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Review paper

Nutrition principles and recommendations in different types of hepatic encephalopathy

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Abstract

Appropriate nutrition – in terms of both quantity and quality – is not only one of the main life processes. A well-balanced diet including sufficient amounts of minerals and vitamins supports proper human development and functioning from fetal development to very advanced old age; it promotes regeneration after intensive exercise and is a key element for successful treatment of most acute and chronic diseases, including liver diseases.

Key words: encephalopathy, diet, diagnostic tools.

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Introduction

General nutrition recommendations in patients with liver diseases are similar to the general well-balanced dietary recommendations, except for elimination diets indicated in some genetic or metabolic diseases. However, patients with advanced liver disease, especially with cirrhosis, often present with malnutrition or even cachexia, which requires different caloric intake and qualitative composition of the diet as well as an additional supply of vitamins or micronutrients [1].

Encephalopathy is a serious, transient or permanent functional central nervous system (CNS) impairment, which can be either congenital or acquired. Hepatic encephalopathy (HE), also known as portosystemic encephalopathy, has a complex and variable clinical manifestation. This neuropsychiatric condition is caused by an acute injury to the previously healthy liver parenchyma. It can also develop secondarily to chronic liver disease or portal vein confluence abnormalities, with or without portal hypertension as well as portacaval anastomosis. Regardless of aetiology, common characteristics of hepatic encephalopathy include mental disorder, neurological disorder and liver damage, which all show qualitative and quantitative variability. Sometimes damage to other internal organs can be present, too [2].

There are different classification systems applicable to encephalopathy (see Table 1). The primary division classifies encephalopathy into manifest and latent. However, from the clinical perspective the key is severity grading (from a minimally altered mental state in grades 0/1 to coma in grade 4) and classification by duration and characteristics of neurological symptoms into episodic, persistent, or minimal.

Malnourishment

Approximately 60% of patients with cirrhosis were shown to be malnourished or even cachexic. Paradoxically, malnutrition has been increasingly more often diagnosed in overweight and obese patients. The concomitant non-alcoholic steatohepatitis is an additional pathology to further impair liver function. The causes of malnutrition in these patients vary and include insufficient food intake (insufficient caloric intake and unbalanced diet), often secondary to the loss of appetite, malabsorption, dyspepsia and impaired metabolism of carbohydrates and lipids [3].

Table 1. Classification and grading of encephalopathy

Type and aetiology	Grade		Duration	
A – associated with acute liver failure	Minimal	Latent	Episodic	Spontaneous
B – associated with portal-systemic bypass	1		Persistent	
C – associated with cirrhosis	2	Manifest	Chronic	Definitive
	3			
	4			

Progressive malnutrition is associated with risk of multiple complications. The most serious of them are gastrointestinal bleeding, spontaneous peritonitis, hepatic encephalopathy and hepatorenal syndrome.

Dietary management of patients with hepatic encephalopathy

The optimum therapeutic approach in each patient with cirrhosis and hepatic encephalopathy should include appropriate dietary management to complement medical treatment. The recommended dietary management is a three-step process, which consists of (1) nutritional status assessment, (2) nutritional status optimisation and (3) nutritional status monitoring. Quantitative and qualitative dietary improvements, keeping an appropriate mealtime schedule and supplementing fibre and vitamins in daily diet help limit the number of decompensation episodes and prevent encephalopathy progression; such management improves overall survival as well as the MELD (Model For End-Stage Liver Disease) and Child-Pugh scores [4, 5].

Nutritional status assessment

There is no single, perfect tool for nutritional status assessment. Clinical examination is an obvious basis. The objective assessment methods applicable to nutritional status evaluation include bioelectric impedance analysis (BIA), dual X-ray absorptiometry (DXA), hand-grip dynamometry, computed tomography (CT) or nuclear magnetic resonance (NMR) imaging to assess muscle mass, body mass index (BMI), Subjective Global Assessment (SGA), the CONUT scale [6] (Table 2), the Royal Free Hospital Nutritional Prioritising Tool and many others.

Body mass index calculation is a good starting point in nutritional status assessment. It differentiates between 3 types of patients: underweight, normal weight and overweight/obese. Each group may be affected by malnutrition. Subjective Global Assessment is a tool routinely used in hospitalised patients. A score over 3 is indicative of malnutrition [7].

Bioelectrical impedance analysis and DXA, which determine the amount of adipose tissue, are generally reliable nutritional assessment tools. However, the scores may be unreliable in patients with cirrhosis complicated with ascites or peripheral oedema.

Using CT or NMR to determine muscle mass is unfortunately very expensive, so it can be used in a limited number of carefully selected cases only.

Table 3 shows the interpretation and patient management guidelines based on the Royal Free Hospital Nutritional Prioritising Tool (RFH-NPT) [8].

