IJBCS
ISSN: 2147-1428

Original Article

International Journal of Basic and Clinical Studies (IJBCS)
2013;2(2): 35-48 Demirel B et al.

A Research on the Significance of Branched Chain Amino Acids (BCAAs) in the Diets of Liver Cirrhosis Patients*

Birsen Demirel[a] M. Seyit Mercanligil[a] Selcuk Disibeyaz [b]
Fatma Nisanci Kilinc [c] Fatma Celik[d]

[a] Department of Nutrition and Dietetics, Health Science Faculty, Eastern Mediterranean University, Famagusta, T.R.North Cyprus, via Mersin10,Turkey
[b] Turkish Higher Proficiency Hospital Gastroenterology Clinic.Ankara, Turkey
[c] Department of Nutrition and Dietetics , Health Science Faculty, Kırıkkale University, Kırıkkale, Turkey
[d] Department of Public Health, Medical Faculty, Dicle University, Diyarbakır, Turkey

Financial disclosure: none declared.

Abstract

This research has been realized with an aim of observing the effect of increasing the branched chain amino acid amount in the diets of liver cirrhotic patients on the treatment of the disease on 13 patients 7 of which are female and 6 of which are male of ages 37-71 with liver cirrhosis classified according to its viral etiology hospitalized at Turkish Higher Proficiency Hospital Gastroenterology Clinic. The patients anthropometric measuring Body Mass Index (BMI), Triceps Skin-fold Thickness (TST), Mid Arm Circumference (MAC) and blood samples for some biochemical parameters especially branched-chain amino acids (BCAA) and aromatic amino acids (AAA) analysis have been taken 3 times , in the Beginning , at the end of the 15 days diet treatment in harmony with chronic hepatic disease (Treatment I) and at the end of 1 month enrich from BCAA oral enteral product supported diet period from BCAA's provided as a supplement to this diet (Treatment II) . The blood BCAA levels of patients have increased between Beginning – Treatment II and Treatment I – Treatment II periods and this increase has been found statistically significant ($p<0.05$) . The ratio of BCAA/AAA has increased in Treatment II and this increased has been found statistically significant ($p< 0.05$). According to this study, adding of oral enteral products BCAAs to the diets of chronic liver disease patients can increase in blood BCAA/AAA ratio and decrease in blood ammoniac levels, thus result in improving the prognosis of the disease.

Key words : Liver Cirrhosis, BCAAs, AAAs, Oral Enteral Nutrition.

* The current study was presented at ESPEN Congress in 2003, Cannes "A research concerning the importance of BCAA's in patients with liver cirrhosis." Clinical Nutrition 22 (2003): S59."

IJBCS
ISSN: 2147-1428

Original Article

International Journal of Basic and Clinical Studies (IJBCS)
2013;2(2): 35-48 Demirel B et al.

Introduction

The liver is a central organ for regulating metabolism, and a variety of metabolic disorders are frequently seen in patients with chronic liver disease. Liver cirrhosis is an advancing , fatal , chronic disease characterized by various symptoms stemming from hepatocellular inadequacy and portal hypertension(1-3).

Prevalence of chronic liver diseases, including liver cirrhosis, is increasing worldwide. Specific dietary recommendations are needed in patients with chronic liver diseases in order to help prevent and treat liver decompensation because malnutrition is an independent predictor of mortality (4). Protein-calorie malnutrition is a common manifestation in cirrhotic patients with reported incidences as high as 65-90% . PEM affects largely the patients quality of life and survival. Thus diagnosis of and intervention for PEM is important in the clinical management of the liver cirrhosis. Supplementation with BCAA is indicated to improve protein malnutrition(5). Patients with chronic liver disease exhibit a progressive loss of fat and muscle mass leading to mixed protein–energy malnutrition. The severe loss of muscle mass and body cell mass have convincingly been shown to carry a grave prognosis . Inadequate nutrient consumption, maldigestion , increasing intestinal protein losses, dysfunctions in hepatic protein production, changes of metabolism and increasing energy need are among causes of malnutrition (6). Advanced cirrhosis of the liver is associated with altered metabolic, nutritional and hormonal status. Together, these alterations have marked repercussions on amino acid and protein metabolism (7).

