Nutrition in end stage liver disease

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This chapter will focus on studies within the last 5 years of nutrition in end stage liver disease, but earlier studies illustrating the present state of affairs will also be mentioned. The first part will focus on descriptive epidemiological studies that help to set the scene for the intervention studies, which will be described in the second part. Each part will discuss liver cirrhosis, acute liver failure and liver transplantation separately.

The aim is to provide the reader with sufficient background for the decision in clinical practice about when to see nutrition support as an important part of treatment of the patient.

Key words: liver cirrhosis; acute liver failure; liver transplantation; nutrition support; branched-chain amino acids.

PREVALENT OF MALNUTRITION AND ITS RELATION TO CLINICAL OUTCOME AND PHYSIOLOGICAL FUNCTION

Cirrhosis

Malnutrition is common in chronic liver disease and should be seen as a complication in line with ascites, esophageal varices, hepatic encephalopathy (HE), and treated as such.

In an Italian multicenter study of more than 1,400 patients with cirrhosis, the prevalence of low body weight relative to height was only 5%, but 20% of the patients had a recent weight loss >10% of usual body weight and malnutrition, as measured by mid-arm-muscle-area (MAMA) or mid-arm-fat-area, was present in 30% of the patients.1 In a follow-up to that study, it was found that within the Child–Pugh classes A
and B, survival was related to MAMA, but not in class C, suggesting that nutritional status is more important in patients with a better prognosis.\textsuperscript{2} Another study found that mid-arm-circumference (MAC) was independently associated with survival and improved the prognostic accuracy when combined with the Child–Pugh score.\textsuperscript{3}

Even in mild disease, Child–Pugh class A, 25\% of the patients were found to be malnourished.\textsuperscript{2} A study which employed total body neutron activation analysis, a method considered by many to be the gold standard for measuring nutritional status, also showed low total body nitrogen content in patients with Child-Pugh class A.\textsuperscript{4} A more recent study, employing calculation of Body Cell Mass (BCM) from measurement of total body water and extracellular water (by isotope dilution), also found a reduction in BCM in Child–Pugh class A patients.\textsuperscript{5} Concomitant with impaired nutritional status in Child–Pugh class A patients, measured as MAC, it was also observed that 48 and 34\% of these patients had a low energy intake (<30 kcal/kg per day) and protein intake (<1 g/kg per day), respectively.\textsuperscript{6}

Even at this early stage of disease, the impaired nutritional status is related to clinical outcome. Child–Pugh class A patients who were categorised as malnourished, either by Subjective Global Assessment (SGA)\textsuperscript{7} or by hand grip strength, had a higher 1 year-rate of major complications and/or death.\textsuperscript{8}

In most of the studies mentioned, nutritional status was further aggravated with increasing severity of disease, Child–Pugh class B and C, but it is noticeable that nutritional problems are already prominent and related to clinical outcome with mild disease. Also, in many of these studies, patients with different etiologies have been included, such as alcohol, virus and cryptogenic cirrhosis and there seems to be no major difference in prevalence or functional impact of malnutrition among the different causes of cirrhosis.

In addition to the clinical outcome variables mentioned above, nutritional status has been associated with impaired measures of physiological function. Knee and ankle muscle strength were decreased in alcoholic cirrhosis, and it was related to Lean Body Mass, as measured by 24 creatinine excretion, rather than to Child–Pugh score or polyneuropathy.\textsuperscript{9} Hand grip strength was related to BCM, as determined by measurement of total body water and extracellular water.\textsuperscript{10} In a study of mainly Child–Pugh class A patients, all patients who were malnourished according to SGA also had decreased hand grip strength.\textsuperscript{6}

Malnutrition is also associated with immuno-incompetence in liver cirrhosis, such as skin test anergy,\textsuperscript{11–13} but the independent association between immuno-incompetence and liver function versus nutritional status has not been explicitly investigated. In one of these studies,\textsuperscript{12} it was shown that with increasing severity of disease, i.e. Child–Pugh score, there was a parallel increase in malnutrition and also anergy.

