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Review Article

Nutrition in Patients with Alcoholic Liver Disease: A Comprehensive Review

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Abstract

A complex interplay exists between a person's alcohol consumption and nutritional status. Patients who consume alcohol, particularly at heavy drinking levels, are affected by changes in their dietary habits and nutrient metabolism. In this review, nutritional status assessment, current knowledge on nutritional deficiencies, malnutrition, need for early nutritional intervention and medical nutrition therapy goals in alcoholic liver disease are deeply discussed.

Keywords: *Nutrition; Alcoholic Liver Disease (ALD); Alcoholic Hepatitis (AH)*

Introduction

Alcoholic liver disease (ALD) refers to a wide histological spectrum of liver pathologies and represents a negatively relevant cofactor in the progression of chronic liver injury of different etiology [1,2]. Those etiologies include steatosis with or without fibrosis, alcoholic hepatitis (AH), cirrhosis and hepatocellular carcinoma.

Alcoholic liver disease (ALD) arises because of the excessive and prolonged consumption of alcoholic beverages and is prevalent cause of liver cirrhosis especially in Western countries [3]. The latest World Health Organization's Global Alcohol and Health database established in 2018, has been used to estimate worldwide patterns of alcohol consumption and allow comparisons of alcohol related morbidity and mortality. It is known that European people (59.9%) abuse alcohol in higher rates than any other nations [4,5]. Alcohol accounts for a major portion of global disease burden and is projected to take on increasing importance in those regions over time. The effects of alcohol consumption on mortality are greater than those of tuberculosis (2.3%), HIV/AIDS (1.8%), diabetes (2.8%), hypertension (1.6%), digestive diseases (4.5%), road injuries (2.5%) and violence (0.8%) [5].

Alcohol intake classified as heavy drinkers who consume 5 drinks per day at least once a week and chronic alcoholics who drink in binges 6 or more drinks daily [6]. Lower alcohol intake limit for potential development of ALD in women is daily intake of alcohol above 2 drinks and 4 drinks in men. There are many other possible factors that affect the development of ALD other than the amounts [7].

These factors include the drinking patterns such as dose, duration and type of alcohol consumption and associated risk factors including obesity, iron overload, concomitant infection with viral hepatitis, and genetic factors.

When alcohol consumed in excess, it has negative effect on nutritional status of the drinker. For example, alcohol can alter the intake, absorption into the body, and utilization of various nutrients. Consequently, patients with ALD frequently have poor nutritional status. This contributes to malnutrition and deficiencies in proteins, amino acids and certain vitamins in this population. In addition, alcohol exerts some harmful effects through its breakdown that results toxicity. Evidence shows that patients with ALD frequently have poor nutritional status. Therefore, early nutritional approaches may be useful in the treatment and may improve response to treatment, alleviate symptoms, and improve quality and quantity of life. The American Association for the Study of Liver Disease guidelines recommend that all ALD patients must be screened for both protein-calorie deficiency and any specific micronutrient deficiencies (i.e. vitamin and mineral deficiency) [8].

In this review, nutritional status assessment, current knowledge on nutritional deficiencies, malnutrition, need for early nutritional intervention and medical nutrition therapy goals in alcoholic liver disease are discussed.

The nutritional status of the patients with ALD

A complex interplay exists between a person's alcohol consumption and nutritional status. Patients who consume alcohol, particularly at heavy drinking levels, are affected by changes in their dietary habits and nutrient metabolism. Therefore, even if the drinkers consume sufficient calories, protein, vitamins, and minerals deficiencies may develop due to inadequate absorption from gastrointestinal tract. Thus, patients' body cells cannot absorb and use the nutrients they consume. On the other hand, many alcoholics do not consume a balanced diet and alcohol replaces other essential nutrients in the diet. Due to these reasons, patients are faced with overall reduced nutrient intake. Consequently, assessment of nutritional status is important in order to determine need for nutritional interventions in the treatment of patients with ALD.

