Effects of prolonged oral nutritional support in malnourished cirrhotic patients: results of a pilot study

Lina CUNHA (1), Marcel HAPPI NONO (1), Anne Laure GUIBERT (2), Delphine NIDEGGER (3), Philippe BEAU (1), Michel BEAUCHANT (1)

(1) Service d’Hépato-Gastroentérologie et d’Assistance Nutritive, (2) Service Diététique, CHU La Milétrie ; (3) Institut de Santé Publique, Faculté de Médecine, 86021 Poitiers Cedex.

SUMMARY

Objectives — The aim of this prospective study was to evaluate the acceptance and the effects of nutritional supplementation in malnourished ambulatory patients with liver cirrhosis.

Methods — From June 1999 through June 2000, alcoholic cirrhotic patients with moderate to severe malnutrition as assessed with the Detsky index were included in the study. Patients were instructed to consume, in addition to their regular diet, a commercial solution that provided 500 kcal/day. Physical examination, dietary recalls and laboratory tests were performed at 1, 2 and 3 month.

Results — Twenty-nine patients with a mean age of 52 years were included. The Child-Pugh grade was A in 6 patients, B in 14 and C in 8. Eighteen patients (62%) completed the 3 month study protocol. Mean non-alcohol calorie intake increased significantly by 31% at 1 month and by 48% at 3 months. At the same time alcohol calorie intake decreased significantly by 68% and 77%, respectively. Subjective improvement in nutritional status was associated with significant improvement of mean Child-Pugh score (P = 0.0007) and triceps skinfold thickness (P = 0.005). The increase of mid-arm circumference was not significant.

Conclusion — This study showed that oral supplementation in ambulatory patients with liver cirrhosis is feasible and associated with a concomitant reduction of alcohol intake.

RÉSUMÉ

Effets de l’administration prolongée d’un supplément nutritionnel oral chez le cirrhotique dénutri : résultats d’une étude pilote

Lina CUNHA, Marcel HAPPI NONO, Anne Laure GUIBERT, Delphine NIDEGGER, Philippe BEAU, Michel BEAUCHANT

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Objectifs — Le but de cette étude pilote était d’évaluer chez le malade cirrhotique dénutri l’acceptabilité et les effets d’un supplément nutritionnel oral prolongé prescrit en ambulatoire.

Méthodes — Entre juin 1999 et juin 2000, les malades ayant une cirrhose d’origine alcoolique et une dénutrition modérée ou sévère selon l’indice de Detsky, ont été inclus dans l’étude. Ils ont été proposés une correction de la dénutrition par des conseils diététiques et un supplément nutritif oral de 500 kcal/jour. Une visite était effectuée 1, 2 et 3 mois après l’inclusion pour une enquête alimentaire, et la mesure des paramètres anthropométriques et biologiques nutritionnels et hépatiques.

Résultats — 29 malades ont été inclus, d’âge moyen 52 ans. Six malades étaient classés Child-Pugh A, 14 B et 8 C. Dix-huit malades (62 %) ont complété les 3 mois d’étude. L’apport calorique non alcoolique augmentait significativement de 31 % au premier mois et de 48 % au 3e mois, et était associé à une réduction significative de l’apport calorique alcoolique de respectivement 68 % et 77 %. L’amélioration subjective de l’état nutritionnel a été associée à une amélioration significative du score de Child-Pugh (P = 0,0007), et de l’épaisseur cutanée tricipitale (P = 0,005). L’augmentation du périmètre brachial n’était pas significative.

Conclusion — Notre étude montre la faisabilité de la correction de la dénutrition du malade cirrhotique par une supplémentation orale à domicile. Cette prise en charge a été associée à une amélioration significative des paramètres anthropométriques et du score de Child-Pugh et s’est avérée en outre bénéfique sur la consommation d’alcool.

