Digestive and Liver Disease 47 (2015) 819–825

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Review Article

Diagnosis and treatment of nutritional deficiencies in alcoholic liver disease: Overview of available evidence and open issues

Roberta Elisa Rossi[a,b,*], Dario Conte[a,b], Sara Massironi[a]

[a] Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Italy
[b] Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy

ARTICLE INFO

Article history:
Received 29 January 2015
Accepted 30 May 2015
Available online 8 June 2015

Keywords:
Alcoholic liver disease
Enteral nutrition
Nutritional deficiencies
Nutritional support
Parenteral nutrition
Protein–energy malnutrition

ABSTRACT

Malnutrition is common in alcoholic liver disease and is associated with high rates of complications and mortality. In this article, the current literature was reviewed to highlight the relevance of proper nutritional management providing levels of evidence, when available. A PubMed search was performed for English-language publications from 1980 through 2014 with the keywords: alcoholic liver disease, nutritional deficiencies, nutritional support, enteral nutrition, parenteral nutrition, and protein–energy malnutrition. Manuscripts focused on nutritional approach in patients with alcoholic liver disease were selected.

Although nutritional support for malnourished patients improves the outcome of hospitalization, surgery, transplantation and reduces the complications of liver disease and the length of hospital stay, specific guidelines are scanty. Both enteral and parenteral nutrition appear to improve nutritional parameters and liver function; however data on survival is often conflicting. As micronutrient depletion is common in alcoholic liver disease and each deficiency produces specific sequelae, all cirrhotic patients should be screened at baseline for deficiencies of micronutrient and supplemented as needed.

In summary, protein–energy malnutrition and micronutrient depletion are clinical concerns in alcoholic liver disease. Nutritional therapy, including enteral nutrition, parenteral nutrition and micronutrient supplementation should be part of the multidisciplinary management of these patients.

1. Introduction

Alcoholic liver disease (ALD) is the most prevalent cause of advanced liver disease in Western countries and represents a negatively relevant co-factor in the progression of chronic liver injury of different aetiology [1,2].

The term "ALD" includes a wide range of liver injury, including steatosis with or without fibrosis, alcoholic hepatitis (AH), cirrhosis and hepatocellular carcinoma, and represents one of the most common indications for liver transplantation (LT) in Europe and the United States [3].

Complete alcohol withdrawal represents the key treatment for ALD although possibly insufficient when facing with cirrhosis or severe AH [4]. Several medical approaches have been studied, but evidence about their effect on survival is still lacking [5].

Muscle wasting, weight loss, and nutritional deficiencies commonly occur in ALD, the underlying mechanisms including poor dietary intake (due to anorexia, altered sense of taste and smell, and nausea and vomiting), maldigestion and malabsorption (related to concomitant pancreatic insufficiency and bile acid deficiency, respectively), bacterial overgrowth due to reduced motility, loss of proteins secondary to portal hypertension, hypermetabolic state, insulin resistance, and impaired protein synthesis due to cytokine-induced inflammatory responses [6–8]. As malnutrition correlates with both higher rates of complications (variceal bleeding, ascites, encephalopathy, infections, and hepato-renal syndrome) and mortality, its finding in ALD may identify those patients at higher risk of hepatic decompensation and/or liver-related death [8], as clearly demonstrated by a recent study on 363 AH patients, reporting a one year mortality of 14% and 76% in those with mild or severe malnutrition, respectively [4]. Furthermore, malnutrition has also been associated with a longer stay in intensive care units, longer length of hospital stay, and higher mortality after LT [8].

Although no difference in the prevalence and severity of malnutrition has been observed between ALD and viral-related liver disease in one series [9]. Caly et al. reported a poorer nutritional

* Corresponding author at: Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Via F. Sforza 35, 20122 Milano, Italy. Tel.: +39 02 55033445; fax: +39 02 55033644.
E-mail address: robertaelisa.rossi@gmail.com (R.E. Rossi).

http://dx.doi.org/10.1016/j.dld.2015.05.021
1590-8658/

Table 1
Grades of clinical recommendations based on literature studies strength.

Grade of recommendation	Evidence derived from
A	Meta-analysis of randomized controlled trials
B	At least one randomized controlled trial, one controlled study without randomization or one other type of quasi-experimental study
C	Comparative, correlation studies, or case-control studies
D	Expert committee reports or opinions or clinical experience of respected authorities, or both

status in patients with alcoholic cirrhosis compared to those with hepatitis C-related cirrhosis [10].

Nutrition plays an important role as supportive therapy, and the American Association for the Study of Liver Disease guidelines recommend that all ALD patients be screened for both protein–calorie deficiency and any specific micronutrient deficiencies (i.e. vitamin and mineral deficiency) [4].

