Patients at risk of malnutrition: assessment of 11 cases of severe malnutrition with individualised total parenteral nutrition

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Objective: To describe and assess the efficacy and safety of individualised nutritional support during the first week of total parenteral nutrition in moderately to severely malnourished patients who are susceptible to the refeeding syndrome.

Method: Retrospective observational study carried out between January 2003 and June 2006, including adult patients with moderate to severe malnutrition who received ≥ 5 days total parenteral nutrition. The nutritional support was described and the appearance of severe hydroelectrolytic and metabolic disturbances were assessed during the first week of nutrition.

Results: The study included 11 patients with a mean body mass index of 15.4 kg/m². These patients received an average of 23 Kcal/kg/day. They did not show any signs of severe hydroelectrolytic or metabolic disturbances. Three patients presented with hypophosphataemia, five with hypopotassemia and four with hypomagnesemia, all of which were mild to moderate and with the exception of two cases, all were corrected within one week of feeding.

Conclusions: Individualised nutritional support in moderately to severely malnourished patients does not produce refeeding syndrome. Individualised nutrition is an essential strategy for avoiding complications associated with overfeeding.


INTRODUCTION

Refeeding syndrome (RS) is a complication associated with nutritional support, which has considerable morbidity and mortality. It is defined as severe hydroelectrolytic and metabolic disturbances which appear after beginning oral, enteral or parenteral nutrition in patients that are underweight, severely malnourished or suffering from starvation. Moderate to severe malnutrition may be
identified using body mass index values (BMI) of < 17 kg/m² or weight loss of ≥ 10% over a period of 3-6 months, or both. Weight loss of > 10% over two months is considered as a risk of RS. Other factors are prolonged starvation, chronic alcoholism, anorexia nervosa, neoplasias and chronic vomiting.

The syndrome manifests clinically as disturbances in fluid balance (sodium and water retention or dehydration due to osmotic diuresis); hyperglycaemia due to excess carbohydrates; severe electrolyte depletion: hypophosphataemia (serum phosphate of < 1.5 mg/dl), hypokalaemia (serum potassium of < 2.5 mEq/l) and hypomagnesaemia (serum magnesium of < 1 mg/dl) and thiamine deficit, which may lead to Wernicke’s encephalopathy. These disturbances may produce complications of the cardiovascular, haematological, pulmonary and neuromuscular systems. Its exact prevalence is not known since the syndrome often goes undiagnosed. In order to prevent the syndrome, patients at risk must be identified so that they may be given nutritional support that is appropriate for their needs. It is particularly important that these patients are identified during the first week, since this is when electrolyte and cardiac disturbances occur.

The objective of this study is to describe the efficacy and safety of individualised nutritional support during the first week of total parenteral nutrition (TPN) and the clinical results in patients at risk of developing RS.

METHOD

This is a retrospective, observational and descriptive study, which included all adult patients (> 18 years old) with moderate to severe malnutrition (> 10% weight loss within 2 to 6 months or BMI of ≤ 17 kg/m²), who received ≥ 5 days of TPN between January 2003 and June 2006, and who were considered as being at risk of developing RS. All patients received individualised TPN, which was adjusted to the grade of malnutrition, nutritional requirements and initial pathology. Patients were monitored during the daily rounds and feeding was modified according to the patients’ clinical evolution and analytical parameters. Nutrition support pharmacists established the composition of the TPN, which was normally prepared as an all-in-one solution and administered through a central venous line.

Basal energy expenditure (BEE) was calculated using the Harris-Benedict equation, based on a maximum non-protein caloric input of 1.3 x BEE. The energy input was mixed with glucose, which was the only source of carbohydrates and an emulsion that consisted of soya (20%), or soya and olive oil (20 and 80% respectively), was used as the source of lipids. All patients were given an electrolyte supplement in the TPN, in accordance with daily recommendations for adults. These were adjusted daily depending on plasma values, clinical state and drug treatment. In cases of mild electrolyte deficits, inputs were increased in line with published recommendations and in the case of severe deficits, additional electrolyte infusions were given. All patients were given a multivitamin complex in the TPN; this contained all vitamins except phytomenadione, as well as a standard solution of micronutrients for adults. None of the patients were given a thiamine supplement, except for that already included in the multivitamin content (3.51 mg).

