



## RECOMMENDATIONS FOR SPECIALIZED NUTRITIONAL-METABOLIC TREATMENT OF THE CRITICAL PATIENT

### Recommendations for specialized nutritional-metabolic treatment of the critical patient: Nonsurgical abdominal disease. Metabolism and Nutrition Working Group of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)<sup>☆</sup>



Recomendaciones para el tratamiento nutrometabólico especializado del paciente crítico: patología abdominal no quirúrgica. Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)

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## Introduction

The different nonsurgical abdominal disease conditions are characterized by common features that allow them to be addressed jointly when talking about specialized nutritional treatment (SNT). Severe acute pancreatitis (SAP), acute liver failure (ALF) and short bowel syndrome (SBS) are critical clinical conditions characterized by increased morbidity-mortality. The metabolic condition found in these disorders comprises hypermetabolism and hypercatabolism, and SNT must be started as soon as possible following hemo-

dynamic stabilization of the patient. Enteral nutrition (NE) is the nutritional technique of first choice, while parenteral nutrition (PN) is used when EN fails, or as a complement to the latter. Standard diets are the most widely used option, though there are also specific diets which in some cases help improve the nutritional parameters.

## Questions

### 1. Can patients with severe acute pancreatitis be fed via the gastric enteral route? When is postpyloric enteral feeding indicated?

Patients with SAP should receive SNT from the time of diagnosis, since oral intake is unlikely to be possible over the next 5–7 days, and the degree of hypercatabolism is markedly elevated.

The absence of nutrients causes atrophy of the digestive mucosa, intraluminal bacterial overgrowth, increased intestinal permeability and bacterial translocation. Enteral nutrition significantly lowers the incidence of infectious complications, shortens hospital stay and reduces mortality among patients with SAP in comparison with the use of PN.<sup>1,2</sup>

The enteral route is the best strategy for the supply of nutrients. The nasogastric route versus the nasojejunal route remains the subject of research. The jejunal route preserves pancreatic resting conditions. This, and the fact that administration via this route is totally safe,<sup>3</sup> implies that SNT via the jejunal route is recommended as first choice in patients with SAP,<sup>1</sup> especially in cases of particularly severe acute pancreatitis. Despite these recommendations, different randomized studies have shown the gastric route in patients with SAP to afford similar results, and is equally safe,<sup>4</sup> being a valid feeding option in SAP – though it must be taken into account that less seriously ill patients were included in these studies. In cases of intolerance to SNT via the gastric route, SNT using the jejunal route is indicated as a measure prior to PN.

Different studies have related the early introduction of EN to a decrease in infectious complications, a shorter stay in the Intensive Care Unit (ICU), and even lesser mortality among patients with SAP.<sup>5,6</sup> Translocation and infection in pancreatic necrosis, among other processes, conditions the prognosis of SAP, and since EN reduces bacterial translocation, the optimum time for introducing EN is within the first 24–48 h, once the initial resuscitation phase has passed.<sup>1–3,6</sup>

### 2. When is parenteral nutrition indicated in patients with severe acute pancreatitis, and what should its composition be?

Some of the criteria indicating intolerance of EN in patients with SAP are increased ascites and/or intraabdominal hypertension, the presence of high-output intestinal and/or pancreatic fistulas, or the presence of occlusions at some point within the digestive tract.

Although some authors propose delaying the start of PN until day 5–7 of the clinical course in patients where EN is contraindicated,<sup>7</sup> most investigators agree that in those

patients in which enteral feeding is not contemplated in the first three days, PN should be introduced in the first 24–48 h, once hemodynamic stabilization has been achieved.<sup>8</sup>

No studies have evaluated the administration of different lipid formulations or different amino acid compositions in PN of patients with SAP. Lipid emulsions are not contraindicated, and the energy supply therefore should be mixed (carbohydrates and lipids), with close monitoring of the plasma triglyceride concentrations and glycemia.

No data are available on the benefits of EN at trophic doses in patients with SAP that receive PN, though in the same way as with the rest of critical patients, the administration of a minimum nutrient supply via the enteral route may have beneficial effects.

