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Chapter 10

Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: Hyperglycemia and diabetes mellitus

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Abstract

Hyperglycemia is one of the main metabolic disturbances in critically-ill patients and is associated with increased morbidity and mortality. Consequently, blood glucose levels must be safely and effectively controlled, that is, maintained within a normal range, avoiding hypoglycemia on the one hand and elevated glucose concentrations on the other. To accomplish this aim, insulin is often required, avoiding protocols designed to achieve tight glycemic control.

To prevent hyperglycemia and its associated complications, energy intake should be adjusted to patients' requirements, avoiding overnutrition and excessive glucose intake. Protein intake should be adjusted to the degree of metabolic stress.

Whenever patients require artificial feeding, the enteral route , if not contraindicated, should be used since parenteral nutrition is associated with a higher frequency of hyperglycemia and greater insulin requirements. Enteral nutrition should be administered early, preferably within the first 24 hours of admission to the intensive care unit, after hemodynamic stabilization. Specific diets for hyperglycemia, containing low glycemic index carbohydrates and fibre and enriched with monounsaturated fatty acids, can achieve good glycemic control with lower insulin requirements.

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Key words: *Hyperglycemia. Diabetes mellitus. Artificial nutrition. Glycemic control.*

RECOMENDACIONES PARA EL SOPORTE NUTRICIONAL Y METABÓLICO ESPECIALIZADO DEL PACIENTE CRÍTICO. ACTUALIZACIÓN. CONSENSO SEMICYUC-SENPE: HIPERGLUCEMIA Y DIABETES MELLITUS

Resumen

La hiperglucemia es una de las alteraciones metabólicas predominantes en los pacientes críticos y se asocia con un aumento de la morbimortalidad. por ello, es necesario realizar un control efectivo y a su vez seguro de la glucemia, esto es, mantener la normoglucemia en un rango que evite el riesgo de desarrollar hipoglucemia, por un lado, y las cifras elevadas de glucemia, por otro. Para conseguirlo, en la mayoría de los casos es necesario el tratamiento con insulina evitando protocolos dirigidos a conseguir cifras estrictas de glucemias.

Con el fin de prevenir la hiperglucemia y sus complicaciones asociadas, el aporte energético debe adecuarse a los requerimientos de los pacientes, evitando la sobrenutrición y el aporte excesivo de glucosa. El aporte proteico se ajustará al nivel de estrés metabólico. Siempre que el enfermo requiera nutrición artificial y no esté contraindicada debe emplearse la vía enteral, ya que la nutrición parenteral se asocia a mayor frecuencia de hiperglucemia y mayores necesidades de insulina. La administración de la nutrición enteral debe ser precoz, preferiblemente dentro de las primeras 24 h de ingreso en UCI, tras la estabilización hemodinámica. Las dietas específicas para hiperglucemia que contienen hidratos de carbono de bajo índice glucémico, fibra y ricas en ácidos grasos monoinsaturados podrían conseguir un mejor control glucémico con menores necesidades de insulina.

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Palabras clave: *Hiperglucemia. Diabetes mellitus. Nutrición artificial. Control de glucemia.*

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

SENPE: Spanish Society of Parenteral and Enteral Nutrition.

Introduction

In critically-ill patients the development of hyperglycemia secondary to the acute lesion stress is common even in non-diabetics. Hyperglycemia and the metabolic consequences of insulin resistance increase morbidity and mortality in critically-ill patients[1], because they enhance the occurrence of infections and multiple organ failure, mainly due to proinflammatory effects and cell toxicity per se of high glycemia values.

What should be the nutritional support route and when should it be started?

Whenever the gastrointestinal tract is intact and the patient requires artificial feeding, the enteral route must be used in the first 24-48 hours of stay, over the parenteral, which is associated with a higher frequency of hyperglycemia and insulin needs[2]. Although it is known that gastroparesis of diabetic patients can make gastrointestinal tolerance more difficult[3], the enteral route allows for a better control of blood sugar levels and prevents complications derived from hyperglycemia in critically-ill diabetic patients or those with stress hyperglycemia[2] (Ia).

