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Original article

How much protein and energy are needed to equilibrate nitrogen and energy balances in ventilated critically ill children?

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SUMMARY

Background & aims: Protein and energy requirements in critically ill children are currently based on insufficient data. Moreover, longitudinal measurements of both total urinary nitrogen (TUN) and resting energy expenditure (REE) are lacking. The aim of this study was to investigate how much protein and energy are needed to equilibrate nitrogen and energy balances in ventilated critically ill children on the basis of daily measurements of TUN, REE and protein and energy intakes. Comparisons were made with the guidelines of the American Society for Parenteral and Enteral Nutrition and the Dietary Reference Intakes.
Methods: Children with an expected duration of mechanical ventilation $\geq$72 h were prospectively recruited. TUN was measured by chemiluminescence, and REE was measured by indirect calorimetry. Generalised linear models for longitudinal data were used to study the relation between protein intake and nitrogen balance and to calculate the minimum intake of protein needed to achieve nitrogen equilibrium. A similar approach was used for energy. Results were compared to the recommended values.
Results: Based on 402 measurements performed in 74 children (median age: 21 months), the mean TUN was high at 0.20 (95% CI: 0.20, 0.22) g/kg/d and the REE was 55 (95% CI: 54, 57) kcal/kg/d. Nitrogen and energy balances were achieved with 1.5 (95% CI: 1.4, 1.6) g/kg/d of protein and 58 (95% CI: 53, 63) kcal/kg/d for the entire group, but there were differences among children of different ages. Children required more protein and less energy than the Dietary Reference Intakes.
Conclusions: In critically ill children, TUN was elevated and REE was reduced during the entire period of mechanical ventilation. Minimum intakes of 1.5 g/kg/d of protein and 58 kcal/kg/d can equilibrate nitrogen and energy balances in children up to 4 years old. Older children require more protein.

1. Introduction

In critically ill children, optimal nutritional support, especially adequate amounts of energy and protein are associated with decreased mortality and morbidity [1]. It can be difficult to estimate energy and protein requirements in healthy children because these requirements vary with age, growth velocity, modifications in body composition and physical activity [2]. The task is even more complex in patients in paediatric intensive care units (PICUs) where nutritional needs are influenced by various factors such as the patient's disease, treatments, fever and reduced physical activity.

Current nutritional recommendations for critically ill children are based on little evidence, as highlighted by the Cochrane

Abbreviations: A.S.P.E.N., American Society for Parenteral and Enteral Nutrition; CRP, C-reactive protein; DRI, Dietary Reference Intakes; REE, resting energy expenditure; PICU, paediatric intensive care unit; PRISM, Pediatric Risk of Mortality; TUN, total urinary nitrogen; WHO, World Health Organization.

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Collaboration [3]. The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) provides recommendations on protein intake while acknowledging that these recommendations are based on insufficient data [4]. A recent systematic review on protein balance concluded that longitudinal studies including measurements of both protein and energy balances are needed in critically ill children [5].

The paucity of studies can be explained by the difficulty in measuring nitrogen and energy balances as these measurements require technical and financial resources. According to the World Health Organization (WHO) [6], the major method currently available to determine protein needs is to measure nitrogen balance, which requires a precise quantification of both nitrogen intake and nitrogen losses. Total urinary nitrogen (TUN) must be measured [6] and not estimated from the urinary urea content, which is highly variable in critically ill patients [7]. Similarly, determining the energy balance demands the precise measurement of resting energy expenditure (REE) by indirect calorimetry [4].

Although researchers should measure TUN and REE in critically ill children, clinicians are often constrained to estimating protein and energy needs because of limited resources. In a European survey conducted in 111 PICUs, measurements of REE were only performed in 19 units. As an alternative, energy needs were estimated from weights and ages, according to methods developed for healthy children [8].

The primary aim of this study was to assess how much protein and energy are needed to equilibrate nitrogen and energy balances in ventilated critically ill children on the basis of daily measurements of TUN and REE. The secondary aim was to compare these results with the recommended values of the A.S.P.E.N. guidelines [4] and the Dietary Reference Intakes (DRIs) [2].