Decreased serum ratio of branched-chain amino acids (BCAAs) (leucine, isoleucine and valine) to aromatic amino acids (AAAs) (phenylalanine and tyrosine) is a hallmark of liver cirrhosis and is caused by several factors, including reduced nutritional intake, hyper metabolism, and ammonia detoxification in skeletal muscle (3). Low serum BCAA/AAA ratio reduces biosynthesis and secretion of albumin in hepatocytes, and is also associated with the prognosis of patients with chronic liver disease. Affects almost all systems of body and forms a wide clinical table. The high morbidity and mortality of cirrhosis is secondary to these devastating complications. The quality of life and survival of patients with cirrhosis can be improved by the prevention and treatment of complications (8).

This study has been planned with an aim of observing the effect of supporting the diet of patients with liver cirrhosis with an enteral supplement containing BCAA for treatment of the disease.

Subject and Methods

This research has been commenced on 15 patients with liver cirrhosis classified according to its viral etiology hospitalized at Turkish Higher Proficiency Hospital Gastroenterology clinic , whereas 2 patients with liver cirrhosis has been deteriorated and developed exitus within the period the research has been undertaken. Because of that the research has been undertaken on 13 patients with liver cirrhosis (7 of which are female and 6 of which are male) between ages 31-71.

The patients participated in the research has been evaluated by a doctor of Gastroenterology department, patients with no complications but with viral etiology have been taken in the research in different

time periods. The research has been carried on in two levels. At first level of research (Treatment I) the patients participated in the research have been observed in the hospital with their diets (50-60gr. Prot/day-1.2-1.5 gr/kg/day) (5), applied for 15 days in harmony with liver and with a with inquiry method the nutrition they have consumed everyday (morning-noon-night and between) has been recorded in the daily consumption form. At the second level of the research (Treatment II) in addition to their diets a rich product has been provided for a month, to the patients observed with regular hospital diet in harmony with chronic hepatic disease for 15 days, containing oral enteral product enriched branched-chain amino acids to patients (HEPATONUTRİL-Clinical Nutrition- 2 pack/day). At this level the patients have been observed at home. Besides they were followed by phone and visits to their home. All patients have well tolerated the oral enteral product. Nutritional assessment was based on anthropometry, biochemical markers and food consumption record all period of study . Anthropometric measurement consisted of triceps skinfold thickness (TST) and midarm circumference (MAC). TST and MAC were measured using standard methods (10). Serum albumin and prealbumin were utilized as biochemical nutritional markers. Although nonspecific, serum albumin and prealbumin has been used to assess change in nutritional status and stratifying risk of malnutrition(11).

According to food consumption record the daily consumption amount of energy and food elements have been calculated with use of nutrition combination tables. The BMI (kg/m^2) of the patients participated in the research has been calculated by measuring of TST (mm), MAC(cm) the weight (kg) and height (cm) and their blood has been taken for biochemical analysis (total protein, albumin, globulin, pre-albumin, ammoniac, total bilirubin, direct bilirubin, Alkaline phosphatase(ALP), Gamma glutamyl transpeptidase(GGT), Aspartate Aminotransferase (AST),Alanine Aminotransferase (ALT), sodium, potassium, creatinine, Blood Urea Nitrogen(BUN), C- Reactive Protein (CRP), Haemoglobin(Hb), Hematocrit(Hct), Platelets (Plt), Prothrombin time (PT), BCAA, AAA) three times, first in the beginning of the study, second at the end of the 15. day and third at the end of the enteral product supported diet in the following 1 month treatment.

Statistical Analyses

SPSS statistical package program has been used for evaluating the data on windows medium. arithmetic mean(x), standard deviation (SD), values of all data belonging to every three period Beginning (B),Treatment I (TI), Treatment II(TII) have been calculated (10). Repeated three group of Beginning ,Treatment I, Treatment II was analyzed by using one way repeated ANOVA test . The significant differences was found by ANOVA was also analyzed by using Post Hoc Bonferoni test (11).Before using ANOVA test the normality of variables was confirmed by using Kolmogorov-Simirnov test .Wilcoxon marked rank test has been applied on statistical evaluation of average energy and food elements that patients consumed within Treatment I and Treatment II periods(11). All hypothesis were two tailed and the significant results were accepted while $p \leq 0.05$.

Results

Age and anthropometric measuring of female patients participated in the research according to the beginning and treatment periods is shown in table 1 and

statistical evaluation of these values is shown in table 2.

As seen in table 1 female patients' ages are found as 62.57 ± 9.12 years and heights are found as 151.42 ± 4.57cm. Besides the weighted BMI, TST, MAC and values of female patients have been increased when compared to the Beginning. But when the differences between the periods have been statistically evaluated, the difference of weighted BMI and TST values have been found trivial whereas the difference of MAC values between Treatment I and Treatment II periods has been found statistically significant (p>0.05).

