ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

METABOLISM OF NUTRITION IN LIVER CIRRHOSIS

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Manuscript Info

Manuscript History:

Received: 25 September 2014
Final Accepted: 16 October 2014
Published Online: November 2014

Key words:

Nutritional requirement, Calories, Gluconeogensis, polyunsaturated, Ascites, hypophosphatemia.

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Abstract

It is very important to maintain proper nutrition in the case of cirrhosis of liver**.** Nutrition has long been recognized as a prognostic and therapeutic determinant in patients with chronic liver disease. This article is based on a selective literature review of metabolism of nutrients and nutrition in liver cirrhosis. In cirrhosis poor oral food intake is a predictor of an increased mortality. Patients with liver cirrhosis exhibit abnormal metabolism, including increased fat oxidation and decreased glucose oxidation. Calorie intake is essential but is often difficult to attain because of necessary protein and sodium restrictions. When the ascites and edema are severe, sodium intake may need to be restricted below 500 mg as they get lessen, sodium intake may be slowly liberalized up to 2500 mg if body weight does not increased. Nutritional requirements are very poor in liver cirrhosis due to the restriction of sodium and deficiencies of various nutrients or due to malnutrition.

Introduction

Liver Cirrhosis is the most serious or final stage of liver injury and degeneration. The normal liver tissue is gradually destroyed and inactive fibrous connective tissue replaces the liver cells. [1]. Nutrition has long been recognized as a prognostic and therapeutic determinant in patients with chronic liver disease [2] and, therefore, has been included as one of the variables in the original prognostic score introduced by Child and Turcotte. [3] Numerous descriptive studies have shown higher rates of mortality and complications, such as refractory ascites, variceal bleeding, infection, and hepatic encephalopathy (HE) in cirrhotic patients with protein malnutrition. [4-12]. In malnourished cirrhosis patients, the risk of postoperative morbidity and mortality is increased after abdominal surgery.[13] In cirrhosis or alcoholic steatohepatitis (ASH), poor oral food intake is a predictor of an increased mortality. In nutrition intervention trials, patients with the lowest spontaneous energy intake showed the highest mortality. [14- 20]

Effect of cirrhosis on nutritional state

Protein energy malnutrition with coexisting features of kwashiorkor like malnutrition and marasmus is commonly observed in patients with cirrhosis. [21,22]. Prevalence and severity of malnutrition are related to the clinical stage of chronic liver disease increasing from 20% of patients with well compensated disease up to more than 60% of patients with severe liver insufficiency.[23] Patients with cirrhosis frequently suffer from substantial protein depletion. Etiology of liver disease does not seem to influence the prevalence and degree of malnutrition and protein

depletion [22, 23] and the higher prevalence and more profound degree of malnutrition in alcoholics obviously result from an unhealthy lifestyle and low socioeconomic conditions. In hospitalized cirrhotics, fatigue, and psychomotor dysfunction often lead to insufficient oral nutrition. [24, 25]

Metabolism of nutrients in liver cirrhosis

The functional integrity of the liver is essential for the utilization of nutrients. The liver influences the nutritional status by its production of bile acids and its role in the intermediate metabolism of proteins, carbohydrates, fats and vitamins. [26] Patients with liver cirrhosis exhibit abnormal metabolism, including increased fat oxidation and decreased glucose oxidation. Increased fat oxidation manifests as starvation after an overnight fast, because of a lack of glycogen stores in liver cirrhosis [27].

1. **Carbohydrates:**

The utilization of oxidative fuels is characterized by an increased rate of lipid oxidation in the fasting state and the frequent occurrence of insulin resistance (even in Child–Pugh class A patients) [28-30 & 37]. In the post absorptive state, glucose oxidation rate is reduced and hepatic glucose production rate is low despite increased gluconeogensis due to a depletion of hepatic glycogen. [31] Insulin resistance affects skeletal muscle metabolism: glucose uptake and non oxidative glucose disposal, such as glycogen synthesis are reduced, while glucose oxidation and lactate production are normal after glucose provision. [32, 28, 31] It is not known to what extent glucose deposition as glycogen is impaired just in skeletal muscle or in both muscle and liver. [33, 32] Some 15 to 37% of patients develop overt diabetes, indicating an unfavorable prognosis. [34, 35].