Malnutrition may also impair mental function in cirrhotic patients, since it was suggested that increased degradation of endogenous proteins contributed aromatic amino acids that would increase HE.\textsuperscript{14} However, the possible association between nutritional status and HE has not been examined.

It should be emphasised that there is no ‘Gold Standard’ for routine clinical screening or assessment of nutritional problems in patients with cirrhosis. It is often stressed that BMI may be unreliable for nutritional evaluation due to the accumulation of fluid in patients with cirrhosis. This is a problem only in patients who may have a falsely normal BMI due to the accumulation of fluid. In most cases, a clinical judgment of the amount of ascites is possible which can be subtracted from the measured body weight. Patients with ascites who have a low BMI are of course malnourished. As an alternative to BMI, it has been suggested to use bioimpedance analysis or other more...
sophisticated methods, but it should be stressed that the simple methods, such as SGA or anthropometrics methods including MAC do provide information on clinical course as related to nutritional status (see above). A low MAC combined with low hand grip strength has a high sensitivity and specificity of identifying patients with a low BCM, as determined by isotope dilution, while SGA was not associated with BCM. This suggests that a combination of simple objective measurements of MAC and hand grip strength give a better reflection of BCM than the SGA which is limited by being a multivariate subjective method.

The use of bioimpedance analysis for calculating body cell compartments by equations that are not validated in patients with cirrhosis is dubious. Direct use of results from bioimpedance analysis (resistance and phase angle) may be more appropriate. It has been shown that phase angle is more closely related to survival than MAMA, total body potassium or lean body mass estimated from 24 hours creatinine in patients with cirrhosis. The approach of vector analysis based on resistance and phase angle, as a functional measure of cell mass and/or cell function may become of value in the future.

In the guideline for nutrition screening published by the European Society for Clinical Nutrition and Metabolism (ESPEN), it is emphasised that the tool used for nutritional screening should have a high degree of predictive validity, i.e. that the patients identified to be malnourished/at nutritional risk should expect to benefit from nutritional intervention by an improved clinical outcome. None of the methods used for evaluation of nutritional status mentioned above have been validated in this way in patients with cirrhosis (see further in the section on Intervention). The ESPEN guidelines also stress that screening for nutritional risk should include quantitative information on BMI (or MAC when body weight is unreliable/unobtainable), recent weight loss and recent dietary intake and, for hospitalised patients, an evaluation of severity of disease as an index of nutritional requirements. For patients with cirrhosis, such a complete screening process has not yet been undertaken, although the SGA does contain most of these elements in a non-quantitative form. The ESPEN guideline also underlines that plasma albumin is not useful for nutritional screening, since many factors related to the disease process and hydration status, rather than nutritional status, influence plasma albumin levels. This certainly also applies to patients with cirrhosis.

**Acute liver failure and transplantation**

In patients with acute liver failure, no studies are available demonstrating that nutritional status plays an independent role for the clinical course.

Several studies have shown that the risk of postoperative complications is high in malnourished cirrhotic patients. In liver transplantation, the nutritional status at the time of operation, as evaluated clinically, was suggested to be the only variable among those related to survival after liver transplantation that could be treated. In an analysis with an extensive set of variables related to liver function and nutritional status, it was determined that a low BCM, as measured with bioimpedance analysis, combined with increased resting energy expenditure (REE), predicted mortality irrespective of Child–Pugh classification. In a later study there was no association between outcome and nutritional status, measured as BCM by isotope dilution or MAC, but as the authors pointed out, their malnourished recipients had received nutritional supplements while
waiting for transplantation.\textsuperscript{21} The presence of malnutrition has been estimated to increase cost of liver transplantation by 40%.\textsuperscript{22}

