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NUTRICIÓN HOSPITALARIA ES PROPIEDAD DE SENPE

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GUIDELINES FOR SPECIALIZED NUTRITIONAL AND METABOLIC SUPPORT IN THE CRITICALLY-ILL PATIENT

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RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL DEL PACIENTE CRÍTICO

Este suplemento especial de Recomendaciones para el soporte nutricional del paciente crítico ha sido publicado simultáneamente en español en Med Intensiva 2011; 35 (Supl. 1): 1-85

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Chapter 1

Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Introduction and methodology

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Abstract

The Recommendations for Specialized Nutritional Support in Critically-Ill patients were drafted by the Metabolism and Nutrition Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC) in 2005. Given the time elapsed since then, these recommendations have been reviewed and updated as a Consensus Document in collaboration with the Spanish Society of Parenteral and Enteral Nutrition (SENPE).

The primary aim of these Recommendations was to evaluate the best available scientific evidence for the indications of specialized nutritional and metabolic support in critically-ill patients. The Recommendations have been formulated by an expert panel with broad experience in nutritional and metabolic support in critically-ill patients and were drafted between October 2009 and March 2011.

The studies analyzed encompassed metaanalyses, randomized clinical trials, observational studies, systematic reviews and updates relating to critically-ill adults in MEDLINE from 1966 to 2010, EMBASE reviews from 1991 to 2010 and the Cochrane Database of Systematic Reviews up to 2010. The methodological criteria selected were those established in the Scottish Intercollegiate Guidelines Network and the Agency for Health Care policy and Research, as well as those of the Jadad Quality Scale. Adjustment for the level of evidence and grade of recommendation was performed following the proposal of the GRADE group (Grading of Recommendations Assessment, Development and Evaluation Working Group).

Sixteen pathological scenarios were selected and each of them was developed by groups of three experts. A feedback system was established with the five members of the Editorial Committee and with the entire Working Group. All discrepancies were discussed and consensus was reached over several meetings, with special emphasis placed on reviewing the levels of evidence and grades of recommendation. The Editorial Committee made the

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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: INTRODUCCIÓN Y METODOLOGÍA

Resumen

El Grupo de trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC) elaboró en 2005 unas recomendaciones para el soporte nutricional especializado del paciente crítico. Dado el tiempo transcurrido se consideró oportuno la revisión y actualización de dichas recomendaciones, planificándolas como un documento de consenso con la Sociedad Española de Nutrición parenteral y Enteral (SENpE).

El objetivo primario planteado para el establecimiento de las recomendaciones fue evaluar la mejor evidencia científica disponible para las indicaciones del soporte nutricional y metabólico especializado en el paciente crítico. Las recomendaciones se han realizado por un panel de expertos con amplia experiencia en el soporte nutricional y metabólico de los pacientes en situación crítica y se han llevado a cabo entre octubre de 2009 y marzo de 2011.

Se analizaron metaanálisis, estudios clínicos aleatorizados y observacionales, revisiones sistemáticas y puestas al día referentes a pacientes críticos en edad adulta en MEDLINE de 1966 a 2010, EMBASE reviews de 1991 a 2010 y Cochrane Database of Systematic Reviews hasta 2010. Se seleccionaron los criterios metodológicos establecidos en la Scottish Intercollegiate Guidelines Network y los de la Agency for Health Care policy and Research, además de la escala de valoración de la calidad de Jadad, ajustando la gradación de la evidencia y la potencia de las recomendaciones siguiendo la propuesta del Grupo GRADE (Grading of Recommendations Assessment, Development and Evaluation Working Group).

Se seleccionaron 16 situaciones patológicas que fueron desarrolladas, cada una, por grupos de 3 expertos, estableciéndose un sistema de feedback con los 5 miembros del Comité de Redacción y con la totalidad del Grupo de trabajo. En diferentes reuniones se discutieron y consensuaron todas las discrepancias, poniéndose especial énfasis en el repaso de los niveles de evidencia y grados de recomendación establecidos. El Comité de Redacción procedió al ajuste final para su presentación y aproba-

final adjustments before the document was approved by all the members of the Working Group. Finally, the document was submitted to the Scientific Committees of the two Societies participating in the Consensus for final approval.

The present Recommendations aim to serve as a guide for clinicians involved in the management and treatment of critically-ill patients and for any specialists interested in the nutritional treatment of hospitalized patients.

Nutr Hosp 2011; 26 (Supl. 2):1-6

Key words: *Specialized nutritional support. Critically-ill-patient. Recommendations. Clinical evidence.*

ción definitiva por todos los miembros del Grupo de trabajo. Finalmente el documento se presentó a los comités científicos de las dos sociedades participantes del consenso para su aprobación definitiva.

Las presentes recomendaciones pretenden servir de guía para los clínicos con responsabilidades en el manejo y tratamiento de los pacientes críticos y para todos los especialistas interesados en el tratamiento nutricional del paciente hospitalizado.

Nutr Hosp 2011; 26 (Supl. 2):1-6

Palabras clave: *Soporte nutricional especializado. Paciente crítico. Recomendaciones. Evidencia clínica.*

Introduction

Specialized nutritional support (SNS) in critically-ill patients has long been one of the most controversial therapeutic interventions, and preference has been given to other treatments that were considered more important to improve the clinical course of these patients. However, in recent years numerous clinical trials have caused this situation to change.

There is sufficient evidence that malnutrition is an independent risk factor for morbidity, with an increased rate of infections, ICU and hospital stay, days of mechanical ventilation, difficulty for wound healing and increased mortality[1]. At the same time, the evidence on the efficacy and impact of nutritional support for improved overall results in the clinical course of these patients has increased in the last decade[2].

Assignment of a patient to the category of 'critically-ill' is often conflicting in medical literature. This means that the results of nutritional support, both beneficial and harmful, are often transferred from patient groups not necessarily critically-ill to this particular population group, with the errors that this can entail. It is clear that the population of critically-ill patients is not a homogeneous population, based on their assignment to either the surgical, trauma or medical area, and within these, to their specific disease, whose level of severity should be established on the corresponding scales. In addition, it is a type of patients who may experience changes and/or complications during their course that may significantly modify their severity and therefore their prognosis and treatment.

SNS in critically-ill patients has different controversial aspects, such as the indication for nutritional support itself, the type of nutrient substrates to be used, or the administration route. On the other hand, the scientific methodological difficulties in validating such indications may be in opposition to bioethical assessments, because ethics may be easily infringed if nutritional support is stopped for greater or lesser length of time in patients who are not clearly within the groups in which a benefit from the nutritional support has been confirmed. We find ourselves in a situation where on one hand it is argued that the association between malnutrition and increased morbidity and mortality is clearly established, while on the other it is argued that a clear indication cannot be established unless it is based on prospective randomized controlled studies. However, the term 'critically-ill patient' refers to a group of patients with diverse diseases, with sometimes very different or even opposing metabolic responses, so overall recommendations cannot be established for all patients admitted to an intensive care medicine department or to other critical care units, whatever the cause of admission.

The appearance of substrates with clear pharmaconutrional action has complicated even more the panorama and makes it increasingly important that SNS is also aimed at modulation of metabolism, inflammatory and immune responses to specific clinical situations, once the indication for nutritional support has been established.

This has led different scientific societies to consider the need for adaptation of their previously published recommendations[3,4].

Therefore, the Metabolism and Nutrition Working Group (GTMyN) of the Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC), considered the need to review and update the SNS recommendations previously published by the group[5], with the aim of evaluating the currently available evidence for nutritional and metabolic support in different diseases that may occur in critically-ill patients, in order to aid daily clinical practice decision-making.

The unique feature of these guidelines from those previously published remains that of providing specific recommendations for the different populations of critically-ill patients, an aspect that is not considered in other guidelines and which makes them a unique reference in the literature.

Methods

The primary aim for establishing the recommendations was to evaluate the best available scientific evidence for the indications of specialized nutritional and metabolic support in critically-ill patients, with special attention to the assessment of the nutritional status, the nutrient substrates that should be provided, the adminis-

Table I
Diseases and clinical situations included in the recommendations

1.	Introduction, methods, and terminology
2.	Indications, time of initiation and routes of nutrient delivery
3.	Nutritional assessment
4.	Macronutrient and micronutrient requirements
5.	Acute renal failure
6.	Liver failure and liver transplantation
7.	Severe acute pancreatitis
8.	Respiratory failure
9.	Gastrointestinal surgery
10.	Hyperglycemia and diabetes mellitus
11.	Oncohematological patient
12.	Obese patient
13.	Critically-ill burnt patient
14.	Multiple trauma patient
15.	Septic patient
16.	Neurocritical patient
17.	Cardiac patient

tration route and the time of initiation of nutritional support, as well as the existing evidence on the provision of pharmaconutrients.

The recommendations have been formulated by an expert panel, all of whose members belonged to the GTMyN of the SEMICYUC, with extensive experience in nutritional and metabolic support in critically-ill patients. At the ordinary meeting of the group held on 29-30 October 2009, the project prepared was submitted by the editorial staff responsible for it. The primary aim was to update the recommendations prepared in 2005, for which a work plan was designed after discussion of the subjects to be covered and final consensus by the members of the group present at the meeting (Table I).

The recommendations were based on analysis of the literature existing on each subject. The studies analyzed encompassed meta-analyses, randomized clinical trials, observational studies, systematic reviews and updates relating to adult critically-ill patients (over 18 years of age). The databases consulted were MEDLINE from 1966 to 2010, EMBASE reviews from 1991 to 2010, and the Cochrane Database of Systematic Reviews up to 2010. After discussing the methodology to be used for establishing the corresponding evidence, the methodological criteria selected were those established in the Scottish Intercollegiate Guidelines Network (SIGN)[6] and the Agency for Healthcare Policy Research (AHCPR)[7] (Table II). For establishing the quality of the studies, Jadad quality assessment scale was used[8]. Grading of evidence and the strength of the recommendations was adjusted according to the proposal of the GRADE group (Grading of Recommendations Assessment, Development and Assessment Working Group)[9].

After establishing the methodology, the table of contents of the chapters was circulated to all members of the GTMyN for selection of the authors who would be responsible for writing each, based on their own experience. It was agreed by consensus that each chapter should be written by 3 authors. In each chapter, the most relevant questions related to each disease would be established by the authors, after reaching a consensus between them on the final drafting. Irrespective of the specific questions about each subject, it was recommended to ask some or all of the following:

- What amount and type of energy substrates do they need? *(note:* depending on their importance in the condition involved, this will be given overall or separated into 2 questions, for carbohydrates and lipids).
- What are the protein requirements and the characteristics of their provision?
- What are their requirements for micronutrients, vitamins and fiber?
- What is the most recommendable type of formula? Does it require specific nutrients?
- What is the most recommendable route of administration?

Each chapter was reviewed by at least 3 members of the Editorial Committee, who recommended to authors the changes to be made in each subject before giving them their agreement. The final approval of each chap-

Table II
Grades of recommendation and levels of evidence[6,7]

Grades of recommendation	*Levels of evidence*	*Requirements*
A	Ia	Meta-analysis of randomized controlled trials
	Ib	At least one randomized controlled trial
B	IIa	At least one well-designed controlled study without randomization
	IIb	At least one other type of well-designed quasi-experimental study
	III	Well-designed non-experimental descriptive studies, such as comparative studies, correlation studies or case-control studies
C	IV	Expert opinions and/or clinical experience of respected authorities

ter and of the recommendations included in it was based on discussion at several meetings of the GTMyN until a final consensus on the contents of each subject was reached. This system of preparation of recommendations (progressive feedback) was used for all chapters. Any discrepancies or points on which any member of the group expressed his/her disagreement were discussed and agreed on by consensus, putting special emphasis on reviewing the levels of evidence and grades of recommendation established. The Editorial Committee then proceeded to make the final adjustment of each chapter, including the literature review, for its submission and final approval at the meeting of the GTMyN held in March 2011.

The final step of the process was submitting the final document to the scientific committees of the SEMICYUC and the Spanish Society of Parenteral and Enteral Nutrition (SENPE), to establish the final consensus between both scientific societies.

Terminology and definitions used

In the process of preparation of the recommendations, specific terms were used, some of which are shown below:

– *Increased gastric residual volume.* Volume of diet aspirated through nasogastric tube, considered indicative of gastric ileus. The most commonly used volume is of 200 mL, though it ranges from 100 to 500 mL; the latter is used by the GTMyN. Residual volume is checked every 8-24 h.

– *Nitrogen balance.* Measurement of equilibrium status of nitrogen in the body. It is considered neutral when intake equals excretion, positive when intake exceeds losses, and negative when excretion is greater than intake.

– *Bronchoaspiration.* Defined as the passage of nutritional content to the airway. Regurgitations of small volume (silent) are common, but large ones causing acute respiratory failure range from 1-4%. The underlying cause is related to disturbances in swallowing in neurological patients, and in patients with gastric nutrition to an increased volume of gastric residue secondary to the decrease in gastric emptying.

– *Glycemic control.* It consists of the administration of insulin as a continuous infusion to normalize blood glucose values in critically-ill patients with hyperglycemia. There is controversy on the blood glucose values to be maintained, since a strict glucose control (between 80 and 110 mg/dL) increases the incidence of severe hypoglycemia and mortality in critically-ill patients. An adequate and safe value would range between 110 and 150 mg/dL.

– *Diarrhea.* A disorder consisting of an increased number and volume of daily bowel movements, with evacuation of liquid or semi-liquid stools. Feces may contain mucus, blood, pus, or an excessive amount of fat, depending on their etiology. In critically-ill patients, diarrhea is considered as 5 or more daily bowel movements or an estimated total volume in 24 h greater than 2,000 mL.

– *Pharmaconutrients.* A group of substrates that in addition to their intrinsic nutritional effect stimulate mediators that enhance immunity, inhibit proinflammatory factors, and attenuate response to aggression, whose use has been shown to reduce the infection rate in severely-ill patients. Such group includes amino acids, such as glutamine and arginine, ω-3 fatty acids, and some trace elements and vitamins.

– *Severe hypoglycemia.* We speak about severe hypoglycemia when blood glucose values are below 40 mg/dL. It is the most common complication of insulin therapy in diabetic patients and in critically-ill patients receiving insulin therapy as a continuous infusion to maintain blood glucose values in the range considered as "normal blood glucose" (80-110 mg/dL). Untreated cases cause seizures, coma and even death.

– *Insulin resistance.* Inability of insulin to exert its usual biological effects at concentrations that are effective in normal subjects. It usually appears in the hypermetabolic state typical of the critically-ill patient, associated or not with obesity, type 2 diabetes mellitus, dyslipidemia and hypertension.

– *Malnutrition.* This is a nutritional state in which a deficiency, excess, or imbalance of energy, protein, and other nutrients causes measurable adverse effects in body tissues (structure, size and composition), as well as in their function and clinical results. It may be due to unbalanced or insufficient nutrition or to inadequate absorption or use.

– *Micronutrients.* Dietary elements used for metabolic or structural purposes and found in very small amounts in the body. They include trace elements and vitamins.

– *Enteral nutrition.* The term 'enteral nutrition' is used to encompass all forms of nutritional support involving the use of "dietary foods for special medical purposes", as defined in the European Union regulation, irrespective of the route. It includes oral nutritional supplements, and nutrition via nasogastric or nasoenteral or percutaneous feeding tubes.

– *Early enteral nutrition.* The term 'early enteral nutrition' is used to encompass all forms of nutritional support that involve the use of "dietary foods for special medical purposes" and that are administered to the patient within 24-48 h of admission, irrespective of the administration route. Its use has been associated with a reduction in infectious complications and mortality in critically-ill patients.

– *Complementary parenteral nutrition (CPN).* It has been defined as the administration of parenteral nutrition supplemental to enteral nutrition, when the calculated nutritional requirements of the patient are not met with enteral intake. CPN should be started when 60% of nutritional requirements are not met at the fourth day of admission, or for at least 2 consecutive days during the hospital stay.

– *Peripheral parenteral nutrition.* This is a type of parenteral nutrition that allows to deliver nutrients directly to the bloodstream via a peripheral line because it has a lower osmolarity than conventional total parenteral nutrition (below 600-900 mOsm/L). Consequently, in most cases the protein-calorie needs of the patient are not met and, therefore, it is only indicated for short periods or until a central venous access is available to allow total parenteral nutrition to be started.

– *Total parenteral nutrition.* The term 'total parenteral nutrition' will be used to encompass all forms of nutritional support that involve the use of intravenous solutions of nutritional substrates (glucose, lipids and amino acids, as well as vitamins and trace elements) and that replace in their entirety the administration of oral or enteral nutrition.

– *Adjusted weight.* Intermediate measure between actual weight and ideal weight (Wi) used as a weight parameter when calculating energy requirements in obese patients. The formula for its calculation is:

Adjusted weight = Wi + correction factor × (actual weight - ideal weight)

Where the usual correction factor is 0.25 for obesity types I and II, and 0.5 for morbid obesity.

– *Ideal weight.* Weight in relation to height associated with lower mortality and lower cardiovascular and metabolic risk for that patient. It can be adjusted using tables, with great interindividual variation, or using formulas. Among the most used is the Hamwi formula:

Men (Wi in kg): 48.08 + (height [cm] - 152.4/2.54) × 2.72
Women (Wi in kg): 45.35 + (height [cm] - 152.4/2.54) × 2.26

– *Calorie requirements.* Amount of nutrients (carbohydrates, fats and proteins) required to maintain an adequate nutritional state. It is recommended to calculate it by indirect calorimetry, though in clinical practice it is often done based on anthropometric variables (height, weight, age and sex), using different predictive equations, including the Harris and Benedit (HB) equation, which measures resting energy expenditure (REE). The calorie range for a critically-ill patient using the above HB equation is obtained by multiplying REE by a factor ranging from 1.1-1.5. It is sometimes simplified by administering an intake of 20-30 kcal/kg/day.

– *Nutritional risk.* The term is used to describe the possibility of a better or worse outcome of the disease or surgery according to current or future metabolic and nutritional status, and is defined by criteria of weight loss, body mass index, subjective global assessment and serum albumin.

– *Overfeeding syndrome.* Clinical condition seen in patients subjected to artificial nutrition that is characterized by hyperglycemia, hyperosmolarity and dehydration, hypertriglyceridemia, liver dysfunction (steatosis and/or cholestasis), azotemia, hypophosphatemia and altered immune function. Its incidence is increased with use of total parenteral nutrition.

Conflicts of interest

The members of the working group who have participated in the preparation of these recommendations have collaborated previously in activities financed by the pharmaceutical industry for marketing of nutritional products. These activities correspond to participation in clinical trials and educational programs, as well as financial assistance for attendance of scientific events.

No pharmaceutical industry has participated in the preparation, discussion, writing and establishing of evidence in any stage of these recommendations.

The process of translation into English by an independent external company, an extraordinary meeting of the GTMyN for the definitive written recommendations, and publication in the print journals that are the official organ of expression of the two scientific societies participating in the consensus, were possible thanks to the support of Abbott Nutrition.

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Chapter 2
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Indications, timing and routes of nutrient delivery

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Abstract

This article discusses basic features of nutritional support in critically-ill patients: general indications, the route of administration and the optimal timing for the introduction of feeding. Although these features form the bedrock of nutritional support, most of the questions related to these issues are lacking answers based on the highest grade of evidence. Moreover, prospective randomized trials that might elucidate some o f these questions would probably be incompatible with good clinical practice. Nevertheless, nutritional support in critically-ill patients unable to voluntarily meet their own nutritional requirements is currently an unquestionable part of their treatment and care and is essential to the successful management of their illness.

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Key words: *Early enteral nutrition. Parenteral nutrition. Postpyloric nutrition.*

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: INDICACIONES, MOMENTO DE INICIO Y VÍAS DE APORTE

Resumen

En este artículo se recogen aspectos básicos del soporte nutricional en los pacientes críticos: el relacionado con las indicaciones generales, la vía de administración y el momento más indicado para su inicio. pese a ser aspectos referidos a los cimientos del soporte nutricional, todavía no se ha podido responder con grado máximo de evidencia a la mayoría de las cuestiones que plantea y, además, probablemente no puedan realizarse estudios prospectivos y aleatorizados en el futuro que den respuesta a estas cuestiones, por invadir aspectos incompatibles con la buena práctica clínica. pese a todo ello, hoy día el soporte nutricional de los pacientes críticos, con incapacidad para recibir de forma voluntaria todos los requerimientos nutricionales necesarios, es un punto indiscutible del tratamiento y cuidado que necesitan los pacientes críticos para afrontar con éxito la enfermedad.

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Palabras clave: *Nutrición enteral precoz. Nutrición parenteral complementaria. Nutrición pospilórica.*

Introduction

Nutritional support (NS) is an essential part of the treatment of the critically-ill patient who cannot take oral food. The hypermetabolism characterizing these patients leads them quickly to a state of acute malnutrition[1]. This state of malnutrition and lack of nutritional support is associated with a poorer clinical prognosis[2].

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

Specialized NS (SNS) not only has nutritional interest, but is also a tool to modify the response of the body against aggression. Certain nutrients and their route of administration have a prominent role at specific times in the course of the critically-ill patient.

NS can be administered by the enteral route (EN, enteral nutrition) and/or by the intravenous route (PN, parenteral nutrition), with different access routes, different complications and disparate efficacy.

Is specialized nutritional support indicated in critically-ill patients?

Many patients cannot be nourished orally while admitted to the intensive care unit (ICU). It is not possible to conduct controlled studies, on ethical grounds, to establish what period of fasting should be considered for indicating SNS. There have been reports of increased mortality and longer ICU stay in malnourished than normonourished patients[3]. Although it is necessary to go back to the study by Sandstrom et al.[4] to confirm increased mortality due to nonadministration of NS to patients who did not take oral food for 14 consecutive days, recent studies in critically-ill patients have shown that the cumulative deficit in calorie intake is associated with more complications, both infectious and noninfectious, and a longer period of mechanical ventilation than with complete nutritional intake[5]. A recent meta-analysis analyzing published intention-to-treat studies showed greater mortality in patients receiving delayed enteral nutrition than in those receiving early parenteral nutrition, suggesting that combating malnutrition is more important than the route of nutritional support itself[5] (Ia). In critically-ill patients who will not receive a complete oral diet for 3 days, specialized nutritional support should be started, both enteral[6] (IV) and parenteral[7] (IV).

Does early administration result in a different prognosis?

Early administration of SNS is an indicator of healthcare quality in critically-ill patients[8]. At present, there are several clinical guidelines recommending that EN should be started in these patients within 24-48 h of admission to the ICU[7,9,10] (IV).

Early administration has been associated in some groups of critically-ill patients with improved tolerance of the diet, decreased intestinal barrier dysfunction, reduction of infections and days of hospitalization[11] (Ia), and a decrease in days of mechanical ventilation[12] (Ib).

A problem when analyzing this subject is the inconsistency in the definition of early administration, ranging from 24 to 72 h from admission to the ICU. In addition, the control groups were not uniform, comparing early EN with PN, with delayed EN, with standard care/intravenous fluids or oral nutrition, once intestinal transit is reestablished.

Currently, several meta-analyses in different patient groups in which this problem has been studied have confirmed a significant decrease in mortality and hospital stays in patients with intestinal surgery. A significant reduction in infections and hospital stay was confirmed in a mixed group of acute patients[13] (Ia).

In a meta-analysis that analyzed 14 randomized trials of patients admitted to ICUs[10], a downward trend in mortality ($p = 0.06$) and a statistically significant reduction in infectious complications was found in the early EN group[10] (Ia), though there were no differences in other variables, including length of stay or days on mechanical ventilation. In another recent meta-analysis, early initiation of EN support in the first 24 hours after admission or the aggression was analyzed. Six randomized clinical trials involving 234 patients were included, revealing a significant decrease in mortality and the incidence of pneumonia in the group nourished within 24 hours. While this is the first meta-analysis that has shown a reduction in mortality attributable to early administration of NS, as not all groups of critically-ill patients are represented, the authors themselves recommend the judicious application of these findings in clinical practice[14] (Ia).

When should the calorie objective be achieved?

Several studies have reported that the cumulative calorie deficit in critically-ill patients is associated with an increased rate of infectious complications and a longer ICU stay[5,6] (III).

However, it is not clear what the calorie objective should be and in what period it should be reached. The studies analyzed show that an increase for a short interval in energy intakes may be associated with a better course. A randomized study in patients with severe head injury (SHI) who were administered early EN with a rapidly progressing regimen, showed that patients with a more rapid administration had a significant reduction in the rate of infections and improved neurological scores[15] (Ib). A program for implementing nutritional guidelines in critically-ill patients revealed that patients who achieved a greater nutritional intake during the first week had a downward trend in mortality (27 *vs* 37%; $p = 0.058$) and hospital stay[16] (Ib).

There are no studies proposed on the period to achieve the established energy objectives. The period in which these objectives are to be reached, according to the recommendations of some authors, would be about 48-72 hours after the start of nutritional support[9] (IV).

Does the administration route of nutritional support influence the prognosis of critically-ill patients?

Studies in experimental animals have shown that NS via the parenteral route leads to a change in the intestinal microbiota, loss of intestinal barrier function, disturbances in intestinal macrophage function, and increased release of cytokines[17]. Studies in humans conducted in the 1990s, referring particularly to patients with abdominal trauma and in the postoperative context of abdominal surgery, have shown that when administration of PN is compared with the enteral route in patients with a functional gastrointestinal tract, the use of PN is associated with a significantly higher rate of infection and days of hospitalization[18,19] (Ib).