Supplementing with glutamine via the parenteral route at a dose of 0.5 g of glutamine dipeptide/kg/day in patients with SAP that receive PN has been shown to offer prognostic benefits, with a decrease in infectious complications and of the need for surgery, improved glycemic control, and lesser patient mortality.<sup>9</sup> Such supplementing therefore should be considered, except in patients with multiorgan dysfunction.<sup>10</sup>

The administration of  $\omega$ -3 fatty acids in PN may be considered, since they have been shown to shorten hospital stay and reduce infectious complications and mortality.<sup>11</sup>

### 3. What is the best enteral nutrition formula for patients with severe acute pancreatitis?

Peptide formulas have been used in patients with SAP, since they reduce pancreatic secretion, improving nutrient absorption<sup>12</sup> and shortening hospital stay.<sup>13</sup> However, although very few studies have been made in this regard,<sup>13</sup> it has been demonstrated that polymeric diets are safe and equally well tolerated by patients with SAP that receive EN,<sup>13,14</sup> and they moreover are less expensive than peptide formulas.<sup>14</sup>

Very little scientific evidence is available regarding the benefits of diets enriched with pharmac nutrients among patients with SAP. Specifically, few clinical trials have studied the supplementation of EN with pharmac nutrients such as arginine, glutamine or  $\omega$ -3 fatty acids, and most of them lack the methodological robustness needed in order to be able to recommend their systematic use in patients with SAP.<sup>14</sup>

With regard to the administration of probiotics in patients with SAP receiving EN, although some investigators have reported prognostic benefits and improvements in the inflammatory markers,<sup>15</sup> it is presently not possible to recommend their routine use, since very little clear evidence is available, and not always are the same microbial strains or doses used.<sup>12,14</sup> One study has described an increase in mortality among patients administered probiotics.<sup>16</sup>

A study has reported a significant decrease in local infectious complications and a shortened hospital stay in patients with SAP administered fiber-enriched enteral formulas.<sup>15</sup> However, other studies have obtained contradictory results. Consequently, although the use of such formulas may be considered, the supporting evidence is limited.

#### 4. Should patients with acute liver failure receive a diet modified in nutrient quantity or quality?

The severity of ALF is related to the time from symptoms onset to the appearance of coagulation disorders and encephalopathy. In a retrospective study of 267 patients, the causes were found to be viral hepatitis in 37% of the cases, hepatitis B in 28%, unknown origin in 32%, drugs or toxic agents in 19.5%, *Amanita* in 3%, paracetamol overdose in 2% and miscellaneous causes in 11.6%. The survival rate was 58%.<sup>17</sup>

- Caloric requirements in ALF: this disorder is characterized by an increase in energy expenditure due to hypermetabolism and highly exacerbated catabolism. Indirect calorimetry would be the technique of choice for caloric estimation.<sup>17</sup> Some studies use conventional formulas applying a correction factor of 1.2–1.5 to the calculated basal energy expenditure. The advised energy supply is 25–30 kcal/kg/day.<sup>18</sup> The experts recommend the nutritional calculations to be based on usual body weight.
- Administration of nutritional treatment: enteral nutrition is the option of choice and should be started as soon as possible, adopting the gastric or postpyloric route. Parenteral nutrition should be reserved for those cases in which feeding via the digestive route is not possible. In an observational study with the participation of 33 European hepatology units, 50% of the patients received EN.<sup>19</sup>
- Supply of carbohydrates: severe hypoglycemia is frequent, and is associated to the lack of glycogen production and alterations in glycogenolysis, with increased neoglycogenesis and glucose intolerance secondary to peripheral insulin resistance. Hyperglycemia should be avoided, since it can contribute to increased brain edema due to the loss of glucose transporter regulation at the brain blood barrier. The administration of 1.5–2 g/kg/day is advised,<sup>19</sup> with the use of standard diets.
- Supply of lipids: lipid oxidation is increased in these patients, but there are no data not warranting their use together with carbohydrates as caloric supply. The recommended lipid dose is 0.8–1 g/kg/day.<sup>19</sup>
- Supply of proteins: in ALF, the metabolism of ammonium and urea is altered, and their plasma levels are greatly elevated, being related to the degree of encephalopathy and to the risk of intracranial hypertension. Nevertheless, protein restriction is not indicated. The protein supply should be adjusted according to the ammonium levels to between 1 and 1.5 g/kg/day.<sup>20</sup> Some studies use standard amino acid formulations, though most administer solutions enriched with branched or ramified amino acids to improve the hepatic encephalopathy – with inconclusive results. A Cochrane review based on 37 controlled studies in patients with exacerbated chronic liver failure has evidenced improvement of encephalopathy, with no impact upon patient morbidity-mortality.<sup>21</sup>
- Supply of vitamins, oligoelements and ions: these are to be supplied daily from the start of nutritional support. Hypopotassemia, hypomagnesemia, hypophosphatemia and hypocalcemia are frequent in ALF and need to be corrected.<sup>22</sup>

#### 5. Should special enteral nutrition formulas be used in patients with short bowel syndrome?

Short bowel syndrome is a malabsorption syndrome caused by anatomical or functional loss of the small bowel. The affected individuals present chronic diarrhea, dehydration and macro- and micronutrient deficiencies that require EN and, sometimes, PN.