**CAUSES OF MALNUTRITION IN CIRRHOSIS**

The liver plays a central role in the metabolism of most nutrients. In chronic liver disease, glucose intolerance or frank diabetes mellitus is frequent, alterations in amino acid metabolism play a role for the development of HE, decreased hepatic protein synthesis contribute to hypoalbuminemia and ascites and reduced bile acid synthesis is responsible for fat malabsorption. Ascites, and inflammatory processes in the diseased liver, cause decreased appetite. In alcoholic liver disease, alcohol by itself changes hepatic metabolism of some vitamins. All these changes were listed in an early review.\textsuperscript{23} For more recent reviews, see.\textsuperscript{24–26} It remains impossible, however, to name one or a few functions that are quantitatively of major importance for the impaired nutritional state. In the following, recent studies related to macronutrients, minerals and vitamins will be discussed.

**Energy**

The average REE was found to normal in a study of 473 patients, as compared to values predicted by the Harris–Benedict equation, but 34% the patients had an REE > 120% of the expected value. In these hypermetabolic patients, total body potassium was lower, suggesting an association between increased REE and malnutrition, at least in some patients.\textsuperscript{27} Exercise-induced increase in oxygen uptake was found to be normal in patients with cirrhosis.\textsuperscript{28} With a different approach, REE was compared between well-nourished or malnourished cirrhotic patients and it was found that REE was lower in absolute terms in the malnourished patients, that energy expenditure associated with physical activity was equal in the two groups and that both groups were in energy balance.\textsuperscript{29} Only 2 of 50 cirrhotic patients were hypermetabolic in that study. This study concluded that the state of malnutrition is not associated with a negative energy balance, confirming a similar previous study in malnourished cirrhotic patients.\textsuperscript{30} In both studies,\textsuperscript{29,30} REE and dietary intake were decreased in proportion to body size and both REE and dietary intake were lower than those of the healthy population. Therefore, hypermetabolism may contribute to the development of malnutrition, but when the state of malnourishment is reached, it appears that a new steady state is reached, i.e. that REE, mainly determined by lean body mass, is adapted to the new condition. In young healthy individuals, however, intake exceeds expenditure (hyperphagia) after an experimental weight loss.\textsuperscript{31} The same study showed that elderly did not show hyperphagia after weight loss. The biochemical basis of this abnormality is not known, and it seems that patients with cirrhosis also have a defect in the signalling between being underweight and compensatory excess dietary intake.

**Protein**

Protein requirement is increased in clinically stable patients with cirrhosis, to an average requirement of about 0.8 g/kg per day. With the customary addition of 2 SD’s, a recommendation of about 1.2 g/kg per days is reached.\textsuperscript{32–34} Protein requirement can be
increased due to decreased absorption, decreased synthesis of body protein, increased degradation of body protein, or increased hepatic urea production with increased urinary nitrogen excretion and/or increased intestinal protein loss. In these studies, faecal nitrogen excretion was not increased, i.e. neither malabsorption nor increased intestinal loss was responsible. Investigations with stable isotopes suggested that there is an increased rate of endogenous protein degradation both in the fasting state and in the diurnal fasting/fed state. The increase in breakdown of body protein was associated with an increase in plasma amino acids, suggesting that the primary event is increased protein breakdown rather than increased hepatic urea formation. The increased degradation in the fasting state may be due to low glycogen reserves, prompting an early switch to gluconeogenesis from amino acids origination from body protein stores, as based on the observations in Owen’s study. The increase in the diurnal fasting/fed state, as based on preliminary data, may be due to a relative lack of branched-chain amino acids (BCAA—see further on BCAA below), e.g. for removal of ammonia, based on the observations in the study by Hayashi. A single meal does not increase whole body protein synthesis in patients with cirrhosis, in contrast to the increase seen in healthy volunteers. This defect was suggested to be due to the insulin-insensitivity also observed in the study.

Together, these studies indicate that the increased protein requirement is due to both a defect in meal-induced protein synthesis and increased protein degradation during feeding as well as fasting. However, a note of caution is warranted since the methods for measuring protein metabolism are still being debated, not the least in patients with cirrhosis.