What should be the characteristics of energy supply?

It is important to adjust calorie needs to the metabolic stress status of the patient. This attempts to prevent overnutrition, that, in addition to contributing to hyperglycemia[1] (IV), enhances insulin resistance and liver failure. Overnutrition is mainly related to parenteral nutrition (PN)[4] (IV).

One of the most controversial issues is the distribution of the total calorie requirements and, particularly, the carbohydrate/lipid ratio. The American Diabetes Association (ADA)[5] sets out that critically-ill diabetic patients may receive either a standard formula (50% carbohydrates) or a formula low in carbohydrates (33-40%). In contrast, the European Association for the Study of Diabetes[6] recommends that fat content in diet should not exceed 35% and that carbohydrate intake should be within 45-60% of the daily calorie needs.

There are specific enteral formulae for diabetics containing fewer carbohydrates (35-40%) and more fats (40-50%), with predominance of monounsaturated fatty acids (MUFA) (> 60% of the total fat content). New formulae have been developed that, in addition to reducing fat content, increase their low glycemic index carbohydrates[6]. In studies performed in non-critically-ill patients, both types of formulae reduce the glycemic and insulinemic response to intake and, furthermore, diets rich in slow-digestion carbohydrates do not raise post-prandial triglyceride levels, unlike diets rich in fats[7,8]. Therefore, it is recommended to use low-glycemic index carbohydrates, such as starch (preferably), fructose at lower doses, and more recently, isomaltulose and sucromalt, amongst others[8] (Ib).

With regard to lipids, it is recommended to increase MUFA, as they improve glycemic control, lipid metabolism and insulin secretion in non-critically-ill patients with type 2 diabetes[7] (Ib), [8] (IIa). Furthermore, it is recommended to reduce polyunsaturated fatty acids (PUFA) of the ω-6 series to prevent proinflammatory eicosanoids to increase[9].

Regarding PN, the use of mixtures of carbohydrates with fructose or polyols (xylitol) offers conflicting results regarding a better glycemic control when compared to mixtures with glucose[10,11] and currently are scantly used.

In general, patients with type 2 diabetes benefit from fat-high diets, as diets very rich in carbohydrates affect the lipid profile of the patient and increase the risk of cardiovascular diseases.[3]

What should be the protein intake and its characteristics?

Seriously ill patients with hyperglycemia and particularly diabetics show deep metabolic changes in the absence of insulin, such as an increased basal energy expenditure (BEE) and a negative net protein balance. Both insulin and amino acids stimulate protein synthesis, though its effects depend on its relative concentration. In hyperaminoacidemia states, it has been suggested that additional insulin doses do not increase protein synthesis, probably related to the insulin resistance level of each patient[12].

There is no adequate evidence to define a specific nitrogen supply to critically-ill diabetic patients or those with stress hyperglycemia. It is recommended to adjust protein needs to the metabolic stress level of the patient: 1.3-1.7 g of proteins/kg/day according to their metabolic state, in order to prevent exacerbation of protein catabolism.

Do other specific nutrients play any role in nutritional-metabolic support in these patients?

Glutamine

The parenteral administration of glutamine has been associated with an improved glycemic control[13] through several potential mechanisms: *a)* through the metabolism of glutamine to glucose in the glucose-glutamine cycle; *b)* increasing insulin secretion; *c)* improving the sensitivity to insulin of the striate muscle; *d)* increasing the oxidation of free fatty acids, and *e)* decreasing the inflammatory response. It has been proven that glutamine improves insulin sensitivity in seriously ill patients[14], and 2 multicenter clinical trials have shown that patients receiving TPN enriched with

glutamine have fewer infectious complications and better metabolic tolerability[15,16] (Ib).

Eicosapentaenoic acid and gamma linolenic acid

There are no studies with enteral nutrition (EN) or PN that show significant effects of ω-3 fatty acids on glycemic control.

