

DIETARY THERAPY IMPACT FOR CIRRHOTIC PATIENTS WITH HEPATIC ENCEPHALOPATHY

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DIETARY THERAPY IMPACT FOR CIRRHOTIC PATIENTS WITH HEPATIC ENCEPHALOPATHY (Abstract): BACKGROUND: Malnutrition is prevalent in all forms of liver disease and it is associated with increased number of complications and increased short and long term mortality. AIM: to evaluate the level of serum ammonia, recurrence of hepatic encephalopathy (HE), improvement of mental status and of the nutritional status after one month of high protein high calorie (HPHC) diet the effect of a dietary therapy on cirrhotic patients with HE. MATERIALS AND METHODS: Our study was designed as a descriptive prospective analysis of patients with cirrhosis and a previous episode of HE, admitted in Gastroenterology Department of Elias Emergency Hospital, during one year (January 2010-January 2011). The diagnosis of cirrhosis was based on the medical history, physical examination, biochemical findings and imagistic methods. It was evaluated mental status, serum level of ammonia and nutritional parameters, before and after one month diet. RESULTS: A significant decrease in the blood ammonia levels was observed. A significant number of patients showed an improvement of their mental status assessed by West Haven scale after diet. A significant improvement of number connection test (NCT) scores was also noted. Body weight was slightly but significantly increased after a month of diet. Mid-arm muscle circumference (MAMC) increased after one month diet, but not statistically significant. CONCLUSIONS: The HPHC diet has a beneficial effect on the patients with cirrhosis and hepatic encephalopathy, more significant regarding the mental status, level of the serum ammonia and the body weight. It was noted an improvement of mid arm muscle circumference. Key words: hepatic encephalopathy, diet, malnutrition, liver cirrhosis.

KEY WORDS: MALNUTRITION; HEPATIC ENCEPHALOPATHY; SERUM AMMONIA; HIGH PROTEIN HIGH CALORIE DIET.

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INTRODUCTION

Malnutrition has a high prevalence in all forms of liver disease, ranging from 20% in compensated liver disease to more than 80% in those patients with decompensated liver disease and 100% in hospitalized patients with acute alcoholic hepatitis superimposed on cirrhosis [1]. Patients with alcoholic cirrhosis have a higher incidence

of malnutrition than those with nonalcoholic liver disease.

Protein-calorie malnutrition (PCM) can be identified in all clinical stages, but is easier observed in advanced stages of liver disease [2].

There are a number of factors that contribute to malnutrition in patient with liver disease such as decreased calories

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intake, decreased nutrients absorption or impaired metabolic absorption [3].

Many descriptive studies have shown higher rates of complications and mortality in cirrhotic patients with protein malnutrition as well as reduced survival when such patients undergo liver transplantation [4].

Hepatic encephalopathy (HE) is a neuropsychiatric condition that leads to mental status changes and abnormal neuromuscular function in patients with acute and chronic liver failure [5].

More than 35% of hospitalizations are related to HE, with lengths of stay between 5 and 7 days [6].

Two forms of HE are recognized: minimal hepatic encephalopathy (MHE) and overt hepatic encephalopathy (OHE). Patients with MHE have no clinical symptoms of HE, but subtle deficits in cognitive function that can be detected by psychometric or neurophysiologic testing. OHE is characterized by symptoms ranging from trivial lack of awareness to loss of consciousness, and is usually assessed using the West-Haven grading system [7].

Multiple recent studies have shown the importance of maintaining the positive nitrogen balance via increased protein and caloric intake in cirrhotic patients [5]. Negative nitrogen balance due to protein restriction leads to protein-calorie malnutrition (PCM) [8], and decrease the survival rate in patients with liver cirrhosis [5].

The end point was to evaluate the level of serum ammonia, recurrence of HE, improvement of mental status and the nutritional status in patients with liver cirrhosis before and after 1 month of high protein high calories diet.

MATERIALS AND METHODS

Our study was designed as a descriptive prospective analysis of patients with cirrhosis and a previous episode of HE, admitted in Elias Emergency Hospital, Gastroenterology Department, during one year (January 2010-January 2011).

Inclusion criteria were: age between 18 and 80 years, documented liver cirrhosis in a stable hemodynamic condition, compliance to dietary recommendations and medical treatment, with a previous episode of HE.

Exclusion criteria were: overt hepatic encephalopathy (OHE) stage III or IV (West Haven criteria), active gastrointestinal bleeding, ongoing alcoholism, sepsis, liver failure, hepatocellular carcinoma or other known malignancies.

The diagnosis of cirrhosis was based on the medical history, physical examination, biochemical findings and imagistic methods (ultrasound and/or computed tomography).