A systematic review analyzing 13 randomized trials comparing use of the enteral route with the parenteral route in critically-ill patients found that patients with PN showed a higher number of infectious complications than the group with EN. Some studies included reported lower costs and a lower hyperglycemia rate when using the enteral route, though no difference was seen in mortality or in duration of mechanical ventilation[20] (Ia). Some authors[21] have considered that the higher rate of infectious complications associated with PN could be related to less strict glycemia management protocols than those used currently. A recent review noted that some of the severe complications of PN referred to more than 2 decades ago. These do not occur today due to increased knowledge of PN in terms of calorie and protein needs, which has decreased provision of macronutrients, as well as improved control of glucose levels and improved management of central catheters[22] (IV).

A meta-analysis on intention-to-treat studies[5] (Ia) states that patients receiving EN initiated more than 48 hours after ICU admission had greater mortality than the group with PN, which led authors to recommend the use of PN if critically-ill patients were not able to receive EN in the first 24 hours, arguing that the complications associated with malnutrition for not starting nutrition early were greater than the complications from parenteral administration.

The access technique and protocol for maintenance of the IV catheter for PN or the feeding tube for the EN, as well as the different composition of nutrients for parenteral or enteral administration, and the method of delivery of both administration routes, are the origin of the different complications related specifically to the route of administration. In the incidence study of complications conducted by the Metabolism and Nutrition Working Group of the SEMICYUC in 2005, including over 800 patients with SNS, a different rate of complications was observed referring specifically to the route of administration[23,24].

What are the indications for postpyloric enteral nutrition?

The mechanical complications of EN are very common, particularly increased gastric residue due to sustained gastroparesis. This complication frequently leads to inadequate intake or even to discontinuation of the diet. The prevalence study of complications of SNS conducted by the Metabolism and Nutrition Working Group of the SEMICYUC in 2005 shows up to 25% of discontinuation of the diet at some time during treatment as a result of this complication[23]. It has been shown using radioisotopes that patients with a nasojejunal tube have a lower rate of microaspirations than with a nasogastric tube[25] (Ib). However, when it was attempted to relate this finding to a lower rate of pneumonia from bronchial aspiration, no benefit was found[26] (Ib). In a meta-analysis[27] (Ia) of 11 randomized trials comparing the gastric and jejunal routes, no reduction was seen in the rate of pneumonia, both with simple jejunal tubes or double lumen tubes for gastric decompression. To this should be added the difficulty in tube insertion, the frequent need for accessory techniques for placement and the higher rate of complications in their use. In specific conditions, such as severe acute pancreatitis, or in patients with elevated gastric output, their use may be considered for the purpose of reducing the use of PN in these patients[28].

What are the indications for complementary parenteral nutrition?

Several studies[16,29] (IIa) have shown that in daily clinical practice it is difficult to reach the nutritional objectives during the first days of hospitalization due to discontinuations of the diet related to gastrointestinal intolerance[30] or other reasons (radiological examinations, endoscopic techniques, surgical procedures), with the result that nutritional intake in up to 60% of patients is less than that prescribed[31]. The low intake of EN is associated with increased complications[32]. Numerous authors recommend that at least 80% of needs should be covered, though the objective should be 100% of nutritional requirements[33,34] (IV). However, some studies show surprising results, in the sense that critically-ill patients do not appear to benefit from the complete provision, suggesting that it is more appropriate to administer 33-66% of nutritional objectives[35] (IIb). There is agreement in all recommendations to prevent hypernutrition. Some groups of experts recommend combining complementary PN if after 72 hours from admission at least 60% of calorie and protein needs[34] (IV) has not been achieved.

In the patients who did not receive the planned intake of EN and whose requirements were completed with PN, a reduction in hospital stay has been noted, with no difference in the mortality rate[36] (Ib). In these cases, a daily assessment of the amount to be supplemented should be performed to prevent exceeding nutritional needs[8] (IV). In patients with intact gastrointestinal tract, PN started at the same time with EN does not have benefits[37] (IV).

Recommendations

– Critically-ill patients who are not expected to receive a complete oral diet for at least 3 consecutive days should receive specialized nutritional support (C).

– In critically-ill patients, enteral nutrition started early decreases infectious complications and length of stay, and shows a trend towards reduction in mortality (A).

– In certain groups of critically-ill patients, earlier enteral administration (within 24 hours) significantly reduces mortality and incidence of pneumonia (A).

– An attempt should be made to cover the energy objective within the first 48-72 hours after onset of enteral support (C).

– Parenteral nutrition is associated with a higher rate of infectious complications than enteral nutrition, but no differences have been shown in mortality or days of mechanical ventilation (A).

– Delay in reaching the nutritional objectives with enteral nutrition may be associated with complications that outweigh its benefits over parenteral nutrition (B).

– Complementary parenteral nutrition should be started when 60% of nutritional requirements are not met at the fourth day of admission, or for at least 2 consecutive days during the hospital stay (C).

– Routine or standard use of the nasojejunal tube in critically-ill patients is not associated with increased efficacy in provision of enteral nutrition or a lower rate of infectious complications (A). In a situation of persistent increase in gastric output with a high risk of bronchial aspiration or severe pancreatitis, its use can be considered (C).

Conflicts of interest

The authors state that they have participated in activities financed by the pharmaceutical industry for marketing of nutritional products (clinical studies, educational programs and attendance at scientific events). No pharmaceutical industry has participated in the preparation, discussion, writing and establishing of evidence in any stage of these recommendations.

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Chapter 3
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Nutritional assessment

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Abstract

Current parameters to assess nutritional status in critically-ill patients are useful to evaluate nutritional status prior to admission to the intensive care unit. However, these parameters are of little utility once the patient's nutritional status has been altered by the acute process and its treatment. Changes in water distribution affect anthropometric variables and biochemical biomarkers, which in turn are affected by synthesis and degradation processes. Increased plasma levels of prealbumin and retinol —proteins with a short half-life— can indicate adequate response to nutritional support, while reduced levels of these proteins indicate further metabolic stress. The parameters used in functional assessment, such as those employed to assess muscular or immune function, are often altered by drugs or the presence of infection or polyneuropathy. However, some parameters can be used to monitor metabolic response and refeeding or can aid prognostic evaluation.

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Key words: *Nutritional status. Biochemical variables. Energy balance.*

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: VALORACIÓN DEL ESTADO NUTRICIONAL

Resumen

Los parámetros existentes para valorar el estado nutricional en los pacientes críticos tienen utilidad para evaluar el estado de nutrición previo al momento del ingreso en la unidad de medicina intensiva. Sin embargo, su valor es escaso una vez interferidos con los cambios derivados de los procesos agudos y por su tratamiento. Así, los cambios en la distribución hídrica alteran especialmente las variables antropométricas y algo similar ocurre con los principales biomarcadores bioquímicos, que además se ven afectados por los procesos de síntesis y degradación. El incremento plasmático de las proteínas de vida media corta, prealbúmina y retinol, nos puede informar de una respuesta adecuada al soporte nutritivo y su disminución, de nuevas situaciones de estrés metabólico. Los parámetros de estimación funcional, como los de función muscular o los inmunológicos, están interferidos en muchos enfermos por fármacos o por la presencia de infección o polineuropatía. Sin embargo, algunos parámetros sí que se pueden utilizar para monitorizar la respuesta metabólica y la renutrición o bien son de importancia pronóstica.

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Palabras clave: *Estado nutricional. Variables bioquímicas. Balance calórico.*

Introduction

In the physiopathology of malnutrition related to critical illness, a significant role is played by the different levels of acute or chronic inflammation, leading to an altered body composition and a loss of functions including cognitive, immune and muscle function[1,2] (IV). Increased catabolism may in more severe cases contribute to mortality or, conversely, be self-limited if the critical disease itself is resolved[1] (IV).

The assessment of nutritional status in critically-ill patients aims:

– To assess nutritional status at the time of admission to the intensive care unit (ICU).
– To identify the group of patients most likely to benefit from receiving nutritional support.

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

– To identify individually the causes and consequences in terms of morbidity and mortality of malnutrition.
– To identify the limits of the different available techniques of nutritional assessment and their applicability to critically-ill patients.

What value do anthropometric variables and structured questionnaires have in the nutritional assessment of the critically ill?

Weight

It measures in a simplified way total body components. Its diagnostic capacity as an indicator of nutritional status may be improved if it is used to construct indicators such as percent weight loss and body mass index (BMI). An involuntary weight loss greater than 10% within the last 6 months or current weight below 90% of the ideal weight are classical signs of malnutrition. It is an adequate indicator in surgery and chronic diseases and of malnutrition on admission.

Body mass index

It evaluates the correlation between weight and height. Indices < 18.5 kg/m^2 are indicative of malnutrition and are associated with a significant increase in mortality in surgical patients. In contrast, indices > 30-35 kg/m^2 suggest overweight-obesity and allow to assess overnutrition. It has recently been observed that critically-ill patients with higher BMI values showed a greater risk of developing acute respiratory distress syndrome and a longer hospital stay than patients with normal weight[3] (IIb).

Other anthropometric variables

The most commonly used are the triceps skin fold and arm circumference (AC). While the former is the most widely used method to estimate subcutaneous body fat and AC has been postulated as an indicator of the state of preservation of the muscle compartment, both methods are of little value in the nutritional assessment of the critically ill.

Subjective global assessment

It is the structured questionnaire that has been validated in a large part of the population, based on clinical interpretation and on some symptoms and physical parameters. The subjective global assessment (SGA) of nutritional status, performed by experts, is a good indicator of malnutrition and may predict the course of ICU patients[4] (III), though this appears to be questioned in elderly patients[5] (III). Evaluated by experts, it is the most reliable malnutrition parameter on admission.

What biochemical variables are recommended for assessing the nutritional status of the critically ill?

As with anthropometric parameters, biochemical variables are affected by the response of the body in the acute phase and are influenced by nonnutritional disorders in critically-ill patients, so their interest in interpreting nutritional status is limited.

Biochemical variables indicative of muscle protein status[6,7] (III)

– Creatinine/height index. This measures muscle catabolism. Its values are influenced by the amount and protein content of the diet and age. It is not a useful parameter in renal failure. In critically-ill patients, this index detects malnutrition on admission, but has no prognostic or follow-up value alone.

– 3 methylhistidine (3-MH). It is an amino acid derived from muscle protein metabolism. Its values increase in situations of hypercatabolism and decrease in the elderly and malnourished patients. In critically-ill patients, it is a parameter for monitoring nutrition, renutrition, and muscle catabolism.

– Urea excretion. This is a standard method for measuring protein catabolism. It also estimates creatinine and uric acid loss. Its values vary in relation to intravascular volume, nitrogen intake and renal function. In the critically-ill patient, it is an index of the intensity of the metabolic response to stress.

– Nitrogen balance. It is a good renutrition parameter in postoperative patients with stress or moderate malnutrition. It may be useful to establish if a patient is catabolic, in equilibrium, or anabolic. In critically-ill patients, it is not valid as a parameter for malnutrition and nutritional monitoring, but as an index of nutritional prognosis. To monitor nitrogen intake, urea may also be used.

Biochemical variables indicative of visceral protein status[6-8] (III)

– Albumin. It is the biochemical parameter most commonly used for nutritional assessment. A significant reduction in albumin concentrations is associated with an increased rate of complications and mortality. Its plasma concentration is highly influenced by changes in water content. Albumin values on admission are prognostic. However, these values are poorly sensitive to acute changes in nutritional status due to the long half-life of albumin of about 20 days.

– Prealbumin or transthyretin. Its half-life, 2 days, makes it a parameter for monitoring the course of critically-ill patients, where it has been seen that is the most sensitive parameter to changes in nutritional status. However, its values are affected by factors unrelated to this status. Its plasma concentration may reflect both a state of malnutrition or be the consequence of the severity of the underlying condition, so its values are not suitable for monitoring nutritional status in patients with systemic inflammatory response. Nevertheless, there are also studies showing its value on admission and as a good predictor of nutritional risk and morbidity and mortality in patients with artificial nutrition[9,10].

– Retinol-binding protein. Its short half-life, 12 h, also makes it a marker for nutritional monitoring, but its values do not rise rapidly with nutritional support until an anabolic status has returned. Its values increase with vitamin A intake, and decrease in liver disease, infection and severe stress. It has a relative value in patients with renal failure.

– Transferrin. It has a low sensitivity and specificity when analyzed individually. Its plasma values are increased in iron deficiency anemia and decreased in liver disease, sepsis, malabsorption syndrome and non-specific inflammatory states.

Chronic iron deficiency, multiple transfusions, and changes in intestinal absorption invalidate it as a nutritional parameter in critically-ill patients. Its half-life is 8-10 days.

– Somatomedin. This is a low molecular weight peptide, whose synthesis is regulated by the growth hormone and insulin factor 1. It has a short half-life and is stable in serum. It is a good marker of nitrogen balance in severely-ill and hypercatabolic patients and a good parameter for nutritional monitoring of malnourished patients. It has prognostic values for mortality in critically-ill patients with acute renal failure[11] and has been shown to be a more appropriate parameter than transferrin and retinol-binding protein for assessing metabolic status in surgical patients during the stress phase since, unlike these parameters, it is not influenced by the stress level of the patient[6]. Complexity of its measurement and its high cost limit its use.

– Cholesterol. A low serum cholesterol value has been observed in malnourished patients, with renal failure, liver failure and malabsorption syndrome. The presence of hypocholesterolemia may be suggestive of malnutrition in critically-ill patients and is associated with an increase in mortality.

What functional estimation parameters are useful in nutritional assessment of the critically-ill patient?

Muscle function parameters[5] (III)

Analysis of muscle strength, both actively (strength of respiratory muscles, grasping capacity) and passively (contraction and muscle relaxation response to different electrical intensities), was used as an indicator of nutritional status. Its values were more sensitive and specific in predicting surgical complications, than biochemical markers such as albumin or transferrin[12]. However, in critically-ill patients muscle function tests may be altered by highly diverse factors such as the use of sedation analgesia, muscle relaxants or the presence of myopathy and/or polyneuropathy.

Immune function parameters

The reduced total lymphocyte count (< 1,500), CD3/CD4 ratio (< 50) and absence of the delayed cell mediated immune response have been associated with malnutrition. In critically-ill patients, both lymphocyte counts and immune function tests may be altered by a large number of clinical situations or by medication. These parameters may be of value in monitoring the course of critically-ill patients showing a deficiency in immunity on admission.

The activity of mitochondrial complex I in peripheral blood mononuclear cells decreases with malnutrition and rapidly increases after refeeding, and thus may be a good marker of the nutritional status[13] (IIb).

There is no evidence of its usefulness in critically-ill patients or in the study of possible confounding factors in such patients. Measurement of the apoptosis rate of oral epithelium may be another noninvasive technique to determine nutritional status, though this technique requires further studies for it to be validated[14] (III).

Are nutritional prognostic indices of value in critically-ill patients?[6,12] (III)

These indices have been designed for predicting surgery risk, the development of postoperative complications and the indication to start nutritional support on patient admission, based on assessment of nutritional status. They are not adapted to critically-ill patients and are of little value in them.

Are there other less common parameters useful for nutritional assessment in critically-ill patients?

The difficulty in assessing the presence of malnutrition in critically-ill patients leads to the need to search for other methods for its detection. Neutron activation analysis, which measures total body nitrogen, bioelectric impedance, which allows calculation of total body water volume, and potassium isotopes, which are used to estimate total lean tissue mass, are techniques of limited clinical value in critically-ill patients at present. Energy balance (defined as the difference between the prescribed calories and dietary administered calories) and the adaptation of diet are valid tools, since a low-calorie diet and persistently

Table I
Assessment and follow-up parameters

When to measure	*Parameter*
On admission	Weight, height, weight loss, BMI, albumin, cholesterol
Daily	Energy balance, urea
Once a week	Adjust requirements to stress factor, nitrogen balance, creatinine/height index, prealbumin, retinol-binding protein (RBP) changes

BMI: Body mass index.

negative energy balances are associated with adverse clinical outcomes[15] (IIb).

Serum leptin concentrations may be a good predictor of nutritional status, as has been shown in studies done in the elderly, but there is still not sufficient evidence for their value in critically-ill patients[16,17].

Recommendations

– The anthropometric parameters or biochemical markers most commonly used to evaluate nutritional status should not be recommended in clinical practice in critically-ill patients (C).

– To assess nutritional status on admission, weight loss, BMI or SGA may be used. To monitor renutrition, nitrogen balance, prealbumin, retinol and 3-MH may be used. To assess metabolic response, urea excretion, nitrogen balance and 3-MH may be useful. As prognostic parameters, nitrogen balance and albumin may be used (C).

As a guide, the assessment and follow-up parameters proposed in Table I may be used.

Conflicts of interest

The authors state that they have participated in activities financed by the pharmaceutical industry for marketing of nutritional products (clinical studies, educational programs and attendance at scientific events). No pharmaceutical industry has participated in the preparation, discussion, writing and establishing of evidence in any stage of these recommendations.

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Chapter 4

Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Macronutrient and micronutrient requirements

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Abstract

Energy requirements are altered in critically-ill patients and are influenced by the clinical situation, treatment, and phase of the process. Therefore, the most appropriate method to calculate calorie intake is indirect calorimetry. In the absence of this technique, fixed calorie intake (between 25 and 35 kcal/kg/day) or predictive equations such as the Penn State formula can be used to obtain a more accurate evaluation of metabolic rate.

Carbohydrate administration should be limited to a maximum of 4 g/kg/day and a minimum of 2 g/kg/day. Plasma glycemia should be controlled to avoid hyperglycemia. Fat intake should be between 1 and 1.5 g/kg/day. The recommended protein intake is 1-1.5 g/kg/day but can vary according to the patient's clinical status.

Particular attention should be paid to micronutrient intake. Consensus is lacking on micronutrient requirements. Some vitamins (A, B, C, E) are highly important in critically-ill patients, especially those undergoing continuous renal replacement techniques, patients with severe burns and alcoholics, although the specific requirements in each of these types of patient have not yet been established. Energy and protein intake in critically-ill patients is complex, since both clinical factors and the stage of the process must be taken into account. The first step is to calculate each patient's energy requirements and then proceed to distribute calorie intake among its three components: proteins, carbohydrates and fat. Micronutrient requirements must also be considered.

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Key words: *Macronutrients. Micronutrients. Enteral nutrition. Parenteral nutrition.*

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RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: REQUERIMIENTOS DE MACRONUTRIENTES Y MICRONUTRIENTES

Resumen

Los pacientes críticos presentan modificaciones importantes en sus requerimientos energéticos, en las que intervienen la situación clínica, el tratamiento aplicado y el momento evolutivo. Por ello, el método más adecuado para el cálculo del aporte calórico es la calorimetría indirecta. En su ausencia puede recurrirse al aporte de una cantidad calórica fija (comprendida entre 25-35 kcal/kg/día) o al empleo de ecuaciones predictivas, entre las cuales la fórmula de penn State proporciona una evaluación más precisa de la tasa metabólica.

La administración de carbohidratos debe tener un límite máximo de 4 g/kg/día y mínimo de 2 g/kg/día. Deben controlarse los valores de glucemia plasmática con el fin de evitar la hiperglucemia. Respecto al aporte de grasa, debe estar entre 1-1,5 g/kg/día. El aporte proteico recomendado se encuentra entre 1-1,5 g/kg/día, aunque puede variar en función de las características de la propia situación clínica.

Debe prestarse una atención especial al aporte de micronutrientes. No hay un acuerdo unánime sobre los requerimientos de éstos. Algunas de las vitaminas (A, B, C, E) son de gran importancia para los pacientes en situación crítica, con especial atención en pacientes sometidos a técnicas continuas de reemplazo renal, grandes quemados y alcohólicos, aunque los requerimientos específicos para cada uno de ellos no han sido establecidos. El aporte de los requerimientos energéticos y proteicos a los pacientes críticos es complejo, dado que debe tener en cuenta tanto las circunstancias clínicas como su momento evolutivo. La primera fase del proceso es la del cálculo de las necesidades energéticas de cada paciente para, en una fase posterior, proceder a la distribución del aporte calórico entre los 3 componentes de éste: proteínas, hidratos de carbono y grasas, así como considerar la necesidad de aportar micronutrientes.

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Palabras clave: *Macronutrientes. Micronutrientes. Nutrición enteral. Nutrición parenteral.*

What methods can we used to estimate requirements and energy supply?

Indirect calorimetry and Fick method

Indirect calorimetry is the method clinically considered as gold standard. It shows several problems for its application, such as expensive equipment, need for time to perform measurements, staff with experience and lack of availability in most units. In addition, it tries to predict total energy expenditure (TEE) based on measurements performed within a short time interval (5-30 min), evidencing changes up to 20% during the day. Thus, to resting energy expenditure (REE) we should add 15-20% to calculate TEE, though it is most accurate to maintain the measurements for24 h to establish TEE[1] (III). The Fick method has not shown a good correlation with calorimetry and is rarely used in daily practice[2,3] (III).

Estimation methods

The literature includes over 200 formulae to estimate the energy expenditure (EE), none of which have shown a good correlation to measurements taken by indirect calorimetry. However, its use is recommended when calorimetry cannot be performed. For selecting the most appropriate formula, the type of patients evaluated to define them must be considered[4,5] (IIb). A study has been recently published, that includes 202 critical patients undergoing mechanical ventilation comparing indirect calorimetry using different formulas to calculate baseline EE. The authors concluded that the Penn State formula provides a more precise evaluation of the metabolic rate in critically-ill patients on mechanical ventilation[6] (Ib).

Correlation between measured and calculated energy expenditure

All the methods have shown a poor correlation with the EE measured, with overestimation in 80% of the cases, so it is considered that critically-ill patients are often a different population than that used as the basis for these formulae. The correlation is not good because the multiple variables of critically-ill patients[7] are not considered (III). A recent study shows that there is no good correlation between the intake of a fixed amount of calories (25 kcal/kg/day) and indirect calorimetry[8] (IIa), obtaining better results with the latter.

Energy supply

The needs will change based on the metabolic phase where the patient is: initial catabolic phase or recovery anabolic phase. If EE cannot be measured, a supply as close as possible to the requirements measured by indirect calorimetry in the initial phase is recommended to increase in more advanced convalescence phases, based on studies that show a higher incidence of infections as compared to negative calorie balance[9,10] (III) and better results with a positive calorie balance[11] (Ib). Some authors recommend supplementing with parenteral nutrition (PN) when the requirements are not met (60-70% of enteral supply). A meta-analysis of studies comparing enteral nutrition (EN) with mixed nutrition, applied from the patient admission, shows no lower incidence of infectious complications, days of stay at ICUs, or days on mechanical ventilation[12] (Ia).

The weight to be used in the formula will depend on body mass index (BMI) (see chapter 12). In patients with BMI < 18 kg/m^2 it is recommended to use the current weight, to prevent renutrition syndrome, and for all other patients the weight prior to the aggression, as the current weight shows major changes as a result of the initial resuscitation.

In recent years permissive hypoalimentation during the first phases of the critically-ill patient (18 kcal/kg body weight/day) is becoming increasingly accepted[13] (III), expecting to achieve the full objective of the requirements (25 kcal/kg/day) after the first week. Recent studies support this approach finding better clinical outcomes when calorie intake, during the first days of the catabolism phase, is between 33 and 66% of the estimated requirements[14] (IIb). Lower supplies would be associated with an increased number of bacteremias[15] (III) and higher with a higher complication rate[16] (IV). However, this recommendation cannot be established without a prospective study, which is not available yet.

What type of carbohydrates and what amount should be supplied in critically-ill patients?

Glucose is still the main calorie substrate in critically-ill patients. A glucose infusion at 4 mg/kg/min only suppresses neoglucogenesis in 50% and protein catabolism in 10-15%, so it is recommended never to administer a glucose supply greater than 4 g/kg/day. In general, carbohydrates represent 50% of the global energy requirements, though this percentage may vary depending on individual factors and the severity of aggression. Because of the supply and the metabolic stress, hyperglycemia occurs and has been associated with poorer clinical outcomes[17] (III). Multiple studies and meta-analyses were performed[18,19] (Ia), some of which recommend maintaining blood sugar at values between 140 and 180 mg/dL, using insulin if this limit is exceeded , though there is no consensus about the most appropriate limit value (see chapter 10). Higher values would be related to worse clinical outcomes, particularly in infectious complications, and attempting to maintain lower values would be associated with a higher incidence of severe hypoglycemia, without achieving benefitial effects on mortality.

In PN they are administered as dextrose and in EN as more complex sugars, disaccharides, maltodextrins, and starches, usually using those with a lower glycemic index.

What type of lipids and what amount should be provided in critically-ill patients?

Lipid intake must be a fundamental part of nutritional support since, in addition to providing energy in a small volume, it is essential to prevent essential fatty acids deficiency (at least 2% of calories as linoleic acid and at least 0.5% as linolenic acid) and to maintain the structure of cell membranes, and also to modulate intracellular signals[20,21] (IIb). Compared to carbohydrates, lipid supply causes a lower effect on thermogenesis, lipogenesis, stimulation of insulin release, CO_2 production and glycemia values. It is generally considered that ω-3 fatty acids may counteract the proinflammatory effects of ω-6[22] (III).

Fat supplying is safe and well tolerated at an amount of 0.7 to 1.5 g/kg/day[23] (IIa). It should be administered at concentrations of 30 or 20% vs 10%, resulting from a decreased supply of phospholipids (phospholipids/triglycerides ratio of 0.04 at the 30% concentration) and longer perfusions rather than in short periods to prevent changes in pulmonary ventilation/perfusion. There are various commercial formulations in the form of long-chain triglycerides (LCT), but currently the mixtures with middle-chain triglycerides (MCT), fish oil, or olive oil have been shown to be well tolerated and are used with preference over LCT. However, it is difficult to make a specific choice on the type to be used as non of them has shown significant advantages over the other[24,25] (IIb). They must not be administered, or their supply should be reduced, when plasma triglyceride levels are greater than 400 mg/dL[26]. Up to 40% of non-protein calories may be provided. With regard to EN, diets with a high ω-3 content from fish oil should be particularly indicated for patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS)[27] (Ib), [28] (III) (see chapter 8).

