RECOMMENDATIONS FOR SPECIALIZED NUTRITIONAL-METABOLIC MANAGEMENT OF THE CRITICAL PATIENT

Recommendations for specialized nutritional-metabolic management of the critical patient: Indications, timing and access routes. 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: indicaciones, momento de inicio y vías de acceso. Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)

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Introduction

The metabolic reaction to stress forms part of the adaptive response seeking to survive acute illness, and is characterized by the activation of a series of metabolic mechanisms that increase the supply of energy substrates to the vital body tissues. The persistence of aggression over time rapidly leads to energy-protein depletion and acute denutrition. Under these circumstances it is unlikely for the body to have enough metabolic reserves to cover the endogenous energy requirements – giving rise to an energy debt that is associated to a poorer short- and even long-term patient prognosis.

Specialized nutritional support or management (SNS) traditionally has been regarded as a complementary measure in the case of the critically ill, seeking to preserve lean mass and help in the response to stress, though it is also useful for modifying the metabolic response to aggression, preventing oxidative cell damage and modulating the immune response. Certain nutrients and their administration route play an important role in different evolutive stages of the disease process. In this regard, SNS can be administered via the enteral route in the form of enteral nutrition (EN) and/or via the intravenous (i.v.) route in the form of parenteral

nutrition (PN), with different access routes, complications, and levels of efficacy.

Questions

Is specialized nutritional support indicated in the critical patient?

Oral feeding is not possible in many critical patients. Such individuals constitute a heterogeneous population in which the degree of severity should be established based on the pertinent scales. The classification of a patient as being critically ill is conflictive, since it is common practice to extrapolate results from studies on SNS corresponding to patient groups not adequately assessed as critically ill subjects. The reference in this respect should be a patient requiring mechanical ventilation (MV) and in whom the time required to restore oral feeding cannot be predicted.[1]

Thus, in order to establish the indication of SNS, due consideration is required of the time during which the patient will not be able to resume complete oral feeding. There are nutritional screening tools for the in-hospital population that define 5 days of fasting as the period for assessing nutritional risk in the context of severe illness,[2] though other indices do not assess time but the type of disease and its severity. The Nutric Score (nutrition risk in critically ill score) quantifies the risk of developing adverse events potentially modifiable through aggressive and early SNS. A simplified score of >4 points is associated to poorer clinical outcomes, and aggressive SNS would probably afford benefits in this context.[3] The nutritional risk increases in the presence of evidence of malnutrition upon admission, a body mass index (BMI) <18.5 kg/m^2, weight loss >10%, fasting or an involuntary decrease in food intake. Moderate or severe malnutrition in a critical patient requires the early start of SNS.

The correct time for starting SNS has not been clearly defined. No controlled studies have been made to determine the fasting period to be considered for indicating SNS. However, some randomized controlled trials (RCTs) have analyzed the absence of SNS for a limited number of days versus the early introduction of SNS. In patients with peritonitis, significant improvement was observed in terms of mortality among those subjects fed via jejunostomy compared with those not fed until oral intake was resumed.[4] In cases of severe trauma, differences were seen in terms of mortality, duration of stay and days of MV.[5] Surgical patients receiving SNS suffered fewer infections and severe complications.[6] The available studies on patients with medical disease conditions are more limited. A series of individuals with organophosphorus compound intoxication subjected to prolonged MV with minimum EN showed no clinically relevant differences with respect to patients treated only with glucose saline solutions.[7]

When should enteral nutrition be started?

The early introduction of SNS via the enteral route is regarded as a proactive management strategy that can reduce the severity of the disease and the incidence of complications, with a favorable impact upon the clinical outcome. However, earliness in caloric supply could result in nutritional overload, with an increased production of reactive oxygen species, mitochondrial damage and the inhibition of autophagia as a protective mechanism, since the endogenous production of glucose covers up to 50–70% of the energy expenditure during the first few days. These changes could explain some clinical benefits associated with hypocaloric feeding in the early stages of critical illness.[8]

The first problem in interpreting the studies that evaluate timing of the start of EN is the inconsistency in defining earliness, which ranges from 24–72 h after admission to the Intensive Care Unit (ICU). There is growing consensus in defining early SNS as support starting in the first 24–48 h of admission to the ICU, following adequate patient resuscitation and hemodynamic stabilization. A second problem is the design of the different RCTs as regards both the route and amount of nutritional support of the patients under study, and the diversity of the control groups used: late EN, late PN or standard care (intravenous glucose and/or oral feeding once intestinal transit has been ensured).

In the last 15 years a number of RCTs have been carried out to clarify the convenience of starting early EN (in the first 24–48 h) or late EN (>72 h). In most cases, the control groups corresponded to late EN, though in some studies complementing with late PN was used. These trials have been pooled in 6 different systematic reviews, one of which used the first 24 h of admission as criterion for early EN.[9] The early introduction of EN was associated to a decrease in the incidence of global infectious complications in four meta-analyses, and specifically to a decrease in pneumonia in one of them.[9] Three analyzed differences in days of hospital stay, though in only one of them was stay found to be significantly shorter.[8] In sum, early EN reduces infectious complications, with a clear tendency toward lower patient mortality.

When should enteral nutrition be started in hemodynamically unstable patients?

The start of EN requires correct patient resuscitation and hemodynamic stabilization. The enteral presence of nutrients exerts direct favorable effects upon the gastrointestinal tract and increases mesenteric blood flow. The stabilization of patients under conditions of shock may require the use of high-dose inotropic agents and vasodilator drugs, which under conditions of low cardiac output could result in splanchnic hypoperfusion and a risk of mesenteric ischemia. Fifty percent of all critical patients do not receive SNS in the first 48 h due to possible intestinal hypoperfusion and the administration of vasoactive drugs. However, a series of post-heart surgery patients under conditions of low cardiac output and receiving high doses of inotropic agents demonstrated correct tolerance and adequate absorption of nutrients on receiving a hypocaloric diet.[10] The degree of hypotension that places the patient at risk, and the types of patients at increased risk of mesenteric ischemia with EN are not clear; a certain controversy therefore exists regarding the timing and route indicated for feeding the unstable patient. On the other hand, the incidence of intestinal ischemia is less than 1% in critical patients, with a low correlation to shock or the administration of vasopressor drugs.[11] The condition is more common in surgical or trauma cases,

associated to laparotomy, intestinal manipulation, jejunostomy and jejunal diet administration, and is an infrequent complication in medical patients and in subjects receiving EN via the gastric route.

Three prospective cohort studies have analyzed this issue.[12–14] In a series of patients subjected to MV and with a systolic blood pressure of <90 mmHg, of which 75% were receiving vasoactive drugs and presented a Sequential Organ Failure Assessment (SOFA) cardiovascular score of ≥ 3, the mortality rate was found to be lower among those cases in which SNS was started in under 48 h after intubation – the difference being unrelated to the administration route or the different caloric supplies involved. There were more cases of pneumonia in the early nutrition group, though not associated to the enteral route.[13] In another series of patients subjected to MV and receiving vasoactive drugs, a significant decrease in mortality was noted in the early EN group – the effect being more evident in the more seriously ill patients and with a larger number or higher doses of vasoactive drugs.[14] Retrospective studies confirm the safety of this practice, which is able to cover 60–75% of the caloric objectives. Another study established an association between noradrenalin dosage ($\leq 12.5\,\mu g/min$) and good tolerance of EN.[15] Permissive hyponutrition with early EN in septic shock has also been associated to shorter stay and days of invasive MV in the ICU.[16] A recent RCT has analyzed the SNS administration route in patients with shock subjected to MV. The patients received full nutrition (normocaloric diet) on an early basis, with no recorded differences in terms of morbidity-mortality related to the administration route, though the incidence of gastrointestinal complications was higher in the EN group.[17]

In heart surgery patients, different prospective studies under conditions of low postoperative cardiac output have recorded improvements in output and in metabolic response associated to EN, with no evidence of impaired mesenteric perfusion. This confirms that an acceptable caloric target or objective of close to 70% can be assumed, with no increase in complications and with no detected disadvantages associated to the use of early EN in groups of patients subjected to MV and with low postoperative cardiac output requiring 2–4 vasoactive drugs and/or mechanical circulatory assist measures.[10–18]

When should parenteral nutrition be started?

When the digestive tract cannot be accessed by means of a tube, or in situations where EN is contraindicated, the start of PN should be contemplated. Moreover, if EN is unable to meet the nutritional requirements, or if there is clear nutritional risk, PN offers more favorable results than standard care. The administration of PN in malnourished patients reduces the global complications and mortality rate versus standard care. Therefore, when EN is not possible in malnourished patients with an indication of SNS, we should administer PN as soon as possible.[19] In non-malnourished patients or individuals at low nutritional risk, the timing of the start of PN is subject to controversy, since individuals receiving standard care suffer fewer global and infectious complications than those administered PN.[18]