Assessment of the mental status was performed using West Haven scale. Those who were with no abnormalities detected (stage 0) had to perform a conventional Number Connection Test (NCT), using circles numbered from 1 to 25, used for psychometric performance evaluation.

Laboratory tests included cell blood count (CBC), bilirubin, albumin, prothrombin time (PT), serum ammonium, International Normalized Ratio (INR), urea, creatinine, which were used to calculate Child Pugh score and to laboratory evaluation; all markers were measured by standard laboratory methods.

In order to evaluate the nutritional status of the patients with cirrhosis we used mid-arm muscle circumference (MAMC) [9,10], an anthropometric parameter were that is not affected by the presence of ascites or peripheral edema and body weight.

Patients from this study received medical treatment including lactulose in order to obtain 2-3 semisolid stools daily and rifaximin 1200 mg/day.

They were followed for 1 month. During that period they received high caloric high protein (HPHC) diet: 30kcal/kg/day and 1.2g of proteins/kg/day. They were allowed to eat only 100g of poultry meat or fish twice a week. The proteins were from vegetables, cereals or milk products, approximately 20-25% vegetables and fruits,

25-30% cereals and 45-50% milk and milk products. The feeding pattern was designed to provide 4 meals during the day and a late-night snack rich in carbohydrates at 10 p.m. They were asked to choose from a menu with several alternatives by individual preference and tolerance. The tolerance of the cirrhotic patients to dietary recommendation was excellent; no one withdrew from this study because of lack of compliance.

The protocol conformed to the Declaration of Helsinki and Guidelines for Good Clinical Practice in Clinical Trials and was approved by the Elias Emergency Hospital Committee. All patients signed an informed consent.

A descriptive study of the quantitative values was undertaken by using mean and standard deviation values, and qualitative values were expressed as frequencies.

RESULTS

A series of 68 hospitalized patients with cirrhosis, 43 male (63%) and 25 female (37%), was included, the median age was 54 (range 30-68).

The etiology of liver disease was alcoholic in 26 patients (38%), viral-related: B, C, B+D, B+C in 24 (35%), mixed: alcohol + viral in 13 patients (19%) and other etiologies (autoimmune, primary biliary cirrhosis, cryptogenic) in 5 patients (8%).

The degree of liver disease was assessed using the Child Pugh classification. Liver function was relatively well preserved (Child A) in 19 patients (28%), moderately compromised (Child B) in 46 patients (67%) and severely compromised (Child C) in 3 patients (5%).

Clinical examination included the evaluation of the presence of ascites and edema. 53 patients (77%) had ascites, as followed: 33 patients with slight ascites (63%) and 20 with moderate ascites (37%), and 15 patients (23%) didn't have. Only 9 patients had edema (13%).

From all that patients (28) only 10 patients had abnormal NCT (36%),

corresponding to minimal hepatic encephalopathy (MHE).

A significant decrease in the blood ammonia levels was observed after a month of HPHC diet, when all patients included in the study were considered. The decrease in blood ammonia level was observed in all patients as it is revealed in Table I.

Table I The ammonia level and NCT scores before and after HPHC diet

	Before diet (mean)	After diet (mean)	P value
Blood ammonia *	58.3	35.2	<0.0001
NCT scores	62	52	<0.0001

* normal range: 11-33 $\mu\text{mol/L}$

No patient was withdrawn from the study due to a recurrent episode of HE. A significant number of patients showed an improvement of their mental status after diet: 45% from stage I patients (West Haven scale) meaning 10 patients became stage 0. Fourteen patients with stage II (75%) became stage I and only 4 (25%) from 18 patients remained in stage II (Table II).

Table II Evolution of the mental status according to the initial stage of HE assessed by West Haven scale.

	No improvement (%)	1 stage improvement (%)
Initial West Haven stage I	12 (55)	10 (45)
Initial West Haven stage II	4 (25)	14 (75)

That means, after a month of diet, the classification of the patients contains: 38 patients (56%) with stage 0, 26 patients (38%) stage I and only 4 (6%) with stage II. None of these patients worsened the mental status.

The repartition of different stages, before and after the diet, is revealed in Table III.

A significant improvement of number connection test (NCT) scores was also noted

when the initial scores were compared with the scores obtained after a month of HPHC diet.

Taking into account the severity of liver disease, 63% of patients (29 patients) in Child B stage had an improvement in the grade of HE, compared with only one patient (33%) with Child C cirrhosis.

Table III Global repartition of different West Haven stages, before and after the diet

No of patients	Stage 0	Stage I	Stage II
Before diet	28	22	18
After diet	56	38	4

The improvement of HE after the diet was not as good in patients with alcoholic cirrhosis as in patients with viral or mixed etiology. 35% of alcoholic patients improved their mental status after HPHC diet, compared with 43% of patients with viral etiology and with 46% of patients with mixed etiology, but this difference didn't reach statistical significance ($P=0.06$).