What protein requirements and what type must be provided in critically-ill patients?

Although nitrogen losses can be very high, particularly in patients with injuries and burns, very high supplies are not recommended, as while protein supply at an amount of 1.5 g/kg/day decreases protein catabolism by 70%, its increase to 2.2 g/kg/day causes an increase in net protein degradation[29].

In PN, the normal supply is provided by formulations of standard amino acids, where the composition in essential amino acids is similar to the requirements of healthy individuals. The enrichment of PN with branched chain amino acids has been tested, particularly in septic patients[30] (IIa), but there is not sufficient evidence to justify their use (see chapter 15).

Currently there is sufficient evidence for the routine use of glutamine in critically-ill patients[31] (IV), [32] (Ib), [33] (Ib), where it acts as a conditionally essential amino acid. In PN 0.3-0.5 g/kg/day as glutamine-alanine dipeptides are recommended, which are more stable and soluble. Supply in EN has also shown a morbidity and even a mortality reduction in burn and in trauma patients[34] (Ia), though it has not been demonstrated in heterogeneous groups of critically-ill patients yet. Improved control of glycemia metabolism has been confirmed in patients receiving parenteral glutamine, as it would help to reduce insulin resistance[35,36] (IIa).

Intact proteins are generally used in EN. Oligopeptides have shown no clinical benefits in terms of outcomes or gastrointestinal complications. With regard to arginine supply, combined with other substrates by EN, its use is questioned in some specific populations of critical patients (see chapter 15), but some studies found benefits using immunonutrition diets providing arginine[37] (Ib).

What vitamins and trace elements are considered necessary or essential in critically-ill patients?

A combination of antioxidant vitamins and trace elements, including selenium, zinc and copper, can improve outcomes in critically-ill patients[38,39]. A meta-analysis of 15 randomized studies evidences that a combination of antioxidant vitamins and trace elements reduces mortality and the duration of mechanical ventilation, though it does not improve infectious complications or length of stay[40] (Ia).

Vitamin requirements are not established in artificial nutrition for critically-ill patients, though the recommendations of the *Nutrition Advisory Group* of the American Medical Association (AMA-NAG) are followed. Other authors follow the RDA recommendations, even though it is very likely that these are far below the needs of the patients under aggression. Supplying thiamine, niacin, and vitamins A, E and C, as well as other vitamins from complex B is considered to be essential.

Recommendations

– The most reliable method in daily practice to calculate energy expenditure is indirect calorimetry (A). The Fick method and estimation methods do not show a good correlation with energy expenditure measured by indirect calorimetry in critically-ill patients (B).

– In the absence of indirect calorimetry, it is recommended to provide an amount of 25 kcal/kg of current weight/day in patients with a BMI < 30 (C). In patients on mechanical ventilation the estimated calculation of calorie requirements is recommended according to the Penn State equation (B).

– With regard to intravenous administration of glucose, it is not recommended to exceed a supply of 4 g/kg/day (B).

– It is recommended, as most appropriate, to maintain glycemia levels below 150 mg/dl (C).

– The recommended lipid supply in parenteral nutrition is 0.7-1.5 g/kg/day (B).

– Any type of lipid emulsion existing in the current market may be used (B), but it is recommended to avoid single ω-6 supplies in critically-ill patients (C).

– In critically-ill patients, no specific formulation of amino acids has been defined for generic use (C). In general, the supply must be adjusted to an amount of 1-1.8 g/kg/day (B).

– In critically-ill patients intravenous administration of glutamine dipeptides (Ala-Gln) of 0.5 g/kg/day is recommended, complementing parenteral nutrition (A).

– The need for supplying micronutrients (vitamins and trace elements) is set (A), but the amount cannot be established.

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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Chapter 5
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Acute renal failure

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Abstract

Nutritional support in acute renal failure must take into account the patient's catabolism and the treatment of the renal failure. Hypermetabolic failure is common in these patients, requiring continuous renal replacement therapy or daily hemodialysis.

In patients with normal catabolism (urea nitrogen below 10 g/day) and preserved diuresis, conservative treatment can be attempted. In these patients, relatively hypoproteic nutritional support is essential, using proteins with high biological value and limiting fluid and electrolyte intake according to the patient's individual requirements. Micronutrient intake should be adjusted, the only buffering agent used being bicarbonate.

Limitations on fluid, electrolyte and nitrogen intake no longer apply when extrarenal clearance techniques are used but intake of these substances should be modified according to the type of clearance. Depending on their hemofiltration flow, continuous renal replacement systems require high daily nitrogen intake, which can sometimes reach 2.5 g protein/kg. The amount of volume replacement can induce energy overload and therefore the use of glucose-free replacement fluids and glucose-free dialysis or a glucose concentration of 1 g/L, with bicarbonate as a buffer, is recommended.

Monitoring of electrolyte levels (especially those of phosphorus, potassium and magnesium) and of micronutrients is essential and administration of these substances should be individually-tailored.

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Key words: *Acute renal failure. Nutritional requirements. Extrarenal clearance.*

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

Resumen

El soporte nutricional en la insuficiencia renal aguda está condicionado por el catabolismo del paciente y por el tratamiento del fallo renal. En el paciente crítico es frecuente el fracaso hipermetabólico que obliga a técnicas continuas de reemplazo renal o a hemodiálisis diarias. En los enfermos con catabolismo normal (aparición de nitrógeno ureico inferior a 10 g/día) y diuresis conservada se puede intentar un tratamiento conservador. En estos casos es preciso realizar un soporte nutricional relativamente hipoprotéico, con proteínas de alto valor biológico y limitaciones hidroelectrolíticas individualizadas. Es necesario un ajuste del aporte de micronutrientes, siendo el bicarbonato el único buffer utilizado.

Cuando se utilizan técnicas de depuración extrarrenal desaparecen las limitaciones a los aportes hidroelectrolíticos y nitrogenados, pero éstos deben ser modificados en función del tipo de depuración. Los sistemas continuos de reemplazo renal, en función de su flujo de hemofiltración, precisan altos aporte nitrogenados diarios que en ocasiones pueden alcanzar los 2,5 g de proteínas/kg. La cuantía de la reposición de volumen puede inducir sobrecargas energéticas, siendo recomendable utilizar líquidos de reposición y diálisis sin glucosa o con una concentración de glucosa de 1 g/l, con bicarbonato como buffer.

Es preciso monitorizar los valores de electrolitos (sobre todo de fósforo, potasio y magnesio) y de micronutrientes, y realizar aportes individualizados.

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Palabras clave: *Insuficiencia renal aguda. Necesidades nutricionales. Depuración extrarrenal.*

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

Introduction

Acute renal failure has become increasingly common in critically-ill patients, related to factors such as hypotension or shock, aging of the population, use of nephrotoxic drugs (antibiotics, antifungals, combination of antihypertensives and antiinflammatories), multiple examinations with radiocontrasts and as organic failure in multiple organ system failure[1] (IIb).

Nutritional support in acute renal failure is aimed at preserving lean mass and energy reserve, preventing malnutrition, re-establishing an appropriate immune status, and reducing mortality, attenuating inflammatory response and oxidative stress, and improving endothelial function[2]. The lack of large adequately designed studies has precluded a high level of evidence on the recommendations. The heterogeneity of the patient group with renal failure requires a standardization that is to be established with the RIFLE classification (Risk, Injury, Failure, Loss, and End-stage kidney)[3].

Some years ago, water-electrolyte disorders and intolerance to substrate supply involved a frequently insurmountable stumbling block. Currently, treatment stratification by protein catabolism and diuresis, and the application of continuous and discontinuous renal replacement therapy techniques, based on the characteristics of each patient, allow for an adequate nutritional support.

Nutritional support in acute renal failure is related to the catabolism of the underlying disease, the type of treatment provided, the renal replacement technique used, and the presence of previous malnutrition, and is poorly modified by renal failure itself. Catabolism and treatment are essential for the composition of artificial nutrition. In general, patients with normal catabolism receive conventional treatment, stable patients with a moderately increased catabolism are treated with intermittent hemodialysis, and those with a hypercatabolic status are treated with continuous renal replacement techniques.

What are the protein needs and characteristics of their supply?

In these patients protein catabolism should be calculated by the "appearance of urea nitrogen" (AUN) (Table I), which allows for measuring the amount of urea nitrogen (in urine, in the dialyzate and retained due to lack of clearance) generated in catabolic processes[4]. In general, patients with AUN < 5 g/day will receive 0.6-0.8 g of protein/kg/day, and will be treated conservatively if they keep diuresis. Patients with AUN between 5 and 10 g/day require protein supplies of 0.8-1.2 g/kg/day. Based on diuresis and on electrolyte disorders they will receive conservative treatment or extrarenal clearance. When the AUN is > 10 g/day, these patients must receive 1.2-1.5 (and sometimes up to 2.5) g of proteins/kg/day. They require hemodialysis or continuous renal replacement techniques based on their hemodynamic stability[5,6] (IV).

Table I
Calculation of the appearance of urea nitrogen (AUN)

AUN (g/day) = UUN (g/day) + UND (g/day) + CU (g/day)
CU (g/day) = SUNc–SUNi (g/l) × iw (kg/day) × 0.6 + cw-iw (kg/day) × SUNc (g/l)
Total nitrogen output (g/day) = 0.97 × AUN (g/day) + 1.93

AUN: Appearance of urea nitrogen; CU: Changes in the "pool of organic urea"; UND: Urea nitrogen in dialysis fluid; SUNc: Current serum urea nitrogen; SUNi: Initial serum urea nitrogen; UUN: Urinary urea nitrogen; cw: Current weight; iw: Initial weight.

Conservative treatment

Supply must include essential and non-essential amino acids, recommending hypoproteic (up to 1.0 g protein/kg/day) diets (oral or enteral nutrition) with at least 20% of proteins with a high biological value. Exclusive supplies of essential amino acids and histidine are not recommended[7] (IIb).

Hemodialysis and peritoneal dialysis

These techniques allow for a protein supply without restrictions, but cause losses leading to increase the requirements. While protein catabolism degree is highly variable from one patient to another, they are usually patients with moderate hypercatabolism. Intermittent hemodialysis causes a loss of amino acids and peptides of 8-12 g and 1-3 g, respectively, in each session. In addition, depending on the biocompatibility of filters, an increase in inflammatory response may occur. Peritoneal dialysis causes daily protein losses of 13-14 g of proteins, that may increase to 18-20 g if peritoneal irritation occurs and exceed 100 g in severe peritonitis. Supplies of 1.2-1.4 g of proteins/kg/day are recommended in hemodialysis[8] (IV) and 1.2-1.5 g/kg/day in peritoneal dialysis. Diets and mixtures of standard amino acids are usually adequate in most patients[9] (IV).

Continuous renal replacement techniques

Continuous renal replacement techniques are applied to hypercatabolic renal failure requiring supplies of 1.3-1.5 g of proteins/kg/day, to which losses secondary to the technique used should be added. Studies by Davies[10] (IIb) on continuous arteriovenous hemofiltration and Frankenfield[11] (IIb) on venovenous hemofiltration verified daily losses of 10-15 g amino acids in the ultrafiltrate, with a negative glutamine balance (as this accounts for 16% of amino acids of the ultrafiltrate). In septic patients high-flow (more than 35 ml/kg/h)[12] (IV) and very high flow[13] hemofiltration techniques (III) are used, with higher losses. While

Frankenfield, Klein and Druml[14] consider it is adequate to provide 1.5 g of proteins/kg/day, Bellomo[15] (III) and Scheinkestel[16] (Ib), [17] (IIa) recommend supplies of 2.2-2.5 g/kg/day, particularly in continuous high-flow hemofiltration. The need for supplementing them with glutamine is discussed.

What are the energy requirements in acute renal failure?

Acute renal failure does not increase per se the energy requirements, and there may even be a "renal hypocatabolism", particularly in extrarenal clearance, for the hypothermia induced by these techniques. The requirements are established by indirect calorimetry or are calculated multiplying resting energy expenditure (REE) by 1.1-1.2. In the practice they correspond to 25-35 total kcal/kg/day[18] (IIb).

Conservative treatment

The diets or mixtures used will be rich in carbohydrates to limit hyperkalemia, hyperphosphatemia, and hypomagnesemia, that are common in these patients. Supplies of 25 kcal/kg body weight/day[19] (IV) are recommended, with cholesterol-low diets, and a lipid supply of < 1.2 g/kg/day. Occurrence of hypertriglyceridemia limits the amount of calorie intake.

Hemodialysis and peritoneal dialysis

Hemodialysis induces glucose losses, of approximately 25 g per session, while peritoneal dialysis, depending on glucose or polyglucose concentration in the dialysis fluid used, causes a significant glucose and lactate entry, that must be considered when measuring supplies. Patient age is important, and in those over 65 years, 30 kcal/kg/day should not be exceed[18] (IIb), [20] (IV).

Continuous renal replacement techniques

The most commonly used are continuous venovenous hemofiltration, requiring a high amount of replenishment fluid and continuous venovenous hemodiafiltration, requiring infusions of replenishment and dialysis fluid. As compared to mandatory daily loses of 25 g of glucose, inappropriate replenishment and dialysis fluids can include major glucose and lactate supplies[21] (IIb). Solutions free from glucose or with 1 g of glucose/L are recommended, with bicarbonate as *buffer*.

Energy supply should be adjusted to the stress level. As they are almost always hypercatabolic clinical states, protein supply must be high, with a low calorie/nitrogen ratio, limiting the energy needs to 25-35 total kcal/kg/day[22] (IIb).

What electrolyte and micronutrient supplies do patients with acute renal failure require?

The volume restriction is a limiting factor in acute renal failure on conservative treatment, but renal replacement techniques allow for liberalizing supplies and controlling water balance.

Electrolyte control

Conservative treatment requires close monitoring of sodium supply and controlling hyperkalemia, hypermagnesemia, hyperphosphatemia and metabolic acidosis. Extrarenal clearance techniques can maintain sodium, potassium, and bicarbonate within normal ranges (provided dialysis baths and replenishment fluids with bicarbonate and low lactate content are used). In hypermetabolic renal failure, continuous renal replacement techniques obtain better adjustments than intermittent hemodialysis[23] (IIa).

With regards to calcium, hypercalcemia may occur in the intermittent systems and hypocalcemia with continuous techniques, but in the practice they are only clinically relevant when citrate is to be used as system anticoagulant[24] (IIb).

The changes in phosphate values are more relevant. In the conservative treatment and intermittent hemodialysis (and in general in all systems using only the diffusion mechanism), hyperphosphatemia is very common. Nutritional support should be low in phosphates. On the contrary, continuous renal replacement techniques based on the convective mechanism cause major phosphate losses. Replenishment fluids are low in phosphorus to prevent their interaction with calcium and bicarbonate. A close monitoring of serum phosphorus levels is essential to detect severe hypophosphatemia and administer the appropriate supplements[25] (IIb).

Micronutrient supply

Trace elements are comprised in enzyme systems or in proteins, and their losses with extrarenal clearance systems are mild. Standard supplies are recommended in all patients with renal failure. Selenium values are reduced in critically-ill patients, with and without renal failure[26] (Ib). Due to their high antioxidant effect, high supplies are recommended in patients with continuous renal replacement techniques, though they may cause intoxication by selenates. Zinc is low in critically-ill patients, and its deficiency is enhanced with continuous hemofiltration. It must be supplemented, though the standard doses are sufficient[27] (IIa). Iron will be supplied in hyposideremia with low ferritin, but not in inflammation and in oxidative stress, with high ferritin[28] (IIb).

Water-soluble vitamins should be provided at standard doses in conservative treatment and in intermittent dialysis and double doses in patients with continuous procedures. The fear of causing oxalosis with administration of megadoses of vitamin C, limiting supply to 50 mg/day, explains the low values of this vitamin (very important antioxidant) in critically-ill patients, worsening with continuous hemofiltration. Low thiamine values are common despite supplements[26] (Ib).

Fat-soluble vitamins should be administered at standard doses, though in renal failure on conservative treatment or intermittent hemodialysis the dose of vitamin A should be reduced[27] (IIa).

Is there a specific nutritional formula for patients with acute renal failure? Do they require specific nutrients?

In non-hypercatabolic renal failure on conservative treatment or intermittent hemodialysis for oligoanuria, standard diets are inadequate due to their low density and excessive contents of sodium, potassium, and phosphates. Low- or normal-protein diets, with high biological value proteins, high energy density and low content in sodium, potassium and phosphates are recommended. With hemodialysis, normal diets may be used, but sometimes phosphorus chelating agents should be administered. A nitrogen supply only with essential amino acids and histidine is currently not indicated[29] (Ib).

Hypercatabolic patients, on daily dialysis or continuous renal replacement procedures, may be nourished with a high-protein diet, adjusted to the underlying disease[30]. Its composition should be based on the essentiality of some amino acids, requiring in some cases to increase the supplies of tyrosine, taurine, histidine, and branched-chain amino acids. In critically-ill patients, the underlying disease would justify using diets with pharmaconutrients in some cases. With hemofiltration, particularly if high or very high flows are used, the appropriateness of supplementing diets (or parenteral mixtures) with glutamine[31] (IV), [32] (IIb), should be considered, though the contraindication of administration in non-dialyzed renal failure persists.

What is the recommended supply route in acute renal failure?

Whenever possible nutritional support shall be administered by digestive route. Many patients with low catabolism can tolerate oral diet, alone or with supplements, but critically-ill patients usually require enteral nutrition. If there is any contraindication to it, total parenteral nutrition is to be preferred, with glutamine supplements. As soon as gastrointestinal tract is operative, enteral support will be started, as enteral nutrition is an independent predictor of good prognosis[33] (IIb).

Table II
Nutritional requirements in acute renal failure

Non-protein energy	20-30 kcal/kg/day
Carbohydrates	2-5 g/kg/day
Lipids	0.8-1.2 g/kg/day
Proteins (essential and non-essential amino acids)	
Conservative treatment, low catabolism	0.6-0.8 g/kg/day
Extrarenal clearing, moderate catabolism	1.0-1.5 g/kg/day
Continuous renal replacement techniques, hypercatabolism	1.7-2.2 g/kg/day
Administration route	
Conservative treatment, low catabolism	Oral, supplements, EN
Extrarenal clearing, moderate catabolism	EN and/or TPN
Continuous renal replacement techniques, hypercatabolism	EN and/or TPN

EN: Enteral Nutrition; TPN: Total Parenteral Nutrition.

Some circumstances may modify this general criterion.

– Highly catabolic patients using continuous high-flow renal replacement usually require mixed support, since the major supplies make enteral support insufficient, particularly in the first few days of early nutrition[34] (IV).

– Sometimes, the low catabolism of some patients will allow for special parenteral nutritions. One of them is nutritional hemodialysis, using hemodialysis sessions to administer nutrients added to the dialyzate[35] (IIb). This leads to reducing the dialyzer flow and is poorly effective in seriously critically-ill patients, but may be of value in patients on continuous hemodialysis and even on slow continuous ultrafiltration (SCUF). Another of them, in patients with non-hypermetabolic acute renal failure and stable hemodynamics, is nutrition by peritoneal dialysis, with dialysis solutions with glucose or polyglucose and amino acids for absorption in the peritoneum. It is usually inadequate in critically-ill patients[36] (IIa).

When should nutritional support be started in acute renal failure?

It depends on the catabolism of the patient. With a low catabolism, without prior malnutrition, you may wait until a good oral or enteral tolerability is obtained, after correcting water-electrolyte disorders using fluid therapy. Critically-ill hypercatabolic patients on continuous renal replacement techniques should receive early artificial nutrition, since their underlying catabolism is associated with losses secondary to the clearing technique used. The need to start support very early may advise to start mixed nutrition (enteral and parenteral)[37] (IV).

Table II gives a summary of nutritional support in renal failure.

Recommendations

– Protein supply should be adapted to the clinical condition, to the degree of catabolism, and treatment (conservative or extrarenal clearance) performed (B).

– Mixtures of amino acids containing only essential amino acids and histidine should not be used (B).

– Proteins of a high biological value are recommended in non-catabolic patients on conservative treatment (C).

– When extrarenal clearing techniques are used, protein supply should be increased (B). The recommended maximum amount is 2.5 g/kg/day (C).

– With the continuous renal replacement techniques glutamine and taurine supplements are recommended (C).

– In patients on continuous renal replacement techniques, glucose-free replenishment and dialysis solutions or those containing 1 g of glucose/L, with bicarbonate as *buffer*, are recommended (B).

– Electrolyte (phosphorus, potassium and magnesium) and micronutrient values (zinc, selenium, thiamine, folic acid and vitamin C, A and D) must be monitored, individualizing their supplies (C).

– Standard nutrient supply involves no problems in patients with normal catabolism undergoing clearing procedures (C).

– Although enteral (or oral) nutrition is the method of choice, sometimes the clinical condition of the patient leads to performing parenteral or mixed nutrition (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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Chapter 6
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Liver failure and liver transplantation

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Abstract

Patients with liver failure have a high prevalence of malnutrition, which is related to metabolic abnormalities due to the liver disease, reduced nutrient intake and alterations in digestive function, among other factors.

In general, in patients with liver failure, metabolic and nutritional support should aim to provide adequate nutrient intake and, at the same time, to contribute to patients' recovery through control or reversal of metabolic alterations. In critically-ill patients with liver failure, current knowledge indicates that the organ failure is not the main factor to be considered when choosing the nutritional regimen. As in other critically-ill patients, the enteral route should be used whenever possible.

The composition of the nutritional formula should be adapted to the patient's metabolic stress.

Despite the physiopathological basis classically described by some authors who consider amino acid imbalance to be a triggering factor and key element in maintaining encephalopathy, there are insufficient data to recommend "specific" solutions (branched-chain amino acid-enriched with low aromatic amino acids) as part of nutritional support in patients with acute liver failure.

In patients undergoing liver transplantation, nutrient intake should be started early in the postoperative period through transpyloric access.

Prevention of the hepatic alterations associated with nutritional support should also be considered in distinct clinical scenarios.

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Key words: *Liver failure. Liver transplantation. Branched amino acids. Malnutrition.*

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: INSUFICIENCIA HEPÁTICA Y TRASPLANTE HEPÁTICO

Resumen

Los pacientes con insuficiencia hepática presentan una elevada prevalencia de malnutrición. Ésta se encuentra relacionada, entre otros factores, con las alteraciones del metabolismo derivadas de la enfermedad hepática, la disminución en la ingesta de nutrientes y las alteraciones en la función digestiva.

De modo general, en los pacientes con insuficiencia hepática, el soporte metabólico-nutricional debe tener como objetivo el aporte adecuado de los requerimientos contribuyendo, al mismo tiempo, a la recuperación de los pacientes mediante el control o la reversión de las alteraciones metabólicas apreciadas. En los pacientes críticos que presentan insuficiencia hepática, los conocimientos actuales indican que ésta no parece ser un factor fundamental a la hora de considerar la pauta nutricional. Como en otros pacientes críticos, la vía de aporte de nutrientes debe ser la enteral, siempre que ello sea posible.

La composición de la fórmula nutricional debe estar adaptada a la situación de estrés metabólico. A pesar de la base fisiopatológica, clásicamente descrita por algunos autores, que considera al disbalance de aminoácidos un factor desencadenante y mantenedor de la encefalopatía, no hay datos suficientes para recomendar el empleo de soluciones "específicas" (enriquecidas en aminoácidos ramificados y pobres en aminoácidos aromáticos) como parte del soporte nutricional en los pacientes con insuficiencia hepática aguda.

En los pacientes sometidos a trasplante hepático, el aporte de nutrientes debería iniciarse de manera precoz en el postoperatorio mediante una vía de acceso transpilórica. La prevención de las alteraciones hepáticas asociadas al soporte nutricional debe ser también considerada en diferentes situaciones clínicas.

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Palabras clave: *Insuficiencia hepática. Trasplante hepático. Aminoácidos ramificados. Malnutrición.*

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

How can malnutrition be quantified in patients with liver failure?

Malnutrition is a common finding in patients with liver failure (LF). Observational studies to establish the degree of malnutrition have confirmed that malnutrition occurs even in the early stages of the disease, and is more intense in the most seriously ill patients[1] (III). It must be noted that the degree of malnutrition has a significant impact on mortality[2].

The etiology of cirrhosis may also condition the degree of malnutrition. Alcoholism often causes malnutrition "per se." However, malnutrition can also occur in alcoholic patients in withdrawal state. Comparative studies on the effects of the etiology of cirrhosis in malnutrition shows that bleeding is more significant in alcoholic patients than in those with cirrhosis of viral etiology[3] (III).

Nutritional monitoring must be performed through subjective global assessment, loss of muscle mass, and the plasma albumin concentrations, although they are all affected by changes derived from the liver disease. The application of more specific nutritional assessment methods shows significant differences in the definition of malnutrition according to the method used[4] (III).

Does the nutritional status influence the outcome and prognosis of liver failure?

Population studies suggest that malnutrition is a factor influencing the morbidity and mortality of patients with chronic liver disease[5] (III). Some data suggest that preservation of the body lean mass is important in the evolution of cirrhotic patients, as it is associated with lower complications in the evolution[6,7] (III).

In patients candidate to liver transplantation (LT) it is considered that malnutrition affects adversely post-transplant outcome[8,9] (III), though this is controversial, as adverse outcomes are also obtained with this regard[10] (III).

What conditions the choice of the route for supplying nutrients in patients with liver failure?