2. Fats:-

In the fasting state, the plasma levels of free fatty acids, glycerol, and ketone bodies are increased and free fatty acid and glycerol concentrations do not fully respond to low insulin infusion rates as in healthy subjects.[36] Lipids are oxidized as the preferential substrate and lipolysis is increased with active mobilization of lipid deposits. [29, 37]. There is insulin resistance with regard to the antilipolytic activity. After a meal, the suppression of lipid oxidation is not uniformly impaired. [38, 39] Lipid oxidation rates are not reduced and, thus, the net capacity to utilize exogenous fat does not seem to be impaired. [28, 40] Essential and polyunsaturated fatty acids are decreased in cirrhosis and this correlates to nutritional status and severity of liver disease. [41, 42]

3. Protein and Amino acids:-

Protein in cirrhotic patients has been found to be normal or increased. Some authors mainly focused on the presence of increased protein breakdown, while others suggest that a reduced protein synthesis plays the main role. [43] Albumin, but not fibrinogen, synthesis rates correlate with quantitative liver function tests and clinical stages of cirrhosis. [44, 45] Nevertheless, stable cirrhotics apparently are capable of efficient nitrogen retention and significant formation of lean body mass from increased protein intake during oral hyper alimentation. [46] Protein catabolism influences the amino acid imbalance of cirrhosis and indirectly causes nitrogen overload to the liver leading to hyperammonemia. In cirrhotics, after an overnight fast, glycogen stores are depleted and metabolic conditions are similar to prolonged starvation in healthy individuals. It has been shown that a late evening carbohydrate snack was associated with improved protein metabolism in cirrhotic patients. [47- 49] Insulin resistance apparently is without effect on amino acid disposal. [50]. Patients with stable cirrhosis were found to have an increased protein requirement leading to the recommendation of 1.2 g per kgBW contrasting with the recommended minimal intake of 0.8 g per kgBW in healthy humans. [20,46,51,47] Cirrhotic patients exhibit an altered pattern of plasma amino acids characterized by the elevation of aromatic (phenylalanine, tyrosine) and sulfur containing amino acids (methionine) and tryptophan on the one hand and the decrease in BCAA (leucine, isoleucine, valine). [52,53]. Decreased metabolic clearance [54] by the failing liver of aromatic and sulfurous amino acids and increased breakdown in skeletal muscle of BCAA due to portal systemic shunting [55] and hyperammonemia. [56-58] recently, it has been pointed out that, due to the absence of isoleucine from hemoglobin, blood is a protein source of low biologic value leading to BCAA antagonism after upper gastrointestinal hemorrhage. [59] This BCAA antagonism readily explains the long-known clinical observation that blood and vegetable protein represent the two extremes in the hierarchy of food proteins regarding their comagenic potential. More-over, this antagonism leading to hyperammonemia could be overcome by the infusion of isoleucine. [60]

4. Vitamins and Minerals:-

No recommendation on the requirement of micronutrients can be made on the basis of controlled studies. As in other diseases, the administration of micronutrients has no proven therapeutic effect apart from the prevention or correction of deficiency states. Body composition of cirrhotics is altered profoundly and characterized by protein depletion and accumulation of total body water even in Child–Pugh class A patients [61,62] this goes hand-in-hand with salt retention, which does not usually lead to hypernatremia. On the contrary, depletion of potassium,

magnesium, phosphate, and other intracellular minerals frequently occurs. In an early study comparing Parenteral nutrition versus oral diet in cirrhotic patients with ascites, the response to diuretics was poorer in those patients receiving Parenteral nutrition.[63] Zinc and selenium deficiencies have been observed in alcoholic and nonalcoholic liver disease.[64-67] .A deficiency in water soluble vitamins, mainly group B vitamins, is common in cirrhosis, especially that of alcoholic origin.[68.69] Deficiency in fat soluble vitamins has been observed in cholestasis-related Steatorrhoea, bile salt deficiency, and in alcoholics.[70,71] Patients with hypophosphatemia after acetaminophen-induced liver damage have a better prognosis. Severe hypophosphatemia, however, results in respiratory insufficiency and dysfunction of the nervous system and erythrocytes [72] and, thus, serum phosphate levels should be monitored and corrected in order to support liver regeneration.

Nutritional consequences

The type of nutritional care is directly related to the livers function, an understanding of its role in the metabolic process is necessary to determine the character of diet. An organ that performs so many varied functions, when diseased, will have many effects on nutrient digestion and absorption, storage and metabolism that can lead to vitamin and mineral deficiencies and protein energy malnutrition, as shown in Table 1. [73]

Table No. 1:- NUTRITIONAL CONSEQUENCES OF LIVER DISEASE

NUTRIENT	ABERRATION	CONSEQUENCES
Protein and Amino acids	Increased serum levels of tyrosine methionine, phenylalanine, glutamine and sometimes cystine. Decreased serum levels of branched chain amino acids ------ valine, leucine and isoleucine. Reduction in plasma insulin: glucagon ratio	Theory: increased aromatic amino acids in brain. Gluconeogensis, proteolysis of protein and catabolism of tissue.
Carbohydrate	Glucose intolerance due to elevated serum insulin, insulin resistance and growth hormone and glucagon elevation.	Mobilization and utilization of endogenous protein for energy.
Lipid	Decreased synthesis of lipid- transport proteins. Decreased absorption of long chain fatty acids.	Decreased high density lipoprotein. Steatorrhoea.
Vitamins	Decreased formation of 25-OHD_3 in the liver . Decreased degradation of pyriodoxol phosphate. Decreased formation of vitamin A transport protein. Inadequate retention of folate in the liver.	Decreased serum 25-OHD_3 osteoporosis. Possible vitamin B_6 deficiency. Decreased serum vitamin A Night blindness. Possible folate deficiency.

