Macronutrient and Micronutrient Intake in Lung Disease Children

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Contributor: Nicole Knebusch , Marwa Mansour , Stephanie Vazquez , Jorge A. Coss-Bu

The nutritional and respiratory statuses of critically ill patients are interrelated in such a way that they are interdependent while maintaining a balance. Malnutrition is common in pediatric intensive care unit (PICU) patients and is frequently associated with respiratory failure.

children critically ill nutrition support lung disease metabolism

1. Introduction

The nutritional and respiratory statuses of critically ill patients are interrelated in such a way that they are interdependent while maintaining a balance. Malnutrition is common in pediatric intensive care unit (PICU) patients and is frequently associated with respiratory failure [1][2][3][4][5][6][7][8][9][10][11]. Calorie and protein restriction lead to abnormalities in ventilatory control [12], respiratory muscle function [13], pulmonary structural changes [14], and impaired pulmonary defense mechanisms [15]. In short periods of caloric–protein restriction, metabolic functions of the lung are altered, while extended periods contribute to chronic lung disease, which in turn worsens an already-dismal nutritional condition. Therefore, assessing the nutritional status of patients upon admission to the PICU is imperative, as specified in the latest nutritional support guidelines for critically ill pediatric patients [11]. The nutritional assessment identifies patients at risk, including those with sepsis, acute respiratory failure, and acute kidney injury [5][6][7][16][17].

Various components of the respiratory system are affected by nutrition support, including central stimulation, respiratory muscle function, lung parenchyma, and changes in metabolic demand induced by the consumption of substrates (protein, carbohydrates, and fat). Alterations in respiratory muscle function and structure lead to changes in energy consumption and metabolism [18], so in critically ill patients, the relationship between nutritional status and respiratory failure is of paramount importance to the patient's health.

It has been well established that micronutrients play an integral and mutually synergistic role in maintaining the structural and functional integrity of both the innate and adaptive immune systems [19][20]. Vitamins A and D are involved in epithelial maturation and production of antimicrobial proteins, respectively. These functions support the gut and lung's defense mechanisms against infections [19][20][21][22], suggesting that vitamin D deficiency may be associated with a higher risk of respiratory infections [23]. Vitamins C and E support the innate immune system by protecting the epithelial barriers via the induction of collagen synthesis, deactivation of free radicals, and promotion of fibroblast and keratinocyte proliferation and maturation [24][25].

2. Effects of Malnutrition on the Diaphragm and Respiratory Function

The effects of undernutrition and malnutrition on the structure and function of the respiratory muscles including the diaphragm were published in adults admitted to the intensive care unit receiving mechanical ventilation [26][27][28]. Studies in critically ill adults have described a condition called ventilator-induced diaphragmatic dysfunction with loss of diaphragmatic force-generating capacity and muscle fiber atrophy, myofibril necrosis, and disorganization [29][30][31]. Studies in critically ill children admitted to the pediatric intensive care unit receiving ventilatory support have reported similar findings as the adults' studies, with diaphragm atrophy and loss of contractility [32][33][34][35][36][37][38].

Malnutrition and inadequate nutrition intake in critically ill children during admission to the hospital are associated with worse clinical outcomes [11][16][39]. Studies in animals exposed to undernutrition have shown atrophy of the diaphragm and intercostals and reduced amount of elastic and collagen fibers in the alveolar septa [40][41][42]. Ultrasonography has been reported as a useful tool in the evaluation of the structure and function of the diaphragm and other skeletal muscles in critically ill children [43][44][45][46][47][48] A report by Koskelo, EK et al. used ultrasonography to measure muscles in the arms and thighs of 16 children with malignancies; the authors concluded that the ultrasound method combined with anthropometry was useful in the assessment of the nutritional status of children [45]. Two reports concluded that the use of ultrasonography in children to evaluate skeletal muscle thickness was not reliable and more studies were needed before muscle ultrasound is routinely used in critically ill children [44][46]. A recent study by Güngör S [49], compared the diaphragm thickness (DT) in children with primary malnutrition and a healthy control group; the authors found that the right and left DT were thinner in the malnourished group vs. the control group and there was a significant weak positive correlation between weight and height z score and right and left DT; r = 0.297, $p < 0.001$; r = 0.301, $p < 0.001$, respectively.

