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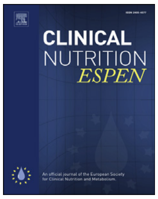

Review

Nutritional support of critically ill adults and children with acute respiratory distress syndrome: A clinical review

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SUMMARY

Acute Respiratory Distress Syndrome (ARDS) continues to be associated with significant morbidity and mortality. Optimization of nutrition remains a significant challenge in these patients. The role of nutrition in supporting convalescence and modulating the disease process has attracted much research attention. While there are similarities in ARDS phenotype between children and adults, there are also significant differences in causation, metabolic responses and outcomes. This review aims to critically evaluate the available evidence for various nutritional practices in managing children and adults with ARDS, and to summarize and compare the recommendations by expert bodies.

There is conflicting evidence regarding the target caloric intake in ARDS. The use of predictive equations for the estimation of resting energy expenditure in ARDS patients remains inadequate. The gold standard of indirect calorimetry is costly and labor intensive, and may not be as accurate in intubated patients with high oxygen requirements. Whilst overfeeding should be avoided, early enteral feeding should be encouraged. There is no evidence of benefit in early commencement of parenteral nutrition in children and adults with ARDS.

Further studies are needed to inform nutritional practice in patients with ARDS, particularly in children, where there remains a paucity of clinical studies.

1. Introduction

Originally described by Ashbaugh et al. in 1967, acute respiratory distress syndrome (ARDS) continues to be a significant healthcare burden in critically ill patients [1,2]. Despite interventions such as low tidal volume ventilation and improved supportive management strategies, mortality remains high from the condition [3].

Malnutrition is prevalent in both critically ill adults [4] and children [5]. Poor nutrition is associated with worse respiratory muscle function [6], increased susceptibility to infections [7] and mortality [8]. Consequently, there has been much interest in investigating whether optimizing nutrition in ARDS might lead to improvement in clinical outcomes.

In this review, we critically evaluate the available evidence for caloric targets, protein provision, as well as enteral and parenteral nutrition (PN) in patients with ARDS. In addition, we consider the physiological differences between children and adults, and relate this to why nutritional strategies should be tailored to different patient groups. Where available, we therefore also compare the current consensus recommendations by specialist nutrition societies. The topics of immunonutrition and specialized formulas/nutrition additives are beyond the scope of this review and we refer the reader to other excellent reviews in these topics [9–14].

2. Methods

We searched for publications in PubMed using the following MeSH headings: “nutritional status” OR “nutrition” OR “nutritional sciences” AND “acute respiratory distress syndrome” OR “acute

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lung injury". We did not limit our search by publication type, but limited our search to English publications and human studies. We hand-searched review articles on ARDS to include additional publications not captured in the initial search. The most recent recommendations by the following specialist groups were compared: American Society for Parenteral and Enteral Nutrition (ASPEN, 2009, 2016), Society of Critical Care Medicine (SCCM, 2016) the European Society for Clinical Nutrition and Metabolism (ESPEN, 2006, 2009); European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN, 2005); the Pediatric Acute Lung Injury Consensus Conference (PALICC, 2015); and the Canadian Critical Care Practice Guidelines (CCPGs, 2015).

2.1. How the acute metabolic response and pathophysiology of ARDS differs between children and adults

The pathophysiology of ARDS, though not completely clear, is associated with the presence of pro-inflammatory cytokines and apoptosis activators, which are thought to play a role in alveolar epithelial damage [15,16]. The diagnosis, progression and outcomes of ARDS in adults are different from children, suggesting differences in pathophysiology and response to the illness [17].

Indeed, adults and children appear to differ in their metabolic response to critical illness. During acute critical illness, adults have been shown to undergo a brief hypometabolic "ebb" phase, followed by a hypermetabolic "flow" phase after fluid resuscitation [18]. The "flow" phase, which typically occurs around day 2 of injury, is characterized by the production of inflammatory cytokines, and a rise in body temperature and respiratory rate [19]. A more detailed review of this metabolic response has been published elsewhere [20]. Briefly, rapid catabolism occurs and energy expenditure increases proportionally to the degree of inflammation [21], although this may be altered by the use of interventions such as cooling [22,23]. Protein catabolism appears to be significant in critical illness in adults, resulting in acute skeletal muscle wasting [24]. It is hypothesized that rapid breakdown of skeletal muscle occurs to provide substrates for production of inflammatory cytokines and gluconeogenesis [25]. Resistance to anabolic hormones such as insulin also occurs, and together with increased gluconeogenesis, often results in stress hyperglycemia [20]. In adults with ARDS, muscle catabolism leads to muscle wasting that eventually results in prolonged functional impairment in survivors [26].