Table 1. The anthropometric measurement and age of **female** patients in the beginning and treatment periods

Anthropometric Measurements	**Beginning** $\bar{x} \pm SD$	**Treatment I** $\bar{x} \pm SD$	**Treatment II** $\bar{x} \pm SD$	**Repeated ANOVA**(p)	**Bonferoni** (p)
Age (years)	62.57±9.126			-	-
Weight (kg)	58.57±8.580	59.42±12.01	60.42±9.571	> 0.05	-
Height (cm)	151.42±4.577			-	-
BMI (kg/m^2)	25.51±3.736	25.84±4.857	26.31±3.922	> 0.05	-
TST (mm)	14.92±5.689	17.85±4.525	19.00±4.000	> 0.05	-
MAC (cm)	24.07±2.812	24.21±3.649	24.57±3.408	< 0.05	**TI-TII**; < 0.05

TI: Treatment I
TII: Treatment II

Age and antropometrie measurements of male patients (n-6) have been checked according to the Beginning (table 2).The age of male patients has been found as 44.16±4.71 years, their heights has been found as 170.8±6.43cm. Besides while the weighted BMI values of male patients have decreased during the treatment periods when compared to the beginning, TST values have increased and MAC values have barely changed. But when the differences between periods have statistically been evaluated (table 2).The difference of weighted BMI and TST values between periods has been found trivial (p>0.05) whereas the difference of values of MAMC between Treatment I and T atment II periods have been found significant (p<0.05).

Table 2. The anthropometric measurements and age of **male** patients in the beginning and treatment periods

Anthropometric measurements	Beginning $\bar{x} \pm SD$	Treatment I $\bar{x} \pm SD$	Treatment II $\bar{x} \pm SD$	Repeated ANOVA(p)	Bonferoni (p)
Age (year)	44.16±4.708			-	-
Weight (kg)	71.75±14.34	70.83±15.74	69.16±16.35	> 0.05	-
Height (cm)	170.8±6.431			-	-
BMİ (kg/m^2)	24.40±4.363	24.23±5.138	23.50±5.050	> 0.05	-
TST (mm)	15.08±11.18	17.58±13.03	21.16±16.46	> 0.05	-
MAC (cm)	25.91±4.340	25.86±5.472	26.08±6.537	< 0.05	**TI-TII**; < 0.05

Biochemical finding values of patients participated in the research have been shown in table 3 according to treatment periods and statistical evaluation of such values has been shown in table 3.

Table 3. The biochemical findings of the patients in the beginning and treatment periods (n=13)

Biochemical Parameters	Beginning $\bar{x} \pm SD$	Treatment I $\bar{x} \pm SD$	Treatment II $\bar{x} \pm SD$	Repeated ANOVA(p)	Bonferoni (p)
Urea (mg/dl)	76.61±73.92	63.76±50.93	47.76±23.60	> 0.05	-
Creatinine (mg/dl)	1.107±177.75	1.069±0.404	0.931±0.360	> 0.05	-
AST (U/L)	117.0±177.75	64.30±51.73	60.92±46.10	> 0.05	-
ALT (U/L)	68.30±97.52	78.00±150.2	51.46±47.26	< 0.05	**B-TI**; < 0.05, **TI-TII**; < 0.05
ALP (U/L)	178.9±116.2	204.0±126.8	156.4±75.58	< 0.05	**B-TI**; < 0.05, **TI-TII**; < 0.05
Total Protein (g/dl)	7.284±2.021	7.484±1.756	8.130±0.976	< 0.05	**B-TI**; < 0.05
Albumin (g/dl)	2.630±0.507	2.846±0.509	3.369±0.649	< 0.05	**B-TII;** <0.05,**TI-TII**; < 0.05
Pre-albumin (g/dl)	0.078±1.77	0.083±2.32	0.096±2.75	< 0.05	**B-TI**; < 0.05, **TI-TII**; < 0.05, **B-TII**;<0.05
Globulin (g/dl)	4.653±1.853	4.638±1.673	4.761±0.958	> 0.05	-
Total Bilirubin (mg/dl)	4.800±6.758	3.928±5.920	3.546±5.554	> 0.05	-
Direct Bilirubin(mg/dl)	1.745±2.734	1.490±3.639	1.426±2.633	> 0.05	-
Sodium (mmol/lt)	136.2±3.443	136.0±5.552	135.3±4.922	> 0.05	-
Potassium (mmol/lt)	4.284±0.786	4.438±0.670	4.446±0.600	> 0.05	-
CRP (mg/lt)	49.03±44.15	45.98±42.27	34.30±33.70	< 0.05	**B-TII;** <0.05,**TI-TII**; < 0.05
Ammoniac (mg/dl)	110.86±50.03	90.67±32.89	67.90±26.66	< 0.05	**B-TII;** <0.05,**TI-TII**; < 0.05
GGT (U/L)	96.00±100.3	75.07±51.18	71.61±40.17	> 0.05	-
PT (sn)	17.36±2.466	16.29±2.612	15.46±2.203	< 0.05	**B-TII;** <0.05

