



RECOMMENDATIONS FOR SPECIALIZED NUTRITIONAL-METABOLIC MANAGEMENT OF THE CRITICAL PATIENT

Recommendations for specialized nutritional-metabolic treatment of the critical patient: The chronic critical patient. Metabolism and Nutrition Working Group of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)^{☆,☆☆}



Recomendaciones para el tratamiento nutrometabólico especializado del paciente crítico: paciente crítico crónico. Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)

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Received 18 October 2019; accepted 9 December 2019

Introduction

The decrease in mortality due to early multiorgan failure has generated a growing population of patients that do not die but remain in the Intensive Care Unit (ICU) with residual vital organ and system functions that cause them to be highly dependent, with a poor prognosis and (among the survivors) poor quality of life: these are the so-called *chronic critical patients* (CCP).

Between 5% and 10% of all patients subjected to mechanical ventilation (MV) progress towards CCP status, with age and comorbidities being risk factors for this condition. Recurrent reactivation of the immune-neuroendocrine axis may lie at the root of the process, inducing an allostatic overload, in CPPs.¹ On the other hand, a coincidence

[☆] Please cite this article as: Cervera Montes M, Gastaldo Simeón RM, Portugal Rodríguez E. Recomendaciones para el tratamiento nutrometabólico especializado del paciente crítico: paciente crítico crónico. Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC). Med Intensiva. 2020;44:81–84.

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

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in time has been observed in the genic expression of innate immunity (systemic inflammatory response syndrome [SIRS]) and adaptive or suppressive immunity (compensatory anti-inflammatory response syndrome [CARS]), with patient progression towards CCP status being conditioned to the magnitude and direction of these changes in genic expression.^{2,3}

Clinically, CCPs exhibit the following features: prolonged MV, weakness secondary to polyneuromyopathy, altered body composition (sarcopenia, fat infiltration, osteopenia and anasarca), neuroendocrine changes (loss of pulsatile growth hormone [GH] secretion), cerebral dysfunction (delirium, coma) and susceptibility to infection. Although 50% of these patients are freed from MV, the in-hospital mortality rate reaches 49%, and the survival rate after 1 year is only 30%. Chronic critical patients may recover or evolve towards a new late organ dysfunction phenotype associated to a state of persistent inflammation causing increased anabolic/catabolic imbalance and a state known as *persistent inflammation, immunosuppression and catabolic syndrome* (PICS). In most cases, however, these patients slowly progress towards a fatal outcome or require admission to a long-stay care institution.⁴ Chronic critical patients are characterized by a certain genomic substrate, though it is still not clear why some of them recover while others progress towards PICS.⁵

There is no established specific treatment for these patients. The attempts to control the neuroendocrine problem lying at the heart of the problem have had no clear impact upon the patient outcome. Prevention is crucial, with interventions in the acute phase of the process, seeking control of the inflammation and endocrine-metabolic alterations and the prevention of muscle dysfunction, being key elements.

The present chapter addresses the nutritional-metabolic interventions that prove useful in CCPs, together with other associated therapies that complete the so-called “*anabolic nutrition*” strategy.

Questions

1. Do the energy and protein requirements of these patients differ from those of the rest of critical patients?

There is no evidence supporting a specific nutritional strategy for CCPs and patients with PICS. The persistence of inflammation, hypercatabolism and anabolic resistance leads to a state of sarcopenia/cachexia; the “*anabolic nutrition*” strategy is the best option for combating this situation, together with resistance exercises. In addition to other actions, “*anabolic nutrition*” proposes a caloric supply of 25–30 kcal/kg/day and a protein supply of 1.5–2 g/kg/day.^{6–9} Special attention should focus on glycemic control (glycemia <150 mg/dl, minimizing its variability), with the avoidance of an excessive caloric supply.¹⁰

2. What is the most adequate feeding route?

Enteral nutrition (EN) is recommended as first-line nutrition support strategy in patients with a functioning gastrointestinal tract. Feeding initially is via a nasogastric tube (NGT); the nasojejunal route offers no objective advantages in this regard.^{11,12} Enteral nutrition, initially on a continuous basis, can be applied intermittently to facilitate other therapeutic actions (e.g., active exercise, early mobilization, etc.).¹³ In any case, it is advisable to have an EN administration protocol based on volumetric objectives and controlled by nursing staff.¹⁴

Percutaneous endoscopic gastrostomy (PEG) should be considered in patients that tolerate EN via NGT if a prolonged duration of feeding is expected (>30 days). It should be considered in the second-third week in those patients with inadequate intake and a moderate to severe risk of malnutrition. The decision to perform PEG should be made on an individualized basis, taking into account the patient preferences, diagnosis and life expectancy.¹⁵ In the recovery phase, CCPs should be evaluated for safety of feeding via the oral route and the suspension of feeding via NGT or PEG once the nutritional targets have been reached.