Nutritional state was assessed using weight loss and BMI, as well as albumin, cholesterol and lymphocyte values in the plasma. Patients were strictly monitored and analysed from the beginning of TPN, in order to detect and correct hydroelectrolytic and metabolic disturbances associated with RS. There were ≥ 2 analytical tests for all patients during the first week and three or more for 9 of the patients. Glycaemia (capillary glycaemia/6 hours), vital signs (heart rate and blood pressure), fluid balance, respiratory rate and mental state were monitored daily.

RESULTS

Of the 449 patients who received TPN in the period indicated, 11 (2.4%) were included in the study. Their baseline characteristics are detailed in table I and table II shows the mean nutritional inputs during the first day and week of TPN.

Four patients (36.4%) died. Two died 4 weeks after completing TPN and two on day 6 and 8 of TPN. None of these patients died from RS (one died from myocardial infarction (MI) and another from neoplasia). The MI is not believed to have been caused by complications associated with TPN.

Table I. Demographic and nutritional characteristics of patients at the beginning of total parental nutrition

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex (males/females)</th>
<th>Diagnosis upon admittance</th>
<th>Length of stay in hospital (days)</th>
<th>Total parenteral nutrition (days)</th>
<th>Actual weight (kg)</th>
<th>Weight loss (kg)</th>
<th>Duration of weight loss (months)</th>
<th>Ideal weight (kg)</th>
<th>Height (cm)</th>
<th>Body mass index (kg/m²)</th>
<th>Basal energy expenditure (kcal/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64.0</td>
<td>7/4</td>
<td>3 gastrointestinal neoplasia</td>
<td>51.7 (95% CI: 19.6-83.4)</td>
<td>12.2 (95% CI: 8.6-15.8)</td>
<td>42.3 (95% CI: 37.0-47.5)</td>
<td>11.3 (95% CI: 7.3-15.2)</td>
<td>2.5 (95% CI: 0.5-4.6)</td>
<td>59.8 (95% CI: 50.7-68.9)</td>
<td>165.0 (95% CI: 156.0-174.0)</td>
<td>15.4 (95% CI: 14.8-16.0)</td>
<td>1,065 (95% CI: 936-1,194)</td>
</tr>
</tbody>
</table>

95% CI: confidence interval.
Totallymphocytes, $10^3$ cells/mcl (1.5-5) 0.9 (0.4-1.5) 0.9 (0.3-1.5) 0.9 (0.2-0.6)

Renal function

Creatinine, mg/dl (0.5-1.2) 0.8 (0.6-1.0) 0.8 (0.4-1.5) 0.8 (0.2-0.6)

Urea, mg/dl (10-50) 48.8 (27.5-70.1) 46.5 (19.0-74.0) 33.8 (16.0-51.5)

Table III. Mean serum analytical parameters at the start, during and the end of the first week of TPN

Mean nutritional inputs for patients on the first day and during the first week of total parenteral nutrition

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Units</th>
<th>Start of TPN</th>
<th>Day 4</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macronutrients:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total kcal/kg/day</td>
<td></td>
<td>20.7 (95% CI: 19.0-22.5)</td>
<td>23.2 (95% CI: 21.4-25.1)</td>
<td></td>
</tr>
<tr>
<td>Non protein kcal of nitrogen</td>
<td></td>
<td>121.2 (95% CI: 112.4-129.9)</td>
<td>120.4 (95% CI: 113.7-127.0)</td>
<td></td>
</tr>
<tr>
<td>Microelements:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, mEq/day</td>
<td></td>
<td>2.3 (95% CI: 1.6-3.0)</td>
<td>2.4 (95% CI: 1.7-3.1)</td>
<td></td>
</tr>
<tr>
<td>Potassium, mEq/day</td>
<td></td>
<td>50.0 (95% CI: 30.3-69.7)</td>
<td>61.5 (95% CI: 48.6-74.4)</td>
<td></td>
</tr>
<tr>
<td>Magnesium, mEq/day</td>
<td></td>
<td>16.0 (95% CI: 10.9-21.1)</td>
<td>15.4 (95% CI: 11.1-19.6)</td>
<td></td>
</tr>
<tr>
<td>Phosphate, mEq/day</td>
<td></td>
<td>14.8 (95% CI: 11.5-18.1)</td>
<td>15.3 (95% CI: 12.0-18.7)</td>
<td></td>
</tr>
<tr>
<td>GGT, U/l (5-36)</td>
<td></td>
<td>67.9 (-10.4-146.2)</td>
<td>66.5 (15.0-118.1)</td>
<td></td>
</tr>
</tbody>
</table>
| Urea, mg/dl (10-50) | | 48.8 (27.5-70.1) | 46.5 (19.0-74.0) | 33.8 (16.0-51.5)

