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### Chapter 7

# Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Severe acute pancreatitis

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#### Abstract

Severe acute pancreatitis (SAP) causes local and systemic complications leading to high catabolic, hypermetabolic and hyperdynamic stress states with marked morbidity and mortality.

In the last decade, nutritional support has become a key element in the treatment of SAP. Thus, specialized nutrition is indicated from admission, with enteral nutrition being preferred to parenteral nutrition. Enteral nutrition should be initiated early using infusion through the jejunum beyond the ligament of Treitz to minimize pancreatic stress.

There are no specific studies that establish the type of diet to be used but experts recommend the use of polymeric diets.

Parenteral nutrition, without a specific formula, is indicated in patients with SAP who are intolerant to enteral nutrition or when the clinical signs of pancreatitis are exacerbated or aggravated by enteral nutrition. Even so, a minimal level of enteral infusion should be maintained to preserve the trophic effect of the intestinal mucosa

In the last few years, several studies of the administration of immunomodulatory diets in patients with SAP have been carried out to demonstrate their effects on the course of the disease. However, there are few clear recommendations on the prognostic benefits of pharmaconutrient enriched diets in these patients. There is substantial scientific evidence suggesting that the only clear indication for pharmaconutrition in patients with SAP is parenteral glutamine administration, which is recommended by all clinical guidelines with distinct grades of evidence.

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Key words: Pancreatitis. Lipids. Enteral nutrition.

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SEMICYUC: Spanish Society of Intensive Care Medicine and Coronary Units. SENPE: Spanish Society of Parenteral and Enteral Nutrition.

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: PANCREATITIS AGUDA GRAVE

#### Resumen

La pancreatitis aguda grave es una patología que cursa con complicaciones locales y sistémicas que condicionan una situación de estrés altamente catabólica, hipermetabólica e hiperdinámica con marcada morbimortalidad.

En la última década, el soporte nutricional se ha convertido en uno de los puntos clave en el tratamiento de la pancreatitis aguda grave. Así, hay indicación de nutrición especializada desde el ingreso, siendo de elección la nutrición enteral sobre la nutrición parenteral administrada de forma precoz más allá del ligamento de treitz, para provocar el mínimo estímulo pancreático. No hay estudios específicos que nos aclaren cuál es el tipo de dieta a administrar, pero los expertos recomiendan la utilización de dietas poliméricas.

La nutrición parenteral, sin una fórmula concreta, quedaría indicada en los pacientes con pancreatitis aguda grave que presentan intolerancia a la nutrición enteral o cuando se agravan los signos clínicos de pancreatitis al administrar la dieta enteral. Aun así, se recomienda mantener una mínima perfusión de nutrición enteral para preservar el efecto trófico de la mucosa intestinal. En los últimos años se han realizado numerosos trabajos referentes a la administración de dietas inmunomoduladoras en pacientes con pancreatitis aguda grave, con la finalidad de objetivar cambios en su evolución. Sin embargo, hay pocas recomendaciones claras en cuanto a los beneficios pronósticos de la administración de dietas enriquecidas en farmaconutrientes, específicamente en pacientes con pancreatitis aguda grave. Sustentada por una evidencia científica relevante, el aporte de glutamina por vía parenteral en pacientes con pancreatitis aguda grave parece ser la única indicación clara de farmaconutrición en pancreatitis aguda grave recomendando su uso todas las guías de referencia para la práctica clínica con diferentes grados de evidencia.

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Palabras clave: Pancreatitis. Lípidos. Nutrición enteral.

#### Introduction

Acute pancreatitis (AP) is one of the most common diseases of the pancreas, with an incidence of 5-80/1,000 inhabitants/year. Patients admitted to the ICU show the severe forms, which account for 15-20% and are associated both with local complications (pancreatic necrosis, infection of necrosis, pancreatic abscess or pseudocyst) and systemic complications (multiple organ failure), with a high morbidity-mortality (over 50% in some series).

It is essential to establish the diagnosis and to stratify severity in the first 48 h, to establish its prognosis and start treatment early, where nutritional support (NS) is essential. In the consensus conference of the Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC), following the steps of the Conference of Atlanta, Severe Acute Pancreatitis (SAP) is defined by the presence of a number of signs and symptoms, including severity scales based on biological or tomographic signs. However, this classification does not include the presence or absence of organ failure, associated with general or local complications, that will be critical in the evolution of patients with SAP<sup>1,2</sup>.

