Enteral nutrition in severely malnourished and anorectic cirrhotic patients in clinical practice

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SUMMARY

Objectives — To determine among severely malnourished cirrhotic patients remaining anorectic during hospital stay which patients may benefit from enteral nutrition in clinical practice.

Methods — A prospective study including malnourished cirrhotic patients fed by enteral nutrition because of inadequate dietary intake after one-month hospitalization was carried out in a department receiving patients from other hospitals. Patients who died during hospital stay (N = 35, group I) were compared to surviving patients (N = 28, group II).

Results — Nutritional status and spontaneous dietary intake on admission to our department were in the same range in the two groups, Pugh score was higher in group I (11.1 ± 1.9 vs 9.1 ± 2.0, P = 0.0001). The delay between previous hospital admission and the outset of enteral nutrition was comparable in the two groups. Its duration and total dietary intake during enteral nutrition were higher in group II (respectively 42.2 ± 30.9 vs 15.2 ± 33.1 days, P = 0.0016 and 41.1 ± 13.0 vs 29.9 ± 10.0 kcal/kg/d, P = 0.0004). Prevalence of side effects was higher in group I (54.3 vs 17.9%, P = 0.0031). Multivariate analysis showed that Pugh score and septic complications were negatively associated with survival (respectively P = 0.0196 and P = 0.0078) while duration of enteral nutrition was positively associated (P = 0.0435). Eighty six per cent of patients receiving enteral nutrition with bilirubin levels above 74 µmol/L may benefit from six-week enteral nutrition (74 ± 0.6 vs 6.3 ± 0.3 g/kg/d, P = 0.0049).

Conclusions — In severely malnourished cirrhotic patients remaining anorectic after one-month hospitalization, patients with bilirubin level below 74 µmol/L may benefit from six-week enteral nutrition with mid-term improvement in liver function and increase in spontaneous dietary intake.

RÉSUMÉ

L'alimentation entérale dans la pratique clinique chez les malades cirrhotiques sévèrement dénutris et anorexiques : bénéfice et facteurs pronostiques

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Objectifs — Le but de cette étude était de déterminer parmi les malades cirrhotiques hospitalisés sévèrement dénutris et restant anorexiques durant le séjour hospitalier, quels malades pourraient tirer un bénéfice de la nutrition entérale en pratique clinique.

Malades et méthodes — Les cirrhotiques sévèrement dénutris et anorexiques admis dans un service de soins de suite et recevant une alimentation entérale en raison de la persistance d’une anorexie un mois après le début de l’hospitalisation ont été inclus dans une étude prospective. Les malades décédés durant l’hospitalisation (N = 35, groupe 1) ont été comparés aux patients survivants (N = 28, groupe 2).

Résultats — L’état nutritionnel et les apports spontanés à l’admission dans le service étaient comparables dans les deux groupes. Le score de Pugh était plus élevé dans le groupe 1 (11.1 ± 1.9 vs 9.1 ± 2.0, P = 0.0001). Le délai entre la première admission et le début de l’alimentation entérale était comparable dans les deux groupes. Sa durée et l’apport nutritionnel durant son déroulement étaient plus élevés dans le groupe 2 (respectivement 42.2 ± 30.9 vs 15.2 ± 33.1 j, P = 0.0016 et 41.1 ± 13.0 vs 29.9 ± 10.0 kcal/kg/j, P = 0.0004). La prévalence des effets secondaires était plus élevée dans le groupe 1 (54.3 vs 17.9%, P = 0.0031). En analyse multivariée, le score de Pugh et les complications septiques étaient négativement associés à la survie (respectivement P = 0.0196 et P = 0.0078) alors que la durée de la nutrition entérale était positivement (P = 0.0435). Quatre vingt six pour cent des malades sous nutrition entérale dont le taux de bilirubine totale était supérieur à 74 µmol/L à l’admission dans le service étaient décédés. Les effets à moyen terme de la nutrition entérale chez les malades survivants étaient une amélioration du score de Pugh (7.5 ± 2.0 vs 9.1 ± 2.0, P < 0.0001) et une augmentation des apports caloriques et protéiques spontanés (29.7 ± 15.3 vs 18.1 ± 10.1 kcal/kg/j, P = 0.0150 et 1.0 ± 0.5 vs 0.6 ± 0.3 g/kg/d, P = 0.0049).