Protein calorie malnutrition is frequent in patients with chronic liver disease, particularly cirrhosis of any cause [1]. Based on anthropomorphic criteria, malnutrition affects up to 20 % of patients with compensated cirrhosis and 60 % of those with severe liver failure [2]. This prevalence is probably an underestimation and would be higher if more sensitive body composition criteria were applied [3]. In the cirrhotic patient, malnutrition favors the development of complications and increases the risk of death 1.7- to 2-fold [4]. Multiple factors are involved [5], associating anorexia, unbalanced diet, protein, trace element and vitamin deficiencies, insulin resistance with increased oxidation of adipose tissue, and increased resting energy consumption correlated with alcohol intake or viral load depending on the cause of cirrhosis. Infections or hemorrhagic complications may also occur.

Several groups [3] have suggested that nutritional support could help improve the nutritional status and liver function and consequently the prognosis in cirrhotic patients. These studies based on parenteral nutrition were designed to evaluate the efficacy of conventional solutions for alcoholic cirrhosis patients or branched amino acids for patients with hepatic encephalopathy [3]. Although no comparative study has been published, enteral nutrition probably provides an equivalent effect to that of parenteral nutrition while avoiding the risk of catheter-related or
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Patients and methods

Between June 1999 and June 2000, the nutritional status of all patients with alcoholic cirrhosis was established on the basis of physical examination, anthropomorphic measurements, and dietary survey. The Detsky index [13] was used to determine malnutrition. Patients found to have moderate or severe malnutrition were invited to participate in a prospective study designed to evaluate the effect of complementary nutritional support on their nutritional status. All patients gave their informed and written consent to participate in the study. The diagnosis of cirrhosis was established on the basis of liver biopsy results and/or concordant clinical and biological findings. Patients were recruited during outpatient consultations or hospitalization. A stable clinical situation without hemorrhagic or infectious complications was required for inclusion. Patients with another cause of chronic liver disease, notably hepatic tumor, or who declined prolonged follow-up were excluded.

The dietary survey was conducted by the same dietitian throughout the study. Total energy intake, protein, fat, and carbohydrate intake, and alcohol intake during the three days preceding the consultation were recorded at inclusion and at 1, 2, and 3 months. The Child-Pugh score [15] and laboratory test results for nutritional markers (fasting serum prealbumin and albumin) were recorded at each visit. Anthropometric parameters, tricipital skin fold measured with a Harpenden Compass, and mid-arm circumference measured half-way between the olecranon and the acromion with a tape measure, were recorded on the non-dominant side by the same investigator (LC).

The nutritional protocol had two parts: a) The first involved dietary counseling twice a week delivered by a physician and a dietitian who advised abstinence from alcohol and prescribed a normal protein-calorie diet. b) The second part consisted of supplementary oral nutrition using a liquid product (Rénutryl®) with a calorie to nitrogen ratio of 1.33 kcal/mL. The product was delivered on medical prescription by public pharmacies. The patients were asked to note the prescribed quantity and the content consumed daily.

A single investigator (LC) conducted the clinical follow-up. Data were recorded on an Excel 98 datasheet and analyzed with Statview (SAS Institute, Berkeley CA). Qualitative variables were expressed as mean ± standard deviation. Qualitative variables were expressed as raw data and percent. Univariate analysis of qualitative variables was performed with the chi-square test or Fisher’s exact test if the sample size was small. Variance of quantitative data recorded at the 1, 2, and 3-month visits was tested with ANOVA for repeated measures. A p value < 0.05 was considered statistically significant.

Results

Twenty-nine patients (twenty-one men and eight women), mean age 52 years (range 30-74) were included. At inclusion, sixteen patients had ascites, known to be refractory in six; eleven patients presented malnutrition alone, and two had had a recent gastrointestinal hemorrhage due to rupture of esophageal varices in one and portal hypertension-related gastritis in the other. The Child-Pugh grades were: A six patients, B fourteen patients, C eight patients (six with refractory ascites). Eighteen patients (62 %) completed the study. Nine (31 %) did not attend the third month visit and two patients died during the course of the study, one and two months after inclusion due to acute severe alcoholic hepatitis which developed during the study course.