SAP causes a systemic inflammatory response leading to a highly catabolic, hypermetabolic and hyperdynamic stress condition<sup>3,4</sup>. The previous nutritional status of the patient will be critical in the evolution; therefore, chronic alcohol intake and obesity are severity-independent factors.

The traditional treatment for SAP was intestinal rest and parenteral nutrition (PN). In the last decade, different studies have shown that this traditional approach is associated with an increased morbidity and an increased mortality risk<sup>5-8</sup>.

A recent study of several intestinal function markers concluded that dysfunction of the intestinal barrier is an early fact during SAP, that is related to infection of pancreatic necrosis, occurrence of multiple organ failure and severity of pancreatitis with mortality increase<sup>9</sup>.

Therefore, the concept of classical NS, limited to reversing the catabolic state, is changing. The emerging data suggest that the route, time, amount and composition of artificial nutrition are aimed at reducing pancreatic secretion, treating and/or preventing associated malnutrition in a severe metabolic-catabolic stress state, modulating inflammatory response and preventing the development of local and systemic infections<sup>10-14</sup>. Nutritional support can be a very important intervention in the management of patients with SAP.

## What are the indications of nutritional support in patients with severe acute pancreatitis?

In SAP there is an indication of specialized nutrition since admission, as these patient will not restart intake in the next 5-7 days and degree of hypercatabolism is maximum<sup>3,4</sup> (IV).

The need for surgery or the development of local complications related to pancreatitis does not change the indication of NS, that should continue to be based on the severity and efficacy of intake to reach the calculated nutritional requirements.

## Is enteral nutrition advisable in patients with severe acute pancreatitis?

Absence of enteral feeding induces gastrointestinal mucosa atrophy, bacterial overgrowth, increased intestinal permeability, and bacterial translocation. In an experimental study of AP, enteral nutrition, as compared to PN, reduced endotoxemia levels, bacterial translocation in portal and systemic blood, and the number of bacterial colonies in mesenteric nodes and in the pancreas<sup>15</sup>.

The most recent meta-analyses concluded that EN, compared to PN, continues to show a significant reduction in mortality in infectious complications and duration of hospital stay<sup>11,12,16</sup> (Ib).

The latest revision by Cochrane 2010, with an analysis of subgroups with SAP, concluded that EN shows significant benefits over PN by reducing mortality, multiple organ failure, systemic infection and surgical procedures. In addition, it is associated with a trend in reducing hospital length of stay, local septic complications, and other local complications, and all this at a lower cost<sup>13</sup> (Ib).

#### When should be enteral nutrition started?

Studies evaluating the effect of EN on systemic inflammatory response in patients with SAp show a faster reduction of APACHE II and inflammatory markers<sup>9,10,14,16</sup>. It has been shown that bacterial colonization and infection occur a few hours following the onset of pancreatitis. A mortality reduction has been seen in several series, excluding studies starting NS after 48 h<sup>16,17</sup>. The existence of previous malnutrition (as in the case of SAP of alcoholic origin) is another reason for starting early EN. Considering that EN started as soon as possible improves the disease process, we should recommend early EN in SAP, in the first 24-48 hours following admission, after the initial resuscitation phase<sup>5,12-14,16,17</sup> (Ib).

#### How should enteral nutrition be administered?

Some studies in SAP have shown that exocrine secretion in response to cholecystokinin and other secretagogues is markedly reduced<sup>18</sup>. On the other hand, EN flow distal to the ligament of Treitz stimulates minimally pancreatic secretion, respecting "pancreatic rest". Randomized studies on EN vs PN have been published, where EN was administered in the jejunum,

with no complications secondary to the site<sup>5,6</sup>. It is therefore concluded that the use of jejunal nutrition<sup>12,14,16</sup> (Ib) is safe for SAP. The use of a dual lumen catheter, which allows for jejunal infusion together with gastric decompression, monitoring the quantity and appearance of gastric output, enhances tolerability and management of EN in these patients.

However, randomized studies comparing EN by gastric versus jejunal route in SAP have demonstrated similar outcomes<sup>19,20</sup> (Ib), though the comparison of severity is difficult to establish, so the gastric route can be also used in some cases.

#### What is the most advisable type of formula?

There is a single study in pancreatitis where the objective is to assess the type of diet administered. This study includes a small number of seriously ill patients with pancreatitis, and concludes that both oligomeric and polymeric diets are well tolerated in patients with pancreatitis<sup>21</sup> (IIb).