Fiber

The ADA recommends administration of dietary fiber in diabetic patients, due to its lower glycemic index[5]. A metaanalysis showed no significant benefits in seriously ill patients[16] (Ia), though a subsequent study demonstrated that specific diets containing fiber improved glycemic control, though without emphasis in seriously ill patients[7] (Ib).

Trace elements and vitamins

There is no evidence that antioxidant vitamins at doses higher than the requirements are safe or beneficial[17] (IIb). The contribution of oxidative stress in diabetic complications and, particularly in seriously ill patients, is not evident, as tissue damage occurs in diabetic patients but not in patients with insulin resistance, as in the case of stress hyperglycemia occurring in critically-ill patients. There are no evidences of the efficacy of antioxidants in the prevention or control of the complications associated with hyperglycemia[18] (IV).

Can any specific diet be recommended in critically-ill patients with hyperglycemia?

Specific enteral diets for the control of hyperglycemia are characterized as rich in MUFA and containing low-glycemic index carbohydrates and fiber[19]. Very few studies have been performed to date and, though they show no differences in morbidity-mortality with the use of a conventional diet, they achieve a better control of glycemia and a lower need for insulin[19] (Ib), [20,21] (III). A recent study evidences also a lower variability in blood sugar levels when a specific enteral diet is used in patients with type 2 diabetes[22] (III).

Should blood glucose values be normalized in critically-ill patients?

Different studies have shown that hyperglycemia is an independent risk factor for a poorer prognosis in critically-ill patients[23,24].

The outcomes of a study in a population of critically-ill surgical patients maintaining a tight glycemic control, from 80 to 110 mg/dl by continuous perfusion of insulin[25] and demonstrating a reduction of 3.4% of the risk of death at the ICU, could not be reproduced in subsequent studies[26,27]. Even subsequent publications evidence an increased mortality in the group of patients maintaining strict blood glucose levels (80-110 mg/dl), mortality related to the high incidence of severe hypoglycemia[28-30] (Ib).

The largest multicenter study conducted to date (NICESUGAR)[30] included 6,104 patients from mixed ICUs and compared 2 ranges of blood glucose levels: 80-108 mg/dL (strict) versus < 180 mg/dL (conventional). The incidence of severe hypoglycemia was higher in the strict control group (6.8 vs 0.5%; $p < 0.001$) and 90-day mortality in the strict control group was significantly higher (27.5%) than in the conventional group (24.9%) (95% CI, 1.02-1.28; $p = 0.02$)[30] (Ib). The mean blood glucose achieved in the strict control group was 114 mg/dL vs the conventional group 144 mg/dL.

Two recent metaanalyses shows that in all critically-ill patients, the strict control of blood glucose levels (80-110 mg/dl) significantly increased severe hypoglycemia, without improving survival as compared to the conventional control group[31,32] (Ia).

It has been demonstrated that the variability of blood glucose levels along the patient evolution may affect mortality, even if it occurs between blood glucose ranges considered as appropriate[33]. In the cohort of 66,184 patients evaluated by the ANZICS (Australian and New Zealand Intensive Care Society), the variability of blood sugar levels over the first days of evolution was associated with an increased adjusted mortality when compared to the appearance of severe hypoglycemia[24] (III).

Recommendations

– It is recommended to monitor blood glucose values in all critically-ill patients (A).

– It is recommended, as most appropriate, to maintain blood glucose levels below 150 mg/dl (C).

– It is recommended to start treatment with insulin when blood glucose levels exceed 150 mg/dL (C).

– Continuous insulin perfusion protocols, will be designed to prevent strict blood glucose levels (80-110 mg/dL) in order to reduce the risk of severe hypoglycemia (B).

– It is recommended that continuous insulin perfusion protocols should be designed to avoid the variability of blood glucose levels (C).

– Energy supply should meet patient requirements avoiding overnutrition (C).

– Specific diets for hyperglycemia may decrease insulin requirements in these patients (B).

– In patients with parenteral nutrition it is recommended to use glutamine supplements in order to contribute to hyperglycemia control (B).

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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