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Chapter 6

Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Liver failure and liver transplantation

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Abstract

Patients with liver failure have a high prevalence of malnutrition, which is related to metabolic abnormalities due to the liver disease, reduced nutrient intake and alterations in digestive function, among other factors.

In general, in patients with liver failure, metabolic and nutritional support should aim to provide adequate nutrient intake and, at the same time, to contribute to patients' recovery through control or reversal of metabolic alterations. In critically-ill patients with liver failure, current knowledge indicates that the organ failure is not the main factor to be considered when choosing the nutritional regimen. As in other critically-ill patients, the enteral route should be used whenever possible.

The composition of the nutritional formula should be adapted to the patient's metabolic stress.

Despite the physiopathological basis classically described by some authors who consider amino acid imbalance to be a triggering factor and key element in maintaining encephalopathy, there are insufficient data to recommend "specific" solutions (branched-chain amino acid-enriched with low aromatic amino acids) as part of nutritional support in patients with acute liver failure.

In patients undergoing liver transplantation, nutrient intake should be started early in the postoperative period through transpyloric access.

Prevention of the hepatic alterations associated with nutritional support should also be considered in distinct clinical scenarios.

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Key words: *Liver failure. Liver transplantation. Branched amino acids. Malnutrition.*

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SEMICYUC: Spanish Society of Intensive Care Medicine and Coronary Units.

SENPE: Spanish Society of Parenteral and Enteral Nutrition.

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: INSUFICIENCIA HEPÁTICA Y TRASPLANTE HEPÁTICO

Resumen

Los pacientes con insuficiencia hepática presentan una elevada prevalencia de malnutrición. Ésta se encuentra relacionada, entre otros factores, con las alteraciones del metabolismo derivadas de la enfermedad hepática, la disminución en la ingesta de nutrientes y las alteraciones en la función digestiva.

De modo general, en los pacientes con insuficiencia hepática, el soporte metabólico-nutricional debe tener como objetivo el aporte adecuado de los requerimientos contribuyendo, al mismo tiempo, a la recuperación de los pacientes mediante el control o la reversión de las alteraciones metabólicas apreciadas. En los pacientes críticos que presentan insuficiencia hepática, los conocimientos actuales indican que ésta no parece ser un factor fundamental a la hora de considerar la pauta nutricional. Como en otros pacientes críticos, la vía de aporte de nutrientes debe ser la enteral, siempre que ello sea posible.

La composición de la fórmula nutricional debe estar adaptada a la situación de estrés metabólico. A pesar de la base fisiopatológica, clásicamente descrita por algunos autores, que considera al disbalance de aminoácidos un factor desencadenante y mantenedor de la encefalopatía, no hay datos suficientes para recomendar el empleo de soluciones "específicas" (enriquecidas en aminoácidos ramificados y pobres en aminoácidos aromáticos) como parte del soporte nutricional en los pacientes con insuficiencia hepática aguda.

En los pacientes sometidos a trasplante hepático, el aporte de nutrientes debería iniciarse de manera precoz en el postoperatorio mediante una vía de acceso transpilórica. La prevención de las alteraciones hepáticas asociadas al soporte nutricional debe ser también considerada en diferentes situaciones clínicas.

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Palabras clave: *Insuficiencia hepática. Trasplante hepático. Aminoácidos ramificados. Malnutrición.*

How can malnutrition be quantified in patients with liver failure?

Malnutrition is a common finding in patients with liver failure (LF). Observational studies to establish the degree of malnutrition have confirmed that malnutrition occurs even in the early stages of the disease, and is more intense in the most seriously ill patients[1] (III). It must be noted that the degree of malnutrition has a significant impact on mortality[2].

The etiology of cirrhosis may also condition the degree of malnutrition. Alcoholism often causes malnutrition "per se." However, malnutrition can also occur in alcoholic patients in withdrawal state. Comparative studies on the effects of the etiology of cirrhosis in malnutrition shows that bleeding is more significant in alcoholic patients than in those with cirrhosis of viral etiology[3] (III).

Nutritional monitoring must be performed through subjective global assessment, loss of muscle mass, and the plasma albumin concentrations, although they are all affected by changes derived from the liver disease. The application of more specific nutritional assessment methods shows significant differences in the definition of malnutrition according to the method used[4] (III).

Does the nutritional status influence the outcome and prognosis of liver failure?

Population studies suggest that malnutrition is a factor influencing the morbidity and mortality of patients with chronic liver disease[5] (III). Some data suggest that preservation of the body lean mass is important in the evolution of cirrhotic patients, as it is associated with lower complications in the evolution[6,7] (III).

In patients candidate to liver transplantation (LT) it is considered that malnutrition affects adversely post-transplant outcome[8,9] (III), though this is controversial, as adverse outcomes are also obtained with this regard[10] (III).

What conditions the choice of the route for supplying nutrients in patients with liver failure?

No controlled studies have been performed comparing enteral nutrition (EN) to parenteral nutrition (PN) in patients with advanced LF. However, it may be stated that, as in other diseases, EN should be the first route to be considered when specialized nutritional support is indicated. Esophageal or gastric varicose veins and the presence of coagulopathy are contraindications commonly used in the clinical practice for placing a nasogastric tube, though this contraindication is not supported by clinical studies and has been discussed by some authors[11] (IV). In a randomized study evaluating the efficacy of EN in patients with bleeding for esophageal varicose veins, no significant difference was seen in rebleeding in patients with a feeding catheter and those receiving oral nutrition[12] (Ib). However, the procedure should be performed after assessing the related risks and benefits.

Parenteral nutrition should be used in these patients when: *a)* the gastrointestinal tract is not functional due to the presence of gastrointestinal bleeding; *b)* EN is not well tolerated; *c)* EN is insufficient to provide nutritional requirements, and *d)* there is a high risk of aspiration as a result of consciousness disorders related to advanced states of encephalopathy.

What amount and quality of energy substrates are required?

Nutritional supply must be conditioned by the degree of malnutrition and the type of disease, related or not to the progression of LF. There are no controlled studies that establish the optimum nutritional supply in patients with LF in critical situation. Therefore, nutritional similar supplies are similar to those given to other critically-ill patients, with some changes suggested by the physiopathological characteristics of the LF.

The total recommended calorie supply is within 25-40 kcal/kg/day[13-15] (IV).

With regard to the distribution of the energy supply, it must be considered that patients with LF are at a high risk of hypoglycemia (for limitation in storage of glycogen and liver neoglycogenesis).

There are no data contraindicating fat supply within nutritional support in patients with LF. The recommended lipid supply limit is similar to that of other critically-ill patients. Various clinical studies show that intravenous fat infusion causes both an increase in triglyceride plasma levels and an increase in their metabolism and excretion. Comparative studies between the different lipids in patients with LF have not shown significant differences[16,17]. Studies with indirect calorimetry in severe LF show a reduction in glucose oxidation and an increase in fat oxidation[18] (III).

What should be the characteristics of protein supply?

It is classically considered that a high protein intake may cause encephalopathy. However, some studies indicate that normal protein supply does not lead to an increased encephalopathy, while protein restriction has adverse effects upon protein metabolism[19] (Ib). The limitation of protein supply is not indicated "routinely" in these patients; it should only be considered in patients in an unstable situation and always conditioned by demonstration of encephalopathy related to increased protein intake.

Are there any formula or specific nutrient recommended in liver failure?

The mechanisms leading to an amino acid pattern characteristic of liver failure, the role played by this pattern in the occurrence of liver encephalopathy, and the effect of branched-chain amino acids (BCAA) upon protein turnover are the pathophysiological basis to justify the increased BCAA in LF.

Most studies with oral supplements of BCAA were conducted in outpatients with chronic liver disease, to assess their impact on disease progression. In general[20-22] (Ib), [23] (III), the use of BCAA allows for establishing some positive effects (improved Child score, fewer hospital admissions, lower encephalopathy) but differences were not seen in patient mortality. Several revisions have been performed about this matter[24,25]. The data are not conclusive due to the heterogeneity of the populations studied and the variability in the type of nutrition used. The results of the Cochrane review, based on 11 controlled studies including 556 patients, suggest that supplements with BCAA impact favourably encephalopathy improvement, but is not associated with other effects on morbidity and mortality[26] (Ia).

The indication for administering this type of solutions to patients with LF is, therefore, controversial. It is important, in any case, to assess the amino acid profile of the solution enriched with BCAA that is decided to be administered to the patient, as this could be deficient in other amino acids and, therefore, affect the nutritional efficacy of treatment.

Regarding other formulations, such as diets enriched with casein or amino acids of plant origin, the results of its use have not been adequately tested[27].

What are the vitamin and trace elements requirements?

Patients with advanced disease show a high risk of micronutrient deficiency. The etiology of the situation is multifactorial, with co-adjuvant factors involved, such as an inadequate intake, gastrointestinal absorption deficiency and their increased clearance. Supplements with Zn and Mg should be administered in LF, particularly in the most seriously ill[28] patients (III).

According to this, the vitamin requirements (both water-soluble and lipid- soluble), and trace elements (Mg, Zn, P) appear to be increased, though studies have not been conducted to outline this situation. The role of vitamin D and K in immune tolerance of the graft is under investigation[29] (III).

How should nutritional support of liver transplant patients be?

Malnutrition is not a contraindication for transplantation, but may adversely affect the progression and prognosis of transplanted patients.

Early postoperative nutritional support, both by enteral[30] (Ib) and parenteral route[31] (Ib), is associated with clinical outcomes benefits. In a study comparing both methods, no differences were seen in the parameters tested[32] (III).

Macro and micronutrient requirements are similar to those recommended for other postoperative situations.

The use of pharmaconutrition may be beneficial in the immediate postoperative period. PN with glutamine improves the course of liver biochemical parameters and reduces hospital stay[33] (Ib). The use of an enteral diet enriched with pharmaconutrients (arginine, ω-3, nucleotides), both before and after transplantation, is associated with a better maintenance of protein reserves and lower incidence of post-operative infectious complications[34] (III).

The administration of a mixture of prebiotics and probiotics, together with EN postoperatively following transplantation, may reduce infectious complications[35] (Ib).

How can liver disease associated with nutritional support be prevented?

Cholestasis associated with PN is a serious complication occurring in pediatric patients receiving long-term PN, and may be an indication for bowel transplant. The limitation of the lipid supplied from infusions based on soybean oil (less than 1 g/kg/day) may contribute to decrease serum levels of bilirubin[36] (III). The use of lipid solutions containing fish oil has shown positive results in prevention of such disorders[37] (Ib), [38] (III).

The main factors for development of liver disease in critically-ill adult patients with nutritional support are the high energy supply (> 25 kcal/kg/day) and the presence of sepsis[39] (III). According to this, controlling both events would be fundamental for the prevention of liver disease secondary to nutritional support. Studies performed on lipid emulsions containing ω-3 fatty acids (fish oil) have also allowed to noticing favorable outcomes in the prevention or reversion of liver disorders secondary to PN[40] (Ib), [41,42] (IIa).

Recommendations

– A calorie intake of 25-40 kcal/kg/day is recommended (C).

– Energy supply should be mixed (carbohydrates/fats) (C). There is no contraindication to intravenous administration of lipid emulsions, though it is recommended that the supply does not exceed 1 g/kg/day (C).

– In patients with a high metabolic stress, the limitation of protein intake is not indicated routinely (C). The regular use of diets enriched with branched amino acids is not recommended in patients requiring enteral nutrition. These diets may be used if the patients develop encephalopathy during enteral nutrition (C).

– Vitamins and trace elements intake (particularly Zn, Mg and P) should be increased (C).

– In patients with liver transplant, early nutritional support should be administered postoperatively following transplant, preferably by enteral route (transpyloric route) (B).

– In patients with liver transplant, macronutrient requirements are similar to those of other situations in the immediate postoperative period. P, Mg and Zn values should be monitored (B).

– It is recommended to use lipid emulsions containing ω-3 fatty acids (fish oil) in patients with liver disorders during parenteral nutrition (B).

Conflict of interests

The authors declare that they have participated in activities funded by the pharmaceutical industry for marketing of nutritional products (clinical studies, educational programmes and attendance to scientific events). No pharmaceutical industry has participated in the preparation, discussion, writing, and establishing of evidences in any phase of this article.

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