No controlled studies have been performed comparing enteral nutrition (EN) to parenteral nutrition (PN) in patients with advanced LF. However, it may be stated that, as in other diseases, EN should be the first route to be considered when specialized nutritional support is indicated. Esophageal or gastric varicose veins and the presence of coagulopathy are contraindications commonly used in the clinical practice for placing a nasogastric tube, though this contraindication is not supported by clinical studies and has been discussed by some authors[11] (IV). In a randomized study evaluating the efficacy of EN in patients with bleeding for esophageal varicose veins, no significant difference was seen in rebleeding in patients with a feeding catheter and those receiving oral nutrition[12] (Ib). However, the procedure should be performed after assessing the related risks and benefits.

Parenteral nutrition should be used in these patients when: *a)* the gastrointestinal tract is not functional due to the presence of gastrointestinal bleeding; *b)* EN is not well tolerated; *c)* EN is insufficient to provide nutritional requirements, and *d)* there is a high risk of aspiration as a result of consciousness disorders related to advanced states of encephalopathy.

What amount and quality of energy substrates are required?

Nutritional supply must be conditioned by the degree of malnutrition and the type of disease, related or not to the progression of LF. There are no controlled studies that establish the optimum nutritional supply in patients with LF in critical situation. Therefore, nutritional similar supplies are similar to those given to other critically-ill patients, with some changes suggested by the physiopathological characteristics of the LF.

The total recommended calorie supply is within 25-40 kcal/kg/day[13-15] (IV).

With regard to the distribution of the energy supply, it must be considered that patients with LF are at a high risk of hypoglycemia (for limitation in storage of glycogen and liver neoglycogenesis).

There are no data contraindicating fat supply within nutritional support in patients with LF. The recommended lipid supply limit is similar to that of other critically-ill patients. Various clinical studies show that intravenous fat infusion causes both an increase in triglyceride plasma levels and an increase in their metabolism and excretion. Comparative studies between the different lipids in patients with LF have not shown significant differences[16,17]. Studies with indirect calorimetry in severe LF show a reduction in glucose oxidation and an increase in fat oxidation[18] (III).

What should be the characteristics of protein supply?

It is classically considered that a high protein intake may cause encephalopathy. However, some studies indicate that normal protein supply does not lead to an increased encephalopathy, while protein restriction has adverse effects upon protein metabolism[19] (Ib). The limitation of protein supply is not indicated "routinely" in these patients; it should only be considered in patients in an unstable situation and always conditioned by demonstration of encephalopathy related to increased protein intake.

Are there any formula or specific nutrient recommended in liver failure?

The mechanisms leading to an amino acid pattern characteristic of liver failure, the role played by this pattern in the occurrence of liver encephalopathy, and the effect of branched-chain amino acids (BCAA) upon protein turnover are the pathophysiological basis to justify the increased BCAA in LF.

Most studies with oral supplements of BCAA were conducted in outpatients with chronic liver disease, to assess their impact on disease progression. In general[20-22] (Ib), [23] (III), the use of BCAA allows for establishing some positive effects (improved Child score, fewer hospital admissions, lower encephalopathy) but differences were not seen in patient mortality. Several revisions have been performed about this matter[24,25]. The data are not conclusive due to the heterogeneity of the populations studied and the variability in the type of nutrition used. The results of the Cochrane review, based on 11 controlled studies including 556 patients, suggest that supplements with BCAA impact favourably encephalopathy improvement, but is not associated with other effects on morbidity and mortality[26] (Ia).

The indication for administering this type of solutions to patients with LF is, therefore, controversial. It is important, in any case, to assess the amino acid profile of the solution enriched with BCAA that is decided to be administered to the patient, as this could be deficient in other amino acids and, therefore, affect the nutritional efficacy of treatment.

Regarding other formulations, such as diets enriched with casein or amino acids of plant origin, the results of its use have not been adequately tested[27].

What are the vitamin and trace elements requirements?

Patients with advanced disease show a high risk of micronutrient deficiency. The etiology of the situation is multifactorial, with co-adjuvant factors involved, such as an inadequate intake, gastrointestinal absorption deficiency and their increased clearance. Supplements with Zn and Mg should be administered in LF, particularly in the most seriously ill[28] patients (III).

According to this, the vitamin requirements (both water-soluble and lipid- soluble), and trace elements (Mg, Zn, P) appear to be increased, though studies have not been conducted to outline this situation. The role of vitamin D and K in immune tolerance of the graft is under investigation[29] (III).

How should nutritional support of liver transplant patients be?

Malnutrition is not a contraindication for transplantation, but may adversely affect the progression and prognosis of transplanted patients.

Early postoperative nutritional support, both by enteral[30] (Ib) and parenteral route[31] (Ib), is associated with clinical outcomes benefits. In a study comparing both methods, no differences were seen in the parameters tested[32] (III).

Macro and micronutrient requirements are similar to those recommended for other postoperative situations.

The use of pharmaconutrition may be beneficial in the immediate postoperative period. PN with glutamine improves the course of liver biochemical parameters and reduces hospital stay[33] (Ib). The use of an enteral diet enriched with pharmaconutrients (arginine, ω-3, nucleotides), both before and after transplantation, is associated with a better maintenance of protein reserves and lower incidence of post-operative infectious complications[34] (III).

The administration of a mixture of prebiotics and probiotics, together with EN postoperatively following transplantation, may reduce infectious complications[35] (Ib).

How can liver disease associated with nutritional support be prevented?

Cholestasis associated with PN is a serious complication occurring in pediatric patients receiving long-term PN, and may be an indication for bowel transplant. The limitation of the lipid supplied from infusions based on soybean oil (less than 1 g/kg/day) may contribute to decrease serum levels of bilirubin[36] (III). The use of lipid solutions containing fish oil has shown positive results in prevention of such disorders[37] (Ib), [38] (III).

The main factors for development of liver disease in critically-ill adult patients with nutritional support are the high energy supply (> 25 kcal/kg/day) and the presence of sepsis[39] (III). According to this, controlling both events would be fundamental for the prevention of liver disease secondary to nutritional support. Studies performed on lipid emulsions containing ω-3 fatty acids (fish oil) have also allowed to noticing favorable outcomes in the prevention or reversion of liver disorders secondary to PN[40] (Ib), [41,42] (IIa).

Recommendations

– A calorie intake of 25-40 kcal/kg/day is recommended (C).

– Energy supply should be mixed (carbohydrates/fats) (C). There is no contraindication to intravenous administration of lipid emulsions, though it is recommended that the supply does not exceed 1 g/kg/day (C).

– In patients with a high metabolic stress, the limitation of protein intake is not indicated routinely (C). The regular use of diets enriched with branched amino acids is not recommended in patients requiring enteral nutrition. These diets may be used if the patients develop encephalopathy during enteral nutrition (C).

– Vitamins and trace elements intake (particularly Zn, Mg and P) should be increased (C).

– In patients with liver transplant, early nutritional support should be administered postoperatively following transplant, preferably by enteral route (transpyloric route) (B).

– In patients with liver transplant, macronutrient requirements are similar to those of other situations in the immediate postoperative period. P, Mg and Zn values should be monitored (B).

– It is recommended to use lipid emulsions containing ω-3 fatty acids (fish oil) in patients with liver disorders during parenteral nutrition (B).

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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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[1,2].

SAP causes a systemic inflammatory response leading to a highly catabolic, hypermetabolic and hyperdynamic stress condition[3,4]. 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[5-8].

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[9].

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[10-14]. 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[3,4] (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[15].

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[11,12,16] (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[13] (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[9,10,14,16]. 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[16,17]. 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[5,12-14,16,17] (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[18]. 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[5,6]. It is therefore concluded that the use of jejunal nutrition[12,14,16] (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[19,20] (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[21] (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[22] (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[2,23,24].

Xian-Li confirmed that the start of PN 24-48 hours after obtaining hemodynamic control reduced complications, hospital stay and mortality[25] (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[12]. 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)[24]. 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[23,26-28] (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[29] and suggest outcome benefits in patients with SAP when nutrition enriched with pharmaconutrients is administered[29,30], though from the design of these studies it is not considered that there is sufficient evidence for recommending them[12,16,24,31,32](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[12,14,33,34] (Ib).

With regard to the administration of probiotics and prebiotics in patients with SAP, currently, and analyzing the data obtained from the studies completed[8,9,35,36] (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[37,38].

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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Chapter 8
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Respiratory failure

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Abstract

Severe acute respiratory failure requiring mechanical ventilation is one of the most frequent reasons for admission to the intensive care unit. Among the most frequent causes for admission are exacerbation of chronic obstructive pulmonary disease and acute respiratory failure with acute lung injury (ALI) or with criteria of acute respiratory distress syndrome (ARDS). These patients have a high risk of malnutrition due to the underlying disease, their altered catabolism and the use of mechanical ventilation. Consequently, nutritional evaluation and the use of specialized nutritional support are required. This support should alleviate the catabolic effects of the disease, avoid calorie overload and, in selected patients, to use omega-3 fatty acid and antioxidant-enriched diets, which could improve outcome.

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Key words: *Respiratory failure. Acute lung injury. Nutritional support. Omega 3 fatty acids.*

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: INSUFICIENCIA RESPIRATORIA

Resumen

La insuficiencia respiratoria aguda grave que precisa ventilación mecánica es una de las causas más frecuentes de ingreso de los pacientes en UCI. Entre las etiologías más frecuentes se encuentran la reagudización de la enfermedad pulmonar obstructiva crónica y la insuficiencia respiratoria aguda con lesión pulmonar aguda o con criterios de síndrome de distrés respiratorio agudo. Estos pacientes presentan un riesgo elevado de desnutrición por su enfermedad de base, por la situación catabólica en la que se encuentran y por el empleo de la ventilación mecánica. Ello justifica que estos pacientes deban ser valorados desde el punto de vista nutricional y que el uso de soporte nutricional especializado sea necesario. El soporte nutricional especializado debe paliar los efectos catabólicos de la enfermedad, evitar la sobrecarga de calorías y utilizar, en casos seleccionados, dietas específicas enriquecidas con ácidos grasos ω-3 y antioxidantes que podrían mejorar el pronóstico.

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Palabras clave: *Insuficiencia respiratoria. Lesión pulmonar aguda. Soporte nutricional. Ácidos grasos omega 3.*

Introduction

Multiple studies have shown that compliance with good practice guidelines in the use of artificial nutrition in ventilated patients may improve the quality of this intervention and, probably, the clinical outcomes such as hyperglycemia, the duration of mechanical ventilation and even mortality[1-4] (III). However, many recommendations given relating to patients with chronic obstructive pulmonary disease (COPD) have a low level of evidence[5] (IV).

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What should be the nutritional support route and when should it be started?

This recommendation affects all patients with invasive mechanical ventilation, including both patients with respiratory insufficiency secondary to COPD and patients with acute lung injury (ALI)/acute respiratory distress syndrome (ARDS). There are no specific recommendations on the best nutritional supply route or the time of onset in patients with acute respiratory failure (ARF), although there is for mechanically ventilated seriously ill patients. By extension, and as in any seriously ill patient, the route of choice is always the enteral, either gastric or postpyloric, and feeding should be started early, within the first 24-48 hours[6] (Ia).

Nutritional support in patients with chronic respiratory failure acutely worsened

Patients with COPD show a prevalence of malnutrition ranging from 25 to 40%[7]. A relevant weight loss is seen (of 5% in the previous 3 months or 10% in the previous 6 months) in 25-40% of the patients with a significant pulmonary impairment, that is, forced expiratory volume in the first second (FEV1) < 50%. Weight and body mass loss is a common complication in patients with advanced COPD, mainly of emphysematous type. Mean survival in these patients with cachexia and FEV1 < 50% is approximately 2-4 years, markedly lower than in those without it[8]. In addition, the low weight (body mass index [BMI] < 20 kg/m^2) or recent weight loss and the value of muscle atrophy, measured through the fat-free mass index, are independent predictor factors of mortality[9] (IIb). They also are factors predicting prognosis following acute worsening and the need for mechanical ventilation, associating both to a higher number of re-admissions and acute worsenings.

The mechanisms responsible for nutritional depletion and cachexia are multiple. Weigh loss with depletion of fat-free mass and BMI reduction in patients with COPD is associated with a greater number of readmissions and acute worsening and a higher mortality[10] (III).

Nutritional support is aimed at both maintaining a stable weight and promoting muscular anabolism. The administration of nutritional supplements in COPD patients with malnutrition does not improve anthropometric measures, pulmonary function, and functional capacity, but may play a relevant anabolic effect and be associated with an improved survival[10] (III), [11] (Ia).

What energy requirements are indicated in patients with chronic obstructive pulmonary disease acutely worsened?

Up to 60% of patients with COPD show a high basal energy expenditure (BEE), particularly when they lose weight[12]. Empirically, since there are no clinical trials in patients with acute worsening of COPD, it appears reasonable to use the generic advice of 25-30 kcal/kg/day. In patients requiring mechanical ventilation it is recommended that carbohydrate supply is 50-70% and fat supply 30-50% of energy requirements. Glucose perfusion must not exceed 4 g/kg/day, since supplies over 5 mg/kg/min increase clearly VCO_2, making difficult disconnection from the ventilator[13] (III). Some randomized, controlled studies have compared the effect of diets rich in carbohydrates (50-100% of total energy) to diets with a lower percentage (30% of the total energy) and only observed adverse events in the cases where the energy amount administered exceeded the needs calculated[14] (III). Thus, the use of specific enteral formulas with low carbohydrate and high fat content is not necessary.

What are the protein requirements of patients with chronic respiratory failure?

In hospitalized patients with acutely worsened COPD, a high protein intake has been recommended, and this recommendation applies to patients on mechanical ventilation. Proteins increase the minute volume, VO_2 and ventilatory response in case of hypoxia and hypercapnia, regardless of the VCO_2, and pH. Although changes have been described in the pattern of amino acids in malnourished patients with severe COPD, there is no scientific evidence that a specific supply of amino acids has significant benefits. Supplies of 1-1.5 g/kg/day are recommended in non-hypercatabolic patients and of 1.5-1.8 g/kg/day in those with an intense aggression.

What micronutrient supply is required in patients with chronic respiratory failure?

For an adequate function of respiratory muscles it is important to maintain adequate values of phosphorus, magnesium, calcium, iron, zinc, and potassium, so it is recommended, particularly in the phase of disconnection from the ventilator, to ensure normal values. Selenium and vitamin A, C and E can be useful due to their antioxidant effect and, in the case of vitamin E, it may also have an anti-inflammatory effect. However, in stable patients it has not been shown that a supply above the daily needs improves significantly the outcome in these patients[15,16].

Nutritional support in acute respiratory failure: acute respiratory distress syndrome (ARDS) and acute lung injury (ALI)

What should be the characteristics of energy and protein supply?

In general, as in other critically-ill patients, energy supply must meet the patient requirements, avoiding overnutrition. It is also important to ensure at least 50-65% of calorie requirements estimated during the catabolic phase, though only observational studies demonstrate the beneficial effect of meeting energy requirements[3,4] (III). In addition, recent large multicenter studies aimed at evaluating strict glycemic control have demonstrated the difficulty to achieve mean calorie intakes above this percentage (from 11 to 16 kcal/kg/day), regardless of the administration route used, and a systematic review does not support the need to ensure these calorie requirements from the first day[17].

This debate is also applicable to protein supplies. There is a consensus in the need to provide proteins above 1-1.2 g/kg/day, but the level of evidence is also very low[4]. In fact, and taking into account the mean calorie supplies, in all above mentioned studies protein supplies are below 1 g/kg/day[3]. It must be noted that in a Spanish observational study of the Metabolism and Nutrition Working Group of SEMICYUC, 20 kcal/kg/day of calorie intake and 1 g/kg/day of protein intake were reached in 50% of the patients, though 30% of them received parenteral nutrition and enteral nutrition, simultaneously[18].

Do pharmaconutrients play any role in nutritional support of patients with acute respiratory distress syndrome and acute lung injury?

Diets based on ω-3 fatty acids (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA), gamma linoleic acid (GLA), and antioxidants are being, in recent years, under study attempting to define their influence on the outcome of this condition.

ω-3 fatty acids, contained in fish oil, are essential in critically-ill patients, and their role has been investigated in the modulation of inflammatory response. One of the findings in uncontrolled activation of the inflammatory response, as seen in ALI/ARDS and in sepsis, is the role of cytokines and eicosanoids derived from lipids. Three clinical trials with enteral nutrition using a commercial formula containing ω-3, fatty acids, GLA, and antioxidants evidenced improvements in the clinical outcomes, both the ICU length of stay and mechanical ventilation days, and mortality in one of them[19-21] (Ib). This has been confirmed in a subsequent meta-analysis[22] (Ia). In addition, an observational study in surgical patients with intra-abdominal sepsis treated with parenteral nutrition enriched with ω-3 fatty acids evidenced a relative mortality reduction for the severity degree in patients as compared to the expected[23] (III).

However, these studies[19-21] used control diets containing high amounts of fat (up to 50% of energy requirements in 2 of them), and a high content in linoleic acid. When several pharmaconutrients are combined, it is difficult to establish the actual benefit of each of them and maybe, most importantly, the control diet used in these studies is inadequate.

Three recent studies approach this subject. The first, not published yet when these *recommendations* were drawn up, compares the effect of ω-3 fatty acid supplements with antioxidants, administered in bolus every 12 h in addition to the standard enteral diet, versus the control, and has been discontinued for treatment futility after recruiting 272 patients[24]. The second study analyzes the inflammatory response in bronchoalveolar lavage of these patients, with no significant differences[25]. And, finally, a Spanish multicenter study using a commercial diet with ω-3 fatty acids, GLA and antioxidants in the treatment of patients with sepsis and ARDS, did not improve gas exchange or decreased the incidence of new organ failures, and although the ICU length of stay was shorter than in the control group, no differences were seen in infectious complications[26].

In parenteral nutrition there are no studies assessing the effect of ω-3 fatty acids in the group of critically-ill patients with ALI/ARDS. There are no studies either in this type of patients with other pharmaconutrients.

Recommendations

– In chronic respiratory failure a total calorie intake of the basal energy expenditure multiplied by a factor between 0.9 and 1.1 is recommended (C).

– Protein supply recommended in critically ill patients with chronic respiratory failure would range from 1.0 to 1.8 g of proteins/kg/day (C).

– Special attention should be paid to potassium, phosphorus, magnesium, and antioxidant intake in patients with chronic respiratory failure (C).

– Specific enteral formulas with low carbohydrate content and high fat content are not indicated in chronic respiratory failure (C).

– In acute respiratory failure, calorie and protein supply should be similar to that recommended for other critically ill patients with a high stress level (B).

– An enteral diet enriched with ω-3 diet fatty acids, GLA, and antioxidants may have beneficial effects in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) (B).

– There are no specific recommendations for the use of ω-3 fatty acids by parenteral route (C).

– There are no specific recommendations for the single use of glutamine, vitamins, or antioxidants supplements (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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Chapter 9
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Gastrointestinal surgery

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Abstract

Gastrointestinal surgery and critical illness place tremendous stress on the body, resulting in a series of metabolic changes that may lead to severe malnutrition, which in turn can increase postsurgical complications and morbidity and mortality and prolong the hospital length of stay.

In these patients, parenteral nutrition is the most widely used form of nutritional support, but administration of enteral nutrition early in the postoperative period is effective and well tolerated, reducing infectious complications, improving wound healing and reducing length of hospital stay.

Calorie-protein requirements do not differ from those in other critically-ill patients and depend on the patient's underlying process and degree of metabolic stress.

In patients intolerant to enteral nutrition, especially if the intolerance is due to increased gastric residual volume, prokinetic agents can be used to optimize calorie intake. When proximal sutures are used, tubes allowing early jejunal feeding should be used.

Pharmaconutrition is indicated in these patients, who benefit from enteral administration of arginine, omega 3 and RNA, as well as parenteral glutamine supplementation.

Parenteral nutrition should be started in patients with absolute contraindication for use of the gastrointestinal tract or as complementary nutrition if adequate energy intake is not achieved through the enteral route.

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Key words: *Gastrointestinal surgery. Nutritional support. Pharmaconutrients. Complementary parenteral nutrition.*

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RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: CIRUGÍA DEL APARATO DIGESTIVO

Resumen

El estrés de la cirugía gastrointestinal y la enfermedad crítica representan una gran agresión sobre el organismo, lo que ocasiona una serie de cambios metabólicos que pueden conducir a una situación de desnutrición grave, con aumento de las complicaciones posquirúrgicas, mayor morbimortalidad y prolongación de la estancia hospitalaria.

En estos enfermos la nutrición parenteral es la más utilizada, pero se ha visto que la nutrición enteral administrada de forma precoz en el postoperatorio es efectiva y bien tolerada, con disminución de las complicaciones infecciosas, mejoría de la cicatrización de las heridas y menor estancia hospitalaria.

Las necesidades caloricoproteicas no difieren de las de otros pacientes críticos, y dependerán de la patología basal del paciente y de su grado de estrés metabólico.

En caso de intolerancia a la nutrición enteral, en especial si se debe al aumento del residuo gástrico, se deben utilizar procinéticos para optimizar el aporte calórico. En caso de suturas proximales se debe recurrir a la colocación de sondas que permitan la nutrición en yeyuno de forma precoz.

La farmaconutrición tiene efectos beneficiosos en este t ipo de enfermos, con indicación de mezclas de arginina, omega 3 y RNA por vía enteral, así como la suplementación con glutamina en nutrición parenteral.

La nutrición parenteral deberá iniciarse en los pacientes con contraindicación absoluta para la utilización del tracto gastrointestinal, o como nutrición complementaria si no se consigue un aporte calórico adecuado por vía enteral.

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Palabras clave: *Cirugía gastrointestinal. Soporte nutricional. Farmaconutrientes. Nutrición parenteral complementaria.*

Introduction

Surgery is the cause of a number of deep inflammatory and metabolic changes with the primary objective of ensuring the adequate defence of the body and prioritize the metabolic pathways to useful products in the acute stage of the disease.

Malnutrition is associated with changes in body composition, and delayed wound healing, decreased functional capacity, impaired immune function and changes in the different organ systems[1]. Therefore, malnourished patients are at risk of experiencing infectious and cardiorespiratory complications[2,3], increased morbidity and mortality and prolongation of hospital stay. The presence of postoperative ileus and integrity of new anastomosis have led to maintaining fasting with administration of parenteral fluids until the patient starts with bowel sounds or clears gases. However, it has been shown that early postoperative enteral nutrition is effective and well tolerated[4]. Enteral feeding is associated with clinical benefits, such as the reduction in the incidence of postoperative infectious complications and improved healing of tissues[5].

Therefore, the nutritional intervention is essential as part of the treatment of postoperative gastrointestinal patients, including those with good previous nutritional status, since the worsening of nutritional status due to the surgical stress and critical illness will be a determinant factor of poor subsequent outcome.

What should the calorie intake be?

Caloric requirements will be adapted to the stress status of the patient[6-9]. The surgical patient admitted to the intensive care unit (ICU) is usually in a grade 2-3 stress condition, so the calorie supply should be 25-30 kcal/kg/day. In a hyperglycemia state, 20-25 kcal/kg/ day will be required. In the catabolic phase, 20-25 kcal/kg/day will be administered and will be increased to 25-30 kcal/kg/day in the anabolic phase[7] (IV). It is recommended not to exceed 2,000 kcal/day.

What amount and quality of energy and protein substrates is required?

Protein supply will be within 1.2-1.5 g/kg/day of proteins[10] (IV), that could increase in cases of protein loss increase, as in patients with open wounds, burns, or enteropathy with protein loss. Nitrogenated losses in patients with open abdomen are higher than in other surgical patients, with a mean protein loss of 3.5 g of nitrogen in 24 h, so it has been proposed to increase protein supply a mean of 2 g of nitrogen per litre of abdominal fluid lost[11] (III).

Glucose supplied as energy substrate should be adjusted to maintain glycemic values below 150 mg/dL, providing insulin as necessary[12] (Ib) and avoiding protocols for tight glycemic control (80-110 mg/dL).

The minimum amount of lipids required is 1 g/kg/day and its total supply will account for 30% of calorie supply but, sometimes and according to the patient's condition, it may be 40%. Only if there is hypertriglyceridemia (> 400 mg/L) its supply will be withdrawn or stopped[13]. Lipid emulsion including middle-chain triglycerides (MCT) is better metabolized in the mitochondria and has been shown to have advantages over lipid emulsion based on long-chain triglycerides (LCT) alone, with less infectious complications in surgical patients[14] (Ib).

Advances in the understanding of the metabolic, immunomodulating and inflammatory properties of fatty acids have allowed for developing new lipid formulas for modulating the inflammatory response in various situations of aggression. A metaanalysis[15] compares the immune effects of all lipid emulsions, without finding advantages of some over others. The recommendations of the Canadian Critical Care Group on nutritional therapy in critically-ill patients pooled studies based on the nature of the lipid used and found no differences in their clinical outcome[16] (IV). Heller et al., in a randomized prospective study, evidenced that intravenous administration (i.v.) of ω-3 fatty acids at doses of 0.11 g/kg/day for an average of 8.7 days in 661 surgical ICU patients, reduces mortality as compared to mortality predicted by SAPS II[17] (III).

A MCT/LCT emulsion enriched with fish oil, with a high vitamin E content, has been recently launched onto the market. A randomized, double-blind clinical trial performed in postoperative critically-ill patients operated for abdominal aorta aneurysm[18] compared 2 homogeneous groups of patients receiving total parenteral nutrition (TPN) for 5 days. Patients receiving this new fat mixture had a significant increase of eicosapentaenoic acid, leukotriene B5 and vitamin E when compared with the control group, a significant reduction of hospital stay and a non-significant trend towards a lower incidence of pneumonia. Another randomized, double-blind study[19] compared this emulsion enriched with fish oil to LCT in patients undergoing elective thoracoabdominal surgery, finding a trend toward shorter hospital stay. Despite this, for the moment there are not enough data available to recommend the type of lipids that must be used in critically-ill patients with PN and abdominal surgery.