Body weight was slightly but significantly increased after a month of diet. Mean value before diet was 68.3 kg and after the HPHC diet reached up to 69.2 kg ($P=0.008$). Mid-arm muscle circumference (MAMC) increased from 28.6 cm to 29.3 cm after one month diet, but not statistically significant.

DISCUSSION

Hepatic encephalopathy (HE) is a neuropsychiatric condition of impaired mental status and abnormal neuromuscular function that may occur in patients with advanced liver disease and has a potential for full reversibility [8].

Minimal hepatic encephalopathy (MHE) has no recognizable clinical symptoms. It is present in 30-84% of patients with liver cirrhosis. It is diagnosed by neuropsychological tests.

Hepatocellular failure, portosystemic shunting, sepsis, variceal bleeding, excess dietary intake or electrolyte imbalance are

the most common precipitating factors that contribute to develop of HE [8].

European Society for Clinical Nutrition and Metabolism (ESPEN) recommends that patients with liver cirrhosis should receive 35-40 kcal/kg per day [11].

Protein requirements are increased in cirrhotic patients and high protein diets are generally well tolerated in the majority of patients.

The inclusion of adequate protein in the diets of malnourished patients is often associated with a sustained improvement in their mental status. Protein helps preserve lean body mass; skeletal muscle makes a significant contribution to ammonia removal. Protein restriction must be avoided and the recommendation is to maintain 1.2-1.5 g proteins/kg/day [12].

In severely protein-intolerant patients it is recommended branched-chain amino acids (BCAA) supplementation. These amino acids (leucine, isoleucine and valine) cannot be synthesized de novo.

Chronic liver disease is characterized by a decrease in the serum level of BCAA, whereas hyperammonemia increases their utilization [13].

The Fischer ratio, the balance between branched-chain amino acids (BCAA) and aromatic amino acids (AAA), is 3:1 in healthy population. It becomes inverted in cirrhotic patients. BCAA are essential for protein production and prevent the catabolism. AAA are precursors for "false" neurotransmitters such as octopamine and phenylethylamine, contributing to neurologic dysfunction [13].

A meta-analysis of BCAA supplementation revealed the improved rate of recovery from episodic HE, but did not demonstrate a survival advantage [14].

Long-term oral supplementation with BCAA mixture is better than ordinary food to improve the serum albumin level and the energy metabolism in cirrhotic patients [15]. In the same study body weight was slightly but significant increase in the BCAA group.

A significant correlation was established with midarm muscle

circumference (MAMC), but not with triceps skinfold thickness (TST).

In a randomized, double-blind, multicenter study, comparing a supplement of BCAA or maltodextrin the conclusions were that the supplementation with BCAA after an episode of HE does not decrease recurrence of HE. BCAA improve minimal HE and muscle mass [16].

The timing of BCAA supplementation may be crucial. This issue was addressed by a crossover study. At 3 months, a significant increase in serum albumin level was observed in patients administered nocturnal BCAA.

It leads to an increase of serum protein of approximately 10% if given before bedtime [17]. Problems that limit the use of BCAA in the treatment of HE are their taste and expense.

Our study shows that protein and energy requirements for cirrhotic patients may be maintained in patients with HE. It leads to improvement of mental status in 90% of patients. Our study confirms recent studies showing that patients tolerate high-protein diets and benefit of them.

Most patients tolerate HPHC diet without risk of HE. It improves mental status in a significant way. A higher proportion of patients with severe impairment of the mental status improved after one month diet (63%). A lower proportion of patients with alcoholic cirrhosis improved their mental status compared with those with viral or mixed etiology. A significant improvement of number connection test (NCT) scores was also noted after the diet.

A decrease in blood ammonia level was noted not only for patients with improvement of mental status, but also for the patients that maintained their mental status. No one had an increase of serum level ammonia. This HPHC diet had a significant improvement on the body weight and mid arm muscle circumference (MAMC) after a month of treatment.

We used an eating schedule characterized by 4 meals during the daytime a a late evening snack consisting in food

reach in carbohydrates. Like similar studies that referred to reach in BCAA late evening snacks diets, this study shows a better outcome from the mental status and nutritional point of view.

CONCLUSION

High protein high calorie diet had a beneficial effect on the patients with cirrhosis and hepatic encephalopathy. This effect was statistically significant regarding the mental status, level of the serum ammonia and the body weight.

The daily eating pattern consisting in 4 meals and 1 late evening snack contributed to HE improvement, avoiding protein loading in a period of day, but maintaining the protein positive balance.

CONFLICT OF INTERESTS

None to declare.

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