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A VEGETABLE PROTEIN-RICH DIET FOR THE TREATMENT OF LIVER CIRRHOSIS

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Abstract. Twelve patients were administered a vegetable protein-rich diet, which was low in methionine and high in the branched-chain amino acid (BCAA) to aromatic amino acid (AAA) molar ratio, and an animal protein-rich diet, high in methionine and low in the BCAA/AAA molar ratio. These diets were administered successively for one week each. Actually ingested amounts of tyrosine and methionine were significantly lower during the feeding of the vegetable protein-rich diet than the animal protein-rich diet. Serum methionine concentrations increased while on the animal protein-rich diet and decreased following the switch to the vegetable protein-rich diet. No other amino acid concentrations were affected. Significant differences were not observed in nitrogen balance or serum protein concentrations.

Key words: vegetable protein, methionine, branched-chain amino acids, liver cirrhosis, dietary treatment.

Cirrhotic patients are usually treated with a high protein, high energy diet to maintain a well-compensated state. However, plasma amino acid imbalances, high levels of methionine and aromatic amino acids (AAA: phenylalanine and tyrosine) and low levels of branched-chain amino acids (BCAA: valine, leucine, and isoleucine) are common in patients with advanced cirrhosis (1). Normalization of these imbalances by intravenous infusion of BCAA-enriched solutions has induced arousal and prevented hepatic encephalopathy in severe cirrhosis (2). Greenberger *et al.* (3) recently demonstrated the effect of a vegetable protein-rich diet in the prevention of hepatic encephalopathy. In the present study, patients with well-compensated cirrhosis were fed either a vegetable or an animal protein-rich diet, and their clinical state and nutritional status were then evaluated.

MATERIALS AND METHODS

Subjects. Ten males, aged 47 to 65, and two females, aged 39 and 59, who were admitted to Okayama University Hospital, were studied. Diagnoses of liver cirrhosis were made by peritoneoscopic and histologic observations of the liver (Table 1).

Diets. The two test diets, a vegetable and an animal protein-rich diet, and a standard diet were prepared (Table 2). The vegetable protein-rich diet contained 500 g of soybean products such as soy curd, fermented soybean and soy milk, all of which are popular in Japan. The animal protein-rich diet was composed mainly of milk, cheese, meat, fish, and egg. The

TABLE 1. DISEASE FEATURES OF THE CIRRHOTIC PATIENTS

Patient No.	Age (yr)	Sex	HBsAg[a] / Drinking history	Bilirubin (mg/dl)	Total protein (g/dl)	Albumin (g/dl)	GOT (IU/l)	GPT (IU/l)	K_{ICG}
1	65	M	− / +	1.30	6.6	2.7	41	25	0.06
2	60	M	− / −	0.93	6.7	3.3	62	43	0.06
3	63	M	+ / +	5.09	8.1	3.7	640	443	-
4	56	M	− / −	0.95	8.3	4.3	192	209	0.13
5	47	M	+ / −	5.64	7.2	2.9	131	101	0.04
6	51	M	− / −	1.98	7.6	3.5	132	116	0.05
7	61	M	− / +	0.74	9.0	4.3	83	65	0.09
8	51	M	− / −	1.09	7.4	3.1	182	152	0.06
9	39	F	+ / −	1.63	6.7	2.7	169	114	0.04
10	59	F	− / −	0.67	8.1	4.3	67	44	0.12
11	55	M	− / +	1.42	8.0	4.0	140	132	0.10
12	55	M	− / +	1.33	7.0	4.0	94	80	0.09
Normal range				0.22−0.96	6.7−8.5	4.0−5.4	11−40	6−35	0.189±0.010

[a]Hepatitis B virus surface antigen as determined by the presence of specific antibodies.

TABLE 2. COMPOSITION OF STANDARD AND TEST DIETS.

