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Controversies in nutritional support for critically ill children

Johanna R. Askegard-Giesmann, MD[a,*], Brian D. Kenney, MD, MPH[b]

[a] Division of Pediatric Surgery, Riley Hospital for Children, Indiana University, 705 Riley Hospital Dr, Room 2500, Indianapolis, Indiana 46202
[b] Division of Pediatric Surgery, The Ohio State University, Nationwide Children's Hospital, Columbus, Ohio

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ABSTRACT

Nutritional support for critically ill infants and children is of paramount importance and can greatly affect the outcome of these patients. The energy requirement of children is unique to their size, gestational age, and physiologic stress, and the treatment algorithms developed in adult intensive care units cannot easily be applied to pediatric patients. This article reviews some of the ongoing controversial topics of fluid, electrolyte, and nutritional support for critically ill pediatric patients focusing on glycemic control and dysnatremia. The use of enteral and parenteral nutrition as well as parenteral nutritional-associated cholestasis will also be discussed.

Introduction

Nutritional support for critically ill infants and children is an important element of their care. Children have specific requirements for proper growth and neurodevelopment in addition to their maintenance fluid and energy needs. The stress of trauma and surgery can increase these nutritional needs, while adding to their complexity, especially when deciding on the optimal route of administration. Balancing the needs of the patient, with their physiologic and clinical status, is the basis for much controversy, as we attempt to discover the optimal nutritional and fluid administration in these challenging patients.

Energy requirements and physiologic stresses

Malnutrition has been associated with increased morbidity and mortality in critically ill children since 1985[1] and has more recently been associated with an increase in risk-adjusted mortality as well as PICU length of stay.[2] The percentage of patients admitted to the PICU with acute malnutrition, defined as 2 SD below the average weight-for-age, has been reported from 19–32%.[3,4] Malnutrition has also been associated with increased morbidity and mortality in critically ill children.[1] Critical illness also places variable energy demands on patients and attempts have been made to predict those energy needs with standard equations; however, rather inconsistently.[5,6] Providing the proper amount of nutritional support to critically ill children is of paramount importance to their survival and outcomes.

Calculating the correct caloric and energy needs in children can be challenging, and the dangers of inappropriate nutrition can be devastating (i.e., bone demineralization, rickets, cholestatic jaundice, poor wound healing, impaired lung function, and slow growth). Open wounds, such as the open abdomen and burn patients, have additional protein losses. Caloric needs are also altered by several factors such as surgical procedures, stress, hypothermia, infection, and trauma.[7,8] Similarly, intensive care interventions can also decrease energy needs, such as mechanical ventilation, paralysis, or sedation, and a temperature-controlled environment.[6] The Harris–Benedict equation has often been used to calculate the energy needs of children; however, these formulas were based on adult populations and are not easily or correctly applied to the pediatric population. Indirect calorimetry was first performed in children in the beginning of the 20th century by Fritz Talbot and still serves as an appropriate standard for calculating basal metabolic rates.[6] Several studies of critically ill children have shown a significant difference in measured vs. predicted values of energy needs and expenditures when standard equations were utilized.[9–11]

Mehta et al.,[7,12,13] as well as the ASPEN guidelines, recommend indirect calorimetry to estimate the energy needs of the patient, as well as obtaining their baseline nutritional status upon admission to the PICU. This may also help identify patients that may be at risk for refeeding syndrome. Despite these recommendations, few critical care units routinely perform these measurements and its impact on clinical outcomes still needs to be demonstrated.[7] Consequently, it remains an area of controversy regarding initiation and maintenance of nutrition in the ICU.

* Corresponding author.
E-mail address: jaskegar@iupui.edu (J.R. Askegard-Giesmann).

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Fluid management in critically ill pediatric patients—Hypotonic vs. isotonic fluids

Critically ill children are often in need of intravenous fluid resuscitation and vasopressor support. Pediatricians and critically ill trained physicians often differ from surgeons in their fluid administration tactics. Hyponatremia, defined as a sodium level less than 135 mEq/L, is relatively common, especially in critically ill patients, with an incidence reported from 19–50% of hospitalized patients.[14–17] Recent case reports of catastrophic results of hyponatremia causing neurologic morbidity as well as death[18–23] have increased awareness of this problem, and debate continues between the type of fluid to administer to patients, both in the critical care units as well as on the wards.

There are several factors thought to contribute to hyponatremia in the post-operative setting. Volume depletion, pain, nausea, and stress are thought to increase the non-osmotic stimulus for ADH release.[24] Isotonic fluids can assist in mitigating some of these factors, while helping to maintain normonatremia. Opponents argue that istotonic fluids may cause hypernatremia, as well as fluid overload and hypertension. While these side effects are seen in older adult patients whose cardiac and renal function may be impaired, they are rare in the pediatric population.

Several studies have demonstrated the relationship between the administration of hypotonic fluids and hyponatremia in a variety of patient populations.[14,25–27] Choong et al.[25] randomized 258 children after elective surgery to receive either hypotonic or isotonic maintenance IV fluids and reported a significant risk of hyponatremia in the hypotonic group (40.8% vs. 22.7%, RR $=$ 1.82, $p = 0.004$). Similarly, Rey et al.[26] randomly assigned children admitted to 3 PICUs to receive hypotonic vs. isotonic maintenance IV fluids and reported a 5.8-fold increased risk of hyponatremia in the hypotonic group. Caradang et al. retrospectively examined a cohort of normonatremic hospitalized children who had received either hypotonic or isotonic fluids. They found that hyponatremia was more likely to occur with administration of hypotonic fluids, but also found that hyponatremