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## Abstract

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# EFFECT OF A BRANCHED CHAIN AMINO ACID-ENRICHED NUTRITIONAL PRODUCT ON THE PATHOPHYSIOLOGY OF THE LIVER AND NUTRITIONAL STATE OF PATIENTS WITH LIVER CIRRHOSIS

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*Abstract.* A new nutritional product (SF-1008C) containing a high proportion of branched chain amino acids (BCAA) and low proportion of aromatic amino acids (AAA) and methionine was tested to see its effect on the impaired protein metabolism and abnormal nutritional state frequently observed in patients with advanced liver cirrhosis. A sharp increase in plasma BCAA levels and fall of AAA and methionine levels were found following the administration of an SF-1008C-supplemented diet to healthy controls and cirrhotic patients, which the BCAA levels increased only slightly following an isocaloric control diet. Blood ammonia levels increased within the normal range transiently following the diets. The SF-1008C-supplemented diet was given for 2 weeks to cirrhotic patients with histories of hepatic encephalopathy, who were taking a low-protein diet because of hyperammonemia. Serum prealbumin levels, nitrogen balance, molar ratio of plasma BCAA/phenylalanine and tyrosine, the number connection test and electroencephalograms improved during the period of the experimental diet. The results, therefore, indicate that a BCAA-supplemented diet is well tolerated by patients with advanced cirrhosis and useful for treatment of impaired protein metabolism. Furthermore, this product is beneficial in preventing hepatic encephalopathy in cirrhotics.

*Key words :* branched chain amino acid, aromatic amino acid, nutritional product, liver cirrhosis, hepatic encephalopathy.

Plasma amino acid imbalance and lower serum albumin levels in patients with advanced liver cirrhosis indicate the impaired synthesis of protein in the cirrhotic liver and the accelerated protein catabolism in the skeletal muscle. Since blood ammonia levels increase frequently in patients with liver cirrhosis, they must eat a protein-restricted diet for long periods (1). Anorexia, ascites and intestinal bleeding are additional problems in careing for those patients. In fact, diminished calorie and protein intake has been reported in alcoholic and non-alcoholic liver cirrhosis (2). A long-term fast or low protein diet often causes protein-calorie malnutrition, which may induce deterioration of the liver dysfunction and various complications such as hepatic encephalopathy. Water and mineral imbalances and impaired glucose tolerance are also frequently observed

in cirrhotic patients. Therefore, nutrition of those patients should be watched carefully, considering the impaired protein-amino acid metabolism. The appropriate amino acid composition of a diet or nutritional product is essential to nomalize the abnormal serum aminogram. The appropriate amino acid composition of the diet also may be beneficial in the treatment and prevention of hepatic encephalopathy, since both hyperammonemia and serum amino acid imbalance are thought to be encephalopathic factors (3).

A nutritional product (SF-1008C) especially formulated for patients with severe liver disease such as fulminant hepatitis and liver cirrhosis consists of high proportion of BCAA and low proportion of AAA and methionine. To investigate the effect of feeding SF-1008C on the liver pathophysiology, including protein metabolism, and the nutritional state in liver cirrhosis, an SF-1008C-supplemented diet was administered to both healthy controls and cirrhotic patients.

## SUBJECTS AND METHODS

Six patients with liver cirrhosis (four males and two females, Table 1), who were admitted to Okayama University Hospital, and two healthy subjects (29-and 31-year-old males) were adopted as clinical materials for this study. Diagnosis of liver cirrohsis was made by peritoneoscopy and histological observation of liver biopsy specimens. Patients 1, 2 and 3 are well compensated and have neither an abnormality of the carbohydrate metabolism, ascites nor jaundice. Patients 4, 5 and 6 have a history of hepatic encephalopathy.

The content of amino acids and other nutrients in SF-1008C (Otsuka Pharmaceutical Co. Ltd., Tokyo), a soft powder nutritional product, is shown in Table 2. A half pack (one 97-g pack contains 400 kcal and 25.3 g protein) of SF-1008C was dissolved in 175 ml of lukewarm water and served to Patients 1 and 2 and to the two healthy subjects following each meal (9 a.m, 2 p.m. and 7 p.m.) of a low protein diet (1600 kcal and 40 g protein/day). Amounts of the nutrients actually ingested by these subjects were similar and are shown in Table 3.