As seen in table 3 when treatment periods biochemical findings are observed as regard to the beginning, it can be seen that urea, AST, ALT, total bilirubin, direct bilirubin, CRP, ammoniac and GGT values have decreased. Although It's above normal values, an increase in treatment I and a decrease in treatment II have been observed when compared to the beginning. Sodium, Potassium and globulin have shown very little change between periods. When urea, creatinine, AST, globulin, direct bilirubin, sodium, potassium, and GGT values are statistically evaluated (table 3). It is seen that the difference between all periods is statistically trivial ($p>0.05$). The decrease of ALP and ALT values during Treatment II when compared to the beginning have shown statistically trivial difference ($p>0.05$), decrease between Beginning-Treatment I and Treatment I-Treatment II have statistically significant difference ($p<0.05$). Decrease of CRP value in the Beginning-Treatment I period has shown statistically trivial difference ($p>0.05$).It has been found significant ($p<0.05$) in the Beginning-Treatment II and Treatment I-Treatment II periods. The reduction of ammoniac value has been found statistically significant ($p<0.05$) between each and every three period. Total protein, albumin and pre-albumin values of biochemical findings have increased in Treatment I and Treatment II when compared to the beginning (table 3). When the inter-period difference of total protein value statistically examined it has been found trivial in the Beginning - Treatment II and Treatment I- Treatment II periods, found significant between Beginnin- Treatment I ($p<0.05$). The increase of albumin value in Treatment I period according to the beginning has been found trivial ($p>0.05$) whereas the increase between the Beginning-Treatment II and Treatment I-Treatment II periods has been found statistically significant ($p<0.05$). The increase in pre-albumin value has constituted a statistically significant difference in each and every three period a little decrease has been observed at PT value when compared to the beginning. When the difference of PT value between the Beginning -Treatment I and Treatment I-Treatment II period statistically observed the difference is statistically trivial ($p>0.05$).The shortening of PT value between Beginning- Treatment II has been found statistically significant ($p<0.05$).

The BCAA findings of patients participated in the research belonging to the treatment periods and the statistical evaluation of such values are shown in table 4.

Table 4. The BCAA and AAA findings of patients in the beginning and treatment periods(n=13)

		Beginning $\bar{x} \pm SD$	Treatment I $\bar{x} \pm SD$	Treatment II $\bar{x} \pm SD$	Repeated ANOVA(p)	Bonferoni (p)
BCAAs	Isoleucine+leucine	61.29±21.99	69.93±19.95	129.1±98.55	< 0.05	**B-TI**; < 0.05, **TI-TII**; < 0.05, **B-TII**;<0.05
	Valine	73.58±24.82	74.07±28.87	78.58±24.82	< 0.05	**B-TII**;<0.05 **TI-TII**; < 0.05,
AAAs	Methionine	42.99±45.72	41.06±43.75	35.86±30.72	> 0.05	-
	Phenylalanine	92.84±23.91	96.00±20.89	85.97±25.45	> 0.05	-
	Tyrosine	142.07±55.40	126.4±46.31	111.2±44.93	< 0.05	**B-TI**; < 0.05, **B-TII**;<0.05

As seen in table 4, isoleucine+leucine and valine values have increased when compared to the beginning and a decrease (except for phenylalanine's Beginning-Treatment I values) at phenylalanine and tyrosine values have been observed. With regard to statistical evaluation of BCAA findings, increase of isoleucine+leucine values has constituted a statistically significant difference in every three period ($p<0.05$). Methionine and phenylalanine values of AAAs have been found statistically indifferent for each and every period ($p>0.05$). Although tyrosine value between Treatment I-Treatment II periods is statistically trivial ($p>0.05$). It has been observed that statistical difference between Beginning-Treatment II and Beginning-Treatment I periods is significant ($p<0.05$).