With regard to the carbohydrate/lipid ratio, a study[20] compared PN with carbohydrates/lipid ratio of 80/20 to PN with 50/50 ratio, finding a lower nitrogen loss in the 80/20 group, though with a worst control of blood glucose, concluding that a greatest evidence is required to establish a recommendation.

Do specific nutrients play any role in nutritional-metabolic support in these patients?

Glutamine

The patients where elective abdominal surgery is indicated show some degree of malnutrition and a deficit of circulating glutamine for different reasons, most of them associated with their underlying disease (anorexia, intestinal obstruction, blood loss, etc.). This situation worsens postoperatively, since glutamine demands increases in response to the aggression, having demonstrated that circulating and muscle-released glutamine values are inadequate for surgery stress[21]. Several studies have evaluated the role of glutamine supplements in postoperative patients following abdominal surgery[21-26].

A metaanalysis including 9 randomized, controlled clinical trials, with a total of 373 patients undergoing abdominal surgery, concluded that administration of PN supplemented with glutamine (20-40 g/day) has a beneficial effect on nitrogen balance, reduces hospital length of stay and infectious complications[22] (Ia). Dechelotte conducted a multicenter, randomized, double-blind, controlled study, with administration of PN supplemented with glutamine versus PN without glutamine, concluding that in the glutamine group infectious complications are reduced and a better glycemic control is achieved[23] (Ib). Estívariz performed a similar clinical trial including surgical patients with various etiologies, ranging from pancreatic to colon surgery, and concluded that in the PN group with glutamine infectious complications decrease in the subgroup of colon surgery, but not in that of surgery of pancreatic necrosis[24] (Ib). Oguz conducted a study in postoperative patients with colorectal cancer, where enteral nutrition vs enteral nutrition supplemented with parenteral glutamine was administered, in a total of 109 patients, concluding that glutamine supplements reduce the number of postoperative complications and hospital stay[25] (Ib). Kumar compared in patients with peritonitis and abdominal injuries the administration of enteral glutamine (45 g/day) versus conventional EN without finding benefits in the glutamine group[26] (Ib).

Arginine

Arginine supplements are recommended due to their beneficial effect on T cells and their function as nitric oxide precursor. Several studies in critically-ill patients show that when arginine is administered with other pharmaconutrients, infections and hospital stay decrease. These effects are more apparent in cancer patients to undergo elective abdominal surgery[27,28] (Ia), particularly when they have also received this type of nutrition preoperatively. The beneficial effect of pharmaconutrition in wound healing and a reduction in suture dehiscence also appears to be demonstrated in these patients[29] (Ib). Therefore, it is recommended to use diets enriched with arginine, ω-3 fatty acids, and RNA postoperatively following abdominal surgery.

There are no studies to recommend the single use of arginine systematically in EN or PN in surgical patients[6] (IV).

Micronutrients and antioxidants

Given the essential action of micronutrients (vitamins, trace elements) in maintaining immune and antioxidant system function, their supply is necessary in any patient susceptible to these deficiencies, even if of subclinical type. The critically-ill patient has a negative trace element balance and an increased production of free oxygen radicals[30]. Therefore, it is necessary to supply micronutrients and antioxidants in the nutrition of critically-ill postsurgical patients, though there is no evidenced about the exact amount. The studies performed with micronutrients confirmed that selenium supplementation evidenced a trend towards reducing 28-day mortality, though the differences were not statistically significant[31]. In PN 2-4 mg zinc/day are recommended. When there is an inflammatory bowel disease, pancreatic disorders or intestinal fistulas after surgery, losses can account for several times the normal requirements, so it is recommended to increase zinc supply in PN, though an exact dose cannot be given[32].

Fiber

Soluble fibre may be beneficial in patients developing diarrhea while receiving EN. Both soluble and insoluble fibres must be avoided in patients at a high risk of intestinal ischemia or intestinal motility disorders. Cases of intestinal obstruction in non-surgical patients who were given an enteric formulation with insoluble fibre have been described[33].

What should be the best nutritional support route?

In critically-ill patients it has been shown that EN should be started early for its benefits on the clinical outcome. A metaanalysis performed on studies in patients undergoing elective gastrointestinal surgery compared the results of early EN versus fasting. A reduction in the risk of infection and hospital stay was confirmed, with a trend to decreased mortality in the treated group[34] (Ia). In surgical patients who can tolerate enteral diet, early EN is recommended, as it reduces the risk of infection, length of stay and suture dehiscence, particularly if there is a gastrointestinal cancer[35] (IIb). In patients whose anastomosis is located in the proximal gastrointestinal tract (gastrectomy, pancreatoduodenectomy, esophageal resection), jejunal feeding can be given, either through a jejunostomy or a nasojejunal tube, recommending early EN via this route[36,37] (IIb).

In case of impaired intestinal motility, the use of prokinetics such as metoclopramide (10 mg IV 4 times daily) and erythromycin (200 mg twice daily) reduces residual gastric volume and improves the percentage of patients that may be nourished successfully[38] (III).

Is it indicated to administer parenteral nutrition? At what time?

Patients who cannot tolerate EN should receive PN adapted to their calorie-protein needs[9]. TPN will be indicated in case there is an absolute contraindication to EN[39]. In a randomized study, 300 patients undergoing major surgery received continuous PN or glucose alone (300 g/day) for 14 days. The group treated with PN had a lower mortality than the group treated with glucose[40] (Ib). The metaanalysis by Simpson and Doig, who compared PN to EN in critically-ill patients, evaluated 9 studies, finding a lower mortality in the PN group versus the late EN[41] (Ia). There is controversy about the use of early PN. The Canadian Nutrition group[42] (IV) recommends that, if the gastrointestinal tract is affected, early PN may be indicated, since a prolonged fasting period is associated with a poor outcome.

Is it indicated to administer parenteral nutrition as a complement to enteral nutrition?

In critically-ill surgical patients it is often difficult to provide all necessary nutrients by the enteral route. As there are no specific studies in abdominal surgery with complementary PN, following the recommendations of the critically-ill patients in general, the use of PN complementary to EN must be considered if 60% of the energy goal is not met at the third day of admission. If the goal of 20-25 kcal/kg/day is not reached, enteral and parenteral nutrition may be started, as with insulin therapy PN does not involve an additional risk[43,44] (IV).

Recommendations

– In patients undergoing abdominal surgery, the nutritional needs are similar to all other critically-ill patients (C).

– Administration of prokinetics should be considered in patients with intolerance to enteral nutrition (C).

– In surgery of the gastrointestinal tract with proximal anastomosis enteral nutrition using a feeding catheter placed distal to the anastomosis is recommended (B).

– The administration of w-3 fatty acids may be considered to improve outcome in these patients (C).

– The use of diets enriched with pharmaconutrients is recommended in neoplasic patients undergoing abdominal surgery (B).

– Parenteral nutrition in critically-ill surgical patients should be supplemented with glutamine (A).

– In critically-ill surgical patients there are not enough data available to recommend supplementing enteral nutrition with glutamine (C).

– Complementary parenteral nutrition should be started if 60% of nutritional requirements are not achieved on the third day of hospital stay or, during hospital stay, for at least 2 consecutive days (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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Chapter 10
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Hyperglycemia and diabetes mellitus

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Abstract

Hyperglycemia is one of the main metabolic disturbances in critically-ill patients and is associated with increased morbidity and mortality. Consequently, blood glucose levels must be safely and effectively controlled, that is, maintained within a normal range, avoiding hypoglycemia on the one hand and elevated glucose concentrations on the other. To accomplish this aim, insulin is often required, avoiding protocols designed to achieve tight glycemic control.

To prevent hyperglycemia and its associated complications, energy intake should be adjusted to patients' requirements, avoiding overnutrition and excessive glucose intake. Protein intake should be adjusted to the degree of metabolic stress.

Whenever patients require artificial feeding, the enteral route , if not contraindicated, should be used since parenteral nutrition is associated with a higher frequency of hyperglycemia and greater insulin requirements. Enteral nutrition should be administered early, preferably within the first 24 hours of admission to the intensive care unit, after hemodynamic stabilization. Specific diets for hyperglycemia, containing low glycemic index carbohydrates and fibre and enriched with monounsaturated fatty acids, can achieve good glycemic control with lower insulin requirements.

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Key words: *Hyperglycemia. Diabetes mellitus. Artificial nutrition. Glycemic control.*

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: HIPERGLUCEMIA Y DIABETES MELLITUS

Resumen

La hiperglucemia es una de las alteraciones metabólicas predominantes en los pacientes críticos y se asocia con un aumento de la morbimortalidad. por ello, es necesario realizar un control efectivo y a su vez seguro de la glucemia, esto es, mantener la normoglucemia en un rango que evite el riesgo de desarrollar hipoglucemia, por un lado, y las cifras elevadas de glucemia, por otro. Para conseguirlo, en la mayoría de los casos es necesario el tratamiento con insulina evitando protocolos dirigidos a conseguir cifras estrictas de glucemias.

Con el fin de prevenir la hiperglucemia y sus complicaciones asociadas, el aporte energético debe adecuarse a los requerimientos de los pacientes, evitando la sobrenutrición y el aporte excesivo de glucosa. El aporte proteico se ajustará al nivel de estrés metabólico. Siempre que el enfermo requiera nutrición artificial y no esté contraindicada debe emplearse la vía enteral, ya que la nutrición parenteral se asocia a mayor frecuencia de hiperglucemia y mayores necesidades de insulina. La administración de la nutrición enteral debe ser precoz, preferiblemente dentro de las primeras 24 h de ingreso en UCI, tras la estabilización hemodinámica. Las dietas específicas para hiperglucemia que contienen hidratos de carbono de bajo índice glucémico, fibra y ricas en ácidos grasos monoinsaturados podrían conseguir un mejor control glucémico con menores necesidades de insulina.

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Palabras clave: *Hiperglucemia. Diabetes mellitus. Nutrición artificial. Control de glucemia.*

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

Introduction

In critically-ill patients the development of hyperglycemia secondary to the acute lesion stress is common even in non-diabetics. Hyperglycemia and the metabolic consequences of insulin resistance increase morbidity and mortality in critically-ill patients[1], because they enhance the occurrence of infections and multiple organ failure, mainly due to proinflammatory effects and cell toxicity per se of high glycemia values.

What should be the nutritional support route and when should it be started?

Whenever the gastrointestinal tract is intact and the patient requires artificial feeding, the enteral route must be used in the first 24-48 hours of stay, over the parenteral, which is associated with a higher frequency of hyperglycemia and insulin needs[2]. Although it is known that gastroparesis of diabetic patients can make gastrointestinal tolerance more difficult[3], the enteral route allows for a better control of blood sugar levels and prevents complications derived from hyperglycemia in critically-ill diabetic patients or those with stress hyperglycemia[2] (Ia).

What should be the characteristics of energy supply?

It is important to adjust calorie needs to the metabolic stress status of the patient. This attempts to prevent overnutrition, that, in addition to contributing to hyperglycemia[1] (IV), enhances insulin resistance and liver failure. Overnutrition is mainly related to parenteral nutrition (PN)[4] (IV).

One of the most controversial issues is the distribution of the total calorie requirements and, particularly, the carbohydrate/lipid ratio. The American Diabetes Association (ADA)[5] sets out that critically-ill diabetic patients may receive either a standard formula (50% carbohydrates) or a formula low in carbohydrates (33-40%). In contrast, the European Association for the Study of Diabetes[6] recommends that fat content in diet should not exceed 35% and that carbohydrate intake should be within 45-60% of the daily calorie needs.

There are specific enteral formulae for diabetics containing fewer carbohydrates (35-40%) and more fats (40-50%), with predominance of monounsaturated fatty acids (MUFA) (> 60% of the total fat content). New formulae have been developed that, in addition to reducing fat content, increase their low glycemic index carbohydrates[6]. In studies performed in non-critically-ill patients, both types of formulae reduce the glycemic and insulinemic response to intake and, furthermore, diets rich in slow-digestion carbohydrates do not raise post-prandial triglyceride levels, unlike diets rich in fats[7,8]. Therefore, it is recommended to use low-glycemic index carbohydrates, such as starch (preferably), fructose at lower doses, and more recently, isomaltulose and sucromalt, amongst others[8] (Ib).

With regard to lipids, it is recommended to increase MUFA, as they improve glycemic control, lipid metabolism and insulin secretion in non-critically-ill patients with type 2 diabetes[7] (Ib), [8] (IIa). Furthermore, it is recommended to reduce polyunsaturated fatty acids (PUFA) of the ω-6 series to prevent proinflammatory eicosanoids to increase[9].

Regarding PN, the use of mixtures of carbohydrates with fructose or polyols (xylitol) offers conflicting results regarding a better glycemic control when compared to mixtures with glucose[10,11] and currently are scantly used.

In general, patients with type 2 diabetes benefit from fat-high diets, as diets very rich in carbohydrates affect the lipid profile of the patient and increase the risk of cardiovascular diseases.[3]

What should be the protein intake and its characteristics?

Seriously ill patients with hyperglycemia and particularly diabetics show deep metabolic changes in the absence of insulin, such as an increased basal energy expenditure (BEE) and a negative net protein balance. Both insulin and amino acids stimulate protein synthesis, though its effects depend on its relative concentration. In hyperaminoacidemia states, it has been suggested that additional insulin doses do not increase protein synthesis, probably related to the insulin resistance level of each patient[12].

There is no adequate evidence to define a specific nitrogen supply to critically-ill diabetic patients or those with stress hyperglycemia. It is recommended to adjust protein needs to the metabolic stress level of the patient: 1.3-1.7 g of proteins/kg/day according to their metabolic state, in order to prevent exacerbation of protein catabolism.

Do other specific nutrients play any role in nutritional-metabolic support in these patients?

Glutamine

The parenteral administration of glutamine has been associated with an improved glycemic control[13] through several potential mechanisms: *a)* through the metabolism of glutamine to glucose in the glucose-glutamine cycle; *b)* increasing insulin secretion; *c)* improving the sensitivity to insulin of the striate muscle; *d)* increasing the oxidation of free fatty acids, and *e)* decreasing the inflammatory response. It has been proven that glutamine improves insulin sensitivity in seriously ill patients[14], and 2 multicenter clinical trials have shown that patients receiving TPN enriched with glutamine have fewer infectious complications and better metabolic tolerability[15,16] (Ib).

Eicosapentaenoic acid and gamma linolenic acid

There are no studies with enteral nutrition (EN) or PN that show significant effects of ω-3 fatty acids on glycemic control.

Fiber

The ADA recommends administration of dietary fiber in diabetic patients, due to its lower glycemic index[5]. A metaanalysis showed no significant benefits in seriously ill patients[16] (Ia), though a subsequent study demonstrated that specific diets containing fiber improved glycemic control, though without emphasis in seriously ill patients[7] (Ib).

Trace elements and vitamins

There is no evidence that antioxidant vitamins at doses higher than the requirements are safe or beneficial[17] (IIb). The contribution of oxidative stress in diabetic complications and, particularly in seriously ill patients, is not evident, as tissue damage occurs in diabetic patients but not in patients with insulin resistance, as in the case of stress hyperglycemia occurring in critically-ill patients. There are no evidences of the efficacy of antioxidants in the prevention or control of the complications associated with hyperglycemia[18] (IV).

Can any specific diet be recommended in critically-ill patients with hyperglycemia?

Specific enteral diets for the control of hyperglycemia are characterized as rich in MUFA and containing low-glycemic index carbohydrates and fiber[19]. Very few studies have been performed to date and, though they show no differences in morbidity-mortality with the use of a conventional diet, they achieve a better control of glycemia and a lower need for insulin[19] (Ib), [20,21] (III). A recent study evidences also a lower variability in blood sugar levels when a specific enteral diet is used in patients with type 2 diabetes[22] (III).

Should blood glucose values be normalized in critically-ill patients?

Different studies have shown that hyperglycemia is an independent risk factor for a poorer prognosis in critically-ill patients[23,24].

The outcomes of a study in a population of critically-ill surgical patients maintaining a tight glycemic control, from 80 to 110 mg/dl by continuous perfusion of insulin[25] and demonstrating a reduction of 3.4% of the risk of death at the ICU, could not be reproduced in subsequent studies[26,27]. Even subsequent publications evidence an increased mortality in the group of patients maintaining strict blood glucose levels (80-110 mg/dl), mortality related to the high incidence of severe hypoglycemia[28-30] (Ib).

The largest multicenter study conducted to date (NICESUGAR)[30] included 6,104 patients from mixed ICUs and compared 2 ranges of blood glucose levels: 80-108 mg/dL (strict) versus < 180 mg/dL (conventional). The incidence of severe hypoglycemia was higher in the strict control group (6.8 vs 0.5%; $p < 0.001$) and 90-day mortality in the strict control group was significantly higher (27.5%) than in the conventional group (24.9%) (95% CI, 1.02-1.28; $p = 0.02$)[30] (Ib). The mean blood glucose achieved in the strict control group was 114 mg/dL vs the conventional group 144 mg/dL.

Two recent metaanalyses shows that in all critically-ill patients, the strict control of blood glucose levels (80-110 mg/dl) significantly increased severe hypoglycemia, without improving survival as compared to the conventional control group[31,32] (Ia).

It has been demonstrated that the variability of blood glucose levels along the patient evolution may affect mortality, even if it occurs between blood glucose ranges considered as appropriate[33]. In the cohort of 66,184 patients evaluated by the ANZICS (Australian and New Zealand Intensive Care Society), the variability of blood sugar levels over the first days of evolution was associated with an increased adjusted mortality when compared to the appearance of severe hypoglycemia[24] (III).

Recommendations

– It is recommended to monitor blood glucose values in all critically-ill patients (A).

– It is recommended, as most appropriate, to maintain blood glucose levels below 150 mg/dl (C).

– It is recommended to start treatment with insulin when blood glucose levels exceed 150 mg/dL (C).

– Continuous insulin perfusion protocols, will be designed to prevent strict blood glucose levels (80-110 mg/dL) in order to reduce the risk of severe hypoglycemia (B).

– It is recommended that continuous insulin perfusion protocols should be designed to avoid the variability of blood glucose levels (C).

– Energy supply should meet patient requirements avoiding overnutrition (C).

– Specific diets for hyperglycemia may decrease insulin requirements in these patients (B).

– In patients with parenteral nutrition it is recommended to use glutamine supplements in order to contribute to hyperglycemia control (B).

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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Chapter 11
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Oncohematological patient

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Abstract

Patients with cancer, irrespective of the stage of their disease, can require admission to the intensive care unit as a result of the complications of their underlying process or the surgical or pharmacological treatment provided. The cancer itself, as well as the critical status that can result from the complications of the disease, frequently lead to a high degree of hypermetabolism and inadequate energy intake, causing a high incidence of malnutrition in these patients. Moreover, cancer causes anomalous use of nutritional substrates and therefore the route of administration and proportion and intake of nutrients may differ in these patients from those in non-cancer patients.

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Key words: *Cancer. Pharmaconutrients. Glutamine.*

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

Resumen

Los pacientes portadores de cáncer, en cualquier fase de su evolución, pueden precisar ingreso en UCI como consecuencia de complicaciones secundarias a su enfermedad de base o de las terapias quirúrgicas o farmacológicas a que se ven sometidos para tratar su enfermedad. La propia enfermedad cancerosa, así como el estado crítico a que pueden derivar como consecuencia de las complicaciones sobreañadidas, con frecuencia condicionan un alto grado de hipermetabolismo y de déficit de ingesta nutricional, lo que conduce en estos enfermos a una alta incidencia de desnutrición. Además, la propia enfermedad cancerosa condiciona una utilización anómala de los sustratos nutritivos, lo que podría condicionar una vía de administración y una proporción y aporte de nutrientes algo diferenciado de los pacientes no tumorales.

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Palabras clave: *Cáncer. Farmaconutrientes. Glutamina.*

Introduction

Cancer patients with solid tumors may enter the intensive care unit (ICU) as a result of certain surgical treatments, applying in these cases the same recommendations as with any surgical patients in ICU. Patients undergoing hematopoietic stem cell transplantation may require admission to ICU for severe complications of the treatment itself: graft versus host disease, hepatic venoocclusive disease, infectious complications, and mucositis.

Malnutrition affects a high number of the patients with solid tumors, and can occur throughout the course of the disease[1]. Cachexia is present in over two thirds of patients dying of advanced cancer and may be the direct cause of a fourth of deaths[2]. The etiopathogenesis of cachexia includes anorexia and metabolic changes associated with neoplastic disease. Anorexia is the consequence of hypophagia, mucositis, gastric repletion, nausea, diarrhea, constipation, mechanical obstruction, and malabsorption. The metabolic changes are mediated by proinflammatory cytokines that cause changes in energy expenditure and metabolism of macronutrients.

In cancer, resting energy expenditure (REE) may be normal, increased, or decreased. The type of tumor and its phase will play a major role in this behaviour[1]. In

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SENPE: Spanish Society of Parenteral and Enteral Nutrition.

turn, the metabolism of macronutrients is impaired in patients with neoplasic disease, which leads to an anaerobic metabolism of glucose, and glycolysis is an ineffective energy production method, which involves that the tumor takes large amounts of glucose at a high metabolic cost. With regards to lipids there is an increase in lipolysis over lipogenesis[3,4]. In addition, tumours produce factors, such as the lipid mobilizing factor, that induce degradation of the adipose tissue with production of fatty acids.

Finally, there is a progressive reduction of the skeletal muscle mass, with relatively preserved visceral protein mass and increased liver protein mass (synthesis of acute phase proteins). Low plasma concentrations of insulin (or its resistance) and the action of different mediators (cytokines, neuropeptides) activate proteolytic pathways.

Are there any specific issues to assess the nutritional state of these patients?

Although nutritional assessment does not require special considerations, specific methods have been validated for cancer patients. Patient-Generated Subjective Global Assessment (PG-SGA) is a procedure combining data on objective and subjective issues derived from the clinical history and from the physical examination[5]. Although this is the procedure of choice, as it has been shown that it may predict prognosis[6,7] (III), it is not always possible to do it at the ICU, because it requires that the patient completes a number of data. However, the subjective global assessment performed by experts is the most reliable malnutrition parameter on admission and represents the recommended tool for critically-ill patients.

What are the energy and protein needs of critically-ill cancer patients?

Several authors have described an increased of REE in cancer patients[8] (III), [9] (Ib), while others have found no changes from healthy controls[10] (III). Evidence suggests that REE is variable based on the type of tumor, disease activity and presence of complications[11] (IIb). In critically-ill oncohematological patients an REE increase of about 20% is estimated in patients with solid tumors,[1] exceeding 10% in hematopoietic stem cell transplant patients[12]. Protein needs are also increased, without differences from those of any critically-ill patient[13] (III).

Does the cancer disease condition the administration route of specialized nutritional support?

There are no studies that show a better response of antitumor therapy, with chemotherapy and/or radiation therapy, on supplementing it with parenteral nutrition (PN) if there is no serious dysfunction of the intestinal route. In contrast, most studies show a higher rate of infectious complications and poorer prognosis when tumor patients are nourished with PN[14] (Ia), [15] (Ib).

The study of Bozzetti et al.[15] (Ib) reported that patients with gastrointestinal tumors, undergoing surgery, have fewer complications if they are administered nutritional support immediately after surgery. This improvement was more evident in previously malnourished patients and in those nourished enterally. Another study, upon comparing the postoperative complications in patients operated for colorectal cancer nourished by enteral versus parenteral route, reported a lower complication rate in the group nourished by enteral route[16] (Ib).

Mucositis can make digestive intake difficult due to the difficulties on placement of naso or orogastric tubes, which may involve the use of pharyngostomies or gastrostomies, or even the use of PN. Furthermore, in patients with hematological tumors, the development of thrombocytopenia may be a relative contraindication due to the bleeding risk. Some preliminary studies suggest that in these cases performing a prophylactic ostomy could reduce the development of malnutrition[17] (III), but there are currently no conclusive studies analyzing in critically-ill patients the advantages of these ostomies or PN over approach with nasogastric tubes.

Do oncological/hematological patients require specific modifications in the enteral or parenteral nutrition formulae?

Lipid supply

Of the studies available in cancer patients, some of them are contradictory in relation to glucose intolerance[18] and others support normal or increased lipid oxidation[3,4] (IV). Thus, some authors suggest that these patients should be recommended to increase lipid supply in PN at values above 35% of energy requirements.

Eicosaepentanoic acid

The anti-inflammatory and antitumor effects of eicosaepentanoic acid (EPA) seen in recent years have led to introducing these nutrients as part of the treatment of cancer patients. However, the studies attempting to demonstrate the efficacy of nutritional support including use of EPA show contradictory results.

Although prolonging survival after oral supplementing with EPA vs placebo could not be reproduced, and even contrary outcomes have been obtained[19], other studies have reported improved outcomes in several clinical parameters. On the one hand, the review performed by the Cochrane in 2007 concluded that there are insufficient data to establish that oral supplements with EPA are superior to placebo, both alone and in combination with high protein supplements, to improve symptoms associated with cachexia[20]. On the other hand, in a systematic review also in 2007, Elia et al.[21] observed a decrease of complications, particularly infectious, as well as a shortening of hospital stay and improved nutritional parameters in patients on enteral nutrition (EN) supplemented with EPA, but concluded that further research is needed to confirm this. Colomer et al.[22], in a systematic review, found benefits in different clinical, biochemical, and functional parameters when administering EPA supplements in diet or as capsules for at least 8 weeks in certain types and situations of cancer. These findings have not been confirmed in critically-ill cancer patients.