Despite the increased requirement for protein, stable malnourished patients with cirrhosis are in nitrogen balance at an intake lower than that of the healthy population, suggesting that they have reached a steady state with the low intake and the same considerations a those given above about the lack of excess energy intake in an underweight state apply to protein intake.

In situations when acute exacerbations further decrease the intake, e.g. due to infections, tense ascites, bleeding, encephalopathic episodes, the possible increase in REE and the increase in protein requirement will of course aggravate the nutritional status rapidly.

**Vitamins and minerals**

Patients with liver cirrhosis often have low plasma levels of vitamins and trace minerals, but the specific causes and specific functional implications of these abnormalities are not known in detail. Magnesium depletion, now also determined as urinary excretion after a magnesium load, is common in end stage liver disease. Zink deficiency is also common and seems to be caused by decreased absorption and a diuretics-induced increase in urinary excretion. Supplementation with zinc increases glucose tolerance. One study reported that zinc supplementation reduced the increase in plasma ammonia after an alanine load, and this was accompanied by an improvement in psychometric tests, liver function tests and Child–Pugh score. However, the effect on psychometric tests was not confirmed in another study. Thiamine deficiency is common in alcoholism and in alcoholic cirrhosis, but it has been found to be equally frequent in hepatitis C virus related cirrhosis. The deficiency was not due to decreased erythrocyte phosphorylation of thiamine in that study, but
other potential causes were not investigated. It was recommended to give thiamine supplements to all patients with cirrhosis.

INTERVENTION STUDIES

Standard nutrition support in patients with cirrhosis

There is no specific meta-analysis available which can guide the reader as to when to give nutrition support to patients with liver cirrhosis. Recently, a meta-analysis was performed of about 30 randomised controlled trials with a total of about 3000 patients given oral supplements or tube feeding. The meta-analysis included a large variety of diagnoses: neurology, gastrointestinal disease, liver disease, malignant disease, elderly, abdominal surgery, orthopaedic surgery, critical illness/injury, burns. The results showed that the rate of complications was reduced from 46 to 28%, that the rate of infections was reduced from 44 to 24% and that mortality was reduced from 24 to 17%. It may therefore be inferred that nutrition support will also improve clinical outcome in patients with cirrhosis, being a part of the malnourished population in hospitals.

The latest systematic review of nutrition support in patients with cirrhosis aimed at defining more precisely in clinical terms when to give nutrition support to these patients. This was based on the information supplied in the randomised controlled studies available, some of which showed an effect on clinical outcome while others did not. It was noted that the positive and no-effect trials had included patients with approximately the same degree of impaired liver function and impaired nutritional status, whereas the studies differed in amount and type of exclusion criteria. The studies with few exclusion criteria, and with a positive effect on outcome, included patients that had a low spontaneous energy and protein intake while the studies with a large number of exclusion criteria, an no effect on outcome, included patients who had a fairly adequate spontaneous intake of energy and protein. It was therefore suggested that nutrition support is indicated in patients with a low spontaneous intake, i.e. below 50 g protein per day, for example due to complications of the disease (infections, tense ascites, bleeding, encephalopathic episodes). It seems rather obvious that nutrition support only works when the spontaneous intake is low. In these studies there was no indication that adequate dietary intake, including protein, aggravated HE. The point of keeping track of dietary intake has been re-emphasised in a study showing that intake of energy and protein during hospital stay is related to mortality and septic complications.

The consensus report of ESPEN on nutrition support in liver disease gave recommendations for various clinical conditions of the patients: malnourished patients who have an inadequate dietary intake and are at risk of fatal complications should receive nutrition support. This recommendation was based on the same evidence as reviewed above. The intervention studies available, which suggest a positive effect on clinical outcome in such patients, gave energy in amounts of 35–40 kcal/kg per day and protein in amounts up to 1.6 g/kg per day and these doses were recommended by ESPEN to be used as a guideline.