When the correlation between BCAA values belonging to the patients and biochemical findings are examined.It has been observed that there be a negative correlation between isoleucine+leucine and ammoniac, AST, ALP, total protein, total bilirubin, direct bilirubin and pre-albumin values. Nevertheless not have all correlations been found significant ($p>0.05$). That there is a negative correlation between valine and ammoniac ALP, ALT, and CRP and that the result is statistically not significant is being seen ($p>0.05$). But that there is a negative correlation between valine and pre-albumin, total protein, AST, total bilirubin, direct bilirubin and that such correlation is statistically significant has been observed ($p<0.05$).

It has been found that BCAA/AAA ratio of patients for treatment II is 1.222±0.949 whereas the beginning ratio was 0.539±0.254 (Table 5). As the results of statistical comparison o f values related to inter-period BCAA/AAA ratios (table 6) are observed a statistically significant increase with regard to BCAA/AAA ratios between the Beginning-Treatment II and Treatment I-Treatment II has been observed ($p<0.05$). No statistically significant increase has been observed between the beginning BCAA/AAA.

Table 5. The arithmetic means of BCAA/AAA ratios of patients with regard to periods

	$\bar{x} \pm SD$
Beginning BCAA/AAA	0.539±0.254
Treatment I BCAA/AAA	0.587±0.292
Treatment II BCAA/AAA	1.222±0.949

Table 6. The inter-period statistical evaluation of values related to BCAA/AAA ratio

Compared groups			T	p
Beginning BCAA/AAA	-	Treatment II BCAA/AAA	0.0	*
Beginning BCAA/AAA	-	Treatment I BCAA/AAA	28.00	**
Treatment BCAA/AAA	-	Treatment II BCAA/AAA	1.00	*

T: Wilcoxon Marked Rank Test value
* : $p<0.05$ **: $p>0.05$

Child score distributions of baseline and treatment periods are given in table 7. Also according to the period of treatment of patients with Child score plot is shown in Figure 1.

Table 7. Distribution of baseline and treatment periods after child score distributions.

Periods	Child A		Child B		Child C		Total	
	S	%	S	%	S	%	S	%
Beginning	3	23.0	6	46.2	4	30,8	13	100.0
Treatment I	4	30.8	5	38.4	4	30.8	13	100.0
Treatment II	4	30.8	6	46.2	3	23.0	13	100.0

As can be seen in Table 7, at the beginning, 23% of patients while positioning in Child A, this ratio in treatment I and II increased to 30.8%. When looking to Child B score, at the beginning, 46,2% of patients while positioning in treatment I and II, 38.4% of patients in treatment I and 46.2% of patients in treatment II again have positioned in Child B. When looking to Child C score, at the beginning and in treatment I, 30,8% of patients while positioning in Child C, this ratio has decreased to 23% in treatment II.

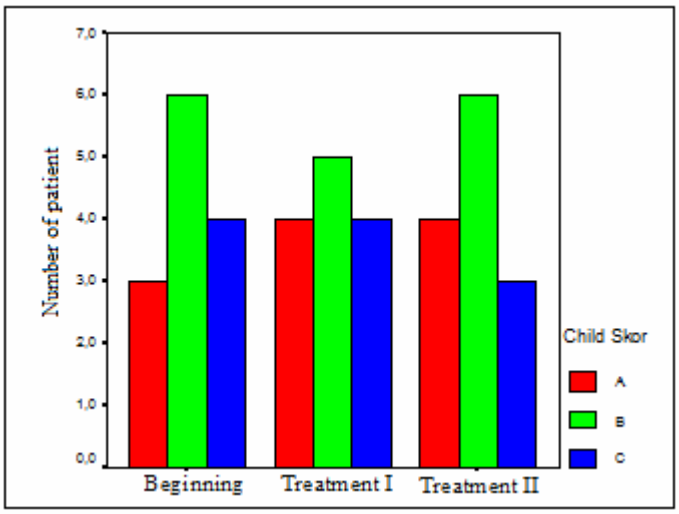

Figure 1. Child score graphics as to patients treatment periods

The averages of daily energy, nutriment elements and most necessary amino acids consumption belonging to 15 days period of (Treatment I) and Treatment II periods of patients participated in the research and statistical comparisons thereof have been shown in table 8. As the consumption amount of branched chained amino acids is found significant ($p<0.05$) the consumption amounts of aromatic amino acids are found statistically trivial when compared between periods ($p>0.05$).

