

Intensive medicine – Guidelines on Parenteral Nutrition, Chapter 14

Intensivmedizin – Leitlinie Parenterale Ernährung, Kapitel 14

Abstract

In intensive care patients parenteral nutrition (PN) should not be carried out when adequate oral or enteral nutrition is possible. Critically ill patients without symptoms of malnutrition, who probably cannot be adequately nourished enterally for a period of <5 days, do not require full PN but should be given at least a basal supply of glucose. Critically ill patients should be nourished parenterally from the beginning of intensive care if they are unlikely to be adequately nourished orally or enterally even after 5–7 days. Critically ill and malnourished patients should, in addition to a possible partial enteral nutrition, be nourished parenterally. Energy supply should not be constant, but should be adapted to the stage, the disease has reached. Hyperalimentation should be avoided at an acute stage of disease in any case. Critically ill patients should be given, as PN, a mixture consisting of amino acids (between 0.8 and 1.5 g/kg/day), carbohydrates (around 60% of the non-protein energy) and fat (around 40% of the non-protein energy) as well as electrolytes and micronutrients.

Keywords: substrate supply, critically ill, sepsis, intensive care

Zusammenfassung

Eine parenterale Ernährung (PE) sollte nicht durchgeführt werden, wenn eine ausreichende orale oder enterale Ernährung möglich ist. Kritisch Kranke ohne Zeichen der Mangelernährung, die voraussichtlich <5 Tage nicht ausreichend enteral ernährt werden können, bedürfen keiner vollen PE, sollten aber zumindest eine basale Glukosezufuhr erhalten. Kritisch Kranke sollten von Anbeginn der Intensivtherapie parenteral ernährt werden, wenn sie voraussichtlich auch nach einem Zeitraum von 5–7 Tagen nicht ausreichend oral oder enteral ernährt werden können. Kritisch Kranke mit einer Mangelernährung sollten – auch neben einer möglichen partiellen enteralen Ernährung – parenteral ernährt werden. Die Energiezufuhr sollte nicht konstant sein, sondern muss an den Verlauf der Erkrankung angepasst werden. Eine Hyperalimentation sollte im akuten Stadium der Erkrankung auf jeden Fall vermieden werden. Kritisch Kranke sollten zur PE eine Mischung aus Aminosäuren (0,8 und 1,5 g/kg/Tag), Kohlenhydraten (ca. 60% der Nicht-Protein Energie) und Fett (ca. 40% der Nicht-Protein Energie) sowie Elektrolyten und Mikronährstoffen erhalten.

Schlüsselwörter: Substratzufuhr, kritisch krank, Sepsis, Intensivtherapie

Indications for PN in critically ill patients

- Parenteral nutrition (PN) should not be instituted when adequate oral or enteral nutrition is possible (C).
- Critically ill patients without symptoms of malnutrition, who probably cannot be adequately nourished enterally

for a period of <5 days, do not require full PN but should be given at least a basal supply of glucose (B).

Commentary

Patients who can be nourished orally or enterally should certainly be nourished this way.

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The negative consequences of PN observed in earlier studies [1] probably occurred as a result of unphysiologic composition and infrequent monitoring of PN (too high energy used, badly monitored BS (blood sugar) levels) rather than because of the parenteral substrate administration. Recent studies [2], [3] have shown that, compared with enteral nutrition, there is not necessarily a connection between PN and a higher rate of complications or a worse prognosis.

Nevertheless, it is concluded by the expert group that enteral application should be preferred, if possible, as it is more physiological, and generally incurring lower costs. Furthermore, with the exception of one study, PN did not have specific advantages over enteral nutrition.

There are still not enough randomised controlled studies to answer the question whether patients should be fed parenterally when they cannot be adequately enterally nourished.

Experiences over the last years have shown that if enteral nutrition is started early, a higher proportion of patients, requiring intensive care, can be adequately nourished enterally after a few days. In one such study [4], it was observed that a reduced nutrition supply over a few days had no negative consequences, as long as the patients showed no symptoms of malnutrition. Adequately nourished patients who can be completely nourished orally or enterally again within 5–7 days do not require PN. For such patients, one should provide at least a basal glucose supply (2–3 g/kg kg/day). However, for malnourished patients one should start early with PN.

Indication for PN

- Critically ill patients should be nourished parenterally from the beginning of intensive care if they are unlikely to be adequately nourished orally or enterally even after 5–7 days (A).

Commentary

In the above-mentioned study [4], the electively operated patients, who were given infusions of only 250–300 g glucose/day and were unable to take adequate nourishment orally after 14 days, showed a 10 times higher mortality than patients who were nourished completely parenterally from the beginning of intensive care. Therefore, post-operative patients who might develop a state of malnutrition, after a period of 8–12 days on only glucose infusions, may be predisposed to a higher rate of mortality. Since it should not be the aim of nutrition therapy to allow the patients to get into a state of malnutrition and then be treated for it, such patients should be nourished parenterally from the beginning of intensive care.

