

## 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.*

### 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

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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: 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  $\omega$ -3 y antioxidantes que podrían mejorar el pronóstico.

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as hyperglycemia, the duration of mechanical ventilation and even mortality<sup>1-4</sup> (III). However, many recommendations given relating to patients with chronic obstructive pulmonary disease (COPD) have a low level of evidence<sup>5</sup> (IV).

#### 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<sup>6</sup> (Ia).

### **Nutritional support in patients with chronic respiratory failure acutely worsened**

Patients with COPD show a prevalence of malnutrition ranging from 25 to 40%<sup>7</sup>. 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<sup>8</sup>. In addition, the low weight (body mass index [BMI] < 20 kg/m<sup>2</sup>) or recent weight loss and the value of muscle atrophy, measured through the fat-free mass index, are independent predictor factors of mortality<sup>9</sup> (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. Weight 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<sup>10</sup> (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<sup>10</sup> (III), <sup>11</sup> (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<sup>12</sup>. 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<sub>2</sub>, making difficult disconnection from the ventilator<sup>13</sup> (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<sup>14</sup> (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<sub>2</sub> and ventilatory response in case of hypoxia and hypercapnia, regardless of the VCO<sub>2</sub>, 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<sup>15,16</sup>.

### **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<sup>3,4</sup> (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<sup>17</sup>.

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<sup>4</sup>. In fact, and taking into account the mean calorie supplies, in all above mentioned studies protein supplies are below 1 g/kg/day<sup>3</sup>. 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<sup>18</sup>.

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

Diets based on  $\omega$ -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.

$\omega$ -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  $\omega$ -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<sup>19-21</sup> (Ib). This has been confirmed in a subsequent meta-analysis<sup>22</sup> (Ia). In addition, an observational study in surgical patients with intra-abdominal sepsis treated with parenteral nutrition enriched with  $\omega$ -3 fatty acids evidenced a relative mortality reduction for the severity degree in patients as compared to the expected<sup>23</sup> (III).

However, these studies<sup>19-21</sup> 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  $\omega$ -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<sup>24</sup>. The second study analyzes the inflammatory response in bronchoalveolar lavage of these patients, with no significant differences<sup>25</sup>. And, finally, a Spanish multicenter study using a commercial diet with  $\omega$ -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<sup>26</sup>.

In parenteral nutrition there are no studies assessing the effect of  $\omega$ -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  $\omega$ -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  $\omega$ -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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