Inadequate nutritional status, increased energy expenditure, airway infection and inflammation, and progression of lung disease are the main characteristics of cystic fibrosis (CF) with malnutrition and chronic lung disease being inextricably interconnected [50][51][52][53][54][55]. An analysis of the Cystic Fibrosis Foundation National CF Patient Registry reported longitudinal relationships between lung function and growth in 968 children over a period of 4 years; the authors concluded that growth and nutritional status are associated with changes in the percent of predicted forced expiratory volume in 1 s (FEV 1%) and that nutritional intervention may slow the decline in lung function in this population [56] A study by Konstan, MW et al. [57] followed a total of 931 children from the ages of 3 to 6 years; the results showed that weight-for-age, height-for-age, and % ideal body weight at 3 years of age were poorly associated with lung disease, but were significantly associated with pulmonary function (forced vital capacity and FEV 1%) at the age of 6 years. The authors concluded that early aggressive intervention aimed at growth and nutrition may affect pulmonary function. Another study by Hart N et al. [58] evaluated diaphragm strength by measuring twitch transdiaphragmatic pressure (Tw Pdi) in 20 patients with CF aged 15.1 ± 2.8 years (SD); the results showed a positive and significant correlation between Tw Pdi and fat-free mass, arm muscle circumference, body mass index, and FEV 1%. These findings indicated that diaphragm strength is preserved in young patients with CF. A study by Hauschild DB et al. [59], evaluated prospectively the association between nutritional status and lung function (FEV 1%) in 38 children (aged 1–15 years, median age of 3.8 years) with CF over a period of 36 months; the results showed that children with nutritional failure at baseline (weight for length and or BMI < 10th) had a relative risk of 5.00 (95% C.I. 1.49–16.76) to have impaired lung function after 36 months. These results indicated that nutritional status was associated with impaired lung function.

The early years in infancy represent a critical period for the development of respiratory diseases later in life [60], and children with malnutrition are more susceptible to repeated and serious episodes of respiratory diseases [61]. Published evidence suggests that children born prematurely have an increased risk of chronic obstructive respiratory diseases in adulthood [62]. Two studies from developing countries reported the association of nutritional status with wheezing and lung function; Hawlader MDH et al. [63], studied 912 children (average age of 4.5 years) in rural Bangladesh and reported that wheezing was significantly associated with stunting and underweight. Ferdous F et al. [64] measured lung function (FEV 1%) in 517 children who had been followed since birth until the age of 9 years; the study found that children who were stunted had lower FEV 1% values compared to children with normal stature. Three large population-based studies evaluated the associations of early childhood growth patterns with lung function and asthma [65][66][67]. The study by den Dekker HT et al. [66] evaluated 24,938 children (age range, 3.9–19.1 years); the results showed that children born with a younger gestational age and children born with a smaller size for gestational age had lower FEV 1% values and had an increased risk of childhood asthma, and greater infant weight gain was associated with higher FEV 1% and risk of asthma. The report by Casas M et al. [65] evaluated 4435 children and performed spirometry at the age of 10 years; the results showed that greater peak weight velocity and body mass index at adiposity peak were associated with lower airway patency in relation to lung volume. A recent study by Voraphani N et al. [67], analyzed data from 652 participants who had at least one set of spirometry data (obtained at ages 22, 26, 32, and 36 years); results showed that maternal nutritional problems during pregnancy, being born small for gestational age, and being underweight in childhood were independent predictors of spirometric restriction in adult life.

3. Caloric and Protein Needs of the Patient with Pulmonary Disease

Based on the nutritional support guidelines of ASPEN (American Society for Parenteral and Enteral Nutrition) (American Society for Parenteral and Enteral Nutrition) and SCCM (Society of Critical Care Medicine), indirect calorimetry can be used to determine the energy requirements of pediatric patients with acute respiratory failure [11]. When indirect calorimetry cannot be used, the use of formulas to estimate basal metabolism is recommended to determine the caloric requirement for each patient [68]. In pediatric patients, the Schofield formula should be used. In addition, it is important to emphasize the inappropriate use of correction factors during the acute phase of the disease as well as the possibility of excessive caloric intake [69][70][71][72]. Following the acute phase of the disease, the caloric intake should be estimated based on the child's nutritional status and age. Infants and young children will need more calories to maintain adequate growth and development.