Food	Standard diet	Animal protein-rich diet	Vegetable protein-rich diet
		(g/day)	
White rice	660	300	350
White bread	-	50	-
Buckwheat noodle	-	-	200
Cornflakes	-	-	50
Milk	400	400	200
Cheese	-	50	-
Meat	60	80	-
Fish	100	60	-
Egg	50	50	25
Soy products	200	-	500
Potato	70	50	50
Vegetable	300	300	300
Fruit	100	200	-
Sugar	20	90	10
Oil	10	10	-
Energy (kcal/day)	1979	1847	1894
Protein (g/day)	90.6	79.1	79.9
Animal protein	49.8	62.3	9.1
Vegetable protein	40.8	16.8	70.8

standard diet was a special hospital diet containing 50 % protein from animal products; this diet is served normally to chronic liver disease patients. There was no difference in energy or protein content between the diets. The BCAA/AAA molar ratio was much higher in the vegetable-based diet (Table 3). Proteins in the vegetable protein-rich diet had very low chemical scores; the first-limiting amino acids were sulfur-containing amino acids (Table 4). During the first week of the study, the patients were served the standard diet. Thereafter, the patients were treated with the animal protein-rich then the vegetable protein-rich, and finally the standard diet each for a week. Food intake was determined during the test period, and ingested nutrients and amino acids were calculated according to the standard Japanese food tables (4).

Analytical method. Clinical and laboratory tests were performed at the end of each week. In the early morning, venous blood was obtained for serum amino acid, total protein, albumin, and choline esterase analyses. After the sera were deproteinized with 5 % sulfosalicylic acid, serum amino acid concentrations were determined using a Hitachi liquid chromatograph (Type 034, Japan). Nitrogen balance was calculated as [actually ingested nitrogen (g/day) - excreted

TABLE 3. AMINO ACID COMPOSITIONS OF THE DIETS.

Amino acid	Standard diet	Animal protein-rich diet	Vegetable protein-rich diet
		(mmole/day)	
Valine	46.4 ± 4.4	39.4 ± 1.1	38.4 ± 0.9
Leucine	58.8 ± 5.8	49.2 ± 1.7	51.6 ± 0.9
Isoleucine	35.3 ± 3.6	28.7 ± 0.5	31.3 ± 0.8**
Phenylalanine	26.0 ± 2.7	22.6 ± 0.6	25.6 ± 0.4***
Tyrosine	21.3 ± 1.8	20.0 ± 0.2	16.1 ± 0.4***
Methionine	14.0 ± 1.8	13.6 ± 0.8	8.9 ± 0.1***
BCAA/AAA molar ratio	2.95 ± 0.04	2.72 ± 0.06	2.91 ± 0.03*

Data are expressed as mean ± SD (n=3). Significance coefficients were calculated by Student's t-test. *$p<0.025$, **$p<0.01$, ***$p<0.001$, compared with the animal protein-rich diet.

TABLE 4. CHEMICAL SCORES OF PROTEINS IN THE DIETS.

Chemical score	Standard diet	Animal protein-rich diet	Vegetable protein-rich diet
Protein Score	86 (S)[a]	90 (S)	71 (S)
Amino acid Score	100	95 (Thr)	86 (S)
A/E[b] ratio Egg Score	66 (S)	70 (S)	57 (S)
A/T[c] ratio Chemical Score	59 (S)	62 (S)	49 (S)
EAA[d] index	87	88	85

[a]The abbreviations in parentheses indicate the first-limiting amino acid.
S: Sulfur-containing amino acid (Methionine and Cystine)
Thr: Threonine
[b]A/E: Amino acid to essential amino acid
[c]A/T: Amino acid to total amino acid
[d]EAA: Essential amino acid

urinary nitrogen (g/day)-2]. Significance coefficients were calculated by Student's t-test or Wilcoxon's sign rank test.