Nutritional assessment of the ALD patients should be based on detailed history and physical examination [9]. As nutritional assessment is important because of the early diagnosis of nutritional complication such as malnutrition, the most relevant markers for this purpose is the body mass index (BMI, kg/m^2) and the degree of weight loss. In order to make more comprehensive examination, anthropometric measurements or scoring system for malnutrition such as Nutrition Risk Screening (NRS) or Subjective Global Assessment (SGA) can be used. Nutritional assessment with using SGA, which details are given in the table 1 [10], for ALD patients are preferable as it examines any changes in dietary intake, recent changes in body weight, gastrointestinal symptoms, functional capacity, and physical signs of malnutrition represented by loss of subcutaneous fat, muscle mass, oedema, ascites [11].

A. History
Weight change
Dietary intake change
Gastrointestinal symptoms
Functional capacity
Disease and its relation to nutritional requirements
B. Physical
Loss of subcutaneous fat
Muscle wasting
Ankle oedema
Sacral oedema
Ascites
C. SGA Rating
A = Well nourished
B = Moderately (or suspected of being) malnourished
C = Severely malnourished

Table 1: *Features of the subjective global assessment, SGA.*

Nutritional Deficiencies in Alcoholic Liver Disease

Complications such as weight, muscle loss, malnutrition and wide range of nutritional deficiencies commonly occur in ALD [12]. The underlying causes of malnutrition and nutritional deficiencies are summarized in figure 1 [13].

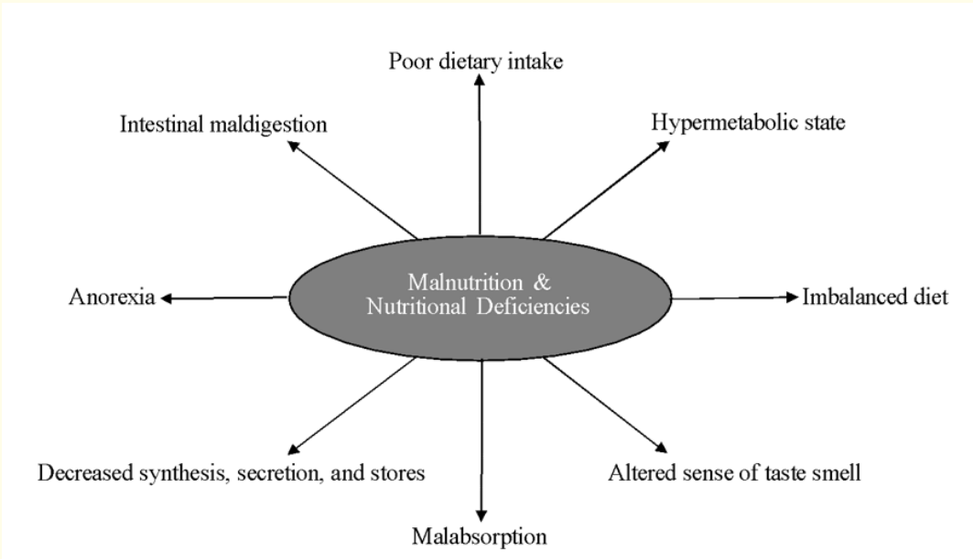

Figure 1: *The underlying causes of malnutrition and nutritional deficiencies.*

Deficiency of the fat-soluble, water-soluble vitamins and various minerals is common in patients with ALD. Deficiencies show specific symptoms, signs and complications. They are often reflected in low serum levels, as well as in neurologic and dermatologic symptoms. Most of ALD patients will require a general, daily vitamin and mineral supplement, with attention to individual serum levels of nutrients that may require additional supplementation.

Decrease in absorption, decreased ability to store fat-soluble vitamins and metabolism of vitamins into their active forms cause vitamin and some mineral deficiencies in ALD. Various vitamins, minerals deficiencies and its mechanism and required interventions were summarized in table 2 [14,15].