Conclusions — Les malades sévèrement dénutris, anorexiques après un mois d’hospitalisation, dont le taux de bilirubine est inférieur à 74 µmol/L peuvent bénéficier de cette assistance nutritionnelle. Le résultat est une amélioration de la fonction hépatique et des apports nutritionnels spontanés.

Introduction

Malnutrition as well as insufficient dietary intake are observed in more than 50% of hospitalized cirrhotic patients [1].

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The principal mechanisms involved in malnutrition are reduction of dietary intake, metabolic abnormalities with hypermetabolism, insulin resistance, increased lipid and protein catabolism and malabsorption [2]. Moreover, malnutrition affects clinical outcome in terms of survival and complications, and is recognized as a prognostic factor [3]. Nutritional intervention has been advocated in order to improve nutritional status and outcome. Modified eating pattern and oral supplementation are usually first recommended, but artificial nutrition is required in anorectic patients who cannot meet their nutrient requirements.
by oral intake “ad lib”. Enteral feeding is usually preferred to parenteral feeding because of the severity of side effects of the latter. Although controlled trials have shown that enteral nutrition is safe and may improve nutritional status and decrease the short-term mortality of advanced cirrhosis, precise indications of enteral feeding in malnourished cirrhotic patients are not well established [4]. Questions such as identification of patients the most likely to benefit from enteral nutrition and when to initiate tube feeding are still debatable in clinical practice.

In a department specifically devoted to complications of liver diseases and receiving patients with a high prevalence of malnutrition and long hospital stay, we have performed a prospective study with the aim to identify patients who can benefit from enteral nutrition. This type of nutrition support was proposed in patients with dietary intake below recommended energy and protein requirements in spite of oral nutritional supplementation, which is pragmatically the most widely accepted indication of this type of nutrition assistance. Among patients receiving enteral nutrition during hospital stay, we compared patients who survived and were discharged after withdrawal of tube feeding with patients who died after initiation of this procedure.

Patients and methods

Patients

All patients with liver cirrhosis receiving enteral nutrition during hospital stay from January 1, 2000 to September 30, 2003 were enrolled in the study. Our unit is specifically devoted to rehabilitation of cirrhotic patients and receives patients from other hospitals in the area of Paris for severe complications of cirrhosis such as severe malnutrition, gastrointestinal bleeding, septic complications, ascites, and encephalopathy. The diagnosis of cirrhosis was based on the usual clinical, biological, and endoscopic findings or liver biopsy. Alcohol intake had ceased for several weeks before hospitalization in our unit. Nutritional status was assessed by anthropometric parameters, severity of liver failure, spontaneous dietary intake on admission into our department, total dietary intake supplied by enteral nutrition, duration of enteral feeding and prevalence of side effects were taken into consideration. Analysis was performed in order to identify prognostic factors.

Nutritional assessment

Body weight and height were measured on or a few days after admission in patients with severe encephalopathy. Mid-arm circumference (MAC) and triceps skinfold thickness (TST) were measured to the nearest millimeter for TST at the non-dominant arm by the same operator. Mid-arm muscle circumference (MAMC) was calculated from MAC and TST. Values of MAC and TST were compared with those of a healthy reference population [5]. A blood sample was collected within 24 h after admission to assay standard biological parameters, transferrin, and C-reactive protein (CRP).