TABLE 1. STATISTICS AND LABORATORY DATA OF THE SIX PATIENTS WITH LIVER CIRRHOSIS

| Clinical findings | Case no | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| Age & sex | 65 M | 73 M | 67 F | 54 M | 57 F | 53 M |
| Height (cm) | 170 | 173 | 152 | 164 | 151 | 167 |
| Weight (kg) | 68 | 76 | 45 | 66 | 53 | 76 |
| Etiology of cirrhosis | Unknown | Alcoholic | Unknown | Alcoholic | Unknown | Alcoholic |
| History of encephalopathy (Years before) | No | No | No | Yes (1) | Yes (0.3) | Yes (2) |
| Low protein diet | No | No | No | Yes | Yes | Yes |
| Serum bilirubin (mg/dl) | 1.1 | 1.0 | 1.2 | 1.7 | 0.6 | 4.1 |
| $K_{ICG}$ | 0.06 | 0.08 | 0.05 | 0.03 | 0.05 | 0.05 |
| Serum ammonia ($\mu$g/dl) | 40 | 28 | 80 | 65 | 100 | 140 |
| Serum prealbumin (mg/dl) | ND | ND | ND | 6.1 | 6.1 | 7.0 |

ND : Not determined.

TABLE 2. NUTRIENT COMPOSITION OF SF-1008C

| Three major nutrients | | Electrolytes (mg/100 g)[a] | | Vitamins (ppm/100 g) | | Amino acid composition (g/amino acid 100 g)[a] | |
|---|---|---|---|---|---|---|---|
| Protein (g/100 g) | | | | | | | |
| Casein | 1.0 | Na | 447 | A | 40.0 | Ile | 14.3 |
| Peptide | 13.0 | K | 332 | $B_1$ | 2.9 | Leu | 15:9 |
| Amino acid | 13.0 | Ca | 123 | $B_2$ | 3.1 | Val | 12.7 |
| Carbohydrate (g/100 g) | | Cl | 444 | $B_6$ | 4.9 | Met | 0.6 |
| Dextrin | 62.1 | P | 199 | $B_{12}$ | 0.01 | Cys | - |
| Lipid (g/100 g) | | Mg | 62.2 | C | 13.8 | Phe | 1.1 |
| Rice oil | 7.0 | Fe | 2.9 | D | 0.4 | Tyr | 0.4 |
| | | Zn | 2.9 | E | 130.0 | Trp | 0.6 |
| | | Mn | 0.4 | K | 0.11 | Thr | 2.0 |
| | | Cu | 0.3 | Pantothenic acid | | Lys | 3.9 |
| | | Co | Trace | | 21.8 | Arg | 6.2 |
| | | | | Nicotinate amide | | His | 1.7 |
| | | | | | 30.3 | Ala | 4.9 |
| | | | | Biotin | 0.5 | Pro | 7.2 |
| | | | | Folic acid | 1.0 | Ser | 1.8 |
| | | | | Choline phosphate | | Gly | 12.0 |
| | | | | | 246.0 | Asp | 3.1 |
| | | | | | | Glu | 5.8 |
| | | | | | | Hypro | 5.5 |
| | | | | | | Hylys | 0.4 |

*a*: Analytic value

TABLE 3. NUTRIENTS OF THE SF-1008C(A HALF PACK/EACH MEAL)-SUPPLEMENTED AND CONTROL DIETS ACTUALLY INGESTED BY TWO HEALTHY SUBJECTS AND TWO PATIENTS WITH LIVER CIRRHOSIS

| | Calorie (kcal/day) | Protein (g/day) | Amino acid (nmoles/day) BCAA | AAA | Methionine | BCAA/(phenylalanine and tyrosine) | Lipid (g/day) | Carbohydrate (g/day) | Non protein calorie/Nitrogen (g) | Nitrogen in SF-1008C/Total nitrogen (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| SF-1008C-supplemented diet | | | | | | | | | | |
| Control 1&2 | 2081 | 75 | 189 | 24 | 5 | 9.2 | 46 | 346 | 152 | 51 |
| Patient 1 | 1786 | 65 | 173 | 18 | 4 | 11.3 | 44 | 289 | 153 | 60 |
| Patient 2 | 1887 | 69 | 182 | 21 | 5 | 10.4 | 45 | 304 | 149 | 56 |
| Control diet | | | | | | | | | | |
| Control 1&2 | 2072 | 74 | 110 | 44 | 11 | 2.8 | 43 | 346 | 149 | 0 |
| Patient 1 | 1768 | 66 | 96 | 39 | 10 | 2.8 | 36 | 296 | 143 | 0 |
| Patient 2 | 1643 | 66 | 100 | 40 | 10 | 2.8 | 34 | 267 | 138 | 0 |

Amounts of the dietary nutrients actually ingested were checked every meal as described previously (9)

In a separate test, the four subjects also ate a control diet similar in calorie and protein content (2072 kcal and 74 g protein/day) to the SF-1008C-supplemented diet with the actual intake of calories, protein, lipid, carbohydrate and amino acid being similar between the healthy controls and the cirrhotic patients. The BCAA/(phenylalanine and tyrosine) molar ratio, however, was much higher in the SF-1008C-supplemented diet (controls, 9.2 and cirrhotics, 10.8) than in the control diet (controls and cirrhotics both 2.8). Blood samples were collected hourly from 3h after breakfast to early the next morning.