95% CI: confidence interval.

Associated with RS, since the patient tolerated the intravenous inputs of fluids and carbohydrates and did not present with cardiac rhythm disturbances, or neuromuscular or pulmonary disorders prior to MI (mechanical ventilation was disconnected four days before). Two patients (18.2%) were admitted to the ICU before beginning TPN. None of the patients presented with hyperglycaemia during TPN (glycaemia > 200 mg/dl).

A patient with a history of hypertriglyceridaemia (triglycerides > 200 mg/dl during the two previous years) presented with hypertriglyceridaemia (triglyceride values at the beginning of TPN were 158 mg/dl and the maximum value measured was 206 mg/dl).

In terms of electrolytes, at the beginning of TPN, 6 patients (54.5%) presented with mild to moderate disturbances and three of these (27.3%) presented with poly-electrolyte disturbances. None of the patients presented with severe disturbances. Two (18.2%) presented with hypophosphataemia (serum phosphate = 1.5-2.4 mmol/dl), 4 (36.4%) with hypokalaemia (serum K = 2.5-3.4 mEq/l) and 4 (36.4%) with hypomagnesaemia (serum Mg = 1.0-1.6 mEq/dl). None of the patients presented with severe electrolyte decompensation or clinical manifestations during the first week of TPN. Six patients (54.5%) presented with mild to moderate disturbances and three (27.3%) with polyelectrolyte disturbances. Three patients (27.3%) developed hypophosphataemia, 5 (45.5%) with hypokalaemia and 4 (36.4%) with hypomagnesaemia. All of the aforementioned disturbances had been corrected by day 7 of TPN, except in the case of one patient with mild hypokalaemia and another with mild hypomagnesaemia. There were no disturbances associated with sodium. Table III shows the electrolyte disturbances during the first week of TPN.

In two patients, thiamine plasma levels were found to be within reasonable ranges (9.5 and 4.9 mcg/dl, normal: 2.0-7.2 mcg/dl).

At the beginning of TPN, 6 patients (54.5%) presented with high alkaline phosphatase (mean: 346.6 U/L; 95% CI: 240.1 to 489.1) which remained altered on day 7 for all 6 patients (mean: 386.0; 95% CI: 237.3 to 539.3), however there were no significant differences from the initial values (p = 0.686).

With regards to the nutritional parameters at the end of the first week of TPN, albumin increased in 4 patients (36.4%) and remained constant in 7 (63.6%). Cholesterol increased in 3 patients, remained constant in 6 and decreased in the other 2. Total lymphocytes increased in 4 patients, remained constant in 3 and decreased in 4.

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DISCUSSION

No cases of RS were observed among the 11 patients who suffered severe weight loss, were at risk of RS and who received individualised TPN. However, there were cases of mild electrolyte disturbances.

A BMI of < 18.5 kg/m² has been linked to increased mortality for hospitalised patients⁷ (RR: 3.53; 95% CI: 2.83 to 4.39). A fundamental strategy for avoiding iatrogeny associated to overfeeding is the nutritional monitoring of patients who are at risk⁴,⁵,⁸,¹¹.

