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Opinion paper

Protein-energy nutrition in the ICU is the power couple: A hypothesis forming analysis

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SUMMARY

Background & aims: We hypothesize that an optimal and simultaneous provision of energy and protein is favorable to clinical outcome of the critically ill patients.
Methods: We conducted a review of the literature, obtained via electronic databases and focused on the metabolic alterations during critical illness, the estimation of energy and protein requirements, as well as the impact of their administration.
Results: Critically ill patients undergo severe metabolic stress during which time a great amount of energy and protein is utilized in a variety of reactions essential for survival. Energy provision for critically ill patients has drawn attention given its association with morbidity, survival and long-term recovery, but protein provision is not sufficiently taken into account as a critical component of nutrition support that influences clinical outcome. Measurement of energy expenditure is done by indirect calorimetry, but protein status cannot be measured with a bedside technology at present.
Conclusions: Recent studies suggest the importance of optimal and combined provision of energy and protein to optimize clinical outcome. Clinical randomized controlled studies measuring energy and protein targets should confirm this hypothesis and therefore establish energy and protein as a power couple.

1. Introduction

Medical innovations during the last 2 decades have allowed patients benefiting from intensive care to survive injuries and critical illness previously felt unrecoverable. These improved outcomes have brought the intensive care unit (ICU) community to a point where a patient's nutritional state has become a limiting factor in their short and long-term clinical outcome. Energy provision for patients in the ICU has drawn attention given its importance for morbidity, survival and recovery [1]. Determining the optimal energy target is required for the accurate prescription of nutrition support, but the best approach remains open to debate [2,3].

Recommendations of the international academic societies for partial or full coverage of energy requirements, as well as the timing of administration, are inconstant and leave ICU physicians without clear guidelines on which to base their practice. For practical reasons, the total provision of energy is generally calculated on the basis of body weight. Protein need is often not calculated separately and thus not taken into account. Thus, protein provision is dependent on the protein content of the nutrition mixture. Although there is a pragmatic rationale for such an approach, proteins *per se* is likely to influence the patient outcome, both for

Abbreviations: ICU, intensive care unit; EN, enteral nutrition; PN, parenteral nutrition; EE, energy expenditure.

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short (immunity) and long (physical function) term outcome [4]. Indeed, some of the latest nutrition trials have reported negative results, but the reported level of protein intake was either far below the recommendations (e.g. EPaNIC) [5] or unbalanced (e.g. REDOX) [6]. Up until now, we have not paid sufficient attention to the possible impact of the simultaneous, adequate administration of energy and protein [4,7,8].

There is a critical need to consider the accurate prescription of *both* protein and calories together with the purpose to improve nutrition of critically ill patients and to reduce mortality and morbidity. This new “Power Couple” is potentially the basis for a new paradigm of critical care nutrition.

We therefore highlight the significant alterations of energy and protein metabolism observed during the critical illness on the basis of published evidence. We also focus on the potential importance of adequate provision of energy and protein to make clear the urgent requirements to achieve and evaluate the importance of the power couple. Although important, topics such as antioxidants, immune-modulating lipids (e.g. study by van Zanten et al. [9]), and the still evolving issues of autophagy will not be discussed in details.

2. Protein-energy nutrition, the “power couple”

The main role of energy provision for critically ill patients can be understood as fundamental for life support, and protein provision as fundamental for maintaining structure and function. The practical question from a clinician would be, “which is more important and useful as target of nutrition provision?” The answer would be: “both”. Targets of provision for energy and protein are interdependent. Providing energy with adequate amount of protein as its component is the pragmatic approach. The key factor for success may be the tailor-made provision for individual patient, in a way to maximize their utilizations and also to look for their synergistic effects.

Although the hypothesis seems promising, it can be clinically challenging to achieve goals for energy and protein at the same time. Moreover, the convenience of energy as a target of nutrition provision has drawn the clinician's focus toward targeted energy provision, and at the same time led significant neglect of providing adequate protein provision. The abundance of commercially available enteral formulas with relatively low protein content for enteral nutrition (EN) and parenteral nutrition (PN) has also contributed significantly to the disregard of reaching adequate protein targets [10]. Indeed, the growing trend towards EN for critically ill patients has also complicated the issue. Intolerance to EN and frequent interruptions due to clinical interventions prevent adequate energy provision [11] leading to insufficient provision of the protein, while the benefits of protein supplementation by EN and PN need further study. In a study by Alberda et al., ICU patients worldwide received on average less than 60% of prescribed energy, and 56% of prescribed protein [12]. This trend is usually more pronounced in patients with greater severity of illness [10].