3. What is the most adequate specialized nutrition support formula in these patients?

No data are available regarding the most adequate nutritional formula in CCPs/PICS, though in general a hyper-proteic polymeric diet is indicated. Some authors advise the use of formulas enriched with pharmac nutrients, based on studies that describe improvements in terms of immune function and inflammation, together with a decrease in infections and shortened stay and duration of MV.¹⁶ The chosen nutritional formula should afford sufficient protein, avoid excessive calories and ensure an adequate provision of micronutrients.

4. What specific nutrients and micronutrients are required?

Trace elements (TEs) such as Cu, Mn, Zn and Fe, and certain vitamins (Vi) such as vitamin E, C and E, and β -carotene, are crucial as coenzymes and antioxidants.¹⁷ These elements are usually deficient in CCPs as a result of redistribution, hemodilution, insufficient intake and treatments such as continuous renal replacement therapy. There is a negative correlation between micronutrient deficit and the severity of the disease process.¹⁸ In a systematic review, Manzanares et al. sought to determine whether TE and Vi replacement is of benefit. The authors concluded that high doses of TEs and Vi improve the clinical outcomes in critical patients, particularly in the more serious cases.¹⁹ However, there is an important gap in knowledge regarding the normal levels, the dosage and the effect of each TE considered isolatedly. What does seem clear is that the existing commercial mixtures are unable to cover the requirements.²⁰

Controversy remains regarding the administration of pharmac nutrients such as arginine, glutamine, leucine, beta-hydroxy-beta-methylbutyrate and creatine, despite

their acknowledged immunological, enteroprotective and anabolic actions. There are no studies of sufficient quality to clearly establish the usefulness of these nutrients in critical patients in general and in CCPs in particular.^{21–23}

5. What other nutritional-metabolic interventions are useful in these patients?

The endocrine-metabolic scenario, together with concomitant factors such as disuse, make a determinant contribution to sarcopenia, cachexia and immune depression in CCPs and PICS.²⁴ Hormone replacement therapy could correct the consequences of the endocrine anomalies, though studies involving the administration of growth hormone, thyroxin and corticosteroids in CCPs have found such measures to be ineffective.²⁵ In rare instances, a lack of effective hypothalamic-pituitary stimulation can result in functional insufficiency requiring replacement with corticosteroids and thyroxin.

Chronic critical patients suffer bone metabolic disorders (elevated reabsorption) – the recognizable risk factors being cytokines, immobilization, endocrine alterations, the administration of corticosteroids, electrolyte and micronutrient disturbances (Mg, P, K, vitamin C, K and D) and secondary hyperparathyroidism. Nevertheless, the clinical benefits of administering bisphosphonates, calcium and vitamin D are subject to controversy – though there is agreement regarding the administration of vitamin D in highly deficient patients.^{26–28}

Prolonged immobilization and disuse are crucial contributors to the appearance of sarcopenia and weakness. A systematic review revealed no impact upon short- and middle term mortality, though improved mobility and muscle strength was recorded.²⁹ In contrast, other studies have highlighted the benefits of an early rehabilitation program guided by objectives consistent with the patient condition.³⁰ In general, early mobilization is advised, with resistance exercises or neuromuscular electrical stimulation – though the indicated duration and frequency are not clear.

Other pharmacological treatments with anabolic effects are currently under study, such as ghrelin, insulin-like growth factor type 1 and muscle modulators such as the myostatin inhibitors and melanocortin-4 receptor antagonists. Due to its anabolic and appetite-stimulating properties, ghrelin improves the symptoms and muscle weakness of chronic patients with cachexia,³¹ and therefore could afford benefits in the rehabilitation of CCPs.

Recommendations

- In the nutritional strategy of chronic critical patients, a hyperproteic polymeric diet is advised (1.5–2 g/kg/day), avoiding caloric overload (25–30 kcal/kg/day) (Quality of evidence [QE]: moderate in favor).
- Systematic pharmaconutrition is not advised; the incorporation of L-leucine, beta-hydroxy-beta-methylbutyrate and L-carnitine to the diet is an option currently subjected to study (QE: low in favor).
- Enteral nutrition via the nasogastric route is recommended. Feeding through a percutaneous endoscopic gastrostomy (PEG) should be evaluated if prolonged

nutrition is expected (>30 days). Recovery of the oral route is desirable (QE: moderate in favor).

- Periodic supplementing with vitamins and oligoelements may be decided, particularly in patients subjected to continuous or frequent intermittent renal replacement therapy (QE: low in favor).
- Vitamin D supplements are suggested in chronic critical patients with confirmed deficits of this vitamin (QE; low in favor).
- Early mobilization is indicated, with resistance exercises and neurostimulation guided by objectives whenever possible (Grade of recommendation: moderate in favor).

Conflicts of interest

Dr. R. Gastaldo-Simeón has collaborated with Fresenius, participating in congresses, and in a study on parenteral nutrition. She has collaborated with Menarini in training workshops in cardiopulmonary resuscitation. Dr. Esther Portugal has received aids from the drug industry for participation in medical congresses (Abbott) and nutrition-related courses (Abbott, Nestle, Vegemat, Fresenius). In addition, she has given a talk for the drug industry (Vegemat). Dr. Cervera declares that he has no conflicts of interest.

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