Nutrition 28 (2012) 840–843

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

Optimal timing for the initiation of enteral and parenteral nutrition in critical medical and surgical conditions

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ARTICLE INFO

Article history:
Received 16 August 2011
Accepted 20 January 2012

Keywords:
Enteral nutrition
Parenteral nutrition
Critically ill patients
Postoperative care

ABSTRACT

The early provision of nutrients as part of specialized therapy for critically ill patients admitted for critical medical and surgical conditions is recommended by various international guidelines. Enteral nutrition is the first option and should be initiated 24-48 h after admission to an intensive care unit. Even after gastrointestinal anastomosis, early oral or enteral feeding is not only safe but also associated with enhanced recovery and fewer complications. Recent studies showed that the use of an enteral diet or parenteral nutrition that contains immune nutrients enhances the recovery of critically ill patients. Although the precise caloric target remains controversial, the general consensus advocates the avoidance of prolonged hypocaloric or hypercaloric feeding. However, there is still debate about the timing of the initiation of parenteral nutrition when enteral nutrition either is impossible or does not meet the nutritional goals. Although controversy remains, two recent studies showed that when enteral feeding is not feasible the early initiation of parenteral nutrition was not associated with palpable benefit.

Introduction

Various consensus statements and guidelines from international societies recommend the early and adequate initiation of specialized nutrition therapy for critically ill patients admitted for medical and surgical conditions [1–5]. Acute or chronic critical illness may lead to various nutritional deficits, including weakness, muscle wasting, delayed recovery, and immune paralysis [5]. Therefore, the early provision of nutrients is key in the multidisciplinary management of these cases. A recent survey that included 514 international respondents found that early specialized nutrition is well accepted around the world. More than 90% of physicians and dietitians strongly recommended the initiation of either enteral or parenteral nutrition within 24-48 h after the patient is admitted to an intensive care unit. In practice, however, substantial disagreement has been evident between this positive perception of nutrition and reported practice patterns regarding the initiation of feeding [6].

Enteral nutrition (EN) has been preferred over total parenteral nutrition (PN) in the past decade for several reasons, including lower morbidity, lower costs, a shorter length of hospital stay, and the preservation of both the mucosal barrier and the immune competence [7,8]. However, most of this evidence was supported by studies that used hypercaloric PN for comparisons with EN. Complications of overfeeding, such as hyperglycemia and hypercapnia, are known to result in overall detrimental clinical outcomes [9]. Therefore, the prescription of less-caloric PN has been adopted by various critical care facilities to avoid the risks of overloading syndrome. Some recent randomized trials [10] and metaanalyses [11] have shown that PN adjusted to this concept is as reliable as EN for critically ill patients.

Although the formulation and caloric goals of PN solutions have changed in recent years, debate still exists about the timing of the initiation of PN when EN either is impossible or does not meet the nutritional goals. Few data have been generated on this matter, and some recommendations contained in current guidelines from different societies are controversial and based on expert opinions and non-randomized data [2,4]. Therefore, we reviewed the recent literature about the role and timing of the initiation of early enteral and parenteral nutrition in critical medical and surgical conditions.

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0899-9007/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.nut.2012.01.013

Early initiation of enteral nutrition

The early initiation of EN is recommended by various international guidelines [1–3,5] based on substantial evidence [11–13]. Modern guidelines endorse the initiation of EN regardless of the presence of traditional parameters, such as the presence of bowel sounds or flatus [12]. In the critically ill patient who undergoes medical or surgical treatments, the provision of nutrients near 100% of the target via the gut may reduce mortality, particularly in malnourished patients [14]. However, underfeeding is common in critically ill patients, mainly because of gastrointestinal dysmotility or hemodynamic conditions [15]. This is valid for critical medical and surgical conditions. The insistence in maintaining EN in cases of splanchnic hypoperfusion may lead to lethal complications such as non-occlusive bowel necrosis. Non-occlusive bowel necrosis has an estimated incidence of 0.3% to 8.5% in the intensive care unit and may occur even in young patients who previously tolerated EN [16,17].