Experts are now calling for more attention to protein when feeding the critically ill patient. Clinical trials of adequate power are needed to examine the effect of nutrition delivery with enhanced protein content (1.2–2.0 g/kg per day) on patient outcome, as well as to determine the optimal dose for critically ill patients [13]. Kreymann et al. made an interesting statement, that determining nutrition requirements in the form of energy to nitrogen (Energy/Nitrogen) ratio when planning nutrition provision may be helpful in optimizing this balance (Fig. 1) [14]. The concept of the Energy/Nitrogen ratio is based on the principle that amino acid oxidation, either of endogenous or of exogenous origins, can be prevented by energy supply from endogenous or exogenous sources. Since there are large variations in energy expenditure, protein loss, and Energy/Nitrogen ratios across various patient populations, defining the nutrition requirements in terms of Energy/Nitrogen ratios may be a good solution to achieving the optimal balance.

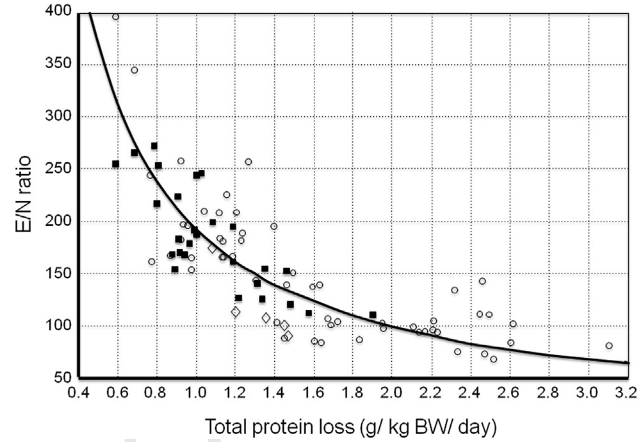

Fig. 1. The relationship between total protein loss and energy expenditure [14]: the energy expenditure was divided by total protein loss to calculate Energy/Nitrogen ratio (E/N ratio). Open circles refer to cohorts of fed patients, filled squares refer to cohorts of fasting patients, and open diamonds refer to cohorts of an undefined state. The E/N ratio decreases as total protein loss increases, indicating that protein loss exceeds energy expenditure when the patient is more catabolic. However, it should also be noted that in this analysis, increased N loss may also be a result of an increase in unutilized N intake.
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It should also be noted that energy expenditure and protein losses are not always equal to the requirements, since there is an optimal amount of energy and protein that can be used by the patient. Elwyn et al. clearly illustrated the relationship between energy and protein provision on nitrogen balance (Fig. 2) [15]. According to their observation, positive nitrogen balance can be achieved either by increasing the provision of energy or protein. Interestingly, a rapid rate of nitrogen accumulation is observed when the caloric intake is increased while the protein intake is unchanged, up to the point where caloric intake reaches 50–60% of the total energy expenditure. As the provision of energy and protein reaches the limit of the utilization by the patient, the rise in the nitrogen balance is attenuated. Although designed to test the

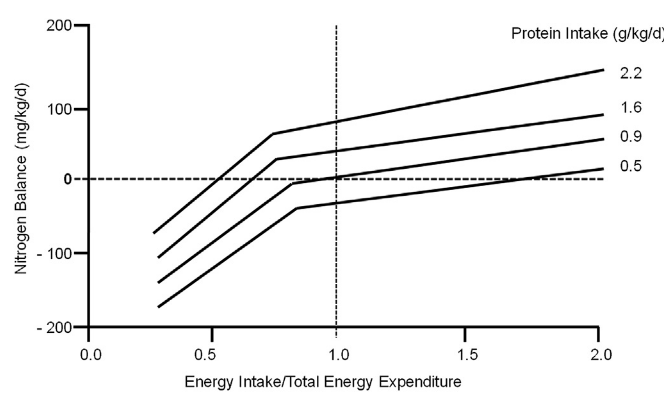

Fig. 2. The influence of energy and protein intake on nitrogen balance [15]: from data generated in 1979 [15], Elwyn et al. had conceptualized that nitrogen balance is a result of various energy and protein provision. Rapid rate of nitrogen accretion is observed with increasing energy intake at a fixed protein intake, until the energy intake approaches to 50–60% of the total energy expenditure, from where the rise in the nitrogen balance is blunted. Thus, similar nitrogen balances can be achieved with either a high protein low-energy, or low-protein high-energy nutrition support regimen.
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