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

M. Planasa, J. F. Fernández-Ortega and J. Abilés

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.

Nutr Hosp 2011; 26 (Supl. 2):50-53
Key words: Cancer. Pharmaconutrients. Glutamine

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 disease1. Cachexia is present in over two thirds of patients dying of advanced cancer and may be the direct cause of a fourth of deaths2. 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.

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

Correspondence: M. Planas.
E-mail: mplanasvil@gmail.com

References
1. SEMICYUC: Spanish Society of Intensive Care Medicine and Coronary Units.
2. SENPE: Spanish Society of Parenteral and Enteral Nutrition.
turn, the metabolism of macronutrients is impaired in patients with neoplastic 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\(^{7}\). 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\(^{9}\) (II), \(^{10}\) (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 tolerance\(^{18}\) and others support normal or increased lipid oxidation\(^{14}\) (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. On the other hand, in a systematic review also in 2007, Elia et al. 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., 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 (IIb), could not be confirmed by other authors. 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 (Ib). In addition, improvements have been reported in nitrogen balance, in immune function, risk of infection, hospital length of stay and healthcare costs (Ib). Effects on mortality have been contradictory (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.

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

- 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 ω-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.

References