Nutrición Hospitalaria

Nutr Hosp 2011;26(Supl. 2):50-53
ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198
CODEN NUHOEQ
S.V.R. 318

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

M. Planas[a], J. F. Fernández-Ortega[b] and J. Abilés[c]

[a]Escuela de Ciencias de La Salud. Universidad de Vic. Barcelona. Spain. [b]Hospital Regional Universitario Carlos Haya. Málaga. Spain. [c]Hospital Costa del Sol. Marbella. Málaga. Spain.

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.*

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.

Nutr Hosp 2011; 26 (Supl. 2):50-53

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

Correspondence: M. Planas.
Escuela de Ciencias de La Salud. Universidad de Vic.
Barcelona. Spain.
E-mail: mplanasvila@gmail.com

SEMICYUC: Spanish Society of Intensive Care Medicine and Coronary Units.
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.

References

1. Lieffers JR, Mourtzakis M, Hall KD, McCargar LJ, Prado MM, Baracos VE. A visceral driven cachexia syndrome in patients with advanced colorectal cancer: contributions of organ and tumor mass to whole-body energy demands. *Am J Clin Nutr* 2009; 89: 1173-9.
2. Tisdale MJ. Cachexia in cancer patients. *Nat Rev Cancer* 2002; 2: 862-71.
3. Zuijdgeest-van Leeuwen SD, Van den Berg JW, Wattimena JL, Van der Gaast A, Swart GR, Wilson JH et al. Lipolysis and lipid oxidation in weight-losing cancer patients and healthy subjects. *Metabolism* 2000; 49: 931-6.
4. Körber J, Pricelius S, Heidrich M, Müller MJ. Increased lipid utilization in weight losing stable cancer patients with normal body weight. *Eur J Clin Nutr* 1999; 53: 740-5.
5. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA et al. What is subjective global assessment of nutritional status? *JPEN J Parenter Enteral Nutr* 1987; 11: 8-13.
6. Gupta D, Lammersfeld CA, Vashi PG, Burrows J, Lis CG, Grutsch JF. Prognostic significance of subjective global assessment (SGA) in advanced colorectal cancer. *Eur J Clin Nutr* 2005; 59: 35-40.
7. Marques de Oliveira MR, Pagotto Fogaça KC, Escobar Gimenes perencin M, Leandro Merhi VA. Subjective aspects of the nutritional status and length of chemotherapy treatment in patients with neoplasias. *Nutr Hosp* 2010; 25: 126.
8. Moses AW, Slater C, Preston T, Barber MD, Fearon KC. Reduced total energy expenditure and physical activity in cachectic patients with pancreatic cancer can be modulated by an energy and protein dense oral supplement enriched with n-3 fatty acids. *Br J Cancer* 2004; 90: 996-1002.
9. Gibney E, Elia M, Jeeb SA, Murgatroyd P, Jennings G. Total energy expenditure in patients with samall-cell lung cancer: results of a validated study using the bicarbonate-urea method. *Metabolism* 1997; 46: 1412-7.
10. Fredrix EW, Soeters PB, Wouters EF, Deerenberg IM, Von Meyenfieldt MF, Saris WH. Effects of different tumor type on resting energy expenditure. *Cancer Res* 1991; 51: 6138-41.