Table 8. The comparison of daily nutrition consumption average of patients for treatment I and treatment II

Energy and Nutrients	Treatment I $\bar{x} \pm SD$	Treatment II $\bar{x} \pm SD$	T	p
Energy (kkal)	1338.3±296.4	1898.46±226.7	1	*
Protein (g)	41.61±10.22	62.23±8.506	1	*
Fat (g)	36.00±8.195	37.0±5.597	37	**
Carbonhydrate (g)	209.61±52.71	317.9±42.35	1	*
Calcium (mg)	573.9±190.3	911.8±174.3	0	*
Iron (mg)	2.76±1.363	3.384±1.556	23	**
Phosphorus(mg)	674.2±190.4	891.4±162.1	4	*
Potassium (mg)	1598.7±478.1	2109.6±457.7	2	*
Sodium (mg)	855.2±273.4	1003.3±324.2	23	**
Vitamin A (IU)	5758.5±3290.01	7344.0±3277.0	25	**
Vitamin C (mg)	92.07±45.17	150.4±61.85	4.5	*
Cholestherol (mg)	113.46±50.16	137.8±56.10	34.5	**
Isoleucine (g)	2.24±0.505	4.772±0.529	0	*
Leucine (g)	3.531±0.855	6.163±0.681	0	*
Valine (g)	2.565±0.738	4.589±0.550	1	*
Methionine (g)	0.972±0,256	1.052±0.189	31	**
Phenylalanine (g)	2.119±0.508	1.939±0.428	38	**
Tyrosine (g)	1.542±0.407	1.391±0.352	36	**

T: Wilcoxon Marked Rank Test value * : $p<0.05$ **: $p>0.05$

Discussion

In recent decades, the role of supplementation of the BCAA in the treatment of liver disease has been studied extensively both in animal models and in humans. A number of studies have reported their favorable effects on hepatic encephalopathy , protein balance , and liver regeneration. Unfortunately, the explanation for the lack of success of enhanced intake of BCAA reported in a number of clinical trials is lacking (9).

In this study the effects of an enriched in the amount of branched chained amino acid in diets of patients with liver cirrhosis have been researched.

There is no gold standard to assess the nutritional status of patients with chronic liver disease. Anthropometric evaluation is essential in any nutritional assessment. The main measurements are weight, height and skinfold thickness. In patients with cirrhosis, some of these indicators become less reliable due to the presence of edema or ascites, which can lead to an underestimation of malnutrition. The tricipital skinfold thickness measures have been proposed as two of the most reliable parameter. Another useful and practical parameter in this group of patients is the BMI (4). But, body weight and BMI were overestimated in cirrhotic patients because of fluid overload. The disadvantage of using BMI to study nutritional status in cirrhotic liver disease patients experiencing salt and water retention was the underestimation of the prevalence and degree of malnutrition.

Clues of protein-calorie malnutrition can be catched with a physical examination. The measuring of triceps skin-fold thickness, subskin fat tissue and mid-arm muscle circumference shows muscle mass. Even though there is water and salt holding at chronic liver patients these measuring provides very accurate information. These measuring are especially significant for findings on the same patients at different times (13).

In this study the anthropometric measuring results of female patients have increased in Treatment II when compared to the beginning period. But this increase has not been found statistically significant (except for Treatment I and Treatment II periods for MAC ($p>0.05$). When anthropometric measuring results of male patients have been examined no statistically significant change has been observed compared to periods except for MAC and TST measuring ($p>0.05$). Since the ascites treatment from the beginning has decreased at the a decrease in the weight has been observed. But statistical increase at TST of patients with liver cirrhosis has shown that TST measure is a more reliable measure that is weight.

The aim of nutritional assessment liver disease patients is to plan a rational treatment by showing the type and degree of malnutrition of patient. In a standard evaluation there are clinic and diet history, physical examination, laboratory examination and body composition measuring (14).

Regarding the biochemical assessment of nutrition, some of the most common and useful indicators are albumin and prealbumin, however, they are synthesized in the liver, and therefore, their value as indicators of nutrition status in the cirrhotic patient is poor, actually, the serum level of albumin does not correlate with anthropometric measures in these patients. In lack of nephropathy and enteropathy which causes protein loss, it can be a good indicator of chronic hepatic disease. The concentration of branched-chain amino acids (BCAAs) and aromatic amino acids are related to the degree of hepatic decompensation, and their particular application in the nutritional assessment needs to be further investigated (15,16,17).