In patients with SBS we need to individualize nutritional treatment, since bowel functionality is conditioned by a range of factors (background disease, length of resected intestine, the anatomical part removed, absence of the ileocecal valve, etc.). In the early stages, priority should focus on the control of dehydration and the electrolytic disorders, particularly hyponatremia and hypomagnesemia. It is advisable to start PN early, with the monitoring of electrolytes and volemia. Subsequently, in the adaptation phase, EN can be gradually introduced until oral feeding proves possible.<sup>23</sup>

A diet rich in complex carbohydrates (50–60%) and low in lipids (20–30%) reduces calorie loss in stools and increases general energy absorption and moist weight, provided at least a portion of colon is preserved. No specific formulas are required, and nutritional supplements may prove useful in accordance with the individualized deficiency involved.<sup>24</sup>

The use of elemental solutions is not regarded as first choice in the management of acute intestinal failure, since the patient may be in the initial secretory phase of SBS. Studies in animals with SBS lacking an ileum have found oligomeric diets to be better tolerated than polymeric diets.<sup>25</sup> There is not enough evidence to recommend the routine use of glutamine<sup>26</sup> or pre- or probiotics.<sup>27</sup> In patients with bowel resections of over 200 cm and a preserved colon, the provision of oxalate should be lowered to reduce its absorption and the risk of nephropathy secondary to accumulation.<sup>28</sup>

Supplementing with vitamins and oligoelements should be individualized, with monitoring of their levels. In patients with terminal ileum resections of over 60 cm in length, vitamin B<sub>12</sub> supplementing is essential.

A new therapy for SBS has been evaluated in recent years, involving the use of teduglutide, a recombinant analog similar to glucagon-2, a natural hormone that regulates the growth, proliferation and maintenance of the cells lining the gastrointestinal tract. Subcutaneous teduglutide is the first long-term medical therapy approved for the treatment of adult patients with SBS dependent upon PN. There are phase III clinical trials demonstrating clinically significant reductions in PN requirements among adults with SBS.<sup>29</sup>

#### Recommendations

- In patients with severe acute pancreatitis, the enteral route is the option of choice – the parenteral route being limited to patients in which EN is contraindicated, proves insufficient or is poorly tolerated (Level of evidence: moderate). Grade of recommendation: moderate).
- In severe acute pancreatitis, EN should be provided via the jejunal route whenever possible (Level of evidence: moderate). Grade of recommendation: moderate), though the gastric route may be a valid and safe alternative in cases

of less severe pancreatitis (Level of evidence: moderate. Grade of recommendation: low).

- In patients with severe acute pancreatitis receiving PN, it is advisable to evaluate the administration of a minimum amount of nutrients via the enteral route (trophic enteral nutrition)(Level of evidence: low. Grade of recommendation: moderate).
- In patients with severe acute pancreatitis requiring PN, it is advisable to supplement PN with  $\omega$ -3 fatty acids. (Level of evidence: low. Grade of recommendation: moderate), with the administration of glutamine at adequate doses, in the absence of contraindications (Level of evidence: moderate. Grade of recommendation: moderate).
- Nutrition via the enteral route is the option of choice in patients with liver failure, and protein restriction is not recommended (Level of evidence: low. Grade of recommendation: moderate).
- In patients with hepatic encephalopathy, branched amino acids can be considered (Level of evidence: low. Grade of recommendation: low).
- In severe acute pancreatitis, short bowel syndrome and acute liver failure, both polymeric and peptidic diets can be used (Level of evidence: moderate. Grade of recommendation: moderate).
- As first strategy in short bowel syndrome, it is advisable to administer nutrition via the parenteral route (Level of evidence: low. Grade of recommendation: moderate).
- In short bowel syndrome it is advisable to administer subcutaneous teduglutide at a dose of 0.05 mg/kg/day to reduce the use of total parenteral nutrition and fluid therapy (Level of evidence: moderate. Grade of recommendation: moderate).

## Conflicts of interest

The members of the working group that have participated in the development of these recommendations have previously collaborated in activities financed by the drug industry dedicated to the marketing of nutritional products. These activities correspond to participation in clinical studies and educational programs, as well to aids for attending scientific events.

The drug industry has not participated in the elaboration, discussion, drafting or scoring of evidences in any of the phases of the present recommendations.

## Note to supplement

This article forms part of the supplement "Recommendations for specialized nutritional-metabolic management of the critical patient. Metabolism and Nutrition Working Group of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)", with the sponsorship of Abbott Nutrition.

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