Spontaneous dietary intake

The patients received the usual diet given in French Hospitals, supplying on average 1800-2200 kcal/d with proportions of carbohydrates, lipid and protein respectively of 55, 30 and 15% energy. The hospital diet was unrestricted except for sodium, which was restricted in patients with ascites. The energy and protein requirements of food consumed were calculated using the CIGUAL database from Mac 2 win software 1990-2000 (Altura Software Inc). Food intake was recorded over a 3-day period after admission by a diettian immediately after each meal by inspecting food served and leftovers. For every patient, food portions remaining on the plate after meals were evaluated (nothing, < 1/2, > 1/2, all) and considered as plate waste. Dietitians listed all snacks, sip feed supplements and personal food items consumed during the study day. Food served was calculated by adding up the nutritional values of the menus and all snacks and sip feed supplements consumed. Food consumed was calculated by subtracting plate waste from the menus and adding all food intakes besides meals. During hospital stay, food intake was monitored and controlled by a hospital dietitian on each week, oral nutritional supplements providing 170 to 300 kcal/day were proposed to all patients with caloric intakes below 30 kcal.kg⁻¹.d⁻¹ (Nutrigel HC+, Crème HP/HC laboratoire Novartis, Clnutren Soupe, Nestle Clinical Nutrition France, Marne La Vallée). Nutritional counselling was provided for each patient on admission and repeated when caloric intake remained low. All patients received vitamin supplements (B1, B6, folic acid, and niacin).

Enteral nutrition

Enteral feeding was proposed to patients with spontaneous caloric intakes below 25 kcal/kg⁻¹.d⁻¹ after 15 days of hospitalization in our department despite oral nutritional supplements or when dietary intake decreased during two consecutive weeks below this cut-off and started after acceptance of the procedure by the patients, provided they were cooperative and with, and had no severe encephalopathy (stage III-IV). Patients received a polymeric diet in the form of a hypercaloric hyperproteic diet (Megareal, Laboratoire Novartis), a hypercaloric normoproteic diet (Nutrodrip Energie, Laboratoire Novartis), or a normocaloric, normoproteic diet (Inkodiet, Laboratoire Fresenius Kabi; Sondalis Iso, Laboratoire Nestlé Clinical Nutrition; Nutrition, Laboratoire Nestlé) according to their estimated nutritional requirements calculated from Harris Benedict equations [6]. The diet was infused continuously into the stomach through a fine-bore nasogastric feeding tube (Kangaroo Pump set: Tyco-Health care UK LTD) with the aid of a constant-infusion pump supplying the diet at a flow of 80-100 mL/h. When encephalopathy occurred, flow was reduced (grade I-III) or stopped (grade IV) until neurological improvement. Tube position was verified by radiography after its placement and every day during treatment by a reference mark located on the tube. Residual stomacal volume was searched four hours after initiation of enteral feeding, the flow was reduced or stopped when residual volume was above 150 mL. The head of the bed was elevated day and night to prevent gastrointestinal reflux and bronchopulmonary aspiration. Patients led by enteral tube could receive a regular oral diet with supplements when possible. Enteral nutrition was withdrawn either when patients increased spontaneous dietary intake and met their nutritional requirements by oral feeding or in case of intolerance or serious side effect.

Biological measurements

Serum transthyretin and CRP were analyzed immunoturbidimetrically on a Synchron CX5 Analyzer (Beckman-Coulter, Roissy, France). Serum albumin concentration was measured by means of the bromocresol green method with the Synchron CX5 Analyzer.

Statistical analysis

Results are given as means ± standard deviation. Comparisons between groups were done with paired and unpaired Student’s t tests as appropriate. Comparisons between percentages were tested with the chi-square test. Multivariate analysis were performed by using a stepwise logistic regression model. The threshold for statistical significance was P < 0.05.

Results

Sixty-three patients were enrolled in the study. Among these patients, 61 had been hospitalized in another hospital before admission in our department with a mean duration of stay of 29.6 ± 18.2 d (median: 29 d). Thirty-five patients died during their hospitalization (group I) and 28 patients survived (group II). Comparisons were performed between these two groups. In group I, etiology of cirrhosis was alcoholism in 32 patients, post-viral C hepatitis in two patients, primary biliary cirrhosis in one patient, in group II etiology of cirrhosis was post-viral C hepatitis in one patient, alcoholism in 27 patients.

