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Long-Term Complementary Dietary Supplement of Vegetable Protein may Decrease Degree of Hepatic Encephalopathy in Patients with Decompensated Liver Cirrhosis

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Abstract: Liver cirrhosis can evoke several complications including hepatic encephalopathy. Protein calorie malnutrition is a well-known complication of liver cirrhosis and regulated control of nitrogen balance can be a very important factor. Tofu is a kind of soy protein in several Asian countries which can be a useful alternative of nitrogen balance in liver cirrhosis patients. Researchers prospectively followed up the cirrhotic patients with decompensated liver cirrhosis up to 5 years and compared the changes of grade in hepatic encephalopathy according to the amount of ingestion of tofu. Data showed significantly lower grade of hepatic encephalopathy in the high ingestion group but there were no significant differences in survival at 5 years follow up. Therefore, vegetable protein such as tofu could be an attractive way of improving nutritional quality for cirrhotic patients and to reduce overall treatment costs.

Key words: Liver cirrhosis, hepatic encephalopathy, vegetable protein, attractive way, nutritional quality

INTRODUCTION

Liver cirrhosis is the end stage of various types of liver disease. It can arouse complications such as coagulopathy, hepatic encephalopathy and portal hypertension with all its complications (Albanis and Friedman, 2001; Munoz, 2008; Pinzani *et al*., 2005). Hepatic encephalopathy is a neuropsychiatric disorder that leads to mental status changes and abnormal neuromuscular function in patients with acute or chronic liver diseases, especially, advanced liver cirrhosis (O'Brien and Williams, 2008; Seymour and Whelan, 1999).

The restriction of dietary protein intake in patients with advanced liver cirrhosis and hepatic encephalopathy became the common practice in the 1970s and 1980s but was not clearly evidence-based (Donaghy, 2002). Increased understanding of the pathophysiology of cirrhosis has shown that most patients with liver cirrhosis do not have the high level porto-systemic shunting and that protein restriction in these patients has no effect on their hepatic encephalopathy (Heyman *et al*., 2006) Furthermore, protein calorie malnutrition is a well-known complication of liver cirrhosis and can be life threatening (Chadalavada *et al*., 2010). Therefore, adjusted control of nitrogen balance in patients with liver cirrhosis can be the very important factor of prognosis. Soy protein is considered the best vegetable protein and is one of the health foods without lactose, fat or cholesterol. Tofu (Korean doobu) is a kind of food made by coagulating soybean ingredients or milk and pressing the resulting curds. Many Asians including Koreans have eaten various foods comprising tofu. There have been few prior studies of cirrhotic patients to elucidate the priority of vegetable protein such as soybean for supplement of protein deficiency in the episodic hepatic encephalopathy. Therefore, to know the relation with grades of hepatic encephalopathy and the amount of soybean ingestion, researchers prospectively followed up the patients with liver cirrhosis up to 5 years and compared the changes of grade in hepatic encephalopathy according to the amount of ingestion of tofu, as soybean dietary protein.

MATERIALS AND METHODS

Researchers selected the subjects with decompensated liver cirrhosis (Child-Pugh score ≥7) from patients of Department of Internal Medicine, St. Mary's Hospital, Daejeon and Republic of Korea. Researchers got an admission from the Institutional Review Board of Human Study in the hospital. The diagnosis of cirrhosis was based on prior liver biopsy or on a combination

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Table 1: Stages of hepatic encephalopathy

Stage	Neurological manifestations
0	Alert and attentive without signs of encephalopathy
1	Alert and attentive but with a least one of the following signs: Dysarthria, ataxia, flapping tremor or obvious decrease in the speed of mental processing
2	Awake but inattentive: disoriented, somnolent, easy to distract, unable to perform easy mental tests (addition, subtraction, remember and a list of numbers) patient's speech is easy to understand
3	Semi-comatose state, marked somnolence or psychomotor agitation. Patient's speech is difficult to understand
4	Comatose State, the patient does not speak and does not follow simple commands

of clinical and imaging data demonstrating portal hypertension and cirrhotic appearance of the liver. We have questioned and recorded the amount of ingestion of tofu on the visit of out patient clinic generally every 2 or 3 months interval without any encouraging of ingestion of tofu. Episodic hepatic encephalopathy was diagnosed based on a sudden change in the mental state from a previously normal consciousness that could not be attributed to another cause. Exclusion criteria to participate in the study were terminal disease (e.g., advanced hepatocellular carcinoma or hepatorenal syndrome), clinically severe distressed state and neurological comorbidities such as old cerebrovascular disease and/or dementia.