A more recent systematic review of all studies of nutrition support also showed that in studies of patients with cirrhosis who fulfil the criteria for being nutritionally at-risk by the ESPEN screening tool NRS-2002, there is a positive effect of nutrition support on clinical outcome.
The ESPEN consensus report also stated, based on the intervention trials available, that in malnourished patients who have an inadequate dietary intake and are at risk of fatal complications, low grade HE (grade I–II) should not be considered a contraindication to nutrition support, including an adequate protein supply. This last statement aimed at changing the clinical routine of reducing protein intake in encephalopathic patients, based on an ill-defined suspicion of encephalopathic patients being protein-intolerant. Iatrogenic protein restriction will of course aggravate malnutrition, in particular when considering the increased protein requirements. This new policy was not immediately accepted.

For patients with HE as their main problem, rather than disease-related anorexia and malnutrition, the ESPEN guideline advised a few days of protein restriction if other obvious causes of HE had been ruled out and protein-intolerance was possible, but after a few days adequate nutrition should be reinstituted.

The need for caution has now been formally investigated in an intervention trial. In this trial, malnourished encephalopathic patients in stage 1–4, median stage 2, were randomised to follow the advice of a gradual increase in protein intake or to adequate protein intake via tube feeding, 1.2 g/kg per day, from the beginning. At the same time precipitating factors were treated when identified: infection or electrolyte disturbances. In 4 out of 10 patients in each group the precipitating factor was not identified. All patients received standard therapy for HE (lactulose followed by neomycin). Outcome of HE and mortality were identical in both groups. The normal protein group had a positive nitrogen balance from day 2, associated with a lower rate of protein degradation compared to the low protein group, at similar rates of protein synthesis. Plasma ammonia at the end of the study was similar in both groups. This study clearly shows that no harm is done when treating malnourished encephalopathic patients with adequate amounts of protein. In addition, the study demonstrates that tube feeding can safely be applied in these patients, since none of the patients developed aspiration pneumonia or significant gastric retention. These conclusions have already received considerable support.

A novel approach is to add pre- and probiotics to a standard tube feeding in order to reduce intestinal bacterial translocation and to improve gut immune function. In a study of patients after liver transplantation, the addition of lactic acid bacteria and fibres indeed resulted in a dramatic reduction in postoperative infections.

Evening meals

The study of Owen showed that after an overnight fast, the splanchnic metabolism in patients with cirrhosis had changed to a metabolic state similar to that of healthy volunteers after a 3 days’ fast, in particular with respect to increased gluconeogenesis from peripheral amino acids derived from body protein. It was suggested that low hepatic glycogen reserves in cirrhotic liver prompt this rapid shift to gluconeogenesis during night hours. It was therefore investigated whether the same amount of protein divided into 4–6 meals including a late evening meal would improve nitrogen balance compared to the usual three main meals pattern. This was indeed found to be the case. The same group later reported that a similar improvement could be achieved by a late evening oral dose of glucose. This approach has been extended to giving BCAA (see further on BCAA below) after breakfast and at night compared to the usual procedure: after breakfast and after dinner. With the night dose of BCAA, the urinary excretion of 3-methylhistidine decreased, both absolute and relative to urinary creatinine excretion. This indicates a lower muscle protein breakdown with the evening
dose of BCAA. It has also been found that one late evening snack with carbohydrate and BCAA improves glucose tolerance to the same degree as the same snack given twice during the daytime. These studies all point to the importance of reducing the length of evening-night time starvation in patients with cirrhosis. Future studies are needed to compare the relative efficiency of the methods described, meal, carbohydrate or carbohydrate with BCAA, for clinical outcome.