ABBREVIATIONS:

MAC : mid-arm circumference
MAMC : mid-arm muscle circumference
TST : triceps skinfold thickness
Characteristics of patients on admission to our department are shown in Table I. Male subjects were predominant in group I (71%) while female subjects were slightly predominant in group II (54%). Patients in group I had a more severe liver failure, 74% of patients in this group belonged to the class C of Child vs 39% in group II. Inflammatory status was in the same range in the two groups. Eleven patients had clinical and biological manifestations of acute alcoholic hepatitis (seven patients in group 1, among them four patients had histologically proven acute alcoholic hepatitis and four patients in group 2). Percentages of patients with acute alcoholic hepatitis were in the same range in the two groups (20 vs 14.3%, \( P = 0.5527 \)). One patient in group I and two patients in group II had hepatocellular carcinoma. Among these two patients, a segmentectomy had been performed in one patient prior admission to our department. Renal function was in the same range in the two groups. Length of hospital stay in our department was longer in group 2 than in group 1 (109.0 ± 87.3 days vs 44.8 ± 44.0 days, \( P = 0.0008 \)).

Nutritional status and spontaneous dietary intake on admission to our department are shown in Table II. Patients in the two groups were severely malnourished, in average half of them had both MAMC and TST below the 5th percentile of a reference population (60% in group I vs 44.4% in group II, \( P = 0.2402 \)). Spontaneous dietary intake was low at the time of admission for the two groups and below the estimated energy and protein requirements (30 to 35 kcal/kg/d, 1 g/kg/d). Nutritional status tended to be more damaged in group I while spontaneous dietary intake on admission were comparable in the two groups.

Characteristics of enteral nutrition are shown in Table III. Mean dietary intake provided by enteral route and oral regular diet during enteral feeding are shown. Enteral nutrition was initiated before admission in our department in 3 patients in group I and 6 patients in group II. Percentage of patients with enteral nutrition before admission tended to be higher in group II than in group I (21.4% vs 8.6%, \( P = 0.1473 \)). However, time between previous hospital admission and start of enteral nutrition was in the same range in the two groups. Regarding the 32 patients in group I and the 22 patients in group II in whom enteral nutrition was initiated after admission to our department, the delay between admission and outset of enteral nutrition was in the same range (mean: 22.8 ± 27.2 days vs 24.5 ± 27.4 days; median: 13.0 vs 14.5 days, \( P = 0.8160 \)). Duration of enteral nutrition was longer in group II than in group I. Energy intake supplied by enteral nutrition and total intake were higher in group II than in group I. Time between withdrawal of enteral nutrition and discharge in group II or death in group I was longer in group II. Side effects were more frequent in group I than in group II (repeated vomiting: 3 vs 3, pneumonia: 2 vs 0, encephalopathy grade 3 vs 1, gastrointestinal bleeding: 2 vs 0). Patients with encephalopathy during enteral nutrition tended to have higher protein supplied by enteral route than patients without encephalopathy (68.3 ± 22.5 vs 53.2 ± 10.5 g/d, \( P = 0.08 \)).

Septic complications during the course or after withdrawal of enteral feeding were more frequent in group I than in group II (spontaneous bacterial peritonitis: 9 vs 1, pneumonia: 8 vs 3, urinary tract infection: 2 vs 1, sepsis characterized negative by culture, fever or hypothermia associated with leucocytosis: 4 vs 1, bacteraemia: 2 vs 1, gastroenteritis: 0 vs 2, spondylitis tuberculosa: 0 vs 1). The overall prevalence of septic complication was 71.4% in group I vs 35.7% in group II (\( P = 0.0046 \)).