Patients were grouped by the mean amount of tofu ingestion such as the low (almost never to under 300 g week^{-1}), middle (300-900 g week^{-1}) and high group (>900 g week^{-1}). Protein content in 300 g of tofu was about 12-15 g and the weight of one piece of commercially sailed one was around 300 g/pack. All patients were supplemented 4.15 or 8.3 g of Branch Chain Amino Acids (BCAAs) (Livact granule, Samil Pharm, Seoul, Republic of Korea). Hepatic encephalopathy was treated similarly in all patients. Correction of precipitating factors was done and was followed enemas of lactulose were administered. Quantifying the mental status with a scale that was an adaptation of the West Haven criteria assessed hepatic encephalopathy (Ferenci *et al*., 2002) (Table 1). The results are expressed as median. The t-test and one-way ANOVA test were used for comparisons among groups of tofu intake for event of hepatic encephalopathy.

RESULTS AND DISCUSSION

Researchers assessed the subjects from 2004-2009 and the clinical characteristics of participants are shown in Table 2. During this period, 80 patients were considered eligible; 24 patients were assigned as the low, 40 patients were middle and 16 patients were high intake group. The baseline demographic and clinical characteristics of

Table 2: Clinical characteristics of patients included in the study

Characteristics	Low (n = 24)	Middle (n = 40)	High (n = 16)
Age	59±12.3	62±8.9	54±10.4
Male/Female	22/2	35/5	12/4
Etiology of cirrhosis			
Hepatitis B	12	25	10
Alcohol	8	12	4
Hepatitis C	1	2	2
Other	1	1	0
Blood tests			
Prothrombin time (INR)	2.1±2.3	2.2±1.9	1.9±1.2
Albumin (g dL^{-1})	3.0±1.5	3.1±1.8	3.3±0.8
Total bilirubin (mg dL^{-1})	1.9±1.7	1.8±1.2	1.7±1.5
Ammonia (mg dL^{-1})	102±39.7	98±54.4	92±28.4
Child-Pugh score	8.3±1.2	8.0±0.8	7.9±1.1

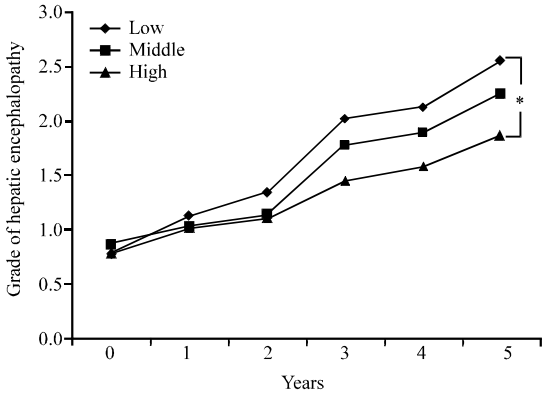

Fig. 1: Changes of grades of hepatic encephalopathy in individual groups for 5 years *; p<0.05

subjects included in the study were similar in groups. There was also no statistical difference of percentage of ingestion of Branch Chain Amino Acids (BCAAs) supplement. There were significant differences in the grades of hepatic encephalopathy between the low and high intake groups (Fig. 1). Data showed lower grade of hepatic encephalopathy in high tofu intake group. However, there were no significant differences in overall survival among groups even though there were slight higher survivals in middle and high tofu ingestion groups compared with the low group (Fig. 2).