Accordingly, the indication for PN should be made prospectively in critically ill patients. The number of days required to re-establish adequate enteral or oral nutrition should be considered at the beginning of the therapy. There are, at present, no established criteria, which could

help in determining, with absolute certainty, which patients are to be nourished parenterally. Therefore, it cannot be avoided that occasionally there are patients on PN who are adequately nourished enterally sooner than expected, and some patients who unexpectedly deteriorate and an indication for PN is established too late.

Combined nutrition therapy (enteral and parenteral nutrition)

- Critically ill and malnourished patients should, in addition to a possible partial enteral nutrition, be nourished parenterally (A).

Commentary

Several studies dealing with patients suffering from severe malnutrition, which have been summarized in one meta-analysis [1], have reported a positive effect of PN with a reduction in complications and mortality.

Energy intake

- The amount of energy supplied should follow the principles stated in the chapter on “Energy expenditure and energy intake” <http://www.egms.de/en/gms/2009-7/000084.shtml>.

This means that the energy supply should not be constant, but should be adapted to the stage, the disease has reached. Hyper-alimentation should be avoided at an acute stage of disease in any case.

Substrate intake

- Critically ill patients should be given, as PN, a mixture consisting of amino acids, carbohydrates, (around 60% of the non-protein energy) and fat (around 40% of the non-protein energy) as well as electrolytes and micronutrients (C).

Commentary

Typical metabolic changes in patients with systemic inflammatory reactions are a reduced oxidation of carbohydrates and an increased oxidation of fat. The disproportion between endogenous glucose production and peripheral glucose oxidation leads to hyperglycaemia in most patients. Accordingly, a lipid supply of 30–50% of energy intake corresponds to the existing pattern of utilization. An increased glucose intake, in such circumstance, does not reduce the endogenous glucose production [5], and leads to a further increase in the already existing hyperglycaemia.

However, it has not been substantiated by studies whether in critically ill patients PN with lipids, and with which kind of lipids, would be more effective than a

carbohydrate intake without lipids with respect to outcome parameters. Therefore, the recommendation of the group to give PN containing fat to critically ill patients is only an expert opinion (C).

The comparative study of Batistella [6], which showed obvious disadvantages when lipids were administered to trauma patients has the following shortcomings: a) not isocaloric in both arms of the study (the energy contents in patients without lipids was about 25% lower) and b) soya bean oil/lipid emulsion was used in the study, the use of which is nowadays controversial for patients in a critical state (see below). Similarly, the higher rate of complications that has been found in the meta-analysis of Heyland et al. [7] for patients given lipid infusions is more a result of the special fat emulsion used than the fat administration in general.

Carbohydrates

(cf. "Carbohydrates" <http://www.egms.de/en/gms/2009-7/000082.shtml>)

- Critically ill patients should predominantly be given glucose as carbohydrate. There is no certain indication for other carbohydrates in critically ill patients (C).

Commentary

Fructose and sorbitol are no longer used because of the grave side effects when there is an inborn incompatibility. With Xylit, a reduction of hyperglycaemia as well as a decrease in hepatic gluconeogenesis was shown in two clinical studies on a small number of patients, when glucose intake was simultaneously decreased. These results have not been confirmed in any further major study. This group does not recommend the use of Xylit, particularly in consideration of observed complications (oxalose).

Hyperglycaemia arising from PN

(cf. "Carbohydrates" <http://www.egms.de/en/gms/2009-7/000082.shtml> and "Complications and monitoring" <http://www.egms.de/en/gms/2009-7/000076.shtml>)

- At all times, a hyperglycaemia caused by PN should be avoided (A).
- If hyperglycaemia occurs, in spite of an adequate insulin supply, the carbohydrate supply should be reduced (C).

Commentary

The study of van den Berghe et al. [8] showed that, for patients requiring intensive care, blood sugar levels of over 110 mg/dl are linked to a significant increase in mortality and morbidity. Insulin can reduce blood glucose level through an increase in cellular glucose uptake and partly through increased glucose utilization as well. The insulin effect can, however, be reduced in particular ill-

nesses such as diabetes mellitus, post-operative insulin resistance, or sepsis.

There were indications in a more recent uncontrolled observational study, that a significantly higher mortality was observed only at blood sugar concentration of >145 mg/dl [9]. In the controlled study from van den Berghe, however, in the group of patients with blood sugar levels between 110–150 mg/dl there was already a significantly higher mortality than in the group of patients in which blood sugar was strictly controlled at values below 110 mg/dl [10]. Therefore, the objective should be to aim for a normoglycaemia with PN, ideally a level between 80 and 110 mg/dl.

Basically two situations can occur:

a) Patients who are euglycaemic before the start of a PN: If there is a significant increase in the blood sugar level to a value considerably >110 mg/dl, while an adequate substrate supply is being administered during the PN, then this should be lowered with a continuous intravenous insulin administration, by means of an infusion pump. It is recommended to have a standardised protocol according to which the insulin dose can be regulated in accordance with the measured blood glucose levels.

If normoglycaemia (<145 mg/dl, ideally <110 mg/dl) is not achieved, even with a maximum insulin dose of approximately 20 IU insulin/h, then the carbohydrate supply should be reduced until the target BS level is attained using this insulin dose. The maximum level of approximately 20 IU insulin/h is not substantiated by any study but is an expert opinion.

