 7.3 g BCAA) was given for two weeks. Pre-albumin serum level was subsequently monitored (before and after intervention) to see if there were any nutritional status changes. Data was analyzed using dependent student T-test with SPSS version 15.0.*

***Results**: There were eligible 16 patients. The average pre-albumin level after diet intervention for two weeks was significantly higher than those before the intervention; i.e. from 5.8 (2.2) mg/dL to 6.8 (2.1) mg/dL, with p = 0.004.*

***Conclusion**: Diet of adequate calories and branched-chain amino acid can improve the pre-albumin serum level in liver cirrhotic patients with malnutrition.*

***Keywords:** cirrhosis, malnutrition, pre-albumin, BCAA*

ABSTRAK

***Latar belakang**: Prevalensi malnutrisi pada sirosis hati masih cukup tinggi, padahal malnutrisi dapat memperburuk prognosis sirosis hati. Pre-albumin merupakan parameter nutrisi yang dapat digunakan untuk evaluasi status nutrisi jangka pendek. Tujuan penelitian ini adalah untuk mengetahui apakah diet dengan kalori dan protein adekuat serta substitusi asam amino rantai cabang (AARC) dapat meningkatkan pre-albumin darah pada pasien sirosis hati dengan malnutrisi.*

***Metode:** Penelitian kuasi eksperimen dilakukan pada pasien sirosis hati yang berkunjung ke Rumah Sakit Koja antara bulan April sampai September 2009. Status gizi diketahui dengan mengukur lingkar lengan atas (LILA). Pasien dinyatakan malnutrisi apabila LILA < persentil 15. Kepada pasien diberikan diet kalori dan protein adekuat dengan substitusi AARC sebanyak 2 x 4 sendok (± 60 g)/hari yang dilarutkan dalam 200 mL air hangat (mengandung ± 7,3 g AARC) selama dua minggu. Perubahan status nutrisi diukur dengan pemeriksaan kadar pre-albumin darah saat sebelum dan sesudah intervensi. Data dianalisis menggunakan uji-T dependen dengan program SPSS 15.*

***Hasil:** Didapatkan 16 pasien yang memenuhi kriteria penelitian. Hasil rata-rata pre-albumin sesudah pemberian diet kalori dan protein adekuat dengan substitusi asam amino rantai cabang (AARC) selama dua*

minggu menunjukkan hasil secara bermakna lebih tinggi dibandingkan sebelum intervensi yaitu dari 5,8 (2,2) mg/dL menjadi 6,8 (2,1) mg/dL; p = 0,004.

***Simpulan**: Kepada pasien sirosis hati dengan malnutrisi dapat diberikan diet kalori dan protein adekuat dengan substitusi AARC untuk memperbaiki kadar pre-albumin darah.*

***Kata kunci**: sirosis, malnutrisi, pre-albumin, AARC*

INTRODUCTION

Malnutrition in liver cirrhosis is commonly associated with increased morbidity and mortality. Malnourished liver cirrhotic patients have higher incidence of encephalopathy, infection, and variceal bleeding.[1,2] Malnutrition develops in patients with liver cirrhosis due to inadequate intake, impaired absorption, and hypermetabolic state.[1] Restricted protein intake is often suggested to liver cirrhotic patients who also have encephalopathy. However, long-term protein restrictions will result in malnutrition, which may lead to increased mortality rate.[2] European Society for Clinical Nutrition and Metabolism (ESPEN) in 2006 recommends a diet plan of 35-40 kcal/kg/day and 1.5 g/kg/day of protein for malnourished liver cirrhotic patients.[3]

Anthropometric examination of mid arm muscle circumference (MAMC) has been considered the most reliable measurement. It can predict survival rate in liver cirrhotic, especially when there is edema and ascites.[4,5] Pre-albumin is a laboratory parameter that is considered most ideal to assess changes in nutritional status, particularly for short-term due to its short half-life (2-3 days).[6] The aim of this study was to find out the overall outcome of calories and protein diet, and substitution of BCAA to enhance pre-albumin serum level in malnourished cirrhotic patients.

METHOD

This study was conducted in Koja Hospital between April and September 2009, with a quasi-experimental pre-and post-test design. The aim was to know the improvement of pre-albumin level after administration of adequate calories and protein intake with BCAA substitution in malnourished liver cirrhotic patients. Samples were taken using consecutive sampling (non-probability sampling) method. Sample size was determined using formula of $n=\left[\frac{(z_\alpha+z_\beta)\times s_d}{d}\right]^2$ with α = 0.025 (one side) and power (β) = 0.90.

The diagnosis of liver cirrhosis was established histologically or based on the presence of at least two of the following characteristic imaging features of esophageal or gastric varices, ascites or increased international normalized ratio (INR) that could not be attributed to any other cause.[4]

Nutritional status was assessed by measuring the mid-arm muscle circumference (MAMC). Patients were considered to be malnourished when MAMC was below the 15th percentile, according to Frisancho reference data (NHANES I and II).[7] Pre-albumin level was determined to assess the nutritional status improvement by using nephelometric technique. The level of 24.8-37.2 mg/dL was considered as normal value.[7,8] Adequate calorie and protein intake with BCAA substitution of 35–40 kcal/kgBW and protein 1.2-1.5 g/kgBW was administered to produce improved nutritional status.[3]

Inclusion criteria were liver cirrhotic patients with malnutrition who had MAMC measurement below the 15th percentile. Subjects were excluded if they had suffered from acute infection, gastrointestinal bleeding, or had been recently discharged from hospitalization within less than two weeks due to acute complication of liver cirrhosis. All patients who met the inclusion criteria were measured for their MAMC and their venous blood samples were drawn for the examination of pre-albumin, albumin and bilirubin level, as well as the prothrombin time. The subjects were informed about adequate calories and protein intake. Afterwards, all subjects were given BCAA substitution 60 g twice daily for two weeks and re-measurement of their pre-albumin level was subsequently carried out. Statistical analysis for the pre-post test design included the paired T-test or Wilcoxon test by using SPSS version 15.