There is theoretical tolerance advantage favorable to the semielemental diet, as it contains small peptides and middle-chain lipids, that do not require pancreatic enzymes to be digested, but, in the opinion of the experts, polymeric diets may be used safely<sup>22</sup> (IV).

#### When should parenteral nutrition be used?

The indication of PN would be subject to the unfeasibility of obtaining an adequate enteral approach, in case of intolerance to EN or when on starting EN the clinical and laboratory signs of the severe acute pancreatitis worsen<sup>2,23,24</sup>.

Xian-Li confirmed that the start of PN 24-48 hours after obtaining hemodynamic control reduced complications, hospital stay and mortality<sup>25</sup> (Ib). Some authors recommend delaying the start of PN for at least 5 days, until the inflammatory response syndrome has subsided, in patients with SAP where EN cannot be started, but they are based on studies not performed on SAP<sup>12</sup>. Thus, following the criterion of indication of PN in critically-ill patients, we consider that PN should be started in patients who require specialized NS, if this could not be started by enteral route or if a total nutritional supply is not achieved, within the first 48 hours following admission. With regard to the composition of PN, there are no data to recommend patterns of specific amino acids or certain lipid formulations in the SAP. No formulation has shown to be superior to another. It must be considered that lipid emulsions are not contraindicated in patients with SAP and, therefore, the energy supply must be mixed (carbohydrates/ fats)<sup>24</sup>. Hypertriglyceridemia and hyperglycemia values must be closely monitored.

In patients receiving PN it may be advisable to simultaneously supply a very low amount of enteral

diet. The purpose of EN, though from a theoretical point of view, would be to maintain the trophic effect of intraluminal nutrient supply on the intestinal mucosa<sup>23,26-28</sup> (IV).

## What specific nutrients are indicated in severe acute pancreatitis?

In recent years multiple studies have been performed on the administration of pharmaconutrition diets in all type of seriously ill patients for the purpose of evidencing changes in their progress. However, there are very few clear recommendations on the prognostic benefits of the administration of diets enriched with pharmaconutrients, specifically in patients with SAP.

With regard to enteral pharmaconutrition in SAP, there is scant scientific evidence and the recommendations on the topic are ambiguous. In the literature published, the benefits with scientific significance make reference to improvements in biochemical inflammation markers<sup>29</sup> and suggest outcome benefits in patients with SAP when nutrition enriched with pharmaconutrients is administered<sup>29,30</sup>, though from the design of these studies it is not considered that there is sufficient evidence for recommending them<sup>12,16,24,31,32</sup>(Ib).

Studies with administration of parenteral glutamine supplements, in patients with SAP receiving PN, have reported prognostic benefits with a shorter hospital stay and a reduction of infectious complications and the need for surgery, as well as a better control of blood sugar levels and faster improvement in biochemical markers of inflammation<sup>12,14,33,34</sup> (Ib).

With regard to the administration of probiotics and prebiotics in patients with SAP, currently, and analyzing the data obtained from the studies completed<sup>8,9,35,36</sup> (Ib), no recommendations can be made for their use, as the literature evidence is rather disparate, not always using the same organisms, and the doses used have been also different.

Few studies about the administration of trace elements and micronutrients with an antioxidant action by parenteral or enteral routes have been performed in patients with SAP<sup>37,38</sup>.

#### Recommendations

- Enteral nutrition by jejunal route is of choice over parenteral nutrition (A).
- Specialized nutritional support in severe acute pancreatitis should be started early, within 48 h of initial resuscitation (A).
- Polymeric and oligomeric diets are equally recommended (C).
- Parenteral nutrition is indicated if enteral nutrition cannot be administered, in case of intolerance to it, or if this leads to worsening of pancreatitis (B).

- It is suggested to assess the possibility for maintaining a minimum enteral nutrient supply, even in patients with intolerance to enteral nutrition and who are on treatment with parenteral nutrition (C).
- The use of glutamine is recommended in patients with severe acute pancreatitis receiving parenteral nutrition (B).
- There are no current recommendations for the use of prebiotics or probiotics in patients with severe acute pancreatitis (C).

#### **Conflict of interests**

The authors declare that they have participated in activities funded by the pharmaceutical industry for marketing of nutritional products (clinical studies, educational programmes and attendance to scientific events). No pharmaceutical industry has participated in the preparation, discussion, writing, and establishing of evidences in any phase of this article.

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