11. Chamouard Cogoluenhes V, Chambrier C, Michallet M, Gordiani B, Ranchere JY, Combret D, et al. Energy expenditure during allogenic and autologus bone marrow transplantation. *Clin Nutr* 1998; 17: 253-7.
12. Nitenberg G, Raynard B. Nutritional support of the cancer patient: issues and dilemmas. *Crit Rev Oncol Hematol* 2000; 34: 137-68.
13. McGeer AJ, Detsky AS, O'Rourke K. Parenteral nutrition in cancer patients undergoing chemotherapy: a meta-analysis. *Nutrition* 1990; 6: 233-40.
14. Bozzetti F, Giannotti L, Braga M, Di Carlo V, Mariani L. Postoperative complications in gastrointestinal cáncer patients: the joint role of the nutritional status and the nutritional support. *Clin Nutr* 2007; 26: 698-709.
15. Bozzetti F, Braga M, Gianotti L, Gavazzi C, Mariani L. Postoperative enteral nutrition versus parenteral nutrition in malnourished patients with gastrointestinal cáncer: a randomized multicentre trial. *Lancet* 2001; 358: 1487-92.
16. Ohrn KE, Wahlin YB, Sjödén PO. Oral status during radiotherapy and chemotherapy: a descriptive study of patient experiences and the occurrence of oral complications. *Support Care Cancer* 2001; 9: 247-57.
17. Gonzalo Marín M, Tapia MJ, García Torres F, Olveira Fuster G, Lainez López M. Evolución de parámetros antropométricos y nutricionales en pacientes con carcinoma de cabeza y cuello con gastrostomía percutánea. *Nutr Hosp* 2010; 25 (Suppl. 2): 45-6.
18. Bozzetti F, Gavazzi C, Mariani L, Crippa F. Glucosa-based total parenteral nutrition does not stimulate glucosa uptake by humans tumours. *Clin Nutr* 2004; 23: 417-21.
19. Takatsuka H, Takemoto Y, Iwata N, Suehiro A, Hamano T, Okamoto T et al. Oral eicosapentaenoic acid for complications of bone marrow transplantation. *Bone Marrow Transplant* 2001; 28: 769-74.
20. Dewey A, Baughan C, Dean T, Higgins B, Jonson I. Eicosapentaenoic acid (EPA, an omega-3 fatty acid from fish oils) for the treatment of cancer cachexia. *Cochrane Database Syst Rev* 2007; (1): CD004597.
21. Elia M, Van Bokhorst-de van der Schueren MA, Garvey J, Goedhart A, Lundholm K, Nitenberg G et al. Enteral (oral or tube administration) nutritional support and eicosapentaenoic acid in patients with cancer: a systematic review. *Int J Oncol* 2006; 28: 5-23.
22. Colomer R, Moreno-Nogueira JM, García-Luna PP, García-Peris P, García-de-Lorenzo A, Zarazaga A et al. N-3 fatty acids, cancer and cachexia: a systematic review of the literature. *Br J Nutr* 2007; 97: 823-31.
23. Anderson PM, Ramsay NK, Shu XO, Rydholm N, Rogosheske J, Nicklow R et al. Effect of low-dose oral glutamine on painful stomatitis during bone marrow transplantation. *Bone Marrow Transplant* 1998; 22: 339-44.
24. Schloerb PR, Skikne BS. Oral and parenteral glutamine in bone marrow transplantation: a randomized, double-blind study. *JPEN J Parenter Enteral Nutr* 1999; 23: 117-22.
25. Coghlin Dickson TM, Wong RM, Offrin RS, Shizuru JA, Johnston LJ, Hu WW et al. Effect of oral glutamine supplementation during bone marrow transplantation. *JPEN J Parenter Enteral Nutr* 2000; 24: 61-6.
26. Brown SA, Goringe A, Fegan C, Davies SV, Giddings J, Whittaker JA et al. Parenteral glutamine protects hepatic function during bone marrow transplantation. *Bone Marrow Transplant* 1998; 22: 281-4.
27. Goringe AP, Brown S, Callaghan U, Rees J, Jebb S, Elia M et al. Glutamine and vitamin E in the treatment of hepatic venoocclusive disease following high-dose chemotherapy. *Bone Marrow Transplant* 1998; 21: 829-32.
28. Gómez Candela C, Castillo R, De Cos AI, Iglesias C, Martín MC, Aguado MJ et al. Effects of parenteral glutamine in patients submitted to bone marrow transplantation. *Nutr Hosp* 2006; 21: 13-21.
29. Wilmore DW, Schloerb PR, Ziegler TR. Glutamine in the support of patients following bone marrow transplantation. *Curr Opin Clin Nutr Metab Care* 1999; 2: 323-7.
30. Da Gama Torres Ho, Vilela EG, Da Cunha AS, Goulart EM, Souza MH, Aguirre AC et al. Efficacy of glutamine-supplemented parenteral nutrition on short-term survival following allo-SCt: a randomized study. *Bone Marrow Transplant* 2008; 41: 1021-7.
31. Pytlík R, Benes P, Patorková M, Chocenská E, Gregora E, Procházka B et al. Standardized parenteral alanyl-glutamine dipeptide supplementation is not beneficial in autologous transplant patients: a randomized, double-blind, placebo controlled study. *Bone Marrow Transplant* 2002; 30: 953-61.