Micronutrient	Causes of Deficiency	Consequences	Supplementation
Folate	Dietary, intestinal malabsorption, losses from renal excretion, decreased live uptake and storage	Megaloblastic anemia	1 mg/day orally
Thiamine	Dietary malabsorption	Alcoholic polyneuropathy, Wernicke-Korsakoff syndrome, high output heart failure	100 mg/day orally or subcutaneously initially for 2 weeks or until repleted
Pyridoxine	Dietary, acetaldehyde displacement from albumin with enhanced urinary excretion	Peripheral neuropathy, altered methionine metabolism, increased AST:ALT ratio	50 - 100 mg/day orally
Vitamin A	Inadequate intake, enhanced metabolism, malabsorption, maldigestion	Night blindness, impairment in immune function, increased risk of hepatic fibrosis.	25,000 - 50,000 IU x3times/week
Calcium	Inadequate intake of calcium and vitamin D, losses from malabsorption and renal excretion	Increased risk for bone loss	1000 - 1500 mg/day
Zinc	Inadequate dietary intake, increased renal excretion due to diuretic therapy	Impairment in immune function, loss in taste sense	220 mg zinc sulfate 1 - 3 divided doses/day

Table 2: *Common micronutrient deficiencies, cause of deficiency, consequences and supplementation in ALD.*

Malnutrition in alcoholic liver disease

ESPEN (European Society Parenteral Enteral Nutrition) defined malnutrition as "A state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease" [16].

Basic diagnostic criteria for malnutrition have been defined by an ESPEN and a similar approach to define diagnostic criteria has been described by a working group of the American Society of Parenteral and Enteral Nutrition (ASPEN) and the Academy of Nutrition and Dietetics (Academy). Malnutrition assessment could be done with any validated nutritional risk screening tool. Reduced body weight, body mass index (BMI) under the 18.5 kg/m^2, appetite change, dietary intake are generally associated with nutritional risk and malnutrition. Similarly, according to the ASPEN and Academy criteria for the potential diagnosis of malnutrition includes at least two factors out of low energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, fluid accumulation, and hand grip strength.

Patients with alcoholic liver disease are faced malnutrition frequently. Complications of malnutrition adversely affect the clinical consequences and include loss of skeletal muscle mass or weight, sarcopenia and changes in energy metabolism [14,17].

It is well known as protein and energy malnutrition is very common among patients with alcoholic liver disease. In a Veterans Administration Cooperative study which includes 363 patients with alcoholic hepatitis, 100% of patients were found to have protein and/or combined protein calorie malnutrition, based on anthropometric and laboratory testing [18]. Additionally, the severity of malnutrition is correlated with disease severity and outcomes.

Reduced oral intake, anorexia, dysgeusia, low quality of diet, hypermetabolism, low-sodium diet, acute hepatitis-cytokines, hyperammonemia of liver disease, other complications of ALD such as gastrointestinal bleeding, encephalopathy, diarrhea, portal hypertensive enteropathy with reduced nutrient absorption, nausea, emesis are factors that lead to malnutrition. The prevalence of malnutrition in ALD has been reported 20% to 60% in outpatients with alcoholic cirrhosis and almost 100% in hospitalized patients with acute alcoholic hepatitis [13,19,20].

Some specific factors such as the duration and amount of alcohol use, time of measurement from last alcohol consumed, the severity and other underlying causes of liver disease, and the contribution of other factors that result in progression of muscle and fat loss can affect the severity of malnutrition in alcoholic liver disease [13].

Nutritional and treatment management of alcoholic liver disease

Nutritional approaches are useful in alcoholic liver disease. The main and preliminary focus in alcoholic liver disease should be complete alcohol withdrawal. If the patient suffers from any detected nutritional deficiency and/or malnutrition, a nutrition therapy should be given by an expert.

Providing nutritional support to ALD patients may improve prognosis since malnutrition is a frequently encountered problem. Societies have recommended oral or parenteral supplements for patients with ALD even at risk of malnutrition [21]. Principle of using oral, enteral, or parenteral nutrition in order to provision of nutritional support are asked often. This issue has been investigated by many clinical trials nevertheless, more clinical data are necessary to standardize or combine these treatments because of a variety of factors such

as inadequate control groups, short duration of the trial, and failure to adequately assess nutritional needs of the patient population [7]. Several studies showed improvement in biochemical markers of liver function or nutritional parameters with nutritional support. In one study, subgroups of patients who achieved nutritional goals and positive nitrogen balance had improved survival compared to those who did not [22]. Moreover, mortality rate was 3.3% in the 30 patients in whom positive nitrogen balance was achieved, but 58% in patients who remained in negative nitrogen balance.