Glutamine

The beneficial results obtained by some authors in patients undergoing autologous transplant of hematopoietic stem cells on supplementing EN with glutamine, with reduced severity and duration of mucositis[23] (Ib), could not be confirmed by other authors[24,25]. PN with glutamine, at doses of 0.5 g/kg/day, may have beneficial effects by reducing local harmful intestinal effects (atrophy) and the liver damage caused by chemotherapy and radiation therapy[26] (Ib). In addition, improvements have been reported in nitrogen balance, in immune function, risk of infection, hospital lengh of stay and healthcare costs[27,28] (Ib). Effects on mortality have been contradictory[29,30] (IIa). In addition, in a randomized, double-blinded study in autologous bone marrow transplantation, high doses of glutamine dipeptide involved a greater number of relapses, mortality and costs[31].

Water, electrolytes, vitamins, trace elements and fiber

No information is available which allows for giving special recommendations on water, vitamins, electrolytes, trace elements and fiber in these patients.

Recommendations

– Patient-generated subjective global assessment is the technique of choice for nutritional status assessment, as it has been shown that it can predict the prognosis of these patients (B).

– Calorie-protein supply in critically-ill oncohematological patients must be similar to that in other critically-ill patients (B).

– In previously malnourished patients with gastrointestinal tumors who undergo surgery it is recommended to administer nutritional support immediately after surgery (A).

– Cancer patients may benefit from parenteral nutrition formulae, with lipid supplies > 35% of total calorie supply (C).

– No adequate data are available to support the use, enteral or parenteral, of w-3 fatty acids supplements in patients with advanced cancer (C).

– In patients undergoing autologous hematopoietic stem cell transplantation, supplementing enteral nutrition with glutamine decreases severity and duration of mucositis (C).

– It is recommended to supplement parenteral nutrition with alanyl-glutamine at doses of 0.5 g/kg/day in bone marrow transplant patients (A).

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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Chapter 12
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Obese patient

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Abstract

As a response to metabolic stress, obese critically-ill patients have the same risk of nutritional deficiency as the non-obese and can develop protein-energy malnutrition with accelerated loss of muscle mass.

The primary aim of nutritional support in these patients should be to minimize loss of lean mass and accurately evaluate energy expenditure. However, routinely-used formulae can overestimate calorie requirements if the patient's actual weight is used. Consequently, the use of adjusted or ideal weight is recommended with these formulae, although indirect calorimetry is the method of choice. Controversy surrounds the question of whether a strict nutritional support criterion, adjusted to the patient's requirements, should be applied or whether a certain degree of hyponutrition should be allowed.

Current evidence suggested that hypocaloric nutrition can improve results, partly due to a lower rate of infectious complications and better control of hyperglycemia. Therefore, hypocaloric and hyperproteic nutrition, whether enteral or parenteral, should be standard practice in the nutritional support of critically-ill obese patients when not contraindicated. Widely accepted recommendations consist of no more than 60-70% of requirements or administration of 11-14 kcal/kg current body weight/day or 22-25 kcal/kg ideal weight/day, with 2-2.5 g/kg ideal weight/day of proteins.

In a broad sense, hypocaloric-hyperprotein regimens can be considered specific to obese critically-ill patients, although the complications related to comorbidities in these patients may require other therapeutic possibilities to be considered, with specific nutrients for hyperglycemia, acute respiratory distress syndrome (ARDS) and sepsis. However, there are no prospective randomized trials with this type of nutrition in this specific population subgroup and the available data are drawn from the general population of critically-ill patients. Consequently, caution should be exercised when interpreting these data.

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Key words: *Critically-ill obese patients. Hypocaloric nutrition. Indirect calorimetry. Predictive equations.*

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

Resumen

El paciente obeso crítico, como respuesta al estrés metabólico, tiene igual riesgo de depleción nutricional que el paciente no obeso, pudiendo desarrollar una malnutrición energeticoproteica,con una acelerada degradación de masa muscular.

El primer objetivo del soporte nutricional en estos pacientes debe ser minimizar la pérdida de masa magra y realizar una evaluación adecuada del gasto energético. Sin embargo, la aplicación de las fórmulas habituales para el cálculo de las necesidades calóricas puede sobrestimarlas si se utiliza el peso real, por lo que sería más correcto su aplicación con el peso ajustado o el peso ideal, aunque la calorimetría indirecta es el método de elección. La controversia se centra en si hay que aplicar un criterio estricto de soporte nutricional ajustado a los requerimientos o se aplica un cierto grado de hiponutrición permisiva.

La evidencia actual sugiere que la nutrición hipocalórica puede mejorar los resultados, en parte debido a una menor tasa de complicaciones infecciosas y a un mejor control de la hiperglucemia, por lo que la nutrición hipocalórica e hiperproteica, tanto enteral como parenteral, debe ser la práctica estándar en el soporte nutricional del paciente obeso crítico si no hay contraindicaciones para ello.

Las recomendaciones generalmente admitidas se centran en no exceder el 60-70% de los requerimientos o administrar 11-14 o 22-25 kcal/kg peso ideal/día, con 2-2,5 g/kg peso ideal/día de proteínas. En sentido amplio puede considerarse la nutrición hipocalórica-hiperproteica como específica del paciente obeso crítico, aunque las complicaciones ligadas a su comorbilidad hace que se planteen otras posibilidades terapéuticas, con nutrientes específicos para hiperglucemia, síndrome del distrés respiratorio agudo (SDRA) y sepsis. Sin embar go, no existe ningún estudio prospectivo y aleatorio con este tipo de nutrientes en este subgrupo concreto de población y los datos de que disponemos se extraen de una población general de pacientes críticos, por lo que deben tomarse con mucha precaución.

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Palabras clave: *Obeso crítico. Nutrición hipocalórica. Calorimetría indirecta. Ecuaciones predictivas.*

Introduction

In the past 3 decades, obesity has reached in developed countries an epidemic nature, with increased prevalence to values close to 30% of the population[1].

It is associated with significant comorbidity, that, in critically-ill obese patients, may affect various organs or systems: cardiovascular, pulmonary, peripheral vascular, hematological, metabolic, hepatobiliary, soft tissues and surgical wounds. Most complications must be diagnosed and treated early, including specialized nutritional support that contributes to global recovery, because they may theoretically increase mortality[2,3].

At present, the role of nutritional support in critically-ill obese patients is controversial[4] (III) in issues such as calculating their needs, method of administration, daily calorie-protein requirements, type of nutrients and time to start.

Obese patients have a similar metabolic response to stress than non-obese patients, which places them at the same risk of nutritional depletion, and may develop energy-protein malnutrition despite their lean mass reserves and excess body fat. They show a fast protein catabolism with relative protein depletion, increased net protein oxidation, and muscle mass degradation[5], and it is likely that therapeutic interventions to increase insulin sensitivity, such as specialized nutritional support itself, may improve its ability to remove or control muscle catabolism.

How does obesity influence mortality in critically-ill patients? Is nutritional support involved in any way in this relationship?

The influence of obesity in the progress and final outcome of critically-ill patients remains controversial. The studies published on the clinical outcome of critically-ill patients, stratified by body mass index (BMI), show significant discrepancies between them regarding the different degrees of malnutrition and/or obesity, particularly those in the extreme groups, malnourished, and morbidly obese[6].

These are observational, cohort or case-control, both prospective and retrospective studies, and no randomized studies have been published. In individual studies, with no intervention, increased mortality has been confirmed in intensive care unit (ICU) in obese versus non-obese patients[2,3,7-9] (III), in medical, surgical and traumatological patients, and also no influence of obesity in mortality[10-14] (III) and even a reduction of this[15] (III).

The metaanalysis by Akinnusi et al[16] (Ia) analyzed 14 studies including 15,347 patients divided into non-obese (BMI < 30 kg/m^2) and obese (BMI > 30 kg/m^2). There were no significant differences in mortality in ICU between obese and non-obese patients (11.4 versus 12.6%; RR: 1.00; 95% CI, 0.86-1.16; p = 0.97) (Ia). In the analysis of sub-groups mortality was lower in obese patients with a BMI of 30-39.9 kg/m^2 than in non-obese patients (RR: 0.86; 95% CI, 0.81-0.91; p < 0.0001). The metaanalysis by Oliveros et al.[17] (Ia) includes 12 studies comparing different groups of BMI to the group of patients with normal nutrition; however, for the analysis they group both mortality at the ICU and hospital mortality. Mortality in the overweight group (BMI: 25-29.9 kg/m^2) is lower than in the group with normal weight (BMI: 18.5-24.9 kg/m^2) (OR: 0.91; 95% CI, 0.84-0.98; p = 0.01). The group of obese patients (BMI: 30-39.9 kg/m2) have a lower mortality than those with normal nutrition (OR: 0.82; 95% CI, 0.68-0.98; p = 0.03), but the high heterogeneity (I^2 of 63.2%) and the lack of specificity for ICU detract validity of data. The metaanalysis by Hogue et al.[18] (Ia) groups 8 studies comparing the different groups of BMI with normal nutrition group and present independent data for their stay at the ICU. No significant differences have been found in mortality at the ICU, though hospital mortality was lower in the group of obese patients (RR: 0.76; 95% CI, 0.59-0.92). As in the other metaanalyses, the high heterogeneity (I^2 of 50-93%) subtracts validity to it, and these data must be considered with caution.

These studies have not evaluated any type of nutritional support and this has not been correlated to mortality or other evolutive parameters. The patients have not been stratified by severity criteria or age groups, although critically-ill obese patients usually have a much younger mean age than non-obese patients.

No study testing and comparing specifically some type of enteral nutrition (EN) or parenteral nutrition (PN) in critically-ill obese patients, evaluated as one of the objectives mortality related to nutritional support; therefore no recommendation may be concluded that prioritizes any type of nutritional support as more effective in the reduction of mortality in critically-ill obese patients[19-23] (IIb).

How can we calculate calorie requirements in critically-ill obese patients?

The use of calorie recommendations based on actual weight may lead to complications such as hyperglycemia and secondary infections[24] (IIa); therefore, there is controversy about the use of the current weight, ideal weight, or weight adjusted for calorie calculation. In this regard, some recommendations are based, either on a fixed percentage energy expenditure (60-70%) or on the current weight (11-14 kcal/kg/day) or ideal weight (22-25 kcal/kg/day)[25].

Adequate evaluation of energy expenditure in nutritional support is conflicting in critically-ill patients. Indirect calorimetry is considered to be the *gold standard*, confirmed by parallel measurements of direct calorimetry[26,27] (Ib). The alternatives commonly used are several standardized predictive equations. They are often inadequate, because the energy requirements of critically-ill obese patients are highly variable and their basic metabolic needs are difficult to predict[28] (IV).

In a recent systematic review[26], but without meta-analysis, Frankenfield et al. validated the use in critically-ill patients of 5 equations and only those of Ireton-Jones 1992 and Penn-State 1998 were considered useful in critically-ill obese patients. However, the data should be taken with caution due to the heterogeneity and the small sample sizes (IV).

A study on 202 critically-ill medical-surgical patients on mechanical ventilation[29] (IIb) compared resting energy expenditure (REE) measured by indirect calorimetry with 8 predictive equations with different variations and 15 different combinations. Only the Penn-State equation was accurate both globally and in the different subgroups, so it is therefore considered to be the advisable equation for use in critically-ill patients, whether obese or not. It was confirmed that neither the severity of the disease as measured by the SOFA, nor fever or traumatic, surgical or medical disease, changed the precision of the equations.

There is agreement in considering that, in critically-ill obese patients, the application of any formula using actual weight overestimates calorie needs, but the value of the different existing alternatives is still controversial, and there is not sufficient evidence to recommend the use of ideal weight or the adjusted weight.

When should artificial nutrition be started in critically-ill obese patients?

Although no studies have been specifically designed to settle this issue, it is considered that the onset of nutritional support in critically-ill obese patients with metabolic stress does not differ from that of non-obese patients[30]. In metabolic stress states, fat deposits of these patients are not sufficient to meet the energy requirements and the high protein catabolism may lead them to significant malnutrition. In obese patients undergoing metabolic stress, it is recommended that artificial nutrition is started early, within the first 36 hours[31] (IV).

What amount and type of energy substrates are required? What carbohydrates/lipid ratio?

Although the undesirable effect of underfeeding has been discussed in critically-ill patients[32], in critically-ill obese patients it has been found that normal protein hypercaloric nutritional support, compared to hyperproteic, hypocaloric supply, leads to fat mass accumulation and enables overfeeding without net protein gain[4], with some agreement in recommending hypocaloric nutrition, not exceeding 60-70% of the calculated calories (11 kcal/kg current weight/day or 22-25 kcal/kg of ideal weight)[25] (IV).

There are few studies based on the current recommendations that analyze nutritional support in this patient group, and most of them refer to PN.

Dickerson[19] (IIb) studied support with PN in 13 surgical critically-ill obese patients, providing 50% of the measured energy expenditure and 2.1 g of proteins/kg ideal weight. A weight loss of 1.7 kg a week was observed, with a positive nitrogen balance and a significant albumin concentration increase, associated with total wound healing, fistula closure and protein anabolism in the group of patients with mild to moderate stress.

The Choban group designed 2 studies with a low-calorie parenteral support. In the first study[23] (IIb), with a randomized, double-blind, prospective design, energy expenditure was measured in 16 obese patients using indirect calorimetry, supplying to a group 100% of the energy expenditure and to the other 50% of the expenditure measured. Both groups received 2 g protein/kg of ideal weight. The duration of the study was 14 days. There were no differences in the overall results, lengh of stay in the ICU, or nitrogen balance. The second[20] (IIb), in 30 obese patients, estimated energy expenditure based on the ideal weight, providing 2 g of protein/kg of ideal weight and administering non-protein calories at a 75/1 ratio to one group (14 kcal/kg) and 150/1 to the other group (22 kcal/kg). No differences were seen in the clinical outcome, but they maintained the same nitrogen balance, and the low-calorie group had a lower need for insulin and lower susceptibility to hyperglycemia.

In a study performed in 40 critically-ill obese patients with EN for at least 7 days[21] (IIb), they were grouped by calorie supply ≥ 20 kcal/kg of adjusted weight or < 20 kcal/kg body weight adjusted per day, with similar protein intake. The low-calorie group, as compared to the normal-calorie group, had a shorter stay at the ICU, shorter duration of antibiotic therapy and a trend towards fewer days on mechanical ventilation without differences in nitrogen balance.

Carbohydrates/lipid ratio as a source of energy has not been tested in critically-ill obese patients, so the standard recommendations should be followed, with a 60/40 or 70/30 ratio of the total non-protein energy, always searching for the best ratio which allows for controlling glycemia at adequate values, as well as triglycerides, that must be maintained below 400 mg/dL[33].

What are the protein needs and characteristics of their supply?

It is recommended that the protein supply accounts for 40-50% of REE, to minimize glucose load without affecting the catabolism of body lean mass[34] (IV). In addition, based on small studies, some randomized[20-24] (IIb), the recommended protein requirements are proportionally higher in critically-ill obese than in non-obese patients, establishing a supply of 1.8-2.1 g/kg ideal weight if BMI is 30-40 kg/m^2 and 2.1-2.5 g/kg ideal weight if > 40 kg/m^2.

What are the micronutrient and vitamin requirements?

The interest in the presumed benefits of micronutrients in critically-ill patients has led to conducting multiple studies on them, particularly those with a higher antioxidant effect, with irregular and often conflicting results. A combination of vitamins, antioxidants, and trace elements, including selenium, zinc, and vitamin E, may improve the overall results in critically-ill patients[35].

In a systematic review of trace elements and vitamins in critically-ill patients[36], alone or in combination, a reduction was seen in mortality, with no effect on infectious complications, particularly if the route was parenteral.

No specific study was performed in critically-ill obese patients, so no recommendations can be given and administration will be adapted to the general recommendations for critically-ill patients[35,36] (IV).

Can any specific nutrition be recommended in critically-ill obese patients?

In a broad sense, low-calorie and high-protein nutrition could be considered as specific of critically-ill obese patients. However, complications linked to comorbidity and the condition of the critically-ill patients lead to considering other therapeutic options. But there are no randomized, prospective studies or literature evidence analyzing the value of nutritional support with specific nutrients in this patients subgroup, so transferring the data applied to a general population of critically-ill patients should be taken with much caution.

Since hyperglycemia is a common metabolic complication in this type of patients, the use of specific enteral formulas containing carbohydrates with a lower glycemic index, supply of monounsaturated fatty acids and fiber should be considered[37,38] (III). The use of diets enriched with w-3 fatty acids and antioxidants may have beneficial effects in ARDS[39] (Ia). Glutamine dipeptide–supplemented parenteral nutrition leads to a better metabolic control and reduce septic complications[40] (III), so its administration in critically-ill obese patients could help to control these varaibles.

Recommendations

– Continuous indirect calorimetry is the gold standard in the assessment of energy requirements in critically-ill obese patients (A).

– None kind of nutritional support has achieved a mortality decrease in critically-ill obese patient (B).

– The energy needs of critically-ill obese patients are highly variable, which complicates estimation of energy needs using the predictive equations (C). Ireton-Jones 1992 and Penn-State 1998 formulas have the best correlation with indirect calorimetry (B).

– Artificial nutrition must be started early in critically-ill obese patients (C).

– In morbid obesity, low-calorie nutritional support is a reasonable choice, providing 50-60% of the measured energy expenditure or 18-20 kcal/kg of ideal weight (B).

– In other types of obesity low-calorie nutrition may also be used, as in morbid obesity, or estimate 20-25 kcal/adjusted weight/day (C).

– Protein supply should be administered, based on BMI, at 1.8-2.5 g/kg ideal weight/day (B).

– There is no clear evidence about the value of specific nutrients in this patient subgroup. Recommendations in this topic should be adapted to those established for the general population of critically-ill patients (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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Chapter 13

Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Critically-ill burnt patient

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Abstract

The response to severe burns is characterized by hypermetabolism (the most hypermetabolic existing model of aggression) and hypercatabolism, with a high degree of destruction of the skeletal musculature. Metabolic disorders are most evident in the first two weeks after the burn, although they can be prolonged in direct relation to the complications that these patients develop. Nutritional-metabolic support is an essential part of the treatment of these patients and should be started early, preferentially through the enteral route, with parenteral nutrition as complementary support. Exact calculation of calorie-protein requirements in these patients is difficult, even when indirect calorimetry is used, due to the high loss of proteins and CO_2 through the skin. Specific pharmaconutrients are indicated, with a high dose of micronutrients. The use of drugs or medications with anabolic effects is also sometimes indicated.

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Key words: *Critically-ill burnt patient. Hypovolemic shock. Complementary parenteral nutrition. Hyperproteic nutrition.*

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

Resumen

La respuesta que se objetiva tras una agresión térmica grave se caracteriza por hipermetabolismo (es el modelo de agresión más hipermetabólica que existe) e hipercatabolismo, con una elevada destrucción de la musculatura esquelética. Los trastornos metabólicos son más evidentes en las 2 primeras semanas tras la quemadura, aunque pueden prolongarse en relación directa con las complicaciones aparecidas. El soporte nutrometabólico forma parte indiscutible del tratamiento de estos pacientes y debe ser precoz, utilizando preferentemente la vía enteral y la nutrición parenteral complementaria. Es dificultoso el cálculo exacto de los requerimientos caloricoproteicos, aun empleando calorimetría indirecta, debido a las elevadas pérdidas cutáneas de proteínas y Co2. Cabe destacar la indicación de farmaconutrientes específicos, de dosis elevadas de micronutrientes y, en algunas situaciones, del empleo de medicaciones o fármacos con efectos anabólicos.

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Palabras clave: *Quemado crítico. Shock hipovolémico. Nutrición parenteral complementaria. Nutrición hiperproteica.*

Introduction

Thermal lesions range from relatively minor to the most severe, devastating lesion that can occur in humans. Once the lesion exceeds 15-20% of the body surface it causes a large number of systemic disorders, including metabolic response to aggression, immune disorders and water loss-poor distribution. Proinflammatory cytokines (IL-6, TNF), hormonal mediators, water loss by evaporation and leak of bacteria or their bioproducts (wound-bowel) play a major role in hypermetabolism and in the protein turnover increase.

Critically-ill burnt patient show pathophysiological particularities, characterized by a special tissue damage and hypovolemic shock secondary to fluid loss. The extremely significant permeability impairment is caused by various mediators (histamine, serotonin, quinines, free radicals and products of the arachidonic acid cascade). Hypovolemia, together with sympathetic stimulation, induces the release of catecholamines, vasopressin, angiotensin-II and neuropep-

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

Table I
Carlson equation for calorie calculation in critically-ill burnt patients

REE = (BME × [0.89142 + 10.01335 × TBSAB]) × m² × AF

AF: Activity factor of 1.25; BME: Basal metabolic expenditure; m²: Total body surface area in square meters; REE: Resting energy expenditure; TBSAB: Total body surface area burnt.

tides "Y", causing vasoconstriction and increased systemic vascular resistances. The initial increase in the resistance is in part due to the increased blood viscosity secondary to blood concentration due to fluid loss (which contrasts with other forms of injury where bleeding with loss of erythrocytes prevail). Vasoconstriction during insufficient resuscitation causes ischemia in the most sensitive organs, namely the kidneys and gastrointestinal tract. Myoglobin excretion is also increased due to rhabdomyolysis, which may contribute to renal damage. When associated with smoke inhalation thermal lesions may be added in the upper airways (that may cause obstruction), chemical lesions in lower airways, and toxicity by carbon monoxide and cyanides (that impair O_2 transport). Electric burns are deeper, with a greater morbidity, and may be associated with other lesions due to falls, falling against objects, or tetanic muscle contractions.

Essentially, the metabolic response to burns (that should be considered an injury model: thermal, electrical) is not different from the response to a injury of another etiology[1] (IV); maybe the differentiation points are both in the high, early skin loss of fluids with proteins, minerals, and micronutrients (acute malnutrition syndrome) and long term stay at the ICU. The magnitude of metabolic response is parallel to the extent and depth of the burns. In this case it reaches a value twofold the normal when the burn affects ≥ 60% of the total body surface area burnt (TBSAB), with persistent hypermetabolism status until coverage and healing of the burnt area is completed.

In summary, the hypermetabolic response that occurs following thermal aggression is characterized by progressive destruction of the skeletal muscle, above that shown in injury-sepsis states. This is where nutritional support, always replacing and trying to modify the metabolic-inflammatory response, plays its role. Therefore, nutritional-metabolic support is an unquestionable part of the treatment of these patients. In addition, the classical concept of young burnt patients, without previous nutritional disorders, should be modified given the increasing percentage of older patients, and with nutritional or metabolic conditions that influence the prognosis and treatment. All these metabolic disorders are more apparent in the first 2 weeks following the burn, but may continue directly related to the complications occurring. Although the medical literature on these conditions is relatively important, the groups analyzed are heterogeneous (burning as a single injury or associated with trauma, inhalation, etc.), involving a very low number of patients, and highly diverse objectives and variables[2] (IV).

Do critically-ill burnt patients show a specific metabolic pattern?

Hypermetabolism

Although in the classical studies it was considered that in these patients the resting energy expenditure (REE) from baseline, calculated by the Harris-Benedict equation, could reach values above 200%, a mean increase has been shown, which does not exceed 170%, but is even lower if seen on the basis of the current treatment of these critically-ill patients[3] (IV). The regular use of an effective sedation and analgesia minimizes the REE increase which involves pathological muscle activity episodes, seizures, pain or those of the management and treatment themselves: mobilizations, tracheal aspiration, etc. In these patients, when adequately sedated, the presence of fever is the main factor of increased REE.

Hypercatabolism

The mean nitrogen loss in burnt patients with no nutritional support exceeds 0.2 g of nitrogen/kg/day (15-20 g/day)[3] (IV). This means a weight loss of 10% in the first week, reaching 20-30% between the second and third weeks, values with a clear correlation with morbidity-mortality increase in patients without nutritional support.

What quantity and type of energy substrates are required in critically-ill burnt patients?

Calculation of calorie-protein requirements

The best method is still indirect calorimetry, though in its absence the formulae previously published should be used. Although there are formulae including the presence of burns (Ireton-Jones), and others based on respiratory physiology assumptions (Penn State) and applicable when the patient is on mechanical ventilation, we can recommend supplying 25 kcal/kg/day + 30-40 kcal × % TBSAB or applying the Carlson et al. equation[4] (Ib) (Table I). This would mean that a patient with over 30% of TBSAB would receive around 2,300-2,800 kcal and 16-18 g of nitrogen.

Carbohydrate supply

It is still the main energy source; glucose is the carbohydrate of choice. A glycemia monitoring and insulin supply protocol is required. While there are no conclusive data about blood glucose levels from which their harmful effects may be concluded[5] (Ia), or the efficacy of close control with insulin for improving prognosis[6] (Ib) it is recommended to monitor blood glucose levels, not permitting sustained hyperglycemia at values above 150 mg/dL, using the required amount of insulin and preventing hypoglycemia. Remember that carbohydrates are the main source of energy in burnt patients, with an optimum best perfusion rate established at 4-5 g/kg/day, though a calorie intake based on carbohydrates of 1,400-1,500 kcal/day[7] must not be exceeded.

Lipid supply

It is usually limited to 20-30% of total non-protein calorie supply, as a low lipid supply involves a better nitrogen retention, lower incidence of infectious complications and shorter stay[8] (Ib). The quality of calorie intake (LCT, MCT/LCT in physical mixture or structuring, oleic acid, ω-3 and their combinations) is under careful assessment. In our experience in these type of patients, emulsions rich in oleic acid cause less liver damage than physical mixtures MCT/LCT and help improving the control of inflammation[9] (Ib).

What are the protein needs and characteristics of their supply in critically-ill burnt patients?

As hypercatabolic patients, critically-ill burnt patients require a protein supply of at least 20-25% of the total calorie supply (> 1.5-2.0 g/kg/day). Non-protein kcal/g of nitrogen ratio will be set at 80:1 and 120:1.