Nutritional status optimisation in hepatic encephalopathy

Table 4 shows the recommended caloric intake, as well as the recommended daily dose of protein and fibre

Table 2. CONUT scale

Parameter	No. malnutrition	Malnutrition severity		
		Mild	Medium	Severe
Serum albumin (g/dl)	> 3.5	3.00-3.49	2.5-2.99	< 2.00
Score	0	2	4	6
Total lymphocyte count (10^3/ml)	> 1600	1200-1599	800-1199	< 800
Score	0	1	2	3
Cholesterol level (mg/dl)	> 180	140-179	100-139	< 100
Score	0	1	2	3
Total	0-4	5-8		> 12
Nutritional status	Normal nutritional status	Moderate malnutrition		Severe malnutrition

necessary for proper body functioning, classified by the patient body weight.

Additionally, patients are advised to increase the number of meals (minimum 5 daily), while decreasing the amount of food per meal. Moreover, all patients with encephalopathy should have an additional evening meal – a bedtime snack, rich in carbohydrates, in order to improve glucose metabolism.

Overweight and obese patients, who require restricted caloric intake (meal size and lipid intake reduction) as well as a dietary modification to include the majority of plant-based proteins and a large dose of fibre, pose the biggest challenge. It is the most difficult to keep a well-balanced diet and an appropriate nutrition level in this patient group.

Nutritional status monitoring in an outpatient setting involves regular weekly appointments to assess the patient's nutritional status. Inpatients should also be assessed on a weekly basis.

Nutrients recommended in patients with hepatic encephalopathy

Protein. Recommended source: plant-based proteins

It is crucial that patients with HE change the type of protein in their diet, switching to plant-based proteins. Additionally, if there is no underlying milk protein intolerance, dairy products are also recommended [9].

The consumption of plant-based proteins offers a wide range of benefits. Products rich in plant-based proteins contain plenty of fibre, which shortens bowel transit time and decreases ammonia absorption. Plant-based proteins contain less methionine and cysteine and more arginine and ornithine, which are metabolised as part of the urea cycle.

Eighty percent of patients show good tolerance of increased plant-based protein intake, without worsening of HE. The mean recommended daily dose for these patients is 30-40 g, that is, 1.2-1.5 g/kg/day. Higher intake causes significant bloating and diarrhoea.

Protein intake according to the type of encephalopathy.

Restricted protein intake is still recommended in patients with an acute manifestation of hepatic encephalopathy.

The initial dose of protein in patients with acute encephalopathy is 0.5 g/kg/day – it should be carefully increased up to 1.0-1.5 g/kg/day. Patients with chronic hepatic encephalopathy benefit from the diet containing plant-based proteins rather than animal-based proteins. Lactulose and rifaximin can be considered, too [9, 10].

Table 3. The Royal Free Hospital Nutritional Prioritising Tool (RFH-NPT)

STEP 1
Has the patient been diagnosed with alcoholic hepatitis or been tube-fed?
No = 0 points
STEP 2
Is oedema present?
No – 0 points, Yes – 1 point
A. BMI (kg/m^2)
> 20 (> 30) = 0 points
18.5-20 = 1 point
< 18.5 = 2 points
B. Unplanned weight loss (%) in past 3-6 months?
< 5% = 0 points
5-10% = 1 point
> 10% = 2 points
C. Patient acutely ill and nutritional intake compromised for > 5 days?
Yes = 2 points
D. Meals are not completed due to fluid overload?
No = 0 points
Sometimes = 1 point
Yes = 2 points
E. Dietary intake reduced > 50% in the last 5 days?
No = 0 points
Yes = 2 points
F. Weight loss in last 3-6 months?
No = 0 points
Yes = 2 points
Hard to say as the patient is on diuretics = 1 point
The Royal Free Hospital Nutritional Prioritising Tool (RFH-NPT) – interpretation and patient management
0 points – low risk of malnutrition
• Routine care
• Re-assessment once a week
1 point
• Routine care
• Patient dietary assessment
• Enhanced caloric intake, bedtime snack
• Re-assessment once a week
2 points
• Appointment with a dietician
• Patient dietary assessment
• Enhanced caloric intake, bedtime snack
• Re-assessment once a week