The major finding of this study is that there is a benefit of ingestion of vegetable protein on the severity of hepatic encephalopathy while there was no significant benefit in survival. The results suggest that patients with decompensated liver cirrhosis can get a benefit by supplement of vegetable protein in the form of tofu. Low plasma concentrations of BCAAs are frequently seen in patients with liver cirrhosis (Fiaccadori *et al*., 1981; Moriwaki *et al*., 2004; Petrides *et al*., 1991) Moreover, the patients with liver cirrhosis have an increased energy requirement. Therefore, those patients have a higher than normal supply of dietary protein is needed to achieve

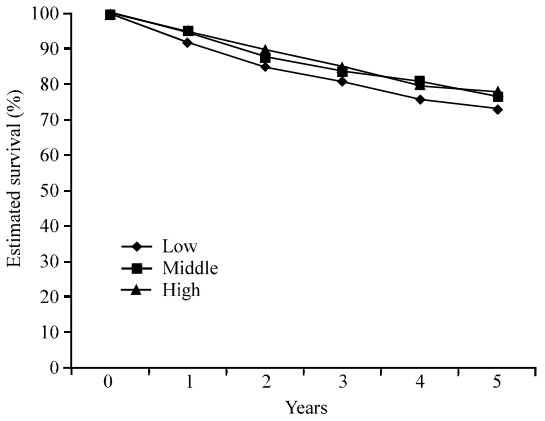

Fig. 2: Estimated overall survival percentage of groups according to intake of tofu for 5 years

nitrogen balance (Kato *et al*., 1998; Marchesini *et al*., 2000). Balance of nutrition in patients with liver cirrhosis can be a very important factor of disease progression and survival.

Several studies have suggested that BCAAs improve plasma acid imbalance as well as protein metabolism in patients with liver cirrhosis (Egberts *et al*., 1985; Horst *et al*., 1984; Rodriguez *et al*., 2003). However, considering cost effectiveness, the efficiency can be somewhat questionable for long-term supplements of BCAAs to decompensated liver cirrhosis because these formulas are expensive and present poor functional characteristics for tube feeding and a bad taste for oral feeding. Therefore, researchers suggest tofu as dietary soy protein can be useful alternative or complementation of BCAAs for dietary supplement of patients with decompensated liver cirrhosis. Soy protein is also one of the best health foods and can help decrease the cholesterol in the body. Engelen *et al*. (2007) suggested that BCAAs supplementation to soy protein enhanced whole body protein synthesis with Chronic Obstructive Pulmonary Disease (COPD) patients and altered to inter-organ protein metabolism in favor of the peripheral compartment.

Therefore, additional supplementation of soy protein with BCAAs can be promising tools of optimizing of amino acid balance in patients with a nutritional deficit. Though there have been controversies about protein intake in patients with hepatic encephalopathy, the objective of nutritional support is to provide adequate nutrients to patients for energy synthesis and normal hepatocyte survival and function (Charlton, 2006). Recently, an interesting animal study was reported by Proot *et al*. (2009). The examination to dogs with congenital porto-systemic shunts showed that soy protein based diet could achieve a significant improvement in hepatic encephalopathy score. As researchers know this manuscript is the first suggestion for an assertion of cost effectiveness in hepatic encephalopathy related with supplementation of vegetable protein to patients with decompensated liver cirrhosis.

CONCLUSION

Consequently, vegetable proteins could be an attractive way of improving nutritional quality and to meet the special amino acid requirements for cirrhotic patients and to reduce overall treatment costs. Moreover, researchers suggest that adjusted feeding of vegetable protein may reduce the chances of episodic hepatic encephalopathy.

LIMITATIONS

However, there are several defects in this manuscript; firstly, the enrolled number of patients was very small. Secondly, researcher could not assess the accurate amount of daily protein intake in individual subjects because there are some possibilities of the erroneous report by patients or other sources of protein. Thirdly, there was continuous decrease in the number of enrolled patients due to patient's death. Even though many defects in this manuscript, to know more long-term effectiveness of supplementation of soy protein in patients with liver cirrhosis, wide enrollment of feasible patients in multiple institutes can be worthy to elucidate the usefulness of vegetable protein.

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