Minerals	Steatorrhoea resulting in calcium soaps and decreased absorption of calcium. Magnesium excreted after alcohol consumption. Zinc excretion increased in cirrhosis.	Decreased serum levels of zinc, magnesium and calcium. Possible zinc deficiency.

Nutrient Requirements in Liver cirrhosis

- Energy

  Energy requirements vary among patients with cirrhosis. In general, energy requirements for patients with end stage liver disease (ESLD) and without, ascites are about l20% to l40% of the Resting energy expenditure (REE). Requirements increase to 150% to l75% of REE if ascites, infection, or malabsorption is present or if nutritional repletion is necessary. This equates to about 25 to 35 calories per kilogram body weight; estimated dry body weight should be used in calculations to prevent overfeeding. [74]. Adequate calorie intake is essential but is often difficult to attain because of necessary protein and sodium restrictions. Calorie intake should be enough to prevent loss of lean body mass. [75].
- Carbohydrates

  Carbohydrate needs is often challenging in liver failure because of the primary role of the liver in carbohydrate metabolism. Liver failure reduces glucose production and peripheral glucose use. The rate of gluconeogensis is decreased with preference for lipids and amino acids for energy. Alterations in the hormones insulin, glucagon, cortisol, and epinephrine are responsible in part for the preference for alternative fuels. [74]
- Lipid

  In cirrhosis, plasma free fatty acids, glycerol, and ketone bodies are increased in the fasting state. The body prefers lipids as an energy substrate, and lipolysis is increased with active mobilization of lipid deposits, but the net capacity to store exogenous lipid is not impaired. A range of 25% to 40% of calories as fat is generally recommended [74]
- Protein

Protein is by far the most controversial nutrient in liver failure, and its management is also the most complex. Cirrhosis has long been thought of as a catabolic disease with increased protein breakdown and inadequate resynthesis, resulting in depletion of visceral protein stores and muscle wasting. [43]. Patients with cirrhosis also have increased protein use. At least one study [46]. Suggests that 0.8 g of protein per kilogram per day is the mean protein requirement to achieve nitrogen balance in patients with stable cirrhosis. Therefore, in uncomplicated hepatitis or cirrhosis without encephalopathy, protein requirements range from 0.8 to I g/kg of dry weight per day to achieve nitrogen balance. To promote nitrogen accumulation or positive balance, at least 1.2 to 1.3 g/kg daily is needed [46]. In situations of stress such as alcoholic hepatitis or decompensate disease [sepsis, infection, gastrointestinal bleeding, severe ascites], at least 1.5 g of protein per kilogram per day should be provided. [43]

- Vitamins and Minerals

  Vitamin and mineral deficiencies occur in alcoholic liver disease as a result of reduced intake and alterations in absorption, storage, and ability to convert the nutrients to their active forms. Vitamin and mineral supplementation is needed in all patients with ESLD because of the intimate role of the liver in nutrient transport, storage, and metabolism, in addition to the side effects of drugs. Vitamin deficiencies can contribute to complications deficiency of pyridoxine, thiamin, or vitamin B12 can result in neuropathy. [75].
- Potassium

  Serum potassium levels must be monitored. Serum potassium may fall due to decreased intake and losses from vomiting, diarrhea &diuretic therapy. [76]
- Sodium

  Ascites and edema are often present with cirrhosis results from the combination of low serum colloid osmotic pressure and portal hypertension. When the ascites and edema are severe, sodium intake may need

to be restricted below 500 mg [77, 76] as they get lessen, sodium intake may be slowly liberalized up to 2500 mg if body weight does not increased [78].

Conclusion

Metabolisms of nutrients are abnormal in liver cirrhosis due to increased fat oxidation and decreased glucose oxidation. Increased fat oxidation manifests as starvation after an overnight fast, because of a lack of glycogen stores in liver cirrhosis. Protein catabolism influences the amino acid imbalance of cirrhosis and indirectly causes nitrogen overload to the liver leading to hyperammonemia. Nutritional needs of liver cirrhosis may vary from patient to patient due to the presence of varying symptoms and presence of ascites, edema and encephalopathy. Zinc and selenium deficiencies have been observed in alcoholic and nonalcoholic liver disease. Zinc deficiency is common in cirrhotic patients from a decrease in hepatic storage capacity. Vitamin A deficiency may arise due to decreased release from the liver. Fat-soluble vitamins are deficient in liver cirrhosis as liver plays an important in metabolism of such nutrients. Nutritional requirements should be met as malnutrition is prevalent in liver cirrhosis.

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