Children, on the other hand, appear to have a different metabolic response during critical illness. Healthy children, unlike adults, have a significant energy and protein requirement for growth and tissue deposition. During critical illness, it is hypothesized that energy for growth is redirected for tissue repair and sustaining organ function [27]. As a result, children who are sedated and supported on mechanical ventilation (MV) do not necessarily demonstrate increased energy requirements [28]. However, like in adults, protein catabolism has shown to be elevated in critically ill compared to healthy children. Whole body protein turnover studies using isotope tracers demonstrated increased protein turnover and a net negative balance in critically ill children compared to healthy controls [29]. Notably, these studies were not specific to children with ARDS, and the catabolic effects of ARDS on functional outcomes have not yet been well described in children. Nevertheless, the presence of different metabolic states indicates the need for nutrition therapy to be tailored to each phase. One difficulty, however, lies in the identification of which phase a patient is in, and when the transition between phases occurs.

2.2. Caloric intake and protein provision

Caloric and protein malnutrition is common in critically ill patients [4,5]. Inadequate energy intake has previously been shown to be associated with increased mortality [8,30], and respiratory muscle dysfunction [6], leading to prolonged dependence on MV and increased susceptibility to infection [7]. This association between malnutrition and increased morbidity [31] and risk-adjusted mortality [32] has also been observed in critically ill children. Nutritional management in critical care has therefore been traditionally centered on ensuring that patients are kept as nutritionally replete as possible. However, more recent studies have called these assumptions into question [33,34].

2.3. Adults

Energy requirements of patients in the intensive care unit (ICU) are traditionally estimated by standard equations. A review evaluating 7 predictive equations concluded that calculated requirements are seldom within 10% of measured energy expenditure, with no consensus as to which standard equation is most accurate [35]. A more accurate method of deriving the Resting Energy Expenditure (REE) is by indirect calorimetry (IC) [36]. This has potential utility in the ICU setting, where some patients confound traditional predictive equations by exhibiting hypometabolism [37]. IC is also particularly useful in patients at the extremes of body mass index (BMI), where predictive equations are increasingly inaccurate [37]. However, IC is costly, requires trained personnel, and is less accurate at high concentrations of inspired oxygen, thereby potentially limiting its use in the ARDS population [36]. Also, while it is the gold standard technique in eligible patients, IC as a technique, is not always accurate [38]. Finally, a practical limitation exists in that IC measurement is not currently widely available in many ICUs [39].

The inflammatory process in ARDS leads to increased protein catabolism and energy expenditure. Adults with ARDS are estimated to have an energy expenditure that is approximately 30% higher than REE [40]. A multi-center cluster randomized trial was conducted to evaluate the clinical effects of evidence-based feeding guidelines, implemented using Browman's Clinical Practice Guideline Development Cycle [41]. However, despite the intervention group achieving caloric goals more often (6.10 vs. 5.02 mean days fed per 10 fed patient-days; difference, 1.07 [95% CI, 0.12–2.22]; $p = 0.03$), there was no statistically significant difference in hospital discharge mortality, or hospital and ICU length of stay (LOS). Furthermore, studies investigating early supplementation of PN have been demonstrated to be associated with adverse clinical outcomes [33,34].

While evidence remains equivocal regarding the benefits of supplementing nutrition early in the disease course of critically ill adults, there are deleterious effects associated with overfeeding.

One of the earlier pieces of research into the interaction between nutrition and ARDS was in the area of carbon dioxide (CO_2) production [42]. This was based on the theory that a high carbohydrate intake might increase CO_2 production, thereby possibly adversely affecting weaning of MV. A subsequent study of 20 stable mechanically ventilated patients, who received PN comprising varying amounts of calories (60% carbohydrate at 1.0, 1.5 and 2.0 times the calculated REE) and proportions of carbohydrate (40%, 60% and 75% of total calorie intake) demonstrated that a higher proportion of calories and not carbohydrate was significantly associated with higher CO_2 production [43]. It may therefore be important to avoid overfeeding in ARDS patients to limit CO_2 production and its potential impact on duration of MV. Furthermore, overfeeding has also been shown to have adverse effects on liver function [44], glycemic control [45] and infection risk [46].

There is emerging evidence to suggest that some measure of caloric underfeeding may possibly confer benefit. In a prospective cohort study of adult medical ICU patients, underfeeding at

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