**BCAA in cirrhosis**

BCAA is still under investigation as a method to treat HE and/or as a nutritional supplement to improve nutritional status and clinical outcome. For recent reviews, see. BCAA, especially leucine, appear to have a special anabolic role as a co-regulator of the rate of protein breakdown, and in experimental animals, also of the rate of protein synthesis. BCAA compete with the serotonin precursor tryptophane for the same amino acid transporter in the blood–brain barrier. The ratio of BCAA/tryptophane is decreased in most patients with cirrhosis, probably due to hyperinsulinemia and/or decreased postabsorptive removal of non-BCAA by the failing liver, and it is therefore believed that a supplement with BCAA may reduce brain uptake of tryptophane.

In a meta-analysis of studies using BCAA for treatment of HE, BCAA was effective when including all studies, but when excluding studies with a low quality (unknown randomisation method, unknown blinding), the effect was neither seemingly nor statistically significant. It was also noted that too few studies were available to carry out a meta-analysis of the effect of BCAA as a nutritional supplement.

Since this meta-analysis, a large multicenter 1-year trial investigated the role of BCAA as a nutritional supplement. The 174 cirrhotic patients were included on the basis of severe liver disease, defined as a Child–Pugh score B or C and evidence of portal hypertension. Neither malnourishment nor encephalopathy were entry criteria. The patients included were not malnourished as determined by MAC or bioimpedance nor overtly encephalopathic. Therefore, the purpose of the study was not to treat malnourishment or encephalopathy, but rather to investigate whether BCAA would be of clinical benefit in cirrhotic patients with moderate–severe disease. The patients were randomised to three groups given different supplements containing either 14 g BCAA or isonitrogenous + isoeenergetic lactalbumin or isoeenergetic maltodextrin. It is a strong methodological feature of this study to include both control groups. BCAA reduced rate of death and further severe progression of liver disease and rate of hospital admissions, increased appetite rating and Quality of Life. The low grade encephalopathy present in some of the included patients did not improve. BCAA increased triceps skinfold thickness, results for MAC were not reported and bioimpedance analysis was not improved. The main problem with the study was a rather large rate of drop-outs in the BCAA group, mainly due to palatability/acceptance issues. This led to a non-significant intention-to-treat analysis for the main outcome variable, death and further severe progression of liver disease. The study does suggest, however, that BCAA has a positive effect on outcome, more than the lactalbumin-based supplement, which in its composition may be more similar to a standard oral supplement. Still, it does remain to be shown that a BCAA supplement is superior to standard products in a successful intention-to-treat analysis.

One of the first studies to employ BCAA was carried out in patients who were protein-intolerant, i.e. tolerating less than 40 g of protein. They were randomised to increase their protein intake to 70 g, either in the form of casein or with a BCAA
supplement.\textsuperscript{69} When encephalopathy worsened, it was considered a treatment failure and the patient was withdrawn from the study. Seven out of 12 patients in the casein group were treatment failures, but only 1 out of 14 in the BCAA group was a treatment failure. This study combines the two potential uses of BCAA: treatment/prevention of HE in malnourished patients who cannot be refed because of protein-intolerance. This is the only study available with this design, and it was the basis of the ESPEN recommendation to use BCAA in this particular situation.\textsuperscript{50} This study of course needs to be verified in other centres, but until more studies are available, this situation remains to be the only clear indication for the use of BCAA in treatment of patients with cirrhosis.

**Hepatic coma and acute liver failure**

There are no recent studies available on nutrition support in hepatic coma. The conclusions from the meta-analysis\textsuperscript{70} still seem to hold: that parenteral nutrition probably improves survival in these patients but the heterogeneity among the studies makes firm conclusions impossible. It should be stressed that most of the trials had tested BCAA containing products, but in most cases they used control treatment without amino acids and therefore it cannot be concluded that it is BCAA, rather a standard amino acid mixture, that may be effective.

For acute liver failure there are no intervention studies available to define the best practice. A survey in Europe showed a surprising variation in feeding techniques (enteral or parenteral) and in composition of feeds.\textsuperscript{71} A large number of centres used standard TPN containing amino acids, despite the fact that these patients have plasma amino acid concentrations that are increased three–fourfold above normal values.