The causes of death in group I were septic complications in 23 cases, gastro-intestinal bleeding in 3 cases (among them one case five days after withdrawal of tube feeding) and terminal hepatic failure in 9 cases. Multivariate analysis with survival as dependent variable and Pugh score, septic complications and gender showed that Pugh score and septic complications were negatively associated with survival (respectively OR = 0.813, IC 95%: 0.406-0.920, \( P = 0.0196 \); OR = 0.119, IC 95%: 0.025-0.571, \( P = 0.0078 \)) while duration of enteral nutrition was positively associated (\( OR = 1.027, IC 95%: 1.001-1.054, P = 0.0435 \)).

Bilirubin median level was 74 μmol/L in group I and 35 μmol/L in group II. Eighteen patients in group I had bilirubin level > 74 μmol/L at the time of admission while twenty-five patients in group II had bilirubin level < 74 μmol/L. The sensitivity and specificity of this cut-off as predictive factor of poor outcome were respectively 51.4% and 89.3%. Positive and negative predictive value of death were respectively 85.7% and 59.5%.

Characteristics of surviving patients on admission and before discharge are shown in Table IV. Pugh score as well as nutrient intake increased. However 15 patients had caloric intake below 30 kcal/kg/d and 14 patients had protein intake below 1 g/kg/d before discharge. Among the 28 surviving patients, anthropometric parameters were measured before discharge in only six patients: TST increased (6.2 ± 1.7 cm ± 4.3 ± 1.3 mm, \( P = 0.0121 \)) while MAMC did not change (18.5 ± 0.8 cm vs 18.4 ± 1.7 cm, \( P = 0.9035 \)).

Discussion

We report the clinical outcome of a group of 63 cirrhotic patients receiving enteral nutrition which was initiated after several weeks of hospitalization in most cases. All these patients were severely malnourished since 53% of them had both MAMC and TST below the 5th percentile of standard values and the majority (58.7%) belonged to the class C of Child. The indication of enteral feeding was insufficient dietary intake with caloric intake below 20 kcal/kg/d and protein intake on average 0.6 g/kg/d. Low dietary intake and anorexia are main causes of malnutrition in hospitalized cirrhotic patients. We have recently shown that decrease in dietary intake paralleled worsening of liver failure: dietary and protein intakes were below requirements (30 kcal/kg/d and 1 g/kg/d), respectively in 80% and 63% of Child C patients [1]. This study in a large series of patients confirmed previous studies showing inadequacy of spontaneous dietary intake in these patients [7, 8]. Several mechanisms including effects of hospitalization and medications, alterations in taste perceptions, abnormalities in gastro-intestinal motility and inflammatory state participate in the reduction of dietary intake [9, 10]. Patients in our present study had increased levels of CRP showing activation of cytokine synthesis such as tumor necrosis factor-α which has a pronounced anorectic effect [11]. Moreover, the liver may be considered as a metabolic sensor and may have a role in the control of food intake [12]. Recommendations of enteral feeding in malnourished cirrhotic patients have been made for more than 20 years [13, 14]. Previous studies have shown that enteral feeding during 3 to 4 weeks was safe and effective in improving liver function and short term clinical outcome [15-17]. Another study has shown that enteral feeding in acute alcoholic hepatitis provided comparable results with corticosteroids [18]. However, enteral feeding is not extensively used in cirrhotic patients in spite of the high prevalence of malnutrition and an inadequate dietary intake in many hospitalized patients. Indications and the real benefit of this nutritional intervention remain controversial. A possible explanation of this fact is that the conditions of enteral feeding in clinical practice are likely to differ from those in controlled studies where patients are randomized and receive enteral feeding soon after admission in hospital. Most physicians are reluctant to initiate enteral nutrition a few days after admission because the general opinion is that...
Table I. – Characteristics of patients on admission to our department.
Caractéristiques des malades à l’admission dans notre service.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Male/female</th>
<th>Age (years)</th>
<th>Ascites (%)</th>
<th>Encephalopathy (%)</th>
<th>Albumin (g/L)</th>
<th>Bilirubin (µmol/L)</th>
<th>Prothrombin index (%)</th>
<th>Child Classification A/B/C</th>
<th>Pugh Score</th>
<th>Transhyretin (g/L)</th>
<th>CRP (mg/L)</th>
<th>Sodium (mmol/L)</th>
<th>Creatinin (µmol/L)</th>
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</thead>
<tbody>
<tr>
<td>Died group I</td>
<td>35</td>
<td>25/10</td>
<td>61.0 ± 11.5</td>
<td>88.6</td>
<td>45.7</td>
<td>23.8 ± 4.8</td>
<td>144.1 ± 160.6</td>
<td>51.9 ± 20.0</td>
<td>0/9/26</td>
<td>11.1 ± 1.9</td>
<td>0.047 ± 0.023</td>
<td>36.7 ± 32.8</td>
<td>131.0 ± 5.9</td>
<td>83.2 ± 50.7</td>
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<tr>
<td>Survived group II</td>
<td>28</td>
<td>13/15</td>
<td>59.2 ± 9.4</td>
<td>60.7</td>
<td>21.4</td>
<td>26.3 ± 4.9</td>
<td>63.3 ± 96.8</td>
<td>66.8 ± 21.6</td>
<td>3/14/11</td>
<td>9.1 ± 2.0</td>
<td>0.072 ± 0.055</td>
<td>27.6 ± 21.8</td>
<td>133.0 ± 4.8</td>
<td>68.3 ± 27.5</td>
</tr>
<tr>
<td>P</td>
<td>0.0439</td>
<td>NS</td>
<td>0.0099</td>
<td>0.0445</td>
<td>0.0409</td>
<td>0.0224</td>
<td>0.0066</td>
<td>0.0086</td>
<td>0.0201</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant

Table II. – Nutritional status of patients on admission to our department.
Statut nutritionnel des malades à l’admission dans notre service.

<table>
<thead>
<tr>
<th>N</th>
<th>Weight (kg)</th>
<th>Height (m)</th>
<th>BMI (kg/m²)</th>
<th>MAC (cm)</th>
<th>MAMC (cm)</th>
<th>TST (mm)</th>
<th>MAMC &lt; 5th perc</th>
<th>TST &lt; 5th perc</th>
<th>MAMC and TST &lt; 5th perc</th>
<th>% patients with Spontaneous</th>
<th>Caloric intake*</th>
<th>Protein intake*</th>
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<td></td>
<td>kcal/d</td>
<td>kcal/kg/d</td>
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<tr>
<td>Died group I</td>
<td>35</td>
<td>59.8 ± 10.5</td>
<td>1.67 ± 0.09</td>
<td>21.2 ± 3.6</td>
<td>20.9 ± 3.7</td>
<td>19.1 ± 3.1</td>
<td>5.8 ± 3.9</td>
<td>86.7</td>
<td>66.7</td>
<td>60.0</td>
<td>32</td>
<td>1072 ± 516</td>
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<tr>
<td>Survived group II</td>
<td>28</td>
<td>55.1 ± 13.5</td>
<td>1.65 ± 0.07</td>
<td>20.2 ± 4.4</td>
<td>21.7 ± 4.1</td>
<td>19.2 ± 3.1</td>
<td>7.9 ± 5.0</td>
<td>66.7</td>
<td>55.6</td>
<td>44.4</td>
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<td>970 ± 433</td>
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<tr>
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</table>

* Data are given for patients in whom enteral feeding was started after admission to our department.
MAC: mid-arm circumference; MAMC: mid-arm muscle circumference; TST: triceps skinfold thickness; NS: not significant
Table III. – Characteristics of enteral nutrition.
Caractéristiques de l'alimentation entérale.