To two cirrhotic patients (Patients 1 and 3), an SF-1008C (a half pack at each meal)-supplemented diet was given at 8 a.m., 12 a.m. and 5 p.m. (shown by arrows in Fig. 6) in order to see the alteration of the plasma amino acid levels throughout the day.

One third of an SF-1008C pack was given at each meal for 2 weeks to three cirrhotic patients (Patients 4, 5 and 6) having had a history of hepatic encephalopathy and hyperammonemia and having been on a low protein diet with the administration of a lactulose solution (60-90 ml/day) (Table 1). During the first week of the study, the patients were served only the low protein diet. Then they were treated with the SF-1008C (one pack/day)-supplemented diet during the 2nd and 3rd week, and again the low protein diet during the 4th week (Fig. 1). Nutritional parameters and liver function tests were analyzed with overnight-fasting blood and urine samples, as shown in Fig. 1. Dietary intake was checked twice a week during the experimental period and the nutrient contents ingested were calculated as reported previously (4).

Blood ammonia levels were determined by an Amitest meter method and the normotest performed by Owren's procedure, as reported previously (5). For amino acid analysis, using a Hitachi amino acid analyzer Type 034, one ml plasma was deproteinized with 1.5 ml of 5 % sulfosalicylic acid, as reported previously (6). Nitrogen balance and serum prealbumin determinations and the number connection test were carried out as reported previously (7). Liver volume was calculated from computerized tomography of the abdomen according to Imamura's procedure (8) and expressed as ml/kg body weight.

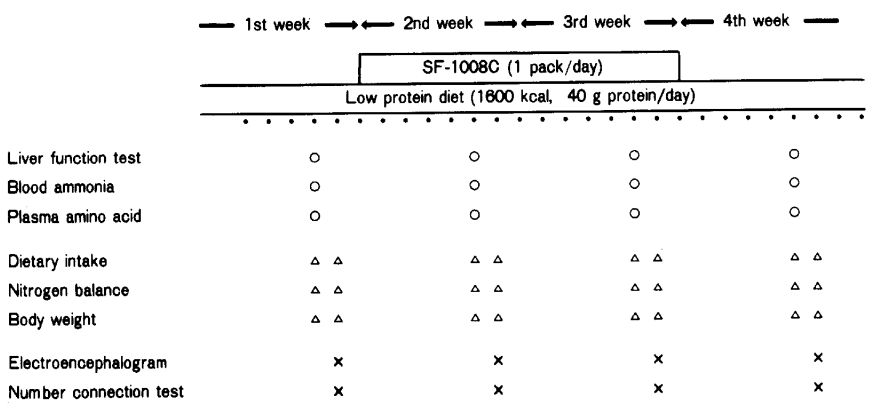


Fig. 1. Schedule of the two week administration of the SF-1008C (one pack/day)-supplemented diet to three cirrhotic patients with previous histories of hepatic encephalopathy on a low protein diet and date for the analysis of the effect of the diet on the pathophysiology of the liver and nutritional state.

## RESULTS

*Alterations in plasma amino acid levels of healthy controls and cirrhotic patients following the SF-1008C (half pack/meal)-supplemented and control diets*

Plasma amino acid levels were determined immediately before and 1, 2 and 3 h after a breakfast of the SF-1008C-supplemented or control diet and early in the morning following a lunch and dinner of the SF-1008C-supplemented or control diet. Plasma BCAA levels in both control subjects and cirrhotic patients, the basal levels of which were not lower in the latter, rose markedly 1 h after having the SF-1008C-supplemented diet in the morning (Fig. 2). Plasma valine levels remained high the next morning, although leucine and isoleucine values returned almost to the basal levels. Plasma BCAA levels increased only slightly following the control diet. Plasma phenylalanine, tyrosine and methionine levels markedly decreased after eating the SF-1008C-supplemented diet, although these levels returned to the basal levels the next morning (Fig. 3). The basal levels of plasma tyrosine were much higher in cirrhotic patients than in healthy controls, a trend that has been observed even in the early stage of liver cirrhosis (9). In cirrhotics, the levels of plasma phenylalanine, tyrosine and methionine were not markedly lowered up to 1 h after the SF-1008C-supplemented diet, and changes in the levels only between apparent 2 h after the administration. When the control