During the acute phase, protein intake is essential due to the increased degradation of proteins [1][2][70][73][74][75][76][77][78]. Age plays a crucial factor since infants and young children require a higher protein intake per kilogram of body weight. According to ASPEN/SCCM, a minimum protein intake of 1.5 g/kg/day is recommended, and this amount should be adjusted based on the levels of biomarkers, such as prealbumin and *C*-reactive protein [1][11].

The goals of nutritional support in the patient with lung disease include (1) adequate caloric intake, (2) adequate protein intake to prevent muscle loss, (3) correction of the cause of respiratory failure, (4) avoidance of excess carbon dioxide production, and (5) reversal of the nutritional-related sequelae of lung disease, which includes optimization of exercise tolerance and normalization of growth, which are particularly relevant in infants and young children [79].

4. Use of Indirect Calorimetry for Optimization of Nutritional Support

Nutrient administration has effects at the level of the respiratory system through physiological and pharmacological processes. An increase in dietary carbohydrate intake increases ventilatory demand secondary to an increase in carbon dioxide production (VCO_2) [80][81][82]. Lipids can have an impact on the vascular tone and inflammatory response of the pulmonary vascular system by serving as precursors of eicosanoid synthesis [83]. Amino acids can increase oxygen consumption (VO_2) and stimulate ventilation through modifications of the respiratory drive [84].

Indirect calorimetry (IC), which uses the gas exchange method, determines the caloric equivalent of VO_2 and VCO_2. For the measurement of energy expenditure in hospitalized patients, this method is considered the gold standard [2][3][73][85][86][87][88][89][90]. IC allows for the calculation of the relative oxidation of the different substrates (carbohydrate, protein, and fat) by obtaining the value of total nitrogen in urine and the use of the respiratory quotient (RQ). Depending on the type of oxidation taking place, the RQ value can range from 0.71 for fatty acid oxidation to 1.0 for carbohydrate oxidation. A value greater than 1.0 indicates a process of lipogenesis, while a value of 0.81 indicates protein oxidation.

Several studies have reported the importance of indirect calorimetry and RQ in caloric adjustment and diet composition in relation to the amount of carbohydrate and fat [2][91][92][93][94][95][96]. The results suggest that the use of IC is necessary for individual adjustment of nutritional support of critically ill patients, particularly those suffering from pulmonary diseases. An excess of carbohydrates will increase breathing effort due to increased carbon dioxide production, resulting in difficulty weaning patients off ventilators.

There have been mixed results when RQ has been used as an indicator of excessive or insufficient caloric intake in critically ill pediatric patients [91][92][93][94][96]. According to Mehta, NM et al. [96], RQ results were obtained for 14 pediatric patients admitted to the PICU. The RQ in hypermetabolic patients [n = 7, 50 ± 64 (SD) kg] was 0.85 ± 0.03 with a caloric intake of 1464 ± 1008 kcal/day, while hypometabolic patients (n = 7, 45 ± 59 kg), had an RQ value of 0.94 ± 0.06 with a caloric intake of 935 ± 559 kcal/day. The authors highlighted the importance of using IC for individualized guidance on nutritional support. Three studies reported sensitivity and specificity values of RQ in pediatric patients as an indicator of excess or lack of caloric intake. The study by Hulst, JM et al. [92] of 95 patients admitted to PICU showed sensitivity and specificity for an RQ value < 0.85 (lack of caloric intake) of 63% and 89%, respectively, while sensitivity and specificity for an RQ value > 1.0 (excess caloric intake) were 21% and 97%, respectively. The report by Dokken M. et al. [91] of 30 mechanically ventilated patients admitted to PICU, reported for an RQ value <0.85 a sensitivity and specificity of 27% and 87%, respectively, and for RQ value > 1.0 a sensitivity and specificity of 21% and 98%, respectively. Liusuwan RA et al. [94], in 74 pediatric patients with burns of >20% body surface area reported: for an RQ value < 0.85, a sensitivity and specificity of 40% and 77%, respectively; and for an RQ value > 1.0 a sensitivity and specificity of 23% and 85%, respectively. The report by Kerklaan D et al. [93] of 78 mechanically ventilated pediatric patients concluded that the identification of patients with an excess or lack of caloric intake using IC and RQ values depended on the definition used to categorize the patients. Thus, it can be concluded that the RQ value identified as an excess or inadequate caloric intake in critically ill pediatric patients has low sensitivity and adequate specificity.

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