The main focus of the nutritional management in ALD patients who are in hypermetabolic state is to meet basal needs and provide additional source as much as possible. It is known that severity of the intrahepatic inflammatory process affects and diversifies the energy requirements in ALD [23-25]. Estimations of the caloric needs of patients with alcoholic liver disease based on the Harris Benedict equation may be inaccurate, and caloric needs deviation ratio is 15% to 18% when compared with measurement using indirect calorimetry [26]. European Society for Clinical Nutrition and Metabolism released general nutrition guidelines for patients with cirrhosis which is also be recommended to patients with ALD. Recommendations on this guidelines includes 30 - 35 kcal/kg energy provision and total energy from carbohydrates, proteins, and fats distributed as 50% to 60%, 25% to 30% (1 - 1,5 g/kg), and 15% to 20% respectively. The unnecessary dietary restriction should be avoided. With exceptions such as if patients present ascites or oedema a low-sodium diet (< 2 g/day) should be recommended or patients with acute hepatic encephalopathy need protein restriction. Small meals such as 4 - 6 times a day including night-time snacks should be encouraged [27]. Other target on nutritional therapy includes screening for deficiencies of serum zinc, calcium and vitamin A, D, E, and K and properly supplemented as needed [12].

To sum up, during intermittent acute illness or exacerbations of the underlying chronic liver disease, above normal protein intake (1.5 g/kg body weight), and hypercaloric diet (40 kcal/kg) improves protein calorie malnutrition and should be considered in the treatment of these patients [28].

Oral nutritional supplementation

Oral supplementation may not be effective because of poor intake and compliance from anorexia, dysgeusia, impaired absorption, and continued hypermetabolic states [29]. Even though, patients in one clinical trial showed tolerance to oral feeding without worsening of and improved liver function in Childs-Pugh class C patients [30].

The nonaromatizable anabolic steroid, oxandrolone, showed benefit when added to oral nutritional supplementation [31]. In another study, when the anabolic steroid oxandrolone was combined at 80 mg/d with oral supplementation, patients who voluntarily consumed at least 2500 kcal per day had improved 6-month survival, liver functions, and nutritional status compared with a control group that took a placebo and had lower voluntary intake of calories [32].

Enteral nutrition

Enteral tube feedings can overcome the effects of anorexia and dysgeusia but not poor enteral absorption and have been shown to be beneficial, well-tolerated, and may improve hepatic function but the impact on skeletal muscle and other nutritional parameters is not conclusive [33].

A short-term study of nasoenteral tube feeding of eight anorectic patients with alcoholic hepatitis was done first on an oral diet and subsequently while receiving an intestinal infusion of a balanced formula that provided 35 kcal/kg of ideal body weight. All subjects showed significant improvement in the intestinal absorption, less than 80% digestibility of total calories, fat, and protein on oral diets, and nitrogen balance [34].

A different prospective study compared the effects of tube feeding with those of a regular diet in alcoholic liver disease. Significant improved was found in hepatic encephalopathy and aminopyrine clearance test of liver function and lowered bilirubin levels in 16 patients fed by enteral formula compared with 16 treated conventionally by hospital diet. The study demonstrate aggressive nutritional intervention could accelerate improvement in alcoholic liver disease [29].

In summary, it appears that enteral formula feeding is safe, maximizes digestion, may have short-term positive effects on liver function, and may improve long-term survival.

Parenteral nutrition

Parenteral nutrition ensures delivery of nutrients and has been used in patients with ALD. In a comprehensive analysis of parenteral nutrition in ALD, short-term benefits on some nutritional parameters were observed but long-term consequences remain unknown. In an analytical review of seven studies including 239 ALD patients showed that parenteral nutrition treatment up to 30 days may improve liver function and nitrogen balance while normalizing the composition of plasma amino acids, but in order to determine long-term metabolic effects, risks, and benefits further studies are needed [35].

In another 2 year follow-up study, 56 patients with alcoholic hepatitis found that those who were randomized to receive supplemental intravenous amino acids and glucose in addition to ad libitum oral intake had improved nitrogen balance, liver function tests, and aminopyrine clearances compared with those receiving supplemental glucose alone during 30 days. It showed no differences in survival during the study period [36,37].

Conclusion

It is wise to keep in mind that parenteral nutrition is associated with significant risks including infections that preclude such supplementation as routine treatment in patients with ALD who have compromised immune function.

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