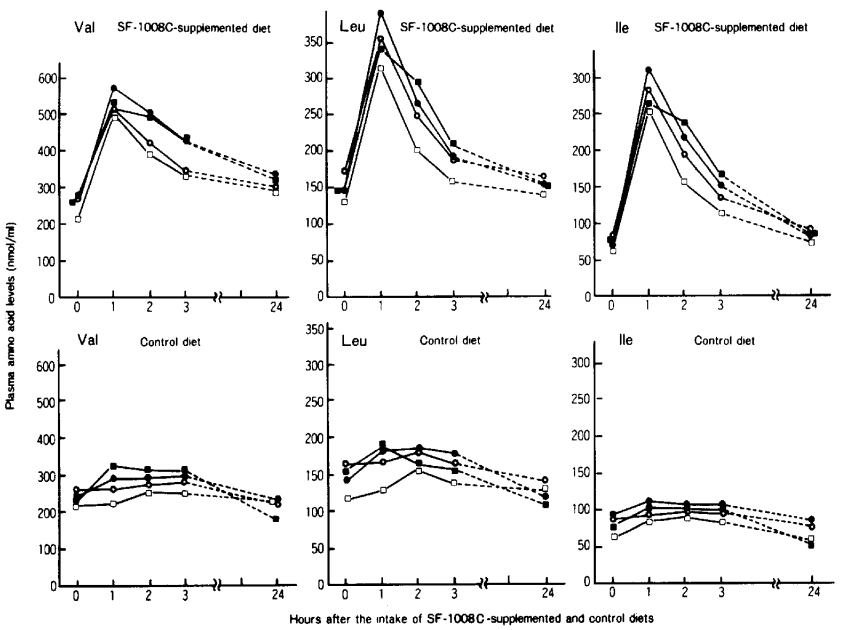


Fig. 2. Time course of plasma BCAA levels following the intake of the SF-1008C (half pack/meal)-supplemented and control diets. □ and ○, control subjects and ■ and ●, cirrhotic Patients 1 and 2. The diet was served at 9 a.m., 2 p.m. and 7 p.m. Other details are described under Subjects and Methods.

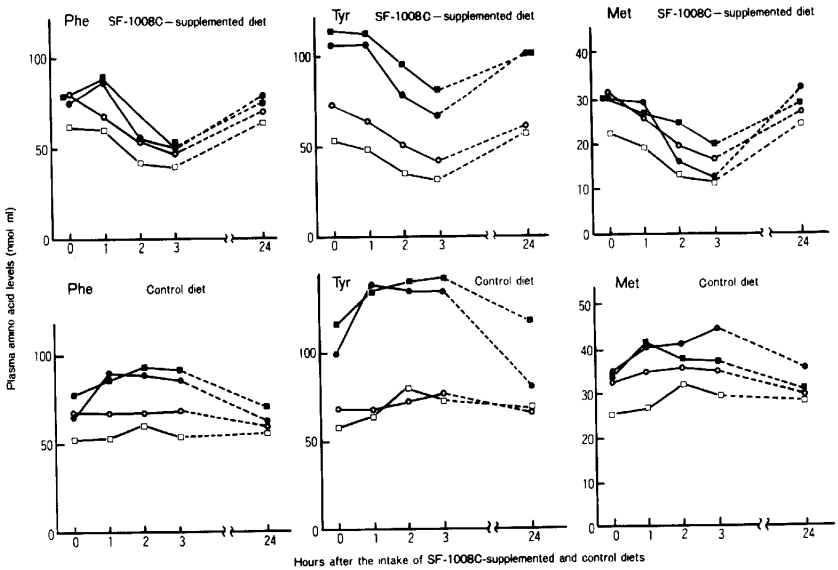


Fig. 3. Time course of plasma phenylalanine, tyrosine and methionine levels after the intake of the SF-1008C (half pack/meal)-supplemented and control diets. Symbols are the same as in Fig. 2.

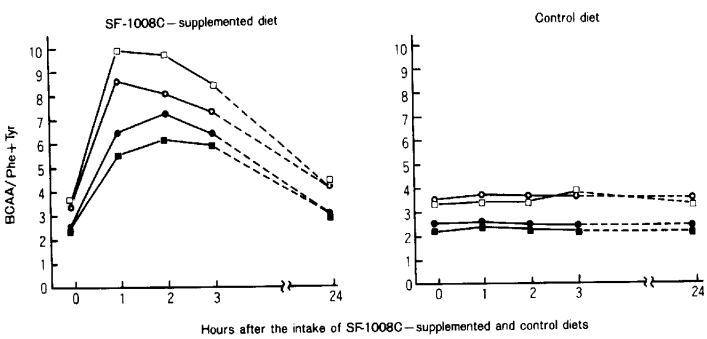


Fig. 4. Alterations in the BCAA/ (phenylalanine and tyrosine) ratio following the intake of the SF-1008C (half pack/meal)-supplemented and control diets.

diet was given to cirrhotic patients, plasma phenylalanine, tyrosine and methionine levels increased 1 to 3 h and again returned to the basal levels the next morning. The BCAA/(phenylalanine and tyrosine) ratio, which was lower in cirrhotics, rose to over the normal range after administration of the SF-1008C-supplemented diet in both control subjects and cirrhotic patients, and remained high the next morning (Fig. 4). The peak of this ratio in cirrhotic patients appeared later and was lower than in control subjects. The ratio did not change significantly with the control diet in both controls and cirrhotics.