Based on the above findings, the present review is aimed at addressing both the main patterns of malnutrition in ALD and the role of nutritional support in this specific setting, reporting the clinical recommendations with pertinent evidence-based strength (Centre for Evidence Based Medicine. Levels of Evidence. http://www.cebm.net/index.aspx?o¼1025, Table 1).

2. Methods

An extensive bibliographical search was performed in PubMed using the following keywords: alcoholic liver disease, nutritional deficiencies, nutritional support, enteral nutrition, parenteral nutrition and protein–energy malnutrition, in order to identify all the pertinent articles published between 1980 and 2014. The reference lists from the selected studies were manually examined to identify further relevant reports. Non-English language papers were excluded. The quality and strength levels of the results were considered and when available meta-analyses and systematic reviews, large epidemiological studies and randomized control trials represented the main source of data.

3. Results

A total of 82 articles with the strongest level of evidence specific to the scope of this review were identified.

3.1. Nutritional assessment

Nutritional assessment in ALD is based on detailed history and physical examination [8]. Of the several clinical markers of malnutrition of which none exclusive, the body mass index (BMI, kg/m^2) and the degree of weight loss are the most relevant ones, in spite of their potential unreliability in presence of fluid retention [8]. A more comprehensive assessment includes anthropometry and scoring systems such as the Nutrition Risk Screening, which considers the amount and duration of weight loss; the BMI for adults; percentile charts for children; the degree of appetite and the ability to eat and retain food (i.e. food intake) and 'stress factors', i.e. the effects of health status on nutritional requirements [8]. A further widely used tool, whose details are given in Table 2, is the Subjective Global Assessment (SGA), based on a standardized questionnaire aimed at assessing 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 or muscle mass, oedema, ascites [8]. In addition, as listed in Table 3, several biochemical markers can help to better define malnutrition, even though albumin, prealbumin, and transferrin may lack accuracy as they are synthesized by the liver; a further critical point is the lack of correlation between these proteins and both the BMI and the lean body mass [8]. Moreover, the widespread use of albumin supplementation in cirrhotic patients can mask actual plasma albumin levels. The total lymphocyte count (TLC) has also been proposed as a useful indicator of nutritional status and outcome, even if its use in patients with hepatic disorders needs further evaluation as few pertinent studies are currently available [11]. Low insulin-like growth factor 1 levels may also be a marker of malnutrition [8], whilst serum creatinine may not accurately reflect the loss of muscle mass in patients with concomitant renal insufficiency. Noteworthy, in patients with chronic illnesses, including cirrhosis, muscle wasting can be assessed by measuring psoas muscle thickness by computed tomography (CT) scanning, a novel accurate, objective marker of nutritional status [8].

Table 2
Features of the subjective global assessment [8].

History
Weight change
Dietary intake change (relative to normal)
Gastrointestinal symptoms (that persisted for >2 weeks), including nausea, vomiting, diarrhoea, anorexia.
Functional capacity: full capacity, dysfunction (working suboptimally, ambulatory, bedridden).
Disease and its relation to nutritional requirements
Primary diagnosis (specify)
Metabolic demand (stress)
Physical (0 = normal, 1+ = mild, 2+ = moderate, 3+ = severe)
Loss of subcutaneous fat (triceps, chest)
Muscle wasting (quadriceps, deltoids)
Ankle oedema
Sacral oedema
Ascites
SGA rating
A: Well nourished
B: Moderately (or suspected of being) malnourished
C: Severely malnourished

SGA, subjective global assessment.

Summary: As per current guidelines, the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends the bedside nutritional assessment using SGA and anthropometric measurements [12].

Grade of recommendation: C.

3.2. Protein–energy malnutrition

Malnutrition, characterized by an altered functional and structural development of an organism, results in an imbalance between the need, intake and utilization of nutrients and is usually associated with poor clinical outcomes.

Patients with chronic liver disease (CLD) are particularly prone to develop malnutrition due to the altered regulation by the affected liver of both the nutritional status and the energy balance. Moreover, the presence of CLD may also decrease the appetite, thus negatively influencing nutrient intake. As no difference

Table 3
Parameters aimed at assessing the presence and degree of malnutrition.

Parameters	Degree of malnutrition		
	Mild	Moderate	Severe
Albumin (g/dL)	3.5–3.0	2.9–2.5	<2.5
Transferrin (mg/dL)	200–150	149–100	<100
Pre-albumin (mg/dL)	22–28	17–10	<10
Retinol binding protein (mg/dL)	2.9–2.5	2.4–2.1	<2.1
Lymphocytes/mm^3	1500–1200	1199–800	<800