In this group of patients , We hypothesized that administration of BCAA will improve liver function and nutritional status in such patients. Therefore, the study was performed to examine whether administration of BCAA one month could help to improve liver function and nutritional status.

In this study total protein, albumin and pre-albumin values have generally increased in treatment I and treatment II when compared to the beginning ($p<0.05$).

Looking at the findings one can see that increases in treatment II is an indicator of nutritious feeding and it has showed the positive effect of treatment with BCAA.

Marchesini.G et al (18), have researched the role of oral supplementation with branched-chain amino acids (BCAA) on 174 patients with in advanced cirrhosis . In patients who remained in this study, nutritional parameters and liver function tests were, on average, stable or improved during treatment with BCAA and the Child-Pugh score decreased (P = 0.013). Also, anorexia and health-related quality of life improved.

Koreeda C. et al (19), reported that nutrient parameters and functional reserve capacity of the liver, and the effects of late evening snack(LES) treatment with BCAA enrichment in liver cirrhosis patients, were evaluated using asialoscintigraphy. They founded serum levels of albumin, tyrosine and molar ratio of BCAA to tyrosine (BTR) were significantly improved.

Blood ammoniac level of chronic hepatic patients has been decreased with improvement of clinical table (20). Ammoniac which is one of the most significant findings at chronic hepatic diseases has been found in high proportions on all patients. But decrease between treatment I and treatment II when compared to the beginning ($p<0.05$) has showed that enteral product supported treatment has made a positive impact a blood ammoniac level of patients with liver cirrhosis.

The liver is involved in the synthesis of many of the proteins required for normal clotting. Thus, the prothrombin time reflects the degree of hepatic synthetic dysfunction. The prothrombin time increases as the ability of a cirrhotic liver to synthesize clotting factors diminishes. PT is a more significant test on severe and acute hepatic diseases than albumin. Longing of PT shows that prognoses is not good (21). In this research it has been observed that PT times of patients has prolonged (table 3). In treatment II the PT results of patients has shortened when compared to the beginning and this has been found that it is statistically significant ($p<0.05$). In blood BCAA results of patients it has been observed that there has been a statistically meaningful increase in BCAA amount at the end of treatment II when compared to the beginnings ($p<0.05$).

The ratio of branched-chain amino acids to aromatic amino acids normally is 3.0-3.5 for patients with liver cirrhosis and the ratio is observed 5.04±1.87 on control group whereas it is observed 1.1±0.62 on patients with liver cirrhosis group ($p<0.01$). The most recent large-scale, multicenter, long-term trials have shown the effects of BCAAs on nutrition, survival, and QOL of patients with cirrhosis by using granulated BCAAs over the course of 1 to 2 y (22-24).

There are various opinions about the mechanism of the decreased levels of BCAA in cirrhosis. BCAAs are used for ammonia degradation in skeletal muscles of cirrhotic patients. A low BCAA level impairs synthesis of proteins such as albumin and destroys muscle proteins (25,26).

The consumption averages of branched-chain amino acids between Treatment I and Treatment II periods have been found statistically significant ($p<0.05$).

As a result of this increase in daily BCAA consumption amount and its positive effects on patient blood biochemical findings formed by rich enteral products from branched-chain amino acids it can be said that the use of products containing BCAA on patients with chronic disease could be useful.

References

1. Takumi Kawaguchi, Namiki Izumi, Michael R. Charlton, and Michio Sata. Branched-Chain Amino Acids as Pharmacological Nutrients in Chronic Liver Disease. Hepatology, 2011;54:1063-1070

2. Kawaguchi T, Yamagishi S, Sata M. Branched-chain amino acids and pigment epithelium-derived factor: novel therapeutic agents for hepatitis C virus-associated insulin resistance. Curr Med Chem 2009;16:4843-4857.

3. Yamato M, Muto Y, Yoshida T, Kato M, Moriwaki M. Clearance rate of plasma branched-chain amino acids correlates significantly with blood ammonia level in patients with liver cirrhosis. Int Hepatol Commun .1995;3:91-96.

4. Moctezuma-Vel_azquez C, et al., Nutritional assessment and treatment of patients with liver cirrhosis, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.03.017.