Daily energy intake is summarized by month in table I. The number of patients who declared continued alcohol consumption was 17/29 at inclusion, 9/29 at the first month, 10/27 at the second and 7/18 at the third. The prescribed quantity of oral supplement was consumed by 19 patients (66 %) and half of the prescribed quantity by four. Six patients did not consume the product. Mean oral supplement calorie intake considering all patients was 362 kcal/d at the first month. At the third month, this level changed little (397 kcal/d) and fourteen patients stated they continued taking the supplement; three took half and one had stopped. There was a significant increase in non-alcohol calorie intake at the first month (+31 %) and at the third month (+48 %). Alcoholic calorie intake deceased simultaneously and significantly (-68 % and -77 % respectively). Again at the first and third month, the proportion of total non-alcoholic calorie intake corresponding to the nutritional supplement was 60 % and 39 %, respectively. This increase was associated with improved protein-lipid-carbohydrate balance.

The time courses of the nutritional parameters and the Child-Pugh score are presented in table II. Subjective improvement in nutritional status was associated with significant improvement in the Child-Pugh score and thickness of the tricipital skin fold. There was no significant change in mid-arm circumference.

One year after onset of the study, four patients had died, two during the study (see above) and two others due to a complication of their cirrhosis (gastrointestinal hemorrhage, hepatic coma and infection) four and six months after inclusion. Three patients were lost to follow-up. Twenty-two patients were living. Among these, seven had developed a complication of portal hypertension: ascites (n = 4) and/or rupture of esophageal varices (n = 2), spontaneous peritonitis (n = 1), hepatorenal syndrome (n = 1). Four of these seven patients had not complied with the nutritional protocol.

Table I. – Time course of energy intake during the 3-month study (mean ± SD).

<table>
<thead>
<tr>
<th>Intake</th>
<th>M0 n=29</th>
<th>M1 n=29</th>
<th>M2 n=27</th>
<th>M3 n=18</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy (kcal/d)</td>
<td>2327 ± 857</td>
<td>2598 ± 840</td>
<td>2665 ± 644</td>
<td>2895 ± 781</td>
<td>0.004</td>
</tr>
<tr>
<td>Total non-alcoholic energy (kcal/d)</td>
<td>1873 ± 679</td>
<td>2457 ± 784</td>
<td>2559 ± 634</td>
<td>2789 ± 772</td>
<td>0.0001</td>
</tr>
<tr>
<td>Nutritional supplement (kcal/d)</td>
<td>362 ± 207</td>
<td>370 ± 200</td>
<td>397 ± 176</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Alcoholic energy (kcal/d)</td>
<td>454 ± 540</td>
<td>141 ± 241</td>
<td>106 ± 215</td>
<td>106 ± 170</td>
<td>0.0001</td>
</tr>
<tr>
<td>Protein (g/d)</td>
<td>65 ± 25</td>
<td>92 ± 32</td>
<td>96 ± 26</td>
<td>99 ± 24</td>
<td>0.0001</td>
</tr>
<tr>
<td>Carbohydrate (g/d)</td>
<td>238 ± 92</td>
<td>316 ± 97</td>
<td>323 ± 93</td>
<td>368 ± 117</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fat (g/d)</td>
<td>74 ± 33</td>
<td>91 ± 36</td>
<td>97 ± 32</td>
<td>102 ± 33</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

Discussion

This study showed that two-thirds of the malnourished cirrhotic patients accepted the ambulatory renutrition protocol centered on repeated dietary counseling and oral nutritional supplementation. This protocol was associated with a significant improvement in certain nutritional parameters and the Child-Pugh score. Improved energy intake coincided with reduced alcohol intake. Nearly half of the increase corresponded to the nutritional supplement. The real benefit which can be attributed to the oral supplement is difficult to distinguish without a control group given dietary counseling alone. In our protocol, nutritional efficacy resulted mainly from dietary counseling repeated monthly, reduced alcohol intake, and regular patient follow-up and care. The exact amount of the nutritional product actually consumed by the end of the third month is difficult to determine but most of the patients stated they continued using the product. As shown in table I, the increase in calorie intake resulted mainly from improved oral intake other than the nutritional supplement.