The average nitrogen balance values were found to be positive on the day of the SF-1008C-supplemented diet (both control subjects and cirrhotic patients, +1.4 g/day) but negative on the day of the control diet (control subjects, −0.5 g/day and cirrhotic subjects, −1.8 g/day). Blood sugar levels in patients with liver cirrhosis increased following either the SF-1008C-supplemented or control diet, the peak being slightly higher with the SF-1008C-supplemented diet, but not exceeding 170 mg/dl (Fig. 5). Healthy subjects showed no significant elevation of the blood sugar concentrations. Blood ammonia levels rose transiently in both healthy controls and cirrhotic patients 1 h following the control diet. However, the levels reached a similar peak 2 h following the SF-1008C-supplemented diet.

The plasma amino acid levels were followed one whole day after administrating the SF-1008C-supplemented diet to two cirrhotic patients (Patients 1 and 3) following each meal of SF-1008C-supplemented diet. Patient 3 ( ■ in Fig. 6), with the lower plasma BCAA levels of the two, maintained a BCAA level within the normal range during the entire day she ate the supplemented diet. The high levels of plasma tyrosine, phenylalanine and methionine levels in this patient were also effectively lowered to values within the normal range during the whole day. Patient 1, with the higher tyrosine levels of the two, showed increased BCAA levels and diminished AAA and methionine levels. The BCAA/ (phenylalanine and tyrosine) ratio in the cirrhotic patients remained higher than the lower limit of the nomal values up to a half day after the SF-1008C-supplemented diet was given.

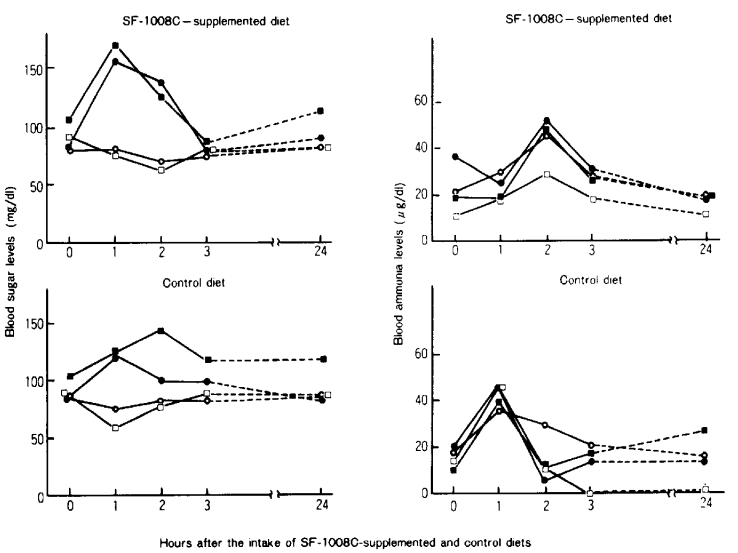


Fig. 5. Time course of blood sugar and ammonia levels after the intake of the SF-1008C (half pack/meal)-supplemented and control diet.

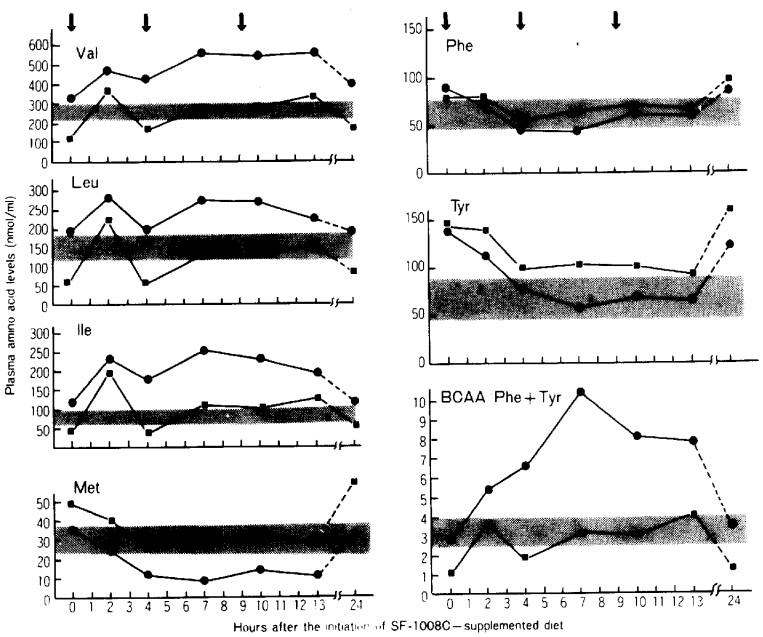


Fig. 6. Alterations in plasma neutral amino acid levels following the intake of the SF-1008C (half pack/meal)-supplemented diet. Two cirrhotic patients ; ●, Patient 1 and ■, Patient 3. The dark band indicates the normal range. Arrows indicate the time of each meal (8 a.m., 12 a.m. and 5p.m.).