RESULTS

Ingested amounts of tyrosine and methionine were significantly lower while on the vegetable protein-rich diet than the animal protein-rich or standard diet (Table 5). Crude fibers were highest in the vegetable protein-rich diet. Improvements were not observed in total serum protein and albumin concentrations or in nitrogen balance during the test period (Table 6). Serum methionine concentrations increased during the feeding of the animal protein-rich diet and then decreased following the switch

TABLE 5. AVERAGE INTAKE OF NUTRIENTS AND AMINO ACIDS

Nutrient and amino acid/day		Standard diet	Animal protein-rich diet	Vegetable protein-rich diet
Energy	(kcal)	1632±314	1602±275	1701±264
Protein	(g)	71.7±10.7	70.8±12.2	66.9±10.2
Animal	(g)	44.2±8.5	52.0±10.5	9.1±1.4***
Vegetable	(g)	27.5±6.2	18.9±1.9	57.8±10.6***
Crude fiber	(g)	3.4±0.6	3.1±0.5	4.3±0.7***
Amino acid	(mmole)			
Valine		34.4±4.9	34.0±6.0	32.1±4.8
Leucine		44.1±6.2	42.1±7.4	42.5±6.1
Isoleucine		26.4±3.5	24.8±4.4	25.9±4.0
Phenylalanine		19.2±2.6	19.3±3.4	21.3±3.4
Tyrosine		16.1±2.1	17.1±2.9	13.9±1.8**
Methionine		10.2±1.4	11.8±1.9	7.5±0.9***
BCAA/AAA molar ratio		2.98±0.04	2.77±0.02	2.85±0.04***

Data are expressed as mean ± SD (n=12). Significance coefficients were calculated by Student's t-test. **$p<0.01$, ***$p<0.001$, compared with the animal protein-rich diet.

TABLE 6. CLINICAL AND LABORATORY DATA.

		Before test diet (Standard diet)	Animal protein-rich diet	Vegetable protein-rich diet	After test diet (Standard diet)
Serum protein	(g/dl)	7.6±0.2	7.7±0.2	7.7±0.1	7.8±0.1
albumin	(g/dl)	3.6±0.2	3.5±0.2	3.5±0.2	3.6±0.1
Bilirubin	(mg/dl)	1.9±0.5	1.7±0.3	1.7±0.4	1.6±0.4
GOT	(IU/l)	161±46	153±46	142±29	156±39
GPT	(IU/l)	134±33	111±30	104±24	105±22
Choline esterase	(△pH)	0.49±0.07	0.50±0.06	0.52±0.07	0.53±0.06
Total cholesterol	(mg/dl)	162±10	167±11	153±11	158±11
Nitrogen balance	(g/day)	0.2±1.0	−0.3±1.1	−0.1±0.9	1.6±0.8

Data are expressed as mean ± SEM (n=12).

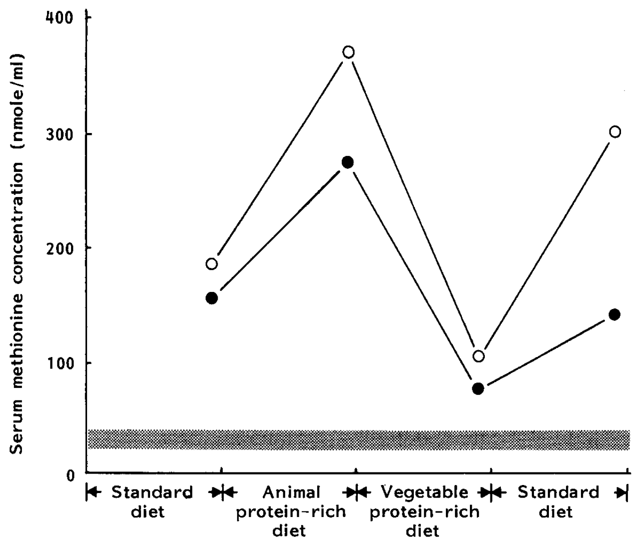

Fig. 1. Changes in serum methionine levels in Patients 3 (●) and 9 (○) during the three different diets. The dark band indicates the normal range of methionine.