In patients who are susceptible to RS, an initial mild caloric input is currently recommended (approximately 20 kcal/kg/day). This may be administered by any means and should be increased slowly during the first week.³,¹³,¹⁵ However, some studies advise that only 25-50% of caloric requirements be administered.²,¹² Some authors recommend minimum glucidic inputs of 100-150 g/day for adults weighing 70 kg (1.4-2.1 g/kg/day)²,¹². There are no recommendations for lipid quantities. The protein input²,⁵,¹² should be 1.2-1.5 g/kg/day, however these recommendations have not been endorsed by any study.

In the present study, the initial caloric input was within the recommended range, however the glucidic input was somewhat higher and no cases of hyperglycaemia were observed.

There are no strict recommendations for electrolyte input. The recommended phosphate input in patients receiving TPN with normal renal function⁴ is 20 to 40 mmol/day. In patients with RS and hypophosphataemia, the following doses of phosphate have been proposed in order to correct mild, moderate and severe hypophosphataemia: 0.08-0.16; 0.16-0.32 and 0.32-0.64 mmol/kg respectively.¹ Two. This should be administered in an intravenous infusion at a maximum speed of 7 mmol/h. However, patients who are severely malnourished may require greater quantities of phosphate.

In the present study, the doses of phosphate are slightly lower than the general recommendations. The appearance of hypophosphataemia in two of the patients may be explained by greater requirements as a result of the patients’ pathologies (one was critically ill and the other had an intestinal fistula). Perhaps higher initial doses should be given in order to prevent such disturbances. However, in studies on cancer patients or those with gastrointestinal fistulas, administering 30-100 mmol/day did not prevent hypophosphataemia.²,⁵,¹²,¹⁴

The recommended magnesium input for patients receiving TPN with normal renal function⁴ is 20-40 mEq/kg/day. In patients with RS, mild to moderate hypomagnesaemia and normal renal function, the recommended input⁴ in bolus is 8-32 mEq (1-4 g) over 6-12 hours.

In the present study the magnesium input was adjusted to the normal recommendations⁴. Perhaps higher initial inputs should be established in order to prevent the appearance of deficits.

The recommended potassium input for patients receiving TPN with normal renal function⁴ is 1-2 mEq/kg/day. In patients with mild to moderate RS, hypokalaemia and normal renal function, the recommended input⁴ is 20-40 mEq in bolus, at a rate of 10-20 mEq/h.

Despite the fact that the inputs used in the present study were within the recommended range, higher initial doses may be required in order to prevent subsequent deficiencies; however in this case potassium should be strictly monitored and analysed.

The recommended sodium input for patients receiving TPN with normal renal function⁴ is 1-2 mEq/kg/day. However some authors recommend that this be restricted in patients who are at risk of RS¹² and that the input should not exceed 20 mEq/day during the first few days, in order to avoid retention of any kind. In the present study the sodium input was within the general recommended range and there were no cases of hypernatraemia. Malnourished patients may present with thiamine deficiencies³,¹¹ which worsen if the patient develops RS. If it is suspected that the patient suffers from a thiamine deficiency, supplements should be administered before administering carbohydrates⁵. The recommended dose is 50-250 mg to be administered at least 30 minutes before beginning TPN⁴. In the present study the only input was 3.51 mg/day. Even so, none of the patients showed symptoms of a deficit and the few plasma levels analysed were within reasonable ranges.

Low levels of nutritional support should be given to patients at risk during the first week. The aim is to re-establish the anabolic metabolism, get rid of mechanisms which may lead to starvation³,¹³ and prevent the appearance of hydroelectrolytic disturbances.¹ Furthermore, patients who are seriously malnourished present reduced protein synthesis with nutritional support⁴. Excess macronutrients may cause severe metabolic complications which affect the hepatic-biliary, renal and respiratory systems.¹⁰,¹⁷. Patients with chronic malnutrition or who are in an acute period of total or partial starvation are more susceptible to these complications if they overfeed⁷,¹⁸. As a result, the aim is not to achieve improved initial nutrition but rather to avoid complications associated with overfeeding. Although the number of patients in the present study is very limited, there were no cases of RS and only mild to moderate cases of electrolyte disturbances. Moreover, despite a moderate initial caloric input, albumin values were maintained or increased in all patients during the first week of TPN.
References

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