*Treatment of cirrhotic patients with the SF-1008C (one pack/day)-supplemented diet*

The pathophysiological and nutritional state of three cirrhotic patients before, during and after treatment with the SF-1008C-supplemented diet are summarized in Table 4. When the patients ate the low protein diet, the daily protein intake was 31.2 g on the average (average protein ingestion 78 % of the served). When the SF-1008C-supplemented diet was administered, the protein intake increased to 59.8 g (the mean ratio 90 %). The nitrogen balance became positive during treatment with the SF-1008C-supplemented diet but became negative again after ceasing the supplemented diet. Elevation of the levels of serum prealbumin, a rapid-turnover protein, was observed gradually after the initiation of treatment with the SF-1008C-supplemented diet, and in the 2nd week of this diet the levels reached a peak of 30 % over the basal levels. Improvement in the slow wave in the electroencephalograms and the rapid performance of the number connection test were observed in all of the patients following the initiation of the SF-1008C-supplemented diet. Hepatic encephalopathy was not detected during the experiment. The blood ammonia levels did not increase even with a greater intake of protein during administration of the SF-1008C-supplemented diet, and other liver functions did not deteriorate with this treatment. Plasma BCAA levels increased

TABLE 4. EFFECT OF THE SF-1008C(ONE PACK/DAY)-SUPPLEMENTED DIET ON THE PATHOPHYSIOLOGY OF THE LIVER AND NUTRITIONAL STATE OF THREE CIRRHOTIC PATIENTS WITH HISTORIES OF HEPATIC ENCEPHALOPATHY

| | Low protein diet (Before) | Low protein diet + SF-1008C 7 days | Low protein diet + SF-1008C 14 days | Low protein diet (After) |
|---|---|---|---|---|
| Energy intake (kcal/day) | 1053± 159 | 1413±221 | 1514±383 | 1189±533 |
| Protein intake (g/day) | 31.2±2.5 | 57.1±5.4 | 59.8±4.5 | 36.0 ±17.9 |
| Urinary N excretion (g/day) | 9.9±2.4 | 8.0±2.8 | 8.6±3.3 | 8.9±3.5 |
| N balance (g/day) | −4.9 ±2.0 | 1.1±3.4○ | 1.0±3.3○ | −3.6±5.3 |
| Serum protein (g/dl) | 6.7±0.6 | 7.0±0.8 | 6.9±0.4 | 7.0 ±1.2 |
| Serum albumin (g/dl) | 3 .0±0.3 | 3.2±0.3 | 3.2±0.4 | 3.3±0.6 |
| Serum prealbumin (mg/dl) | 6.4±0.5 | 7.3±0.8 | 8.3±2.5 | 7.6±0.9 |
| Blood ammonia (μg/dl) | 107±28 | 97±42 | 113±28 | 144±54 |
| Serum bilirubin (mg/dl) | 2.32±1.96 | 2.15±1.23 | 2.30±1.47 | 2.66±1.84 |
| GPT (IU) | 30±10 | 33±12 | 33±15 | 41±17 |
| Normotest (%) | 67.6±5.4 | 60.4±4.8 | 67.2±7.1 | 56.8±1.4 |
| Number connection test (Second) | 79±4 | 67±11 | 57±9◎ | 63±16 |
| Plasma amino acid (nmoles/ml, normal range) | | | | |
| Val (216~306) | 146±31 | 206±52 | 218±74 | 159±44 |
| Leu (113~184) | 89±18 | 110±25 | 123±46 | 94±27 |
| Ile ( 61~106) | 55±12 | 67±13 | 97±49 | 51±14 |
| Phe ( 47~ 76) | 92±20 | 101±25 | 77±16 | 107±23 |
| Tyr ( 46~ 93) | 173±22 | 175±34 | 139±27 | 184±25 |
| Met ( 22~ 39) | 71±9 | 70±10 | 57±7 | 73±11 |
| BCAA/Phe+Tyr | 1.08±0.07 | 1.38±0.08 | 2.01±0.71 | 1.01±0.12 |