In the presence of contraindications to EN, the introduction of early PN on day three (maintaining intravenous glucose for 48 h) or day 8 (after 7 days of hyponutrition) revealed no differences in mortality in the ICU or in hospital, or after 90 days – though the likelihood of live patient discharge from the ICU in the first 8 days was greater in the late PN group.[20] A meta-analysis comparing early PN with different nutritional regimens from day three revealed a tendency toward fewer days on MV, but more days of hospital stay in the early PN group.[21] However, the different nutritional regimens in the controls and the scant difference in starting time between the two groups allowed no conclusions to be drawn regarding the best time to start PN. In another meta-analysis, early PN in the presence of relative contraindications to EN resulted in fewer days of invasive MV and improved muscle recovery over the long term compared with standard care – with no other significant differences in the course of hospital admission.[22] Early PN as an alternative to EN in patients with no contraindication to the latter feeding modality has been described in the CALORIES trial – no differences being observed in terms of infectious complications, mortality or adverse events, except for a lesser incidence of hypoglycemia and vomiting in the early PN group.[23] It should be noted that in this trial, as in many other studies, neither of the two groups were able to cover their respective caloric requirements.

The discrepancies in these trials and the analyses derived from them support the idea that the beneficial or adverse effects are more closely related to the nutritional dose, including protein supply, than to the route employed for administration, or to timing of the start of support. The ideal strategy would be slower energy supply in the first phase of the acute disease, with adaptation to the nutritional objectives after the early phase of aggression. In sum, timing the start of PN remains unclear, and more studies are needed to detect the long term consequences of the caloric debt due to the delay or hyponutrition in critical patients.

What routes can be used to administer specialized nutritional support in the critical patient?

Enteral nutrition is the first choice, because it offers benefits from the nutritional point of view and moreover preserves enterocyte functional and structural integrity. It is the cheapest and most accessible option, and potentially also the safest choice. In contrast to PN, the enteral route would protect the intestinal barrier, with favorable effects upon the intestinal lymphoid tissue, stimulation of enterohormones that intervene in intermediate metabolism, intestinal and liver function, and also immune modulating action.[8,9]

The enteral route with a nasogastric tube is the best choice in the critical patient, and also the least expensive and easiest to use option in the ICU. It is important to implement EN protocols adapted to the reality of the ICU, with implication on the part of the nursing staff and administering a diet based on a certain volume of nutritional formula in accordance with the prescribed dosage, in order to optimize SNS in terms of the administered dose.[24] On the other hand, due evaluation should be made of the need to temporarily suspend EN during diagnostic or therapeutic procedures, in order to avoid significant differences between the pre-

scribed dose and the effectively administered dose.[25] The administration of EN in bolus form may be associated to greater interruption of EN, together with an increased risk of bronchoaspiration. Continuous EN therefore seems to be advisable.[26]

Postpyloric enteral feeding is a valid option in the presence of gastroparesis and a lack of efficacy of the measures adopted to improve EN tolerance (prokinetic agents). This technique should also be considered in the case of a high risk of regurgitation, vomiting or bronchoaspiration (major burn patients, severe acute pancreatitis, traumatic brain injury), since the incidence of such complications can be reduced by postpyloric EN.[27]

Gastrostomy is indicated when prolonged EN is required in the context of dysphagia, which is common in neurocritical patients.[28] Likewise, jejunostomy in the postsurgical setting contributes to preserve digestive tube anatomy and structure, though it affords no improvements in terms of mortality.[4,6]

Total PN (TPN) and complementary PN should be taken into account in order to ensure the minimum nutritional deficit possible; it constitutes a safe and effective alternative, and should be used when EN is contraindicated. The choice between TPN and complementary PN should be established based on the nutritional requirements of the patient, the need for volume restriction, the availability of venous accesses, and the contemplated duration of nutritional support.

The choice of administration route should be based on the prevention of malnutrition and on a correct supply of the necessary nutrients, according to the previously established objectives of nutritional support, independently of the type of route used for administration.

Does the specialized nutritional support administration route influence the patient outcome?

The first 3–5 days of admission, corresponding to the acute phase of the disease process, are characterized by a decrease in intestinal glucose absorption, with greater gastroparesis, which is associated to increased intolerance of EN. The digestion and absorption of EN implies an increase in oxygen and energy demand on the part of the intestine, and an increase in splanchnic blood flow, which may be poorly tolerated under conditions of poor perfusion or shock. The impossibility of providing adequate nutritional support with EN is more a marker of the severity of the disease process than a prognostic factor as such, associated to an increased risk of complications over the patient clinical course.

Although PN traditionally has been associated to an increased risk of infection in the ICU – probably in relation to inadvertent overfeeding and hyperglycemia[29] – improved glycemic control, the decrease in catheter-related infection, and increased safety of the administered formulas currently define PN as a strategy that is as safe and effective as EN.[23,29] In sum, the SNS administration route is not so important; what really counts is the dosage and composition of the administered formula in relation to the prior nutritional assessment of the patient. An increased nutritional deficit – both caloric and proteic – during the first week in the ICU among critical patients with a high nutritional risk is associated to poorer survival over both the short and the long term, as well as to poorer patient quality of life after hospital discharge.[1]

What are the indications of complementary parenteral nutrition?