In acute liver failure, the splanchnic area produces large amounts of ammonia, most likely derived from glutamine removed from the circulation by the portally drained viscera. Ammonia produced in the splanchnic region is taken up in muscle and brain and probably contributes to the production of glutamine in these organs. However, both muscle and brain produce more glutamine than can be accounted for by ammonia and amino acid uptake in these tissues, indicating a severe protein catabolic state.\textsuperscript{72,73} These studies also confirmed earlier studies showing decreased levels of BCAA, despite the increase in total amino acids. It does not seem rational to supply a standard mixture of amino acids to these patients. Future trials on clinical outcome may show clinical benefit from correction of the amino acid pattern by supplying BCAA.

**Transplantation**

Two studies have examined the effect of nutrition support after liver transplantation. Early postoperative enteral nutrition, within 12 hours after transplantation, reduced the rate of viral infections\textsuperscript{74} and showed a tendency to reduced bacterial infections. Postoperative parenteral nutrition reduced the length of stay in the ICU.\textsuperscript{75}

The concept of pre- and postoperative immunonutrition has now also been introduced in liver transplantation,\textsuperscript{76} inspired by the positive results obtained in other types of gastrointestinal surgery.\textsuperscript{77} The study by Plank et al\textsuperscript{76} is a feasibility study with a historic control group and therefore the promising outcome results can only be seen as a stimulus to perform a prospective study. However, it is worth noting from this study that the immunostimulatory effect did not seem to cause an increase in the rate of
rejections and it will be highly interesting to see the results of the prospective trial presently being carried by the authors.

SUMMARY

It has become increasingly clear during the last 10 years that malnutrition by itself is associated with worsened clinical outcome in patients with liver cirrhosis. Simple methods, such as SGA, MAC or the ESPEN screening tool, NRS-2002, may be used to identify patients who are at risk of nutrition-related complications. Inadequate intake in patients with complications raises the alert to initiate nutrition support. In such patients, nutrition support will improve clinical outcome, as a best possible interpretation of the randomised studies available. Standard products can be used in most situations, despite the disturbances in absorption and metabolism of glucose and protein/amino acids. A new study demonstrates that adequate protein intake can safely be given to encephalopathic patients via tube feeding.

In acute liver failure, no intervention studies can govern towards the best practice, but it should be considered that plasma amino acid concentrations are already greatly elevated due to the absent liver function and the increased protein catabolic rate and therefore it does not seem rational to administer standard amino acid solutions in this condition.

In liver transplantation, studies employing standard preparations have also showed improved clinical outcome. A recent feasibility study suggests that immunonutrition is well tolerated after liver transplantation and the results of an ongoing intervention trial are expected with great interest.

Finally, the reader is encouraged to read the ESPEN Guidelines for Enteral Nutrition, which are expected to be published early in 2006. These guidelines also contain an extensive update of enteral nutrition in liver disease.

FUTURE RESEARCH

The effect of nutrition support is based on a systematic review of studies available49 and highly influenced by one study showing improved survival by tube feeding in severely ill patients.78 More intervention studies with standard composition or disease specific compositions are needed before recommendations can be based on a formal meta-analysis.

The role of BCAA is still uncertain. It seems that BCAA is not a useful treatment in patients with HE in general.67 A recent study showed that BCAA improved clinical outcome in not-malnourished cirrhotic patients with moderate–severe liver disease,68 but compliance was unsatisfactory due to palatability problems and therefore a more acceptable formulation of BCAA is needed. It also remains to be settled whether BCAA will improve clinical outcome in malnourished patients, since the disease spectrum of these patients is probably not the same as in not-malnourished cirrhotic patients. The possible role of BCAA in nutrition support of patients with protein-intolerance69 needs to be verified and, in particular, a clinical test for diagnosing protein-intolerance should be developed.
References


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