Table 4. Nutrition principles and recommendations in hepatic encephalopathy

Nutritional status	Normal nutritional status			Moderate malnutrition			Severe malnutrition		
Body weight	Normal/ Underweight	Obesity	Obesity > 40	Normal/ Underweight	Obesity	Obesity > 40	Underweight/ Overweight	Obesity	Obesity > 40
BMI	20-30	30-40	> 40	18-30	30-40	> 40	18-30	30-40	> 40
Caloric intake/day (kcal/kg)	35-40	25-35	20-25	35-40	25-35	20-25	35-40	25-35	20-25
Protein intake/day (g/kg)	1.2-1.5	1.0	1.5	1.2-1.5			1.2-1.5		
Meals	Small but frequent (even 5-7 meals per day)								
Bedtime snack	50 g of complex carbohydrates								
Protein sources	Plant-based, dairy-based if tolerated								
Fibre (g/day)	25-45 especially in obese patients								
Decompensated cirrhosis	Additional medications and supplements in line with therapy goals								
Poorly controlled encephalopathy	Probiotics and branched-chain amino acid (BCAA) supplements may be considered								

Branched-chain amino acids

Branched-chain amino acids (BCAA) include valine, leucine and isoleucine. Temporary BCAA replacement is indicated in patients with acute hepatic encephalopathy. The benefits of BCAA supplementation in patients with chronic HE include decreased frequency of exacerbations. However, there is no improvement in terms of muscle strength or overall survival.

Carbohydrates

Carbohydrates constitute the basis of the diet in patients with liver disease and hepatic encephalopathy, constituting approximately 40-60% of the overall caloric intake. These patients need complex carbohydrates, which should be included in each meal. The bedtime snack, recommended in patients with HE in order to prevent nocturnal gluconeogenesis, should primarily contain complex carbohydrates.

Simple carbohydrates are not recommended and should be avoided. Honey or birch xylitol (especially beneficial in patients with concomitant diabetes) can be used instead as sweeteners.

Lipids

They should constitute approximately 25-30% of the dietary calories. Lipids ensure pleasant taste of foods and affect bowel transit time.

Vitamins

Patients with cirrhosis and HE often present with vitamin B deficiency. The underlying causes of vitamin B deficiency are relatively complex and include their lower intake related to dietary restrictions, malabsorption from the intestine and decreased liver storage capability.

Vitamin B_1 deficiency – apart from that observed in patients with Wernicke's encephalopathy and alcoholic liver disease – may lead to permanent cerebellar damage causing neuropsychiatric symptoms. These are difficult to differentiate from hepatic encephalopathy and irreversible even after liver transplant.

The consequences of vitamin B_2, B_6, B_9 and B_{12} deficiency in patients with advanced liver disease are not yet fully understood; nor is their association with the development and severity of hepatic encephalopathy. The consequences of lipid-soluble vitamin deficiencies are much better known.

Vitamin A is stored in hepatic stellate cells. Hepatic stellate cells activation incurs some vitamin A loss. The vitamin A-deficient cells start collagen production, which significantly affects fibrosis.

The studies show that patients with HE present with significantly reduced vitamin A levels. The level ≤ 0.78 μmol/l in patients with liver disease is associated with an increased mortality risk.

The role of vitamin D is also well understood. Decreased vitamin D levels correlate with increased Child-Pugh scores, whereas a major deficiency is associated with an increased mortality risk in patients with liver disease.

Vitamin E deficiency is particularly marked in alcoholic liver disease. However, only in patients with non-alcoholic steatohepatitis (NASH) does regular vitamin E supplementation offer some biochemical and histological improvement.

Despite the known consequences of various vitamin deficiencies, the proper doses necessary for sup-

plementation in liver diseases have not been determined yet.

Micronutrients

The role of micronutrients in the diet of patients with chronic liver disease and hepatic encephalopathy has been studied for years.

Regularly administered low doses of zinc prevent worsening of liver disease, and – in turn – hepatic encephalopathy. Regular zinc supplementation improved nutritional status in some patients with HE; however, other studies did not confirm this finding.

Patients with cirrhosis tend to have decreased serum levels of magnesium. The regular use of magnesium supplements was shown to improve biochemical parameters (normalising aminotransferase levels), although it did not directly affect the severity of HE.

On the other hand, manganese seems to exert the exactly opposite effect. Some patients with cirrhosis were shown to manifest increased manganese storage all over the body, including the CNS, which exacerbates symptoms of encephalopathy (hence the name 'manganese encephalopathy'). These are rare cases, though [11].

Fibre

Fibre is a crucial nutrient in patients with cirrhosis complicated with HE, regardless of its aetiology.

Fibre, mainly derived from plants, shortens the bowel transit time and, in turn, increases ammonia elimination with faeces. As a result it shows a significant anti-encephalopathy effect.

The recommended daily dose of fibre in patients with hepatic encephalopathy secondary to cirrhosis is 25-45 g – the strength of recommendation is 2B [12].

Probiotics

The qualitative and quantitative changes to the intestinal flora in patients with cirrhosis include decreased numbers of colonies of *Bacteroides*, *Veillonella*, *Streptococcus*, *Clostridium* and *Prevotella*, accompanied by the excessive growth of *Proteobacteria* and *Fusobacterium*.

