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 plantead 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-
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. At the same time, the evidence on the efficacy and impact of nutritional support given to other treatments that were considered more 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 pharmacological 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.

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, 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-
The recommendations have been formulated by an expert panel, all of whose members belonged to the GTMMyN 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) and the Agency for Healthcare Policy Research (AHCPR) (Table II). For establishing the quality of the studies, Jadad quality assessment scale was used. 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).

After establishing the methodology, the table of contents of the chapters was circulated to all members of the GTMMyN 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 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

| Table II |
| Grades of recommendation and levels of evidence |

<table>
<thead>
<tr>
<th>Grades of recommendation</th>
<th>Levels of evidence</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Ia</td>
<td>Meta-analysis of randomized controlled trials</td>
</tr>
<tr>
<td></td>
<td>Ib</td>
<td>At least one randomized controlled trial</td>
</tr>
<tr>
<td>B</td>
<td>Ila</td>
<td>At least one well-designed controlled study without randomization</td>
</tr>
<tr>
<td></td>
<td>Iib</td>
<td>At least one other type of well-designed quasi-experimental study</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Well-designed non-experimental descriptive studies, such as comparative studies, correlation studies or case-control studies</td>
</tr>
<tr>
<td>C</td>
<td>IV</td>
<td>Expert opinions and/or clinical experience of respected authorities</td>
</tr>
</tbody>
</table>
In the process of preparing 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 osmolality 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:

\[
\text{Adjusted weight} = \text{Wi} + \text{correction factor} \times (\text{actual weight} - \text{ideal weight})
\]

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): \(48.08 + (\text{height} \text{[cm]} - 152.4/2.54) \times 2.26\)

Women (Wi in kg): \(45.35 + (\text{height} \text{[cm]} - 152.4/2.54) \times 2.22\)

– **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 Benedict (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, hyperosmolality 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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