2. Material and methods

2.1. Subjects

Children (from birth to age 16 years) who were admitted from January 2008 to April 2010 to the PICU of the University Hospital of Lausanne, Switzerland, with an expected duration of mechanical ventilation of at least 72 h were considered eligible for this study. Exclusion criteria were as follows: a fraction of inspired oxygen (FiO_2) >60%, an air leak around the endotracheal tube >10%, chylothorax, chronic or acute renal disease, severe loss of inflammatory fluid through a pleural or peritoneal drains, exudative enteropathy and therapeutic hypothermia. Out of 448 admissions, 78 children were eligible and three parents refused participation in the study. One patient was excluded after loss of his urine collection. Patients were prospectively studied until extubation or for a maximum of 15 days. The study was approved by the ethics committee of the University Hospital of Lausanne. Written informed consent was obtained from the parents of each child before measurements were made.

Demographic data, diagnoses and Pediatric Risk of Mortality (PRISM) II scores [9] were obtained at admission. The C-reactive protein (CRP) level was recorded each day as a marker of inflammation. Body temperature was obtained during indirect calorimetry measurements. Nutritional status was classified by using the z-scores of either the WHO [10] for children younger than 5 years old or those of the National Center for Health Statistics (NCHS, 2000) for older children. A deviation of more than −2 standard deviations for weight-for-height was considered acute malnutrition, and a deviation of more than −2 standard deviations for height-for-age was considered chronic malnutrition. Weight and height were measured at PICU admission and discharge. For patients admitted as emergency cases, parents provided the last weight value, and height was measured at the patient's bedside.

The research staff did not intervene in the daily management of nutrition support. Energy and protein goals were determined by using the Schofield equation with weight and height [11] and the A.S.P.E.N recommendations [4]. Our protocol uses a progressive increase of nutritional intakes to achieve these goals by at least day 5.

2.2. Measurements of TUN and REE

In all patients, urine was collected through urinary catheters from midday to midday and frozen at −80 °C until the day of measurement. TUN was measured by the chemiluminescence technique with an Antek 7000 analyser (Houston, TX, USA) [12].

REE was measured by indirect calorimetry as soon as possible after PICU admission. Measurements were performed daily until extubation, at the same time each day. The calorimeter (Deltatrac II, Datex-Ohmeda, Helsinki, Finland) was calibrated monthly by the alcohol-burn technique with a burning kit specifically designed for paediatric use, a precise syringe (Model TLL 1010, Hamilton, Switzerland) and a syringe pump (Model 789100, KD Scientific, USA). Before each measurement, the calorimeter was warmed up for 1 h and then calibrated with a reference gas mixture of 95% oxygen and 5% carbon dioxide. In agreement with the bedside nurse, measurements were performed during a period without stressful procedures. In some cases (change in FiO_2, physiotherapy, agitation or suction of the endotracheal tube), the measurement was stopped and restarted at least 30 min after the event. At the end of the measurement, data for each minute were exported with the CaloDatex software (Datex-Ohmeda, Helsinki, Finland) into Excel (Microsoft Office, USA) and analysed in detail.

REE was calculated with the modified Weir's equation [13], using measured values of oxygen consumption (VO_2) and carbon dioxide production (VCO_2). The first 10 min were discarded for all patients to exclude artefacts. A steady state was defined by a coefficient of variation of VCO_2 ≤10% for at least 25 consecutive minutes [14]. For five measurements, steady state was not achieved and these REE and TUN measurements were excluded from the analysis. During the study period, 51 REE and TUN measurements were missed on day one and 16 on day two, mainly because informed consent had not yet been acquired or because the investigators were unavailable.

2.3. Calculation of nitrogen and energy balances

Nitrogen balance was calculated daily as: nitrogen intake minus total nitrogen losses. Nitrogen intake was obtained from total enteral and parenteral feeding from data in a clinical data management system (MetaVision by iMDsoft, Tel Aviv, Israel). Total nitrogen losses included TUN and faecal/miscellaneous (skin, tegumental) losses estimated according to the WHO recommendations [6] as follows: total nitrogen losses (g/d) = TUN (g/d) + faecal losses (0.021 g/d * body weight) + miscellaneous losses (0.001 g/d * body weight). To convert the nitrogen into protein, the usual nitrogen-to-protein conversion factor of 6.25 was used.

Energy balance was calculated daily as: energy intake minus energy requirements. Energy intake was obtained from total enteral and parenteral feeding, including intravenous glucose solutions for medication. Propofol was not used as a continuous infusion for sedation. Energy requirements were considered at REE

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