So far, probiotic supplementation in patients with cirrhosis has varied both in length (between 1 and 6 months), and in dose (between 10^8 and 10^{11} colonies per day). The supplemented bacteria included mainly *Lactobacillus*, *Bifidobacterium*, *Streptococcus thermophilus* and *Bifidobacteria*. A typical dietary supplement contains several strains. It should be noted that administration of probiotics to patients with cirrhosis significantly alters their intestinal flora and decreases the number of pathogenic bacteria, which was confirmed by faecal analysis after a few months of such treatment. Furthermore, probiotics turned out to be beneficial in patients with acute encephalopathy secondary to cirrhosis. It was shown that the 6-month administration of probiotics, mainly containing *Lactobacillus* spp., significantly decreased the risk of HE-related hospitalisation and significantly decreased the CHP and MELD scores. However, neither the recommended dose nor duration of treatment has been determined yet. Not all studies appear to confirm the benefits of using probiotic supplementation in patients with hepatic encephalopathy [13, 14].

Alcohol

Alcohol is strictly contraindicated in all types of HE, just as in all types of cirrhosis, regardless of presence or absence of complications. Alcohol consumption may induce an episode of hepatic encephalopathy; it may also exacerbate or alter its clinical manifestation [15, 16].

Conclusions

1. Patients with cirrhosis and hepatic encephalopathy need a well-balanced and variable diet.
2. Initially, nutritional status assessment should be performed so as to monitor the patient appropriately afterwards.
3. The patient should eat 4-7 meals a day, including a late evening (bedtime) snack.
4. Plant-based proteins are the best source of proteins. Their recommended daily dose is 1.2 g/kg.
5. Ensuring appropriate dietary intake of probiotics and fibre as well as vitamin and micronutrient supplementing are the keys to successful dietary management.

Disclosure

Authors report no conflict of interest.

References

1. Metabolism Consensus Hepatology. 07.2013.
2. Kokot F. Choroby wątroby i dróg żółciowych. PZWL, Warszawa 1991.
3. Sam J, Nguyen GC. Protein-caloric malnutrition as a prognostic indicator of mortality among patient hospitalized with cirrhosis and portal hypertension. Liver Int 2009; 29: 1396-1402.
4. Kalmar DR, Saltzman JR. Nutrition status predict survival in cirrhosis. Nutr Rev 1996; 54: 217-219.
5. Arora S, Mattino C, McAnenny C. The development and validation of nutritional prioritasing tool for use in patients with chironic liver disease. J Hepatol 2012; 56 (Suppl. 2): S241.

6. Taniguchi E, Kawaguchi T, Otsuka M, et al. Nutritional assessments for ordinary medical care in patients with chronic liver disease. Hepatol Res 2013; 43: 192-199.
7. Campillo B, Richardet JP, Bories PN. Validation of body mass index for the diagnosis of malnutrition in patients with liver cirrhosis. Gastroenterol Clin Biol 2006; 30: 1137-1143.
8. Figueiredo FA, Dickson ER, Pasha TM, et al. Utility of standard nutritional parameters in detecting body cell mass depletion in patients with end-stage liver disease. Liver Transpl 2000; 6: 575-617.
9. Nguyen DL, Morgan T. Protein restriction in hepatic encephalopathy is appropriate for selected patients: a point of view. Hepatol Int 2014; 8: 447-451.
10. Bémeur C, Butterworth RF. Nutrition in the management for cirrhosis and its neurological complication. J Clin Exp Hepatol 2014; 4: 141-150.
11. Loguercio C, De Girolamo V, Federico A, et al. Trace elements and chronic and chronic liver disease. J Trace Elem Med Biol 1997; 11: 158-161.
12. Maharshi S, Sharma BC, Sachdeva S, et al. Efficacy of nutritional therapy for patients with cirrhosis and minimal hepatic encephalopathy in a randomizes trial. Clin Gastroenterol Hepatol 2015; doi: 10.1016/j.cgh.2015.09.028 [Epub ahead of print].
13. Rai R, Saraswat VA, Dhiman RK. Gut microbiota: its role in hepatic encephalopathy. J Clin Exp Hepatol 2015; 5 (Suppl 1): S29-36.
14. Andersen H, Borre M, Jacobsen J, et al. Decreased muscle strength in patients with alcoholic liver cirrhosis in relation to nutritional status, alcool abstinence, liver function, and neuropathy. Hepatology 1998; 27: 1200-1206.
15. Jurado García J, Costán Rodero G, Calañas-Continente A. Importance of nutritional support in patients with hepatic encephalopathy. Nutr Hosp 2012; 27: 372-381.
16. Suk KT, Baik SK, Yoon JH, et al. Revision and update on clinical practice guideline for liver cirrhosis. Korean J Hepatol 2012; 18: 1-21.