Traditional nutrition management in either elective or emergency surgeries dictates that during the early days following gastrointestinal resection plus primary anastomosis EN should be withheld until bowel function is reestablished. Postoperative starvation is dictated by the "nil by mouth" policy and continues until bowel movements appear. This policy is applicable to both elective and emergency surgeries and patients who are in an infirmary or intensive care unit during the early postoperative phase. After normal bowel function resumes, a progressive diet, from fluids to normal, is permitted as tolerated by the patient. In contrast, substantial and consistent evidence shows that early oral or enteral postoperative feeding is not only safe but also associated with enhanced recovery and fewer complications [18–20]. A recent metaanalysis that included 15 randomized trails and 1240 patients submitted to gastrointestinal tract resection concluded that early postoperative EN is associated with a significant reduction in total complications compared with traditional postoperative feeding practices. A 45% reduction of all postoperative complications was seen when early postoperative feeding was prescribed. The odds of anastomotic dehiscence were similar (odds ratio [OR], 0.75; 95% confidence interval [CI], 0.39-1.4, $P = 0.39$), indicating that early postoperative feeding is safe. However, nasogastric tube reinsertion tended to be more common in early feeding patients (OR, 1.48; 95% CI, 0.93-2.35; $P = 0.10$), and no advantage of early feeding was evident with regard to either mortality (OR, 0.71; 95% CI, 0.32-1.56; $P = 0.39$) or length of stay (weighted mean difference, −1.28; 95% CI, −2.94 to 0.38; $P = 0.13$) [20].

The provision of EN in critically ill trauma patients may preserve physical gut barrier function and maintain gut-associated lymphoid tissue mass and function. In agreement, another recent metaanalysis based on the results of three randomized trials included 126 trauma patients admitted to a critical care setting. The study showed that the early provision of EN was associated with reduced mortality (OR, 0.20, 95% CI, 0.04-0.91; $P = 0.04$) [21].

Enteral nutrition formulations have changed over the years. An elemental diet was used in the beginning era of early postoperative feeding during the early 1980s [22]. A progressive advance toward either a polymeric or a partially hydrolyzed diet occurred during the next decade [23,24]. Two metaanalyses showed that the perioperative prescription of immune nutrients, especially arginine, is advantageous compared with a standard diet when attempting to reduce the risk of infectious complications and anastomotic dehiscence [25,26]. Arginine-supplemented diets can overcome arginine deficiency, which can occur after surgical trauma. The perioperative administration of enteral arginine supplementation together with ω-3 fatty acids may restore T-lymphocyte function, including CD4 count, and may thus beneficially affect the surgical patient. Furthermore, arginine metabolism via arginase-1 may improve healing by increasing the production of polyamines [27].

One of the aims of nutritional support in critical illness is to minimize lean body mass wasting. In these patients, a rapid consumption of muscle mass and fat is the rule, especially after trauma or septic complications. Although the precise caloric target remains controversial, the general consensus advocates the avoidance of prolonged hypocaloric or hypercaloric feeding [28–32].

Early initiation of parenteral nutrition

The administration of nutrients via the gut either in critically ill medical patients or during the first days following major surgery of the gastrointestinal tract may sometimes be impossible or inadequate, mainly because of ileus or hypotension. Enteral nutrition should be withheld in patients who have a mean arterial blood pressure of less than 60 mm Hg, particularly with the use of fluctuating doses of catecholamine agents to maintain hemodynamic stability [12,17]. In this common situation in daily practice, apprehension about underfeeding critically ill patients progressively increases daily in the intensive care unit. Therefore, the timing of the initiation of PN alone or combined with hypocaloric EN is a major concern [33].

In this context, two important guidelines have put forth conflicting recommendations. The 2009 European Society for Clinical Metabolism and Nutrition guidelines recommend that all patients who are not expected to be on normal nutrition within 2-3 d should receive PN within 24 to 48 h if EN is contraindicated [4]. Supporting this stance, a metaanalysis showed that the early initiation of PN increased the survival of critically ill patients compared with patients who received EN late (OR, 0.29; 95% CI, 0.12-0.70; $P = 0.006$) [11]. In contrast, however, the 2009 American Society for Parenteral and Enteral Nutrition guidelines state that if early EN is not feasible or is unavailable during the first 7 d following admission to the intensive care unit, then no other specialized nutrition therapy (eg, PN) should be provided [2,12].