Mean ± SE ○ $p < 0.10$ ◎ $p < 0.025$

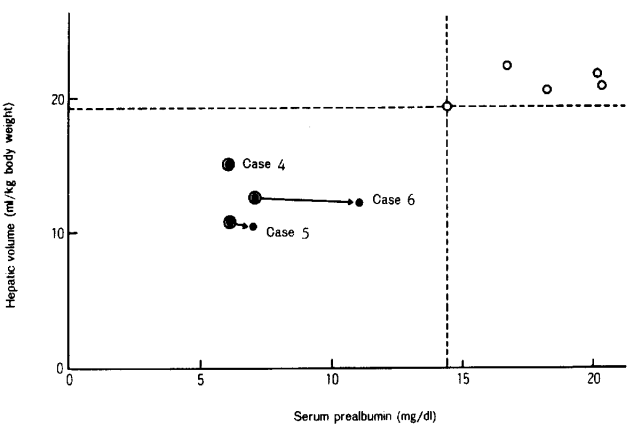


Fig. 7. Changes in the hepatic volume and serum prealbumin levels before and after the two week administration of the SF-1008C (one pack/day)-supplemented diet to cirrhotic patients with histories of hepatic encephalopathy. ○, Hospital controls having no hepato-biliary disease and ◉, cirrhotic patients. ●, Hepatic volume and serum prealbumin levels following the intiation of the SF-1008C-supplemented diet.

upon the treatment, and AAA and methionine levels decreased. The BCAA/(phenylalanine and tyrosine) ratio rose following the start of the SF-1008C-supplemented diet, but returned to the original values after cessation of this diet. The values of liver volume/kg body weight in all cirrhotics were much less than those in the control subjects (Fig. 7). Serum prealbumin levels rose following treatment with the SF-1008C-supplemented diet, even though there was no alteration in the liver volume before and after the treatment.

A representative patient (Patient 5) is described in Fig. 8. She had hyperammonemia of 211 $\mu$g/dl on admission and predominant $\theta$ waves in electroencephalograms. The patient had no complaint while on a low protein diet and under lactulose treatment. When the SF-1008C-supplemented diet was initiated, the daily protein intake increased and urinary nitrogen excretion diminished, so that the nitrogen balance was corrected to nearly jero. A low BCAA/ (phenylalanine

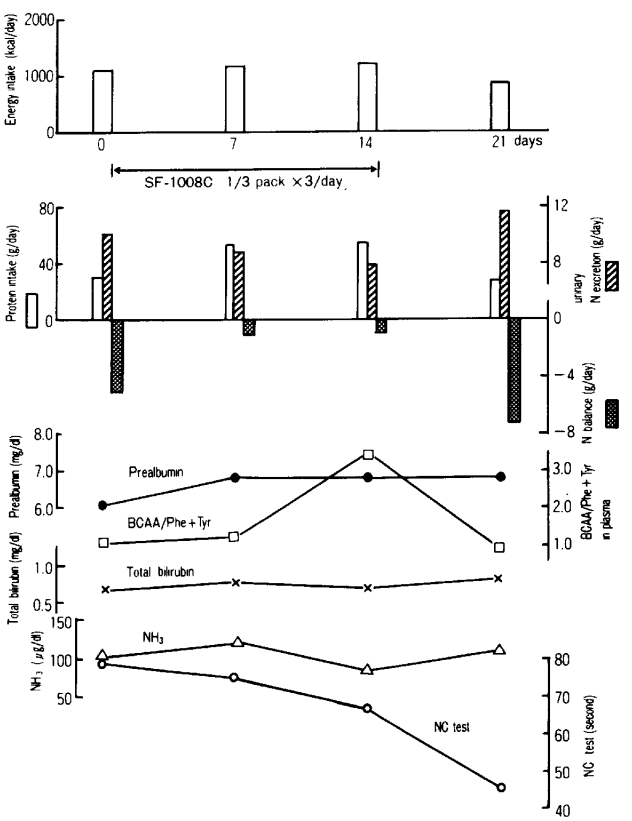


Fig. 8. Several parameters of liver function and nutritional condition before, during and after the administration of the SF-1008C (one pack/day)-supplemented diet to cirrhotic Patient 5 who has a history of hepatic encephalopathy. NC test : number connection test.

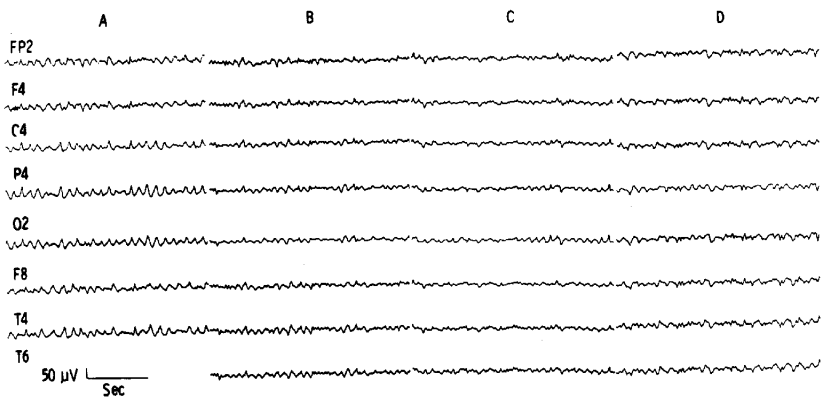


Fig. 9. Electroencephalograms before, during and after the administration of the SF-1008C (one pack/day)-supplemented diet to cirrhotic Patient 5. A, before ; B, a week, and C, 2 weeks after the initiation of the SF-1008C-supplemented diet, and D, a week after switching back to the low protein diet.