TABLE 7. EFFECT OF TWO TEST DIETS ON SERUM AMINO ACID CONCENTRATIONS.

Amino acid (nmole/ml)	Normal range	Before test diet (Standard diet)	Animal protein-rich diet	Vegetable protein-rich diet	After test diet (Standard diet)
Valine	216–306	194.8±18.0	198.3±18.9	200.4±17.8	207.9±6.0
Leucine	113–184	116.8±11.7	118.6±10.4	125.2±12.0	125.1±8.6
Isoleucine	61–106	71.1±6.8	72.5±6.7	79.1±9.7	82.8±9.0
Phenylalanine	47–76	104.4±12.8	98.9±11.2	101.7±12.3	137.5±13.7
Tyrosine	46–93	153.5±22.2	152.6±15.0	147.8±16.2	175.1±18.1
Methionine	22–39	85.3±18.2	103.8±32.3	57.3±7.4**	92.7±22.1
BCAA/AAA molar ratio	2.50–4.62	1.72±0.22	1.66±0.19	1.78±0.20	1.44±0.17

Data are expressed as mean ± SEM (n=12). Significance coefficients were calculated by Wilcoxon's sign rank test. **$p<0.01$, compared with animal protein-rich diet.

to the vegetable protein-rich diet in 8 out of 11 patients. This change was remarkable in 2 patients (Patients 3 and 9) who presented high serum methionine concentrations before the test (Fig. 1). No other amino acid concentrations were significantly affected by the changes in diet (Table 7).

DISCUSSION

Hepatic encephalopathy has been improved by administering a vegetable protein-rich diet to cirrhotic patients (3, 5, 6). Several possible explanations were presented: lower methionine levels, high fiber content, and impaired absorption of vegetable proteins. Methionine has been implicated in the induction of hepatic encephalopathy (7, 8). Horowitz *et al.* (9) reported impairment of the transsulfuration pathway in methionine metabolism in cirrhosis. Impaired ability to eliminate excess plasma methionine after methionine loading has been observed even in cirrhotic patients whose plasma methionine concentrations were within the normal range (9). Increased serum methionine levels were observed in our cirrhotic patients (Table 7), though they were well-compensated. Vegetable protein-rich diets possess low chemical scores because of methionine deficiencies. This lack might be beneficial to impaired methionine metabolism. High serum levels of phenylalanine and tyrosine and low BCAA/AAA molar ratios were also observed in the patients studied. Vegetable protein-rich diets contain significantly low levels of tyrosine. Besides soy products, the vegetable protein-rich diet herein contained foods such as cornflakes and buckweat noodles. Corn protein contains much leucine and has a high BCAA/AAA molar ratio of 4.4. Buckwheat has also a high BCAA/AAA molar ratio due to low tyrosine content. Cheese and milk, being prevalent in animal protein-rich diets, have low BCAA/AAA molar ratios (2.4 and 2.8). However, in our study, the dietary BCAA/AAA molar ratios did not affect the serum ratios. This result may be attributed to the small difference in the ratios between the vegetable and animal protein-rich diets.

Shaw *et al.* (10) reported difficulty in achieving adequate consumption of the vegetable protein diet. Soy products used in this study are very popular in Japan, and patients ingested the vegetable protein-rich diet without any difficulty. It has been suggested that vegetable proteins are absorbed less from the intestines than animal proteins (3). Soy curd and other soy products, however, are reported to be well digested and absorbed (11). Vegetable protein-rich diets are significantly high in crude fibers. Fibers may prevent ammonia production by intestinal flora, or inhibit absorption of ammonia (5).

The cirrhotic patients studied were well-compensated. No patients presented hepatic encephalopathy during the treatment, and they tolerated the high protein diets. In conclusion, use of a vegetable protein-rich diet with soy proteins in the dietary treatment of liver cirrhosis had no deleterious effects on nitrogen metabolism, and should be useful for improving abnormal methionine metabolism.

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