Establishing nitrogen balance in these patients is complex, by including, in addition to nutritional support entries, nitrogen supply which represents the musculoskeletal catabolism given to preserve the visceral protein mass and the major skin losses of the area burnt, as appropriate. It has been shown that supplies of 1.5 g of protein/kg/day are not sufficient to make nitrogen balance positive in the first few days of aggression and, despite the fact that treatments including aggressive protein supplies appear to affect survival, the optimum amount of proteins to be provided is speculation.

In addition, there are various options for modulating the inflammatory response using different protein substrates. About the quality of amino acids it can be stated that, given the current recommendations, glutamine (> 0.3 g/kg/day)[10,11] (IV), both enteral[12,13] (IV) and parenteral[14] (Ib), seems essential as multispecific substrate in the aggression by burning and to generate arginine and glutathione. On a speculation basis, methionine supply appears to reduce catabolism and an additional proline supplement could be advisable for achieving an adequate healing.

What requirements of micronutrients, vitamins, and fiber are needed by critically-ill burnt patients?

These patients may show a deficit of trace elements, such as selenium (related to thyroid hormone disorders in the critically-ill patient), zinc and copper, so it is advised to give high-dose supplements[15] (Ib). They should also receive fat-soluble and water-soluble vitamins attempting to meet the requirements and prevent peroxidation and lesions due to free radicals[16] (Ia). No specific recommendations on fiber supply are known.

Do critically-ill burnt patients require administration of drugs with metabolic implications?

The aggression is associated with increased values of catecholamines and catabolic hormones. Therefore, it is logical to assume that the blockade of this response or the use of anabolic steroids may attenuate hypermetabolism or stop catabolic response[17] (IV).

In critically-ill burnt patients, beta-adrenergic blockers and oxandrolone were used with relatively good outcomes[17] (IV).

Beta-adrenergic receptor blockers (propranolol, metoprolol)

They attenuate hypermetabolism and slow heart rate, decreasing heart oxygen demand while reducing catabolism and lipolysis. There are studies in pediatric populations that show reductions in mortality, the incidence of burn infection, and the time to healing.

Oxandrolone

A testosterone analog, that may be useful for patients with a large burnt body surface.

What is the most advisable supply route?

Specialized nutritional support (SNS) should be adjusted individually, in amount and quality, to the condition and the patient. It should be supplied through the digestive tube preferably and early. In some cases parenteral support will complement or will replace the enteral route when this is insufficient or unusable[18,19] (IV).

Whenever the patient is hemodynamically stable (with no risk of involvement of splachnic area flow), no unwanted increase occurs in gastric residue, and there is no concomitant severe abdominal injury or ileus secondary to drug support, the route of choice is the enteral. Enteral nutrition (EN) has a protective effect on gastrointestinal immune and metabolic functions and is associated with significant reductions of infectious morbidity[20] (Ib). In gastrointestinal administration, using nasoenteral tubes or placing jejunal tubes or gastrostomies should be considered, based on the surgeries required by the patients. In digestive intolerance with elevated gastric residue, the use of prokinetics may contribute to achieve an adequate SNS.

However, for multiple reasons associated with the disease or the treatment, the enteral route may, for several days, not complete nutritional supply, and, therefore, parenteral nutrition (PN) should be used, alone or in combination with EN (complementary nutrition)[21] (IV). An attempt should be always made to maintain the enteral line with an early approach, though the amount of nutrients to be supplied is initially low. However, it must be noted that critically-ill burnt patients, due to their high calorie and protein requirements, are a paradigmatic example of mixed nutritional support (2 or 3 lines): parenteral and enteral, and the parenteral route may be central or peripheral and EN by tube or oral. The purpose is to provide an adequate, balanced amount of nutrients preventing-limiting-modulating the adverse events of the disease.

Recommendations

– The energy supply, in the absence of indirect calorimetry, will be set at 25 kcal/kg/day + 30-40 kcal × % of the total body surface area burnt or according to the Carson formula (B).

– A hyperproteic diet (1.8-2.5 protein g/kg/day) is recommended, with a fat percentage below 30% of the total calorie intake. Thus, glucose supplies above 4 g/kg/day may be justified in these patients (B).

– It is recommended to administer high-dose glutamine supplements (L-glutamine > 0.37 g/kg/day, Gln dipeptide > 0.5 g/kg/day) (A).

– Enteral nutrition (gastric or enteral catheter, surgical ostomies), is of choice. Nevertheless, complementary or exclusive parenteral nutrition will be used if the gastrointestinal approach is not feasible or effective (A).

– High daily supplies of Se, Cu, and Zn are recommended (B).

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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Chapter 14
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Multiple trauma patient

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Abstract

Patients with polytrauma can be viewed as paradigmatic of the critically-ill patient. These previously healthy patients undergo a life-threatening aggression leading to an organic response that is no different from that in other types of patients. The profile of trauma patients has changed and currently corresponds to patients who are somewhat older, with a higher body mass index and greater comorbidity. Severe injuries lead to intense metabolic stress, posing a risk of malnutrition. Therefore, early nutritional support, preferentially through the enteral route, with appropriate protein intake and glutamine supplementation, provides advantages over other routes and types of nutritional formula. To avoid overnutrition, reduced daily calorie intake can be considered in obese patients and in those with medullary lesions. However, little information on this topic is available in patients with medullary lesions.

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Key words: *Mutiple trauma. Glutamine. Calorie requirements. Pharmaconutrition.*

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

Resumen

El paciente traumatizado puede considerarse el paradigma del paciente crítico que, previamente sano, sufre una agresión que pone su vida en riesgo y que determina una respuesta orgánica en nada diferente a la presente en otro tipo de pacientes. El perfil del paciente traumático ha cambiado, siendo en la actualidad algo más mayores, con índices de masa corporal más elevados y con una mayor comorbilidad. Cuando la agresión es grave, su respuesta metabólica es intensa y condiciona un riesgo nutricional. por ello, el soporte nutricional precoz, de preferencia enteral, con aporte proporcionado de proteínas y suplementado con glutamina, condiciona ventajas competitivas con otras vías y tipos de fórmulas nutricionales.

La presencia de obesidad y/o lesión medular debe hacernos considerar una disminución proporcionada del aporte calórico diario, evitando la sobrenutrición, aunque en los pacientes con lesión medular es escasa la información disponible.

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Palabras clave: *Politrauma. Glutamina. Necesidades calóricas. Farmaconutrición.*

Introduction

The profile of injured patients ranges from the young healthy patient suffering an accident when driving a motor vehicle to the somewhat older patient, with associated conditions suffering a precipitation or is run over[1]. Social behavior changes are leading to an increase in patients with overweight, an even clearly obese. These circumstances make the injured patient undergo a higher nutritional risk than those derived from the traumatic aggression in a previously healthy patient and condition a response more in line with the seriously ill patient with complications.

Injured patients show metabolic changes[2] and immunosuppression, with an increased risk of infection and post-traumatic organ failure. The generated hypermetabolic situation must be recognized promptly and be settled readily and for the time needed, as it may last weeks. There are some controversial issues in the nutrition of these patients, such as the time required to start, calorie distribution of macronu-

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

trients, the administration route and the duration of nutritional support.

This chapter excludes brain injury, that will be reviewed in the chapter of neurocritical patients.

When is specialized nutritional support indicated in patients with polytrauma?

In all patients with severe polytrauma and disability or oral nutrition contraindication, artificial nutritional support must be planned. Injured patients with an injury severity score (ISS) > 16 must be considered seriously ill, and, therefore, at an increased nutritional risk, and should be assessed for it[2] (III).

Patients in whom disability for feeding is suspected in the first 5-7 days should immediately start nutritional support, once stabilized[3-5] (IV).

What route should be used to provide the nutrient?

The goodness of enteral nutrition (EN)[6] (III), [7] (IIa), [8,9] (Ib), [10] (Ia) was established from the studies by Moore in 1981, instituting enteral catheters for early nutrition in patients where laparotomy was required for injury reasons.

Ideally, artificial nutrition should be started early, once hemodynamic stability is obtained, by gastric or postpyloric EN[11] (Ib), [12] (III), [13] (IV), not excluding complementary parenteral nutrition (PN) or its exclusive use when it is expected that the patient may not take any food in the first 3 days, or a prolongation of this disability beyond 5-10 days is expected. This supply as complementary PN is object of disagreement between the American Society for Parenteral and Enteral Nutrition (ASPEN)[5] (IV) and the European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations[14] (IV). ASPEN does not recommend it for the first 7-10 days in patients unable to tolerate some amount of EN, as parenteral supplies in patients reaching at least 1,000 enteral calories are associated with a higher infectious morbidity and an increased in late ARDS, with the resulting prolongation of stay and mechanical ventilation[15] (III). Meanwhile, ESPEN[14] (IV) recommends that, given the impact of the calorie deficit on the final outcome, patients with early inability to assume a sufficient amount of calories by enteral route must receive supplemental nutrition by venous route in the first 2 days of progress. There is not sufficient evidence to assume the best recommendation, but as the optimum nutrition is correlated to the better clinical outcomes of the patient at the intensive care unit (ICU), the European position appears to be more advisable, with pending studies to clarify this issue[16] (IV).

An early EN (within the first 24-48 hours of admission), in addition to increasing tolerance, helps avoid gastrointestinal complications such as constipation[17] (III). There is no evidence of superiority of continuous nutrition over intermittent nutrition, with contrary results on oxygen consumption[18,19] (III) and bowel complications, but continuous infusion appears to show a trend towards lower mortality[20] (IIa).

Administration of full doses may be used without this involving an increased intolerance, confirming an increase in regurgitation episodes, but with a better compliance with calorie requirements[21] (Ib). It is recommended to use prokinetics drugs to achieve an effective application of EN[22] (Ia).

What calorie amount should be provided?

Although the available evidence is not unquestionable, there is adequate doctrine to prevent overnutrition[23] (III).

The amount of calories to be provided is obtained by indirect calorimetry, that has been used as comparison pattern for the different predictive formulae. At present, it is accepted that the increase in calorie needs of patients with polytrauma does not exceed 40% of those established by the Harris-Benedict equation, which means 25-30 kcal/kg/day, that in the case of injured obese patients (BMI > 30 kg/m^2) decreases to values < 20 kcal/kg actual weight/day[23,24] (III) (see chapter 12).

In spinal cord injury patients it is estimated that supplies of 20-22 and 23-24 kcal/kg/day may replace the needs of quadriplegic and paraplegic patients, respectively[25-27] (III).

How should feeding be accomplished?

There is no evidence supporting a given calorie distribution in patients with polytrauma, that must be adjusted to the specific particular circumstances of each individual patient and the general recommendations for critically-ill patients. As in any seriously ill patient, a reasonable control of glycemia should be maintained (see chapter 10). Glucose supply will range from 50 to 70% of non-protein calories, with fat supplies from 20-30%. In PN, these lipid solutions should not have a concentration under 20%[28] (Ib) and their composition should include fatty acids derived from fish (ω-3), because of their anti-inflammatory activity[29] (IV). Exclusive supply of ω-6 must be avoided, replacing them in part by others with a lower proinflammatory capacity[30] (Ib).

Pharmaconutrition provides therapeutic benefits to surgical patients and, specifically, patients with polytrauma, either as mixtures of arginine, and ω-3 fatty acids, without glutamine[4] (III), [31] (IV), or with glutamine[32] (IV), either supplemented with enteral[33] (Ib) or parenteral glutamine[34,35] (Ib). A reduction was confirmed in the infection rate, length of stay in the ICU, hospital stay and, in some cases, mortality in septic patients[36] (Ib). A metaanalysis[37] (Ia) supports the use of ω-3 and also questions the use of arginine. The greatest evidence available in patients with polytrauma recommends using glutamine supplementation[38] (Ia), [35-39] (Ib).

Vitamin and/or antioxidant mineral supply reduces the inflammatory response[40] (Ib) and may reduce morbidity and mortality in patients with polytrauma[41] (III).

The attenuation of the inflammatory response, reduction of inflammatory mediators, better and greater hormonal secretion, better healing and better capacity defence, lead pharmaconutrition to be advisable in injured patients, improving the length of stay, both at the ICU and at the hospital, as well as infectious complications and mortality[42] (Ib).

Patients with spinal cord injury

Patients with spinal cord injury show a somewhat different behaviour, and, after a metabolic lethargy period[26,43] (IV), a phase of intense proteolysis starts, which is difficult to control with nutritional support[25] (III), since the pathophysiological base is more related to the denervation/disuse[44] than to the neuroendocrine storm of acute critically-ill patients. In any case, in the first 4 weeks following spinal cord injury, weight loss occurs, which can be estimated at 10-20% of body weight, and about 85% of this is lean mass loss[27,43] (III).

In patients with cervical injury, there are no large nutritional studies performed and potential evidences are based on small series not answering the basic questions related to nutritional support (administration route, requirements, time to start, type of nutrients) in these cases[45] (IV).

Experimental studies in rats, with cervical injuries of different severity, different periods of gastroparesis have been verified, based on the location and severity of the injury (6 weeks for sprains and absence of recovery of gastric motility after cervical section above C5)[46] (IV). Some data suggest that neither the early nutrition support not the adequate compliance with calorie requirements improve the outcomes in cervical injuries[47] (IV), [48] (IIb).

Recommendations

– In the absence of calorimetry a total daily calorie supply of 25-30 kcal/kg/day is recommended in non-obese trauma patients (B).

– In patients with spinal cord injury a nutritional supply of 20-24 kcal/kg/day is recommended (C).

– The use of glutamine is recommended in patients with polytrauma (A).

– It is recommended to use other pharmaconutrients (ω-3, arginine, antioxidants) in the nutritional support of severe trauma patients (C).

– Preferential use of gastric enteral nutrition is recommended, with or without prokinetics, and trans-pyloric enteral nutrition will be considered if neccesary (A).

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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Chapter 15
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Septic patient

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Abstract

Nutritional metabolic management, together with other treatment and support measures used, is one of the mainstays of the treatment of septic patients. Nutritional support should be started early, after initial life support measures, to avoid the consequences of malnutrition, to provide adequate nutritional intake and to prevent the development of secondary complications such as superinfection or multiorgan failure.

As in other critically-ill patients, when the enteral route cannot be used to ensure calorie-protein requirements, the association of parenteral nutrition has been shown to be safe in this subgroup of patients. Studies evaluating the effect of specific pharmaconutrients in septic patients are scarce and are insufficient to allow recommendations to be made.

To date, enteral diets with a mixture of substrates with distinct pharmaconutrient properties do not seem to be superior to standard diets in altering the course of sepsis, although equally there is no evidence that these diets are harmful.

There is insufficient evidence to recommend the use of glutamine in septic patients receiving parenteral nutrition. However, given the good results and absence of glutamine-related adverse effects in the various studies performed in the general population of critically-ill patients , these patients could benefit from the use of this substance. Routine use of omega-3 fatty acids cannot be recommended until further evidence has been gathered, although the use of lipid emulsions with a high omega-6 fatty acid content should be avoided. Septic patients should receive an adequate supply of essential trace elements and vitamins. Further studies are required before the use of high-dose selenium can be recommended.

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Key words: *Sepsis. Septic shock. Glutamine. Arginine.*

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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: PACIENTE SÉPTICO

Resumen

El manejo metabólico nutricional constituye, junto al resto de medidas de tratamiento y soporte, uno de los pilares del tratamiento del paciente séptico. Debe iniciarse precozmente, tras la resucitación inicial, con el objetivo de evitar las consecuencias de la desnutrición, proveer el adecuado aporte de nutrientes y prevenir el desarrollo de complicaciones secundarias como la sobreinfección y el fracaso multiorgánico.

Al igual que en el resto de pacientes críticos, cuando la ruta enteral es insuficiente para asegurar las necesidades caloricoproteicas, la asociación de nutrición parenteral ha demostrado ser segura en este subgrupo de pacientes. Los estudios que evalúan el efecto de farmaconutrientes específicos en el paciente séptico son escasos y no permiten establecer recomendaciones al respecto.

Respecto a las dietas enterales con mezcla de sustratos con diferente capacidad farmaconutriente, su uso no parece aportar, hasta el momento actual, beneficios claros sobre la evolución de la sepsis respecto a las dietas estándar, aunque tampoco hay clara evidencia de que sean perjudiciales.

A pesar de que no hay suficiente evidencia para recomendar el empleo de glutamina en el paciente séptico que recibe nutrición parenteral, éste podría beneficiarse de su uso, dados los buenos resultados y la ausencia de efectos adversos atribuible a la glutamina en los diferentes estudios llevados a cabo en el conjunto de pacientes críticos. No se puede recomendar el empleo rutinario de ácidos grasos ω-3 hasta que dispongamos de mayor evidencia, aunque debe evitarse en estos pacientes el empleo de emulsiones lipídicas con alto contenido en ácidos grasos ω-6. El paciente séptico debe recibir un adecuado aporte de oligoelementos y vitaminas. El empleo de selenio a dosis altas requiere de más estudios para poder recomendarlo.

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Palabras clave: *Sepsis. Shock séptico. Glutamina. Arginina.*

Introduction

Nutritional support in sepsis shows very important limitations in its indications and evaluation. On the one hand, the *Surviving Sepsis Campaign*[1] does not consider specialized nutrition as an issue that must be complied with, but, on the other hand, all reviews performed by experts claim the need for this nutritional support. In addition, the studies published on nutritional support in septic patients are very limited and the results of other populations of critically-ill patients or those suffering another aggression are usually extrapolated. The conclusions on the use of specialized nutritional support in sepsis are usually aimed at improving the hospital length of stay, organ function and other surrogate objectives, and only three studies have been published[2-4] that have reported a decreased mortality. An added difficulty is that most of studies on nutrition and sepsis were conducted with mixtures of nutrients, so it is difficult to allocate the results to one or the other substrate.

Therefore, in this scenario there is a common opinion about the need for feeding septic patients, but there is no definition yet of the quality, the amount, or the timelines for the requirements of substrates.

Is it safe to administer enteral nutrition to patients in septic shock?

As in all other critically-ill patients, provided the gastrointestinal tract is intact and the patient requires artificial nutrition, the enteral route is of choice over the parenteral. The start of enteral nutrition (EN) should be early, within 24-48 hour and after resuscitation of the patient. Splachnic infusion may be compromised in hypotensive patients with inadequate perfusion pressure and, although the reported incidence of intestinal ischemia associated with EN is low and particularly related to postpyloric nutrition[5] (III), [6,7] (IV), and there is no evidence contraindicating the administration of EN in early stages of the shock, it appears to be advisable to recommend, given the fatal consequences of intestinal ischemia, to start EN after patient resuscitation or at least when a stable shock stage has been reached, with an adequate perfusion pressure (doses of vasoactive drugs stabilized, metabolic acidosis and lactate stabilized and/or decreasing, mean blood pressure of ≥ 60 mmHg).

In any case, particularly in the early stages of shock, close monitoring for signs of intestinal intolerance (abdominal distension, increased gastric residue, etc.) is necessary to early identify signs of subclinical intestinal ischemia.

Is the use of parenteral nutrition harmful in sepsis?

In a 1-day observational prevalence study performed in 454 intensive care units (ICUs) in Germany[8] and in 415 patients with severe sepsis or septic shock, it was confirmed that patients with severe sepsis or septic shock receive in Germany a nutritional support preferably with parenteral nutrition (PN), alone or in combination with EN. After analyzing the results, it is concluded that the use of PN was associated with an increased risk of death[8] (III). However, in this study, for its limitations, no adjustment was made with other factors of treatment, for example if the antibiotic therapy was appropriate or resuscitation adequate, and the authors specified[9] that they do not refer to a causal relationship but to an association, and confirm that PN plays a role in patients with contraindications for EN or where the nutritional needs are not achieved by the enteral route.

In contrast, a randomized, controlled, prospective study on PN vs EN enriched with pharmaconutrients (mixture of arginine, ω-3 and antioxidants) in septic patients reported a greater intra-ICU mortality in the enteral group[10] (Ib).

Are diets with mixtures of pharmaconutrients indicated in sepsis?

Only one controlled study has been published on the effects of diets enriched with "immunomodulating" pharmaconutrients (arginine, ω-3, nucleotides, antioxidants) in septic patients in a critical condition. Its results indicate that the use of an enriched diet is associated with lower mortality compared with the use of a control diet[3] (Ib). In the study by Kieft et al.[11], in a group of critically-ill patients for various causes, no differences were seen in terms of mortality, infectious complications, length of stay in ICU and days on mechanical ventilation. An analysis of the patient subgroup with sepsis shows that this was so small (30 patients) that an efficacy study could not be considered in it[11] (Ib).

The metaanalyses published on studies comparing diets enriched with pharmaconutrients with non-enriched diets, do not include a specific analysis of the group of septic patients, because of the few studies available. However, there is a known controversy about the outcomes and recommendations of the different metaanalyses. Heyland et al.[12] suggested that the use of diets enriched with "immunomodulating" pharmaconutrients (IMD) may be associated with increased mortality. Montejo et al.[13], in contrast, concluded that there is sufficient evidence to use IMD in critically-ill patients, considering the benefits associated with their use and the lack of harmful effects. Marik and Zaloga[14], in the last metaanalysis published, concluded that only in the group of patients with sepsis, septic shock, or acute respiratory distress syndrome (ARDS), the use of IMD was associated with a significant decrease of mortality, secondary infections, and stay at the ICU, but provided this formula contained fish oil.

Other formulations enriched with pharmaconutrients, initially designed for acute lung injury (ALI) or ARDS, have been investigated in septic patients. A multicenter study in patients undergoing mechanical ventilation with severe sepsis and septic shock[4] (Ib) reported a 19.4% reduction in the absolute risk of mortality, improved oxygenation, more days free from mechanical ventilation, decreased stay at the ICU and less development of new organic dysfunctions in the group receiving the study diet. A more recent multicenter study[15] (Ib) showed a significant decrease in the mean length of stay in the ICU without affecting mortality or infectious complications in the intention to treat analysis.

Controversy about the use of diets enriched with pharmaconutrients (in the two modalities of arginine/ω-3/antioxidants or EPA/GLA/antioxidants) in septic patients persists. However, the results available do not seem to suffice for contraindicating the use of this type of diets in patients with severe sepsis. In contrast, administration may be followed by benefits.

Is the use of arginine harmful in sepsis?

It is known that sepsis is a condition associated with arginine deficit and arginine has been associated with benefits for sepsis, such as an increase in acute phase reactants, genesis of nitric oxide (NO) with antibacterial activity, action as bowel neurotransmitter and regulator of microcirculation, production of ornithine promoting cell growth and cell differentiation and activity in insulin stimulation, as well as modulation of cell signals from its metabolite, agmatin. However the use of arginine in sepsis is currently questioned in various clinical guides, unlike in other group of critically-ill patients. This is due to the fact that the results expressed in the above mentioned metaanalysis by Heyland et al.[12] on the use of pharmaconutrient formulations that contained arginine and where the authors concluded that the benefits were dependent on the amount of arginine (a higher supply was associated with lower mortality) but also on the target population, and therefore they suggested there was a trend towards increased mortality with arginine supply in critically-ill patients, particularly those with septic shock[12] (IV).

However, to enhance this controversy, in a later metaanalysis[14] the authors concluded that the action of IMD with arginine on the progress of patients with sepsis or systemic inflammatory response syndrome (SIRS) could not be evaluated using the studies reviewed in it[14] (Ia).

With regard to the results using arginine alone in sepsis, the small number of cases studied gives it a low level of evidence. Thus, in 2 studies of the same research group, supplements containing intravenous arginine did not evidence any hemodynamic adverse event, but these results have been only communications and have never been published[16,17] (III). Lorente et al.[18], with the administration of a bolus of 200 mg/kg of L-arginine in a group of 7 patients with septic shock, noticed immediate hemodynamic changes because of pulmonary and systemic vasodilation, though these changes were transient[18] (III).

The increased NO synthesis in sepsis is based on the evidence of the high plasma concentration of its degradation products, nitrates, nitrites (NOx). However, there are disagreements about the real changes in vivo in the genesis of NO and NOx. For the moment, there is only one study that has measured production in vivo of NO in septic patients via its conversion rate in NOx, and reporting slower NOx fractionated synthesis rates in septic patients (n = 6), while the absolute rate was identical to healthy controls (n = 10)[19] (IIb).

As arginine is an amino acid that is decreased in sepsis and it is considered necessary to restore its values, new pathways are under research to restore this deficit supplying citrulline[20].

Is glutamine administration of choice in sepsis?

Although no studies have been performed in humans to evaluate the effect of glutamine on septic patients receiving PN, there is sufficient evidence to the routine use of glutamine in all critically-ill patients receiving PN[21,22] (Ib). After aggression, glutamine plays a major role in inducing mechanisms of cell protection mainly through increasing production of heat shock proteins, as their expression protects against cell damage and against ischemia/reperfusion mechanisms[23] (IIa), which gives it a potential role to prevent progression to multiple organ failure.

With regard to glutamine by enteral route, currently there are insufficient data for recommending it in septic patients and to recommend its intravenous use, as a supplement, when the patient is receiving EN. In a randomized, controlled, prospective study in 55 patients with sepsis and comparing the administration of an enteral diet enriched with glutamine and antioxidants to a standard enteral diet, the intervention group had improved parameters of multiple organ failure versus the control group[24] (Ib), but these outcomes are, however, questioned because the intervention group received a significantly higher protein supply, which may have influenced the results.

What lipid emulsions must be used in sepsis?

The potential benefit of adding ω-3 to EN in critically-ill septic patients shows non-conclusive results, because it is based on studies with diets of different composition from other substrates, different amount and percentage of ω-3 and different comparative agents. Beneficial effects have been reported in terms of mortality, days on mechanical ventilation and days of stay at ICUs with administration of a diet rich in

EPA, with GLA and antioxidants[4], while in other studies, with the same diet, these results could not be confirmed and only reported a reduction in the incidence of nosocomial pneumonia and organ dysfunction.