Few studies have been reported concerning oral nutrition as a means of improving the nutritional status of cirrhotic patients. Cabré et al. [6] compared the efficacy of low sodium enteral nutrition delivered via a nasogastric tube and providing 2115 kcal/d in branched amino acids with that of an isocaloric oral regimen in severely malnourished cirrhotic patients with severe liver failure. Enteral nutrition had to be discontinued in two patients due to intolerance of the nasogastric tube. Mean daily calorie intake in the control group only reached 1320 kcal. These authors demonstrated that at mean follow-up of 25 days, enteral nutrition was associated with a significant improvement in serum albumin and Child-Pugh score but not with anthropometric parameters. Seven patients in each group developed severe infection and mortality at one month was significantly higher in the control group (47 % versus 12 % in the enteral nutrition group), mainly due to infection. These results were confirmed in part by Kaarns et al. [9] who compared enteral nutrition using a standard isocaloric solution (casein) with normal non-supplemented oral nutrition in 16 and 15 cirrhotic patients respectively, most having severe liver failure and ascites. The beneficial effect of enteral nutrition was found to be significant with a more rapid improvement in the encephalopathy and nutritional markers in the enteral nutrition group but with the same mortality at two months (nearly 35 % in both groups). Unlike our series, the patients in these two studies had high serum bilirubin levels and high short-term mortality. This would suggest that most of the patients included in these studies had acute alcoholic hepatitis for which corticosteroid therapy has been suggested to be the only means of improving prognosis [14].

In our study, none of the patients had an acute complication of cirrhosis, with the exception of refractory ascites. Only two patients developed severe acute alcoholic hepatitis during the study, resulting in death in both. It is unlikely that correcting a state of malnutrition alone, even via parenteral nutrition, could modify the prognosis of alcoholic hepatitis [3].

Other authors have demonstrated that it is possible to improve nutritional status by increasing oral intake without using a nasogastric tube [7, 10, 11] in clinically selected patients in stable condition. Two studies [7, 10] concerned patients who were hospitalized for one month and given a diet with controlled protein-calorie content which was progressively enriched. No oral nutritional supplement was used. Both studies reported a positive nitrogen balance [10] and significant improvement in nutritional markers, except for patients with severe liver failure [7].

The short duration (one month) and the requirement for hospitalization are the main drawbacks of these studies. No information was provided concerning longer follow-up, particularly during the first months at home. In the report by Nielsen et al. [10], one third of patients left hospital during the study course, a drop-out rate similar to that in our study. There has been only one report of the long-term effect of oral supplementation in ambulatory patients in comparison with uncontrolled food intake [11]. After one year of follow-up, mortality was the same in the two groups but the patients given oral nutritional support were hospitalized less often and exhibited a more rapid improvement in their nutritional status as assessed with anthropometric criteria. Liver tests improved in both groups, partly due to alcohol abstinence. Hirsch et al. [11] used a 1000 kcal/d oral supplement, about twice that in our study, but reported a mean calorie intake of about 2500 kcal/d, similar to that in our study, and without reporting the precise amount of supplement really absorbed. Such a high calorie level (1000 kcal/d) is probably not compatible with long-term tolerance of nutritional supplements. In our study, the oral intake was 362 kcal/d, in line with the notion that nutritional supplements must be used as an aid to achieve sufficient protein-calorie intake via normal oral nutrition. More recently, Marchesini et al. [16] suggested that branched amino acid oral supplementation products are more effective than the type of product we used in this study. There is however the problem of the acceptability of this type of supplementation.

In conclusion, our study demonstrated that improving nutritional status in cirrhotic patients free of severe acute complications is easily achievable using a low-cost ambulatory oral supplement protocol reinforced by routine hospital dietary counseling but without the need for prolonged hospitalization. This type of nutritional support has a beneficial effect on alcohol intake, which explains both the significant improvement in anthropometric parameters and Child-Pugh score.

Références