Although EN is regarded as the first choice, in actual clinical practice it is only able to cover 45–60% of the calculated nutritional requirements. The reasons leading to caloric-protein deficiency and a possible increase in complications are varied, and include calculation error, interruptions in feeding, and poor gastrointestinal tolerance that limit the administration and absorption of nutrients.[25] Over the days, patients admitted to the ICU accumulate an energy deficit, and the combination of EN and PN can avoid this, making it possible to administer 80–100% of the requirements. Nevertheless, the caloric-protein needs of critical patients are neither clear nor homogeneous in all cases or over the course of admission to the ICU.

In the event of an insufficient EN supply, complementary PN from day four can reduce the incidence of infections and the duration of MV,[30] though such supplementing should be individualized and revised on a daily basis.

When should the caloric objective and the protein objective be reached?

As has been mentioned, the cumulative nutrient deficiency observed when EN is unable to cover the nutritional requirements is associated to adverse effects. Some authors advocate reaching the nutritional objectives in the first 48 h, while others recommend reaching them after one week in the ICU.[20,31]

A RCT including adults with relative contraindications to early EN and randomized to receive early PN (<24 h) or standard care recorded no differences in mortality after 60 days or in the duration of ICU stay – though a decrease in the number of days of MV was observed in the early PN group.[22] In the TICACOS trial,[32] designed to adjust energy supply to the requirements measured by indirect calorimetry, the patient group that received complete energy provision from 48 h of admission showed a nonsignificant decrease in mortality, though with more infections and more days of invasive MV. In contrast, another RCT evidenced a decrease in days of stay, days of invasive MV, infectious complications and the need for renal replacement therapy, as well as improved glycemic control, with the administration of late PN versus early PN[20].

A systematic review[33] including 6 RCTs analyzed the convenience of starting complementary PN on an early (in the first 72 h) or late basis (day 8). The results differed greatly from one study to another. The administration of complementary PN from the first three days of ICU stay reduced the incidence of infections, though no differences in patient mortality were observed versus late complementary PN, and mortality likewise did not depend on whether the patients reached the nutritional objective from day four or day 9.[30] In one of the included studies, hospital stay was found to be shorter when late complementary PN was provided,[20] while in the rest the duration of stay was shorter

in the early complementary PN groups.[31,34,35] One of the studies recorded an increase in infections with early complementary PN.[20] The caloric-protein supply was closer to the established objective when early complementary PN was used.[31,34] Only one of the analyzed studies described fewer days of invasive MV and of renal replacement therapy, fewer infections, and improved glycemic control in the late complementary PN group.[20] On the other hand, the included patient groups were not homogeneous: one study excluded patients subjected to elective surgery,[34] another included mainly post-heart surgery cases,[20] another only contemplated medical patients,[35] and the rest included both medical and surgical cases.[22,30,31]

Recommendations

- It is advisable to start specialized nutritional support in the acute phase in malnourished patients, individuals at high nutritional risk, and in critical patients in which complete oral feeding over the next 5 days is unlikely. (Level of evidence: moderate. Grade of recommendation: high.)
- When specialized nutritional support is indicated and there are no contraindications, it is advisable to start early enteral nutrition (in the first 24–48 h), after adequate patient resuscitation. (Level of evidence: high. Grade of recommendation: high.)
- In patients presenting hemodynamic alterations, with correct resuscitation even in the presence of a low cardiac output, and the administration of one or more vasoactive drugs, enteral nutrition may be started with the adoption of correct monitoring measures. (Level of evidence: low. Grade of recommendation: moderate.)
- The enteral route using a nasogastric tube is the option of choice in the critical patient. (Level of evidence: low. Grade of recommendation: high.)
- In critical patients at nutritional risk and in which enteral nutrition is not possible, parenteral nutrition should be started early (in the first 48 h) at adequate doses, avoiding hypernutrition. (Level of evidence: moderate. Grade of recommendation: moderate.)
- Complementary parenteral nutrition is suggested in patients in which the caloric-protein objective is not reached by day four of the start of nutritional support. (Level of evidence: moderate. Grade of recommendation: moderate.)
- It is advisable to establish protocols to improve nutritional efficacy, with involvement of the entire care team, and to define the indications of postpyloric feeding via gastrostomy and jejunostomy. (Level of evidence: low. Grade of recommendation: high.)

Conflicts of interest

The authors declare that they have no conflicts of interest.

Note to supplement

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