RESULTS

There were 16 patients who had fulfilled the criteria, i.e. 14 (87.5%) male and 2 (12.5%) female subjects. Most subjects (75%) had age range from 40 to 60 years and most of them had Child-Pugh score B (93.8%). No complaint on side effects of BCAA had been reported by the subjects (Table 1).

Statistical analysis showed that the mean pre-albumin levels after adequate calories and protein intake including BCAA were significantly higher than

those before the intervention 5.8 (2.2) mg/dL to 6.8 (2.1) mg/dL, p = 0.004 (Figure 1).

Table 1. Subject characteristics

Variable	n (%)
Sex	
Male	14 (87.5)
Female	2 (12.5)
Age (year)	
< 40	2 (12.5)
40-60	13 (75.0)
> 60	2 (12.5)
BMI (kg/m^2)	
< 16.0	0 (0)
16.0-16.9	1 (6.2)
17.0-18.4	3 (18.8)
Normal (18.5-24.9)	12 (75)
TSF (mm)*	6 ± 2.1
MAMC (cm)*	21 ± 2.2
Child Pugh	
B	15 (93.8)
C	1 (6.2)
Pre-albumin level (mg/dL)*	5.8 ± 2.2

BMI: body mass index; malnutrition cut off point < 16.0 severe, 16.0-16.9: moderate, 17.0-18.4: mild, 18.5-24.9: normal; TSF: triceps skinfold thickness; MAMC: mid-arm muscle circumference (cm); *mean ± SD

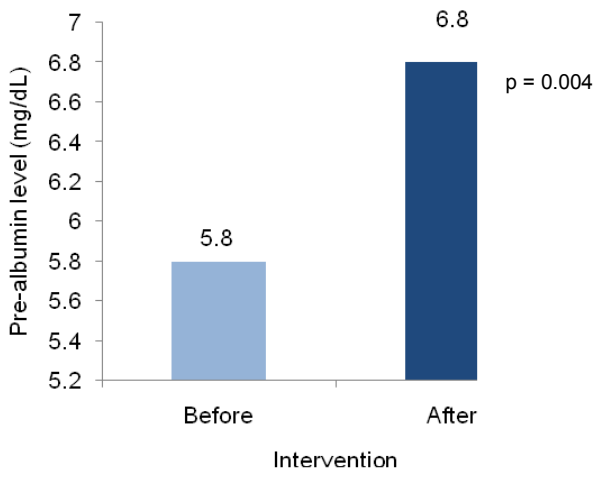

Figure 1. Mean pre-albumin levels before and after intervention

DISCUSSION

Malnutrition may increase mortality and morbidity in patients with liver cirrhosis. Therefore, we should consider an effort to improve nutrition including supplementation of 1.5 g/kgBW/day dietary protein with BCAA substitution. Anthropometric examination of MAMC was determined as the criteria to detect the existence of malnutrition since the MAMC is the least parameter affected by edema and ascites and it is also least affected by impaired liver function.[4]

All subjects in this study were malnourished based on the results of their MAMC measurements, which were below the 15 percentiles. However, when using anthropometric measurements of BMI, there were only as many as four subjects (25%) that expressed malnutrition. Differences in nutritional status based on examination results of BMI and MAMC is consistent with the theory that BMI is less accurate for assessing nutritional status in liver cirrhosis because it has much been influenced by edema and ascites.[4,7] In this study, the changes of BMI and MAMC after intervention were not evaluated because there were no significant anthropometric changes in a short period of time. Hence, pre-albumin was used as the parameter instead.[4,5,8]

Improved nutritional status was observed after BCAA supplementation for two weeks as shown by better pre-albumin level in 16 subjects compared to their condition before treatment.

After treatment, mean value of pre-albumin level increased from 5.8 (2.2) mg/dL to 6.8 (2.1) mg/dL. Improved pre-albumin level has indicated the success of corrective nutritional attempt of the given regimens. Provision of these nutrients, according to ESPEN 2006 guidelines recommendation, is a diet of 35-40 cal/kgBW and 1.5 g protein including BCAA substitution.

Increased pre-albumin level found in this study is consistent with previous studies, which indicated that BCAA may improve nutritional status in malnourished liver cirrhotic patients.[9] Muto et al and Nakaya et al, also found improved serum albumin level in patients with advanced cirrhosis who received BCAA supplementation.[10,11]

We used pre-albumin level as a parameter of nutritional improvement since it has a short half-life (2 days), which is more sensitive to detect any changes of protein-calorie status. Moreover, it is also more sensitive to reflect the patient's current nutritional intake.[12] It is also supported by Beck and Devoto et al, who concluded that pre-albumin is a practical and reliable way to assess the efficacy of nutritional intervention.[6,8]

However, this study has some limitations. The compliance of study subjects may vary and we could not control the diet strictly, which may result in potential errors. Moreover, since the study was conducted in a short period of time, the anthropometric changes could not be evaluated. Therefore, in this study, we only used laboratory changes as the parameter.

CONCLUSION

The mean value of pre-albumin levels in patients with malnutrition and liver cirrhosis after improved nutritional treatment with BCAA substitution given for two weeks is higher than those before the

intervention. Therefore, patients with malnourished liver cirrhosis should be given dietary 35-40 cal/kgBW and 1.5 g protein/kgBW including BCAA substitution to improve their nutritional status. Moreover, further studies of better design and over longer time period of intervention are necessary.

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