As regards their use in PN, the results are somewhat more conclusive and are related to the dose of ω-3 provided. In a prospective study on a survey involving 661 ICU patients with PN ≥ 3 days, with a 10% emulsion of fish oil added to LCT versus a control of LCT, the dose-dependent effects of ω-3 on survival, days of stay, use of antimicrobials and organ dysfunction were evaluated[25]. The most favorable effects were obtained at doses of 0.1-0.2 g/kg/day for survival, infection rates and length of stay. In addition, antimicrobial requirements decreased 26% when comparing doses of 0.15-0.2 g/kg/day to doses < 0.05 g/kg/day[25] (III).

A subsequent randomized, double-blind, controlled study including 166 critically-ill medical patients receiving PN with MCT/LCT, or MCT/LCT supplemented with fish oil, in the subgroup of patients with sepsis[26] no differences were found on both IL-6 or other inflammatory markers, but also on mortality, days of stay at an ICU, days on mechanical ventilation, infectious or bleeding complications[26] (Ib).

A recent randomized, single-blind study[27] including 25 patients with sepsis receiving PN with MCT/LCT versus MCT/LCT/fish oil did not show significant differences in terms of mortality, days on mechanical ventilation or length of stay in ICUs[27] (IIa).

Do antioxidants play a relevant role in patients with sepsis?

The plasma concentration of micronutrients with antioxidant capacity decreases in critically-ill patients, particularly in septic patients[28] (IV). Therefore, special attention should be paid to the supply of trace elements (particularly selenium, zinc and copper) and vitamins in these patients.

It has been suggested that high-dose selenium supplements in patients with severe sepsis or septic shock can improve outcome. However, the studies available to date have found no significant differences versus the control group when analyses by intention to treat are performed[29,30] (Ib). Further clinical studies are required to evaluate the efficacy and safety of selenium in septic patients. The neutral outcomes of these studies may be related to inadequate doses, an inadequate method of administration or an incipient toxicity of sodium selenite, that could have masked a positive effect. The REDOX study, in the recruitment phase, may shed some light on the potential beneficial effect of selenium for these patients[31].

Recommendations

– In patients with septic shock and hemodynamic instability it is recommended to delay the start of specialized nutritional support until the patient has been adequately resuscitated and is in a stable condition (C).

– Parenteral nutrition is a safe route in sepsis when there is no other option for feeding patients (C). Complementary parenteral nutrition could be used when calorie supply requirements may not be reached by the enteral route (C).

– Enteral diets with mixtures of substrates with different pharmaconutrient capacity can provide outcome benefits in septic patients (C).

– Administration of diets enriched with arginine in severe sepsis and septic shock is not cleary associated with deleterious effects in patient outcomes (C).

– When parenteral nutrition is indicated, it is recommended to use glutamine supplements (B).

– In parenteral nutrition it is recommended to use lipid emulsions with low contents in ω-6 (B). Emulsions containing ω-3 may be used in these patients (C).

– High-dose selenium supplements alone may not be recommended routinely in septic patients (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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Chapter 16
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Neurocritical patient

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Abstract

Neurocritical patients require specialized nutritional support due to their intense catabolism and prolonged fasting. The preferred route of nutrient administration is the gastrointestinal route, especially the gastric route. Alternatives are the transpyloric route or mixed enteral-parenteral nutrition if an effective nutritional volume of more than 60% cannot be obtained.

Total calore intake ranges from 20-30 kcal/kg/day, depending on the period of the clinical course, with protein intake higher than 20% of total calories (hyperproteic diet). Nutritional support should be initiated early.

The incidence of gastrointestinal complications is generally higher to other critically-ill patients, the most frequent complication being an increase in gastric residual volume. As in other critically-ill patients, glycemia should be closely monitored and maintained below 150 mg/dL.

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Key words: *Neurocritical patient. Traumatic brain injury. Early nutrition. Hyperglycemia.*

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

Resumen

El enfermo neurocrítico precisa un soporte nutricional especializado debido a su intenso catabolismo y a un prolongado período de ayuno. La vía de administración nutricional preferente es la gastrointestinal, particularmente la vía gástrica, siendo alternativas la vía transpilórica o la nutrición mixta enteral-parenteral en caso de no obtener un volumen nutricional eficaz superior al 60%.

El aporte calórico total oscila entre 20-30 kcal/kg/día, según el período de evolución clínica en que se encuentre, con un aporte proteico superior al 20% de las calorías totales (hiperproteico). El inicio del aporte nutricional debe ser precoz.

La incidencia de complicaciones gastrointestinales es superior al enfermo crítico en general, siendo el aumento del residuo gástrico el más frecuente. Debe establecerse un estrecho control de la glucemia, manteniéndose por debajo de 150 mg/dl como en el resto de los enfermos críticos.

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Palabras clave: *Paciente neurocrítico. Traumatismo craneoencefálico. Nutrición precoz. Hiperglucemia.*

Introduction

Neurocritical patients with brain injury (BI), ischemic or bleeding stroke, or tumor disease, often differ from critically-ill patients in general in several aspects:

– They require drugs and techniques that modify their metabolic status: sedatives, analgesics, barbiturates, muscle relaxation and occasionally hypothermia[1], for at least 5 days, to induce a deep sedation and adequate control of intracranial hypertension.

– BI has a greater incidence in young people and subarachnoid bleeding affects patients between the fourth and sixth decades of life, with adequate nutritional status and, generally, without associated comorbidities. The neurocritical patient with non-subarachnoid vascular disease is generally older, shows a high incidence of metabolic disorders, such as diabetes and hypertriglyceridemia, and the extent of brain recovery is lower, with the resulting longer stay in the ICU[2,3].

– Brain injuries cause gastrointestinal complications, particularly delayed gastric emptying, evidenced

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as increased gastric residue (IGR)[4] in patients receiving enteral nutrition (EN).

– In general, the clinical stabilization period is not long, though the use of vasoactive drugs is common, due to the associated injuries or the need for maintaining an adequate brain perfusion pressure.

– They require long periods of mechanical ventilation related to their low neurological level.

– The neurocritical patient of traumatic etiology develops hypermetabolic and hypercatabolic responses, with a severity not clearly related to severity levels as measured by the Glasgow scale (GCS). Thus, the lower coma grades (GCS, 4-5) show a greater energy expenditure that the higher (GCS, 8-11), and these in turn higher than the intermediate (GCS, 6-7)[5].

– The duration of metabolic response is long, with a peak maximum activity around 2 weeks after admission and a more moderate persistence from the third week[6].

What are the recommended administration routes in neurocritical patients? How can the requirements be calculated?

Specialized nutritional support in neurocritical patients is essential, due to their hypercatabolism and as generally the period with no oral intake and on mechanical ventilation is longer than 3 days[7] (Ib). Administration should be performed early[8-11] (Ib), as in all other critically-ill patients, and preferred administration route is the enteral[12] (Ib). A large study in patients with BI evidenced that a cumulative energy deficit in the first 5 days of progress is related to an increased mortality of 30-40% per 10 kcal/kg of cumulative deficit[13] (Ib). However, there are very few studies comparing early and late EN in neurocritical patients[14].

The semi-seated position, with the head of the neurocritical patient elevated 30º, improves brain distensibility, significantly reduces intracranial pressure[15,16] (IIb) and the risk of bronchial aspiration[17] (IIa).

Except if there is a formal contraindication or if the volume administered with EN is less than 60% of the scheduled volume, the nutrient supply route in neurocritical patients is the enteral. However, there are not enough studies supporting the advantages of EN in contrast to parenteral nutrition (PN). The use of barbiturates for deep sedation is a factor determining intolerance to EN, so the use of PN is preferred in these cases[18] (IIa).

Monitoring and evaluation of calorie intake should be performed using indirect calorimetry, which allows for calculating the total energy expenditure (TEE), the respiratory quotient, and consumption and use of the different substrates[19,20] (Ib). When indirect calorimetry is not available, several formulae have been proposed for estimating the TEE, applying a correction factor within 1.2-1.4 of the basal energy expenditure. However, based on the severity and evolutive patient status, the proposed values for correction factors may underestimate or overestimate calorie needs. Therefore, an adequate calorie intake may be about 20-25 kcal/kg/day in patients with muscle relaxation, and about 25-30 kcal/kg/day in sedated patients. Several factors advise reducing calorie intake, including sedation 20%, analgesia with morphine derivatives 8%, muscle relaxation of 12-28%, treatment with barbiturates of 13-32% and hypothermia or beta blockers 5%[21] (III).

What substrates should be administered to a neurocritical patient?

Calorie supplies should be given by administration of glucose, with supplies under 5 g/kg/day and fats of 0.7-1.5 g/kg/day. Protein supply is about 1.3-1.5 g/kg/day in the acute phase and 1.3 g/kg/day from the second week. According to the increase in protein needs a calorie intake of protein origin over 20% of the total calorie supplies must be maintained[22] (III).

Glutamine is an essential amino acid in stress states[23]. Its administration as dipeptide by the parenteral route in critically-ill patients with injuries[24] showed a decrease in infectious complications and mortality[25,26] (Ia). Their use in BI has been limited because of the theoretical risk of causing an increase in intracerebral glutamate values, leading to an increase in neuronal damage, cerebral edema, and increased intracerebral pressure. Two studies have concluded that the use of intravenous glutamine increases glutamate plasma values, without changes in intracellular values of intracerebral glutamine[27,28] (Ib). A study in neurocritical patients with enteral glutamine[29] (IIa) demonstrated a reduction in the infection rate. In conclusion, the use of glutamine has not been shown to be harmful in the neurocritical patient.

With regard to the use of zinc supplements and other trace elements, there are no conclusive studies which demonstrate an improvement in the variables of clinical outcome and degree of brain recovery in neurocritical patients[30].

What are the most common complications of nutritional support in neurocritical patients?

Neurocritical patients show a high incidence of gastrointestinal complications, the most common being IGR, conditioned by the brain injury itself[31,32] and by the drugs necessary for an adequate control of intracranial pressure (analgesics, sedatives and muscle relaxants).

Transpyloric nutrition is an effective alternative in patients with high IGR[33]. Two studies[34,35] (Ib) evidenced that transpyloric feeding significantly improved the effective volume versus gastric nutrition, and 2 recent publications[36,37] (Ib) have confirmed that transpyloric versus gastric feeding reduces significantly the incidence of late pneumonia. Administration of mixed, enteral and parenteral nutritional support, could also be a valid option in case of gastrointestinal complications, with close monitoring requirements to avoid hyperfeeding. However, there are no studies on the use of mixed nutrition in neurocritical patients.

How should glycemia be controlled?

In these patients, hyperglycemia has been related to an increased rate of infectious and non-infectious upper complications, compared to other groups of critically-ill patients. After the brain injury, a number of changes occur in the metabolism, transport and response to insulin, which are dependent on the type of lesion[38,39].

The increased blood glucose values increase the infection rate and neurological damage. On the contrary, a dramatic reduction in plasma glucose values causes an increased lactate-pyruvate ratio and brain glutamate, that increases brain damage. The gradient between plasma and brain glucose levels is 0.6-0.7, which leads to recommending larger adjustments in the control of glycemia in neurocritical patients[40,41]. There is no consensus on the benefit of intensive or conventional therapy with insulin in neurocritical patients. In a large study[42], no differences in mortality and neurological sequelae were observed between the two groups, though the rate of moderate hypoglycemia rate was higher in the intensive insuline group. Studies evaluating the effect of insulin upon the metabolism and progress variables recommend blood glucose values between 120 and 150 mg/dL, as safety values, in neurocritical patients[7] (IIb). Lower values may induce decreased extracellular glucose reserve and the subsequent brain energy dysfunction. In contrast, increased glycemia values lead to a worsening of prognostic variables, such as neurological recovery, infection rate, mortality, and hospital stay[6,7].

Recommendations

– Due to the severe catabolism state and the unfeasibility of an adequate nutritional supply, neurocritical patients should receive specialized nutritional support in the first three days of their evolution (B).

– High-protein supply is recommended (C).

– Enteral nutrition by transpyloric route is recommended in patients with brain injury since, as compared to the gastric route, it improves the efficacy in enteral supply and reduces the incidence of late pneumonia (B).

– Blood glucose control is recommended as in all other critically-ill patients (A).

– Administration of glutamine dipeptides, intravenously, may be safely used in the neurocritical patient (B).

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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Chapter 17
Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Cardiac patient

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Abstract

Patients with cardiac disease can develop two types of malnutrition: cardiac cachexia, which appears in chronic congestive heart failure, and malnutrition due to the complications of cardiac surgery or any other type of surgery in patients with heart disease.

Early enteral nutrition should be attempted if the oral route cannot be used. When cardiac function is severely compromised, enteral nutrition is feasible, but supplementation with parenteral nutrition is sometimes required.

Sustained hyperglycemia in the first 24 hours in patients admitted for acute coronary syndrome, whether diabetic or not, is a poor prognostic factor for 30-day mortality. In critically-ill cardiac patients with stable hemodynamic failure, nutritional support of 20-25 kcal/kg/day is effective in maintaining adequate nutritional status.

Protein intake should be 1.2-1.5 g/kg/day. Routine polymeric or high protein formulae should be used, according to the patient's prior nutritional status, with sodium and volume restriction according to the patient's clinical situation.

The major energy source for myocytes is glutamine, through conversion to glutamate, which also protects the myocardial cell from ischemia in critical situations. Administration of 1 g/day of omega-3 (EPA+DHA) in the form of fish oil can prevent sudden death in the treatment of acute coronary syndrome and can also help to reduce hospital admission for cardiovascular events in patients with chronic heart failure.

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Key words: *Critically-ill cardiac patient. Cardiac cachexia. Omega-3 fatty acids. Hyperglycemia.*

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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: PACIENTE CARDÍACO

Resumen

El paciente con patología cardíaca puede presentar 2 tipos de desnutrición: la caquexia cardíaca, que aparece en situaciones de insuficiencia cardíaca congestiva crónica, y una malnutrición secundaria a complicaciones de la cirugía cardíaca o de cualquier cirugía mayor realizada en pacientes con cardiopatía.

Se debe intentar una nutrición enteral precoz si no se puede utilizar la vía oral. Cuando la función cardíaca esté profundamente comprometida la nutrición enteral es posible, pero a veces precisará suplementación con nutrición parenteral.

La hiperglucemia aguda sostenida en las primeras 24 h en pacientes ingresados por síndrome coronario agudo, sean o no diabéticos, es un factor de mal pronóstico en términos de mortalidad a los 30 días. En el paciente crítico cardíaco con fallo hemodinámico en situación estable, un soporte nutricional de 20-25 kcal/kg/día es eficaz para mantener un estado nutricional adecuado.

El aporte proteico debe ser de 1,2-1,5 g/kg/día. Se administrarán fórmulas poliméricas o hiperproteicas habituales, según la situación nutricional previa del paciente, con restricción de sodio y volumen según su situación clínica.

La glutamina es la mayor fuente de energía para el miocito, vía conversión a glutamato, protegiendo además a la célula miocárdica de la isquemia en situaciones críticas. La administración de 1 g/día de w-3 (EpA+DHA), en forma de aceite de pescado, puede prevenir la muerte súbita en el tratamiento del síndrome coronario agudo y también puede contribuir a una disminución de los ingresos hospitalarios, por eventos cardiovasculares, en la insuficiencia cardíaca crónica.

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Palabras clave: *Paciente crítico cardíaco. Caquexia cardíaca. Ácidos grasos omega-3. Hiperglucemia.*

Introduction

Malnutrition is present in 50% of patients with chronic congestive heart failure. Heart failure is associated with neurohormonal and immune changes that contribute to a hypercatabolic state, with intestinal malabsorption induced by different factors[1]. Patients with heart disease may present 2 different types of malnutrition: classical heart cachexia, appearing in situations of chronic congestive heart failure (CHF), and a form of malnutrition secondary to complications of cardiac surgery or any major surgery in patients with heart disease[2]. The incidence of cardiac cachexia has been estimated in 12-15% of patients with NYHA grades II-III heart failure. This incidence increases to 10% per year if the grade of heart failure is III-IV[3,4] (IV).

What are the indications of nutritional support in critically-ill cardiac patients?

– CHF. These patients have chronic heart failure (HF) and chronic systemic inflammatory response syndrome (SIRS). Vasoconstriction and stimulation of the sympathetic nervous system are compensatory mechanisms of heart failure, which influences the inadequate use of nutrients[4] (IV).

– Cardiac cachexia. It has been defined as a body mass loss of 27% or decrease of 80-85% from the ideal weight, but the most widely accepted meaning is defined as patients with CHF starting at least 6 months before and a weight loss in the past 6 months of at least 6% from the previous weight. Mortality is very high in cachectic patients, 18% at 3 months, 29% at 6 months, and 50% at 18 months[5] (IV). Factors contributing to that mortality include: a deficient diet, the associated malabsorption syndrome, loss of nutrients through the intestinal and renal tract and imbalance in supply and losses in a hypermetabolism state[6].

– Patients following cardiac surgery and patients with acute heart disease, such as evolution complication of another condition (SIRS, sepsis, etc.). These patients end up behaving as critically-ill patients for nosocomial superinfection, HF refractory to treatment, cardiogenic shock or enlarged cardiomyopathy pending heart transplant.

– Acute coronary syndrome (ACS). These patients usually require oral nutrition, and only enteral nutrition (EN) would be indicated in the course of complications inherent to their condition[7]. Patients in a cardiogenic shock condition on mechanical ventilation, balloon counterpulsation or external ventricular assistance, behave as a chronic critical illness requiring long-term artificial nutritional support[8] (III).

What is the most adequate administration route?

Oral supply is the most appropriate, and if intake is very limited, it may be complemented with nutritional supplements. An early EN should be attempted if the oral route cannot be used. When heart function is severely affected (intraaortic contrapulsation balloon, ventricular assistance, etc.), EN can be performed, but will usually require supplementation with parenteral nutrition (PN) and its start, as a cautionary measure because of the risk of intestinal ischemia, is usually delayed beyond 24-48 hours after admission.

Patient instability, volume limitations, and the frequent changes in bowel function may require establishing total parenteral nutrition (TPN) or, sometimes, complementary parenteral nutrition (CPN)[5] (IV). EN in these type of patients, with the appropriate caution and monitoring, is feasible and beneficial[9] (III).

EN during 2-3 weeks, in patients with heart cachexia, is associated with a faster stabilization of the condition and improved nutritional parameters[10], though with no changes in hemodynamic parameters. There are data evidencing that impaired heart function may reduce the intestinal perfusion causing malabsorption and intolerance to EN[11].

What amount and type of energy substrates are required?

The classical Harris-Benedict equation is acceptable for energy calculation, though easiest approaches have been shown to be useful, such as scheduling 20-25 kcal/kg/day within the first 48 hours and progress to 25-30 kcal/kg/day if required[12,13]. The supplies are often limited for the total volume restriction, and energetic concentrated nutrients should be used (1.5-2 kcal/ml)[14].

There are no specific recommendations related to the percentage of energy substrates that must be contained in the diet of critically-ill cardiac patients. The ratio kcal/g N_2 will be maintained at 100-150/1, decreasing it based on the degree of protein depletion or increase of metabolic stress[15].

Carbohydrate supply

Glucose supply should be adjusted to obtain blood glucose levels < 150 mg/dL, and even in narrower limits postoperatively following heart surgery. Glycemia should be accurately monitored in critically-ill cardiac patients. Acute hyperglycemia is evidenced in 50% of ACS in non-diabetic patients and in 25% of diabetics. It has been proven that sustained hyperglycemia in the first 24 hours in patients admitted for ACS, whether diabetic or not, is a factor of poor prognosis in terms of mortality at 30 days[16,17] (IIb).

Studies such as the DIGAMI (diabetes mellitus, insulin-glucose infusion in acute myocardial infarction)[18] analyzed the metabolism/mortality ratio in ACS. The purpose was to obtain an accurate control of glycemia with high doses of insulin and decrease mortality by 25% at 3 months and by 52% at one year. Although the results were encouraging, they were not significant. The ECLA[19] study reported a mortality reduction of two-thirds when glucose-insulin-potassium were perfused versus placebo, but in subsequent randomized studies, both DIGAMI-2[20] and CREATE-ECLA[21], these objectives were not reached, though it was confirmed that hyperglycemia is an independent predictor of mortality (Ib).

Fat supply

The adverse effects of lipid emulsions on cardiac inotropism only occur when perfusion exceeds 5 mg/kg/min. At the standard doses, without exceeding 2 g/kg/day, all commercial solutions are useful, though emphasis is made on the value of ω-3 fatty acids[22] (IV).

What are the protein needs and characteristics of their supply?

Protein supply should be 1.2-1.5 g/kg/day. In EN, proteins should provide 16-20% of the total energy supply in order to mantain a positive nitrogen balance. The regular polymeric or hyperprotein formulae will be administered, with sodium and volume restriction, according to the previous clinical and nutritional status of the patient[23] (IV).

What is the most advisable type of formula? Are specific nutrients required?

The most advisable type of formula must be modified based on the nutritional status of patients and their needs. Some amino acid may be necessary or useful in cardiac patients, while others have shown a myocardial depressant effect, such as homocysteine, since their values are a risk factor and are frequently increased in patients with HF. They are closely related to the decreased plasma levels of vitamins B_6, B_9 and B_{12}, required for their degradation[24] (IV).

Carnitine

It promotes fat entry in the mitochondria and indirectly activates pyruvate dehydrogenase, that improves glucose oxidation. Carnitine deficiency is associated with myocardiopathy and skeletal muscle dysfunction. Myocardial failure is generally associated with a marked depletion of carnitine of up to 50%. Carnitine administration (3-6 g in divided doses) may lead to improving hemodynamic status and myocardial dysfunction[23,25] (IV).

Glutamine

Experimental studies have shown that its administration, after myocardial ischemia, induces an earlier myocardial recovery, improve cardiac output and restoring ATP/ADP ratio. Glutamine has been shown to increase the synthesis of heat shock protein[26] which is also the greatest source of energy for the myocyte, by conversion to glutamate, also protecting the myocardial cell from ischemia in critical situations[27,28] (IV).

Arginine

As a precursor of nitric oxide, it plays a major role in regulating cardiovascular function, particularly in diabetic patients. Intravenous doses of 3-5 g reduce blood pressure and platelet aggregation. Arginine prevents cardiovascular dysfunction, as it restores nitric oxide synthesis, reduces production of free radicals, and inhibits leukocyte adherence to the endothelium, though in mesenteric ischemic conditions bowel mucosa function may be worsened[29] (IV).

Taurine

It is a non-essential amino acid that contributes to control intracellular calcium values, and therefore appears to be useful to improve myocardial function[25] (IV).

ω-3 fatty acids

They have been shown to have some antiarrhythmogenic potential and could prevent malignant arrhythmia and reduce the incidence of sudden death, acting mainly to prevent it[30,31]. The presence of ω-3 in myocardial cells stabilizes electrically membranes and prolongs the refractory period. They decrease the synthesis of inflammatory prostanoids and modulate the inflammatory response by reducing arachidonic acid catabolytes, preserving endothelial integrity and acting favourably on platelet activity. On the contrary, an excessive supply of ω-6 can increase platelet aggregation and promote chronic inflammation predisposing to plaque unstability[32].

In randomized studies it has been recommended to provide a supplement of 1 g/day of ω-3 (EPA + DHA) as fish oil, for primary prophylaxis of sudden death in the treatment of ACS and for reducing hospital admissions for cardiovascular episodes in CHF[33,34] (Ib), though subsequent studies did not obtain the same results[35] (Ib).

With regard to enteral immunomodulatory diets enriched with arginine, nucleotides, and fish oil, in a randomized, prospective study conducted in 50 patients with poor ventricular function, who were to undergo cardiac surgery, oral supplements of these nutrients were provided during the 5 days prior to surgery, obtaining a lower infection rate, a reduction in the need for positive inotropes and a better preservation of renal function[36] (IIa).

What micronutrient and vitamin requirements are needed?

Vitamin D, calcium, magnesium, zinc, and selenium supplements should be included in an adequate nutritional support for patients with serious heart diseases[37] (IV).

Serious forms of HF have been described in patients with thiamine[38] or selenium deficiency. In patients with ischemic heart disease, after reperfusion processes, supplying antioxidants (vitamin A, C, E and selenium) helps limit myocardial damage[39]. Glutathione peroxidase and tocoferol reduction has been seen experimentally in patients with cardiomyopathy. Therefore, supplements of antioxidants in patients with heart failure, particularly vitamin E (400 IU), may contribute to improve cardiac function[40] (IV).

Severe selenium deficit may cause cardiomyopathy and is characterized by multiple fibrosis foci in the left ventricle. Zinc deficiency is common in patients with CHF and, therefore, the requirements established for these patients must be administred[2] (IV).

Recommendations

– In critically-ill cardiac patients with hemodynamic failure in stable condition, a nutritional support of 20-25 kcal/kg/day is effective for maintaining an adequate nutritional status (B).

– Nutritional formulae recommended in other critically-ill patients will be supplied according to the previous nutritional status, with sodium and volume restriction, in relation to the clinical condition of the patient (C).

– Parenteral nutrition would be indicated for cardiac cachexia, in case of intolerance to enteral nutrition or as complementary nutrition, particularly in patients with cardiovascular surgery (C).

– Hyperglycemia should be closely monitored in patients with acute coronary syndrome and after cardiac surgery, whether or not known diabetics, maintaining values < 150 mg/dL (B).

– Glutamine supply may be beneficial for patients with myocardial ischemia in a critical situation (C).

– In patients with acute coronary syndrome who require enteral nutrition it is recommended to administer at least 1 g/day EPA + DHA (C).

– Supplements with vitamin A, C, B complex, vitamin E, and selenium are recommended to improve heart function (C).

Conflict of interests

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