If the BS falls to a level <80 mg/dl with this therapy, then the carbohydrate intake should be increased again until the target carbohydrate intake for euglycaemic conditions is achieved.

If the BS level falls at the maximum (=target) value of carbohydrate intake, the insulin dose should be lowered.

b) Patients with a BS level >110 mg/dl before commencing PN:

For these patients, hyperglycaemia is a result of a disproportional rate of endogenous gluconeogenesis and glucose oxidation. It is not recommended, under these conditions, to infuse even more glucose as this would only augment the hyperglycaemia.

For this reason, one should start with a continuous insulin infusion. Only when the target BS level can be reached and maintained with a dose of ≤4 IU insulin/h, one should start with an additional glucose supply.

Fats

- No choice of specific fat emulsion is recommended for critically ill patients, because there are no conclusive clinical studies on varying endpoint effects of different lipid emulsions.
- A preferential use of lipid emulsions with a lower content of polyunsaturated fatty acids, relative to pure soybean oil emulsions, appears justifiable in critically ill patients (C).

Commentary

A large number of clinical, ex-vivo and animal studies have shown that the quality of the infused fatty acids has a clinically relevant effects on the immune system. It was observed that classic soybean oil emulsions suppressed the cellular immune response and stimulated the release of interleukins with a pro-inflammatory pattern. One clinical study [6] has also demonstrated that soybean oil emulsions not affect killer cell activity but also induce a higher rate of infection and longer duration of mechanical ventilation and treatment. However, in this study the control group did not receive isocaloric nutrition.

The existing experimental data as well as this clinical study appear to justify the recommendation not to consider pure soybean oil emulsions as the lipid emulsion of choice for critically ill patients.

Alternatives are mixtures consisting of soybean oil and MCT, a mixture consisting of soybean oil or soybean oil /MCT and fish oil, a mixture consisting of 20% soybean oil and 80% olive oil, or a mixture consisting of soybean oil, MCT, olive oil and fish oil, or a mixture consisting of soybean oil, MCT and fish oil. In addition, an emulsion is available with re-esterified medium- and long-chain fatty acids.

No clinical studies have been published to demonstrate an obvious advantage of one of these emulsions over others with respect to relevant clinical outcome parameters in critically ill patients.

Amino acids

- The amino acid intake with PN for critically ill patients should usually be between 0.8 and 1.5 g/kg/day (A).

Commentary

In several clinical studies it was observed that an amino acid infusion of more than 1.5 g/kg/day does not lead to a better nitrogen balance, but instead to an augmented urea production [11], [12], [13], [14], [15], [16]. Although this level has been questioned recently by several authors [17], [18], on the basis of the existing data it is recommended to supply parenteral amino acids between 0.8 and 1.5 g/kg body weight daily. Certain groups of patients (e.g. patients with burns, patients with renal failure) need a higher infusion of amino acids.

Glutamine

- Critically ill patients who are nourished parenterally for longer than 5 days, without receiving any significant nutrition enterally, should be given, in addition to the parenteral infusion of amino acids, glutamine dipeptide in a dose of 0.3–0.4 g/kg body weight/day (equivalent to 0.2–0.26 g glutamine/kg body weight/day) (A).

Commentary

A meta-analysis [19] published in 2002 found that a glutamine supplementation leads to a lower rate of complications and a decrease in mortality rate in critically ill patients. However, the validity of this meta-analysis is limited because it was an evaluation of studies in which both parenteral and enteral glutamine supplementation studies were evaluated together. Furthermore, there was one study dealing only with burn patients [20].

After the publication of the above meta-analysis, two more studies were published, in which critically ill patients were administered additional glutamine parenterally [21], [22]. The investigation by Goeters et al. [22] showed that for patients who were treated with 0.2 g glutamine/kg body weight/day for a period of ≥ 9 days, the mortality over a period of 6 months could be reduced significantly from 66.7% to 40%. These results confirm the results of Griffiths et al. [23], where significant improvement in survival at 6 months was observed mainly in those patients who were treated with glutamine for more than 5 days.

Another study, however, published in 2004 showed in patients with secondary peritonitis [21] only a tendency to a decreased mortality with parental supplementation of glutamine. This was also observed by the study of Powell-Tuck et al. [24] with patients clinically accepted for PN. On the basis of the results of these four studies, it is concluded that a solution of amino acids enriched with glutamine dipeptides should be used at least in patients who need PN for more than 5 days,

Branched-chain amino acids

- In critically ill patients, there is no firm indication for the use of amino acids solutions with a higher proportion of branched-chain amino acids, except for patients with severe hepatic encephalopathy (C).

Commentary

The published small studies [25], [26], [27] using amino acid solutions with an increased proportion of branched-chain amino acids in critically ill patients did not show any advantages in outcome parameters till to date.

The expert group does not see a concrete indication for the use of such a solution at present, since a major study on this is not yet published.

Notes

This article is part of the publication of the Guidelines on Parenteral Nutrition from the German Society for Nutritional Medicine (overview and corresponding address under <http://www.egms.de/en/gms/2009-7/000086.shtml>).

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