5. Hisataka Moriwaki, Yoshiyuki Miwa, Masahiro Tajika, Masahiko Kato, Hideki Fukushima, and Makoto Shiraki. Branched-chain amino acids as a protein- and energy-source in liver cirrhosis, Biochemical and Biophysical Research Communications, 2004,313, 405–409

6. Mathias Plauth, Elke-Tatjana Schütz. Cachexia in liver cirrhosis.International Journal of Cardiology , *85(1)*, *2002*, *83-87.*

7. F. Blonde-Cynober, C. Aussel, L. Cynober. Abnormalities in branched-chain amino acid metabolismin cirrhosis: influence of hormonal and nutritional factors and directions for future research. Clinical Nutrition, 18 (1), 1999,5-138. Goldberg E., Chopra, S.: Overview of the complications, prognosis, and management of cirrhosis, Up to Date, Topic 1263 Version 12.0.May 2013.

9.Holecek M, Branched-chain amino acids and ammonia metabolism in liver disease: Therapeutic implications, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.01.022

10.Jones JM. Reliability of nutritional screening and assessment tools. Nutrition 2004;20(3):307-11.

11. Seres DS. Surrogate nutrition markers, malnutrition, and adequacy of nutrition support. Nutr Clin Pract 2005;20(3):308-13.

12.Celik MY. Biostatistics, Scientific Research , SPSS. Dicle University Press, 2011.

13. Gordon L. Jensen, Pao Ying Hsiao, and Dara Wheeler; Adult Nutrition Assessment Tutorial, J Parenter Enteral Nutr. 2012;36:267-274.

14.Chulaporn Roongpisuthipong, Aphasnee Sobhonslidsuk, Kanokrat Nantiruj and Sriwatana Songchitsomboon, Nutritional Assessment in Various Stages of Liver Cirrhosis, Nutrition 2001,17:761–765.

15. Chang WT, Ker CG, Hung HC, Lee KT, Chen LS, Chiang HC, et al. Albumin and prealbumin may predict retinol status in patients with liver cirrhosis. Hepatogastroenterology 2008;55:1681–5.

16. Fuhrman P, Charney P, Mueller CM. Hepatic proteins and nutrition assessment. J Am Diet Assoc 2004;104:1258–64.

17. Alberino F, Gatta A, Amodio P, Merkel C, DiPascoli L, Boffo G, et al. Nutrition and survival in patients with liver cirrhosis. Nutrition 2001;17: 445–50.

18. Giulio Marchesini, Giampaolo Bianchi, Manuela Merli, Piero Amodio, Carmine Panella, Carmela Loguercio, Fillipo Rossi Fanelli, Roberto Abbiati, Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double-blind, randomized trial .Gastroenterology, 2003, 124(7), 1792-1801.

19. Chizu Koreeda,1 Toshihito Seki,1 Kazuichi Okazaki,1 Sang Kil Ha-Kawa2 and Satoshi Sawada2,. Effects of late evening snack including branched-chain amino acid on the function of hepatic

parenchymal cells in patients with liver cirrhosis. Hepatology Research 2011; 41: 417–422
20. Peter Ferenci, Hepatic encephalopathy in adults: Clinical manifestations and diagnosis, Up to Date, Literature review current through: Jun 2013. Last updated: Tem 10, 2013.
21. Eric Goldberg, Sanjiv Chopra, Diagnostic approach to the patient with cirrhosis, Up to Date. Literature review current through: Jun 2013. Last updated: Mar 09, 2012.
22.Marchesini G, Bianchi G, Merli M, Amodio P, Panella C, Loguercio C, et al. Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double blind, randomized trial. Gastroenterology 2003;124:1792– 801.
23.Muto Y, Sato S, Watanabe A, Moriwaki H, Suzuki K, Kato A, et al. Effects of oral branched-chain amino acid granules on event-free survival in patients with liver cirrhosis. Clin Gastroenterol Hepatol 2005;3:705–13.
24.Kazuyuki Suzuki, Akinobu Kato, Masakatsu Iwai, Branched-chain amino acid treatment in patients with liver cirrhosis, Hepatology Research 30, Supplement, 2004, 25–29.
25.Okuno M, Moriwaki H, Kato M, Muto Y, Kojima S. Changes in the ratio of branched-chain to aromatic amino acids affect the secretion of albumin in cultured rat hepatocytes. Biochem Biophys Res Commun 1995;214:1045–50.
26. Mordier S, Deval C, Bechet D, Tassa A, Ferrara M. Leucine limitation induces autophagy and activation of lysosomedependent proteolysis in C2C12 myotubes through a mammalian target of rapamycin-independent signaling pathway. J Biol Chem 2000;275:29900 – 6.