and tyrosine) ratio in the plasma increased to a normal value in the 2nd week of this diet but again returned to a low ratio after switching back to the control diet. Serum prealbumin concentrations rose markedly in the 2nd week of the SF-1008C-supplemented diet. The patient's electroencephalograms, having showed slow waves before the treatment, improved during the administration of the SF-1008C-supplemented diet but revealed the slow components after ceasing the diet (Fig. 9). The results of the number connection test were much improved after the SF-1008C-supplemented diet. The blood ammonia and serum bilirubin concentrations did not change during and after the treatment.

## DISCUSSION

Elevated AAA and methionine levels and diminished BCAA concentrations in plasma have been reported in patients with decompensated cirrhosis of the liver (10), as observed in Patients 4, 5 and 6. However, in patients with well compensated cirrhosis of the liver, as in Patients 1, 2 and 3, plasma BCAA levels are almost normal, and tyrosine and methionine levels are only slightly high. Improvement of the serum amino acid imbalance was obtained by administering the SF-1008C (a half pack/meal)-supplemented diet, but not by administering the control diet, although the energy and protein content were almost equal in these two diets. Normalization of the plasma aminogram also was found in cirrhotic patients with a history of hepatic encephalopathy by treatment with the SF-1008C (one pack/day)-supplemented diet for 2 weeks. Elevation of prealbumin levels during the administration of the SF-1008C-supplemented diet also suggests that the deficiency of BCAA in patients with liver cirrhosis may be rate limiting of protein synthesis in the damaged liver. BCAA are considered to function not

only as essential amino acids for protein synthesis but also as regulators of protein synthesis and catabolism (11). One can see that the amino acid composition of the protein, and not the amount of protein, is important for the proper nutrition of patients since a standard diet (energy 1710 kcal and protein 75 g/day) containing an equal amount of protein as a BCAA-added diet (energy 1630 kcal and protein 71 g/day) did not increase serum prealbumin and albumin levels (4). Supplementing BCAA and restricting AAA and methionine as well as providing an adequate amount of energy and protein are essential.

Swart *et al.* (12) gave a BCAA-enriched diet to cirrhotic patients who had experienced hepatic encephalopathy in the past and observed a negative nitrogen balance with a daily protein intake of 40 g and a positive nitrogen balance with a daily protein intake of 60 g. Their report also indicates that the patients could tolerate a BCAA-enriched high protein diet well and that the patients with impaired protein metabolism in skeletal muscle was improved on the BCAA-enriched protein diet. As mentioned above, we recognized an increase in the serum prealbumin as well as in the serum BCAA levels following the treatment of cirrhotic patients with a BCAA-added diet (4). Oral administration of GO-80, an amino acid solution which is enriched with BCAA and deficient in AAA and methionine, for a prolong time to patients with chronic hepatic encephalopathy helped them maintain a positive nitrogen balance and recover somewhat from the hepatic encephalopathy (13).

BCAA can be administered in the form of an amino acid-containing capsule as a kind of medication, but it is not easy for patients to take BCAA this way everyday for a long time. In this communication, a new nutrient product, SF-1008C, was used as a drink having a coffee, strawberry or vanilla flavor after each meal of natural foods. All of the patients examined could drink this product without any difficulty, and the diet intake ratio was not diminished upon administration of the SF-1008C-supplemented diet. Therefore, this product can be prescribed to cirrhotic patients in the outpatient clinic, since they can take it easily at home.

Two different diets, an SF-1008C-mixed and control diet, the energy and protein contents of which were similar, were given for 2 weeks to carbon tetrachloride ($CCl_4$)-treated rats with chronic liver injury and untreated rats with normal liver function. In the $CCl_4$-treated rats, after feeding the SF-1008C-mixed diet, ascites were observed less frequently and normotest values as well as serum GOT and GPT activities were improved significantly (7). Plasma tyrosine and methionine levels did not increase in $CCl_4$-treated rats on the SF-1008C-mixed diet and the BCAA/ (phenylalanine and tyrosine) ratio increased slightly. Tyrosine and methionine levels increased in these rats fed the control diet.

Nutrition management of patients with liver cirrhosis using SF-1008C is efficient and safe for improvement of the disturbed plasma amino acid pattern and impaired protein metabolism.

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