The previous nutritional status of the patient before the onset of the critical illness may influence the choice. A metaanalysis showed that the provision of standard therapy (ie, no specialized nutrition) compared with the early initiation of PN in non-malnourished patients reduced infectious complications (relative risk, 0.77; 95% CI, 0.65-0.91; $P < 0.05$) [34]. Conversely, in patients with severe malnutrition or who suffer prolonged illness, the provision of PN is preferred over the maintenance of standard therapy [35,36]. PN formulation with the addition of immune nutrients, such as glutamine [4,37] and ω-3 fatty acids [35], may improve clinical outcomes in critically ill patients as seen with EN.

The role of supplemental PN in critically ill patients is still under debate. The early combination of early EN with early PN was recently reported in a multicenter observational study that involved 21 countries and more than 2900 patients. Interestingly, the most common reasons for the commencement of PN according to the study were "no reason" (almost 40% of cases), followed by prolonged ileus, and "not tolerating EN." These data suggest that the anxiety of providing no nutrients impacts the prescription of supplemental PN. Sixty-day mortality was significantly lower ($P = 0.02$) in the early enteral feeding group (27.8%) compared with the groups with either an early (34.6%) or a late (35.3%) initiation of supplemental PN. In patients who

presented gastrointestinal intolerance to EN, no proven clinical benefit of either early or late combined PN was found. Conversely, the use of early or late PN was associated with a longer hospital stay and lower rate of "discharged alive" at 60 d [38].

Recently, a pivotal multicenter randomized trial that included a large patient sample investigated whether the early or late commencement of PN provides better clinical outcomes in critically ill patients. The authors randomized 4640 patients who were nutritionally at risk and had insufficient EN into groups that received parenteral nutrition that was initiated either early (ie, within 48 h after admission to an intensive care unit; $n = 2312$) or late (ie, on day 8 of admission; $n = 2328$). The results showed that the late-initiation group had a greater chance of being discharged alive from the intensive care unit (hazard ratio, 1.06; 95% CI, 1.00-1.13; $P = 0.04$) and the hospital (hazard ratio, 1.06; 95% CI, 1.00-1.13; $P = 0.04$). Furthermore, the late-initiation group had fewer infectious complications (22.8% versus 26.2%, $P = 0.008$) and stayed fewer days on mechanical ventilation. Finally, costs were reduced significantly in the late-initiation group. The authors concluded that the provision of early PN to supplement insufficient EN during the first week after admission to the intensive care unit in severely ill patients at risk for malnutrition appears to be inferior to the strategy of withholding PN until day 8, while providing vitamins, trace elements, and minerals [39]. The authors used the autophagy theory to explain their results. Autophagy is the only known mechanism that eukaryotic cells possess by which they dispose of intracellular organelles and protein aggregates that are too large to be degraded by the proteasome and is also used to degrade microorganisms that may invade the cell. In mammals, autophagy is induced by starvation and suppressed by nutrient abundance [40]. Insufficiency of the autophagy machinery is caused by chronic illness and aggravated by hyperglycemia [41]. There are however many criticisms for this study. The sample was not homogeneous; 60% was formed by elective patients who underwent cardiac surgery, and the median duration of intensive care unit stay was low (3-4 d). Moreover, the nutritional status of the patients was not considered for early or late commencement of therapy. Furthermore, the patients received intensive insulin therapy, which may have contributed to the increased mortality observed in the early-initiation group. However, this study will certainly impact the present discussion between American and European guidelines on the timing of the initiation of PN for critically ill patients.

Conclusion

The early provision of nutrients via the gut is still the first option for critically ill patients with either medical or surgical conditions. There is no scientific basis to postpone the delivery of food by the oral or enteral route after gastrointestinal anastomosis. However the early or late initiation of PN in critically ill patients, especially in elective non-malnourished surgical patients, is still under debate.

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