<table>
<thead>
<tr>
<th>N</th>
<th>Length of previous hospitalization (d)</th>
<th>Time between Previous hospital admission and outset of EN (d)</th>
<th>Total duration of EN (d)</th>
<th>Intake supplied by EN</th>
<th>Spontaneous intake during EN</th>
<th>Total intake</th>
<th>Time between withdrawal of EN and discharge or death (d)</th>
<th>% patients with side effects of EN</th>
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<tbody>
<tr>
<td></td>
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<td></td>
<td>Energy (kcal/d)</td>
<td>Protein (g/d)</td>
<td>Energy (kcal/d)</td>
<td>Protein (g/d)</td>
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<tr>
<td>Died group I</td>
<td>35</td>
<td>Mean</td>
<td>25.4 ± 15.0</td>
<td>45.1 ± 24.7</td>
<td>15.2 ± 33.1</td>
<td>1150 ± 366</td>
<td>51 ± 18</td>
<td>618 ± 476</td>
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<tr>
<td></td>
<td>Median</td>
<td>24.0</td>
<td>38.0</td>
<td>6.0</td>
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<tr>
<td>Survived group II</td>
<td>28</td>
<td>Mean</td>
<td>34.9 ± 20.7</td>
<td>49.1 ± 36.5</td>
<td>42.2 ± 30.9</td>
<td>1369 ± 449</td>
<td>60 ± 22</td>
<td>802 ± 485</td>
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<tr>
<td></td>
<td>Median</td>
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<td>P</td>
<td>0.0398</td>
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</table>

EN: enteral nutrition; NS: not significant.

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Table IV. – Characteristics of surviving patients on admission and before discharge.
Caractéristiques des malades survivants à l’admission et à la sortie.

<table>
<thead>
<tr>
<th>N</th>
<th>Weight (kg)</th>
<th>Albumin (g/L)</th>
<th>Bilirubin (µmol/L)</th>
<th>Prothrombin index (%)</th>
<th>Pugh Score</th>
<th>Transferrin (g/L)</th>
<th>CRP (mg/L)</th>
<th>Sodium (mmol/L)</th>
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<td>Admission</td>
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<td>55.1 ± 13.5</td>
<td>26.3 ± 4.9</td>
<td>63.3 ± 96.8</td>
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<td>9.1 ± 2.0</td>
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<td>27.6 ± 0.055</td>
<td>133.0 ± 4.8</td>
<td>68.3 ± 27.5</td>
</tr>
<tr>
<td></td>
<td>Discharge</td>
<td>28</td>
<td>53.4 ± 10.5</td>
<td>28.6 ± 5.0</td>
<td>28.6 ± 41.9</td>
<td>75.0 ± 19.8</td>
<td>7.5 ± 2.0</td>
<td>0.114 ± 0.067</td>
<td>9.9 ± 13.6</td>
<td>135.2 ± 6.8</td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td>0.0224</td>
<td>0.0065</td>
<td>&lt;0.0001</td>
<td>0.0028</td>
<td>&lt; 0.0001</td>
<td>NS</td>
<td>NS</td>
<td>0.0271</td>
</tr>
</tbody>
</table>

NS: not significant
spontaneous dietary intake usually increases with improvement of liver function. We have previously shown that oral refeeding with regular diet and supplements as necessary is possible in malnourished cirrhotic patients, dietary intake increased after a long hospital stay with oral nutritional support and the help of dietician [1]. As a result, enteral nutrition is usually carried out in clinical practice in patients with advanced liver disease and remaining anorectic after several weeks of hospitalization. In such condition, the benefit of enteral nutrition is not obvious as shown by a previous study which focused on the relation between nutritional support and patient outcomes in a large cohort of seriously ill hospitalized adults [19]. This study showed that tube feeding was associated with improved survival in coma but decreased survival in acute respiratory failure, multi organ system failure with sepsis and cirrhosis.

Our group of patients had a high mortality rate because of severity of liver failure, in most of them enteral nutrition was started after admission in our department and after failure of oral nutritional support with supplements and dietetic care. These patients are representative of many cirrhotic patients receiving enteral nutrition in clinical practice. Nutritional status and spontaneous dietary intake on admission to our department were in the same range in the two groups of patients, however lower failure observed as Pugh score was more severe in patients who died. Duration of enteral feeding and energy intake supplied by tube feeding as well as total caloric and protein intakes were higher in surviving patients. The prevalence of side effects in surviving patients was close to reported in previous studies, whereas it was more frequent in patients who died [18, 20, 21]. Patients received high protein intake, mainly surviving patients, however this factor doesn't seem to be responsible of the onset of encephalopathy although it has been shown that small intestine in response to enteral nutrition contribute to hyperammonaemia in patients with liver cirrhosis [22]. The most frequent side effects were repeated vomiting and bronchopulmonary aspiration in relation with a damaged gastric motility. Bronchopulmonary aspiration is a very severe side effect since it was the direct cause of death in 5 cases. Therefore, the risk of bronchopulmonary aspiration appears as the principal limiting factor of enteral nutrition in cirrhotic patients with severe liver failure. On the contrary, only two patients had gastro-intestinal bleeding during the course of enteral feeding, showing in agreement with previous results that this technique does not significantly increase the risk of variceal bleeding [4]. Our results show that the factors leading to the risk of bronchopulmonary aspiration, such as neurological disorders and impaired gastric motility should be carefully assessed in cirrhotic patients with severe liver failure before initiation of enteral feeding. Multivariate analysis showed that Pugh score, duration of enteral nutrition and septic complications were the three predictive factors of outcome. Among the factors included in Pugh score, bilirubin level was the most discriminant: 86% of patients receiving enteral nutrition with bilirubin level above 74 µmol/L died. Jaundice in severely malnourished cirrhotic patients remaining anorectic and with pronounced liver failure has a negative prognostic value regarding response of enteral feeding. This result is in accordance with previous studies showing that persistent jaundice has a bad prognostic value in cirrhotic patients with or without alcoholic hepatitis [23, 24]. This cut-off had a low sensitivity but a high specificity of outcome, therefore bilirubin level appears as a useful and simple tool to determine which patients may benefit from enteral feeding. In our series of patients, enteral nutrition was initiated late, in average 6 to 7 weeks after the first admission of patients. This delay may be explained by the lack of assessment of dietary intake in many hospitals. In our department, enteral nutrition was started on average two to three weeks after admission because in our experience spontaneous intake may increase with oral supplementations and dietetic care within this period in two thirds of patients. The lack of difference between our two groups of patients regarding the delay between previous hospital admission of patients and outset of enteral nutrition suggest that this factor is likely not the main factor involved in the outcome of patients. However, we cannot exclude from our results that an earlier initiation of enteral feeding could improve outcome of patients. In surviving patients, enteral nutrition was carried on for more than one month and patients remained hospitalized after withdrawal of tube feeding for a comparable length of time before discharge. Therefore, mid-term effects of enteral feeding could be assessed. We observed improvement in liver function and inflammatory state while spontaneous dietary intake increased but remained below usual requirements in half of the patients. Anthropometric measurements were measured in only six patients and showed an increase in TST, in accordance with a previous study showing that improvement in nutritional status is due to an increase in fat mass [25]. These results show that surviving patients have derived benefit from enteral feeding.

In conclusion, the severity of liver failure, septic complications and duration of enteral feeding are the three independent prognostic factors in malnourished cirrhotic patients receiving enteral nutrition indicating on the basis of low dietary intake and failure of oral supplementation. Mid-term effects of six-week enteral nutrition are improvement in liver function and increase in spontaneous dietary intake. Bilirubin level above 74 µmol/L is a prognostic factor of poor outcome in patients receiving enteral nutrition. The results of an earlier initiation of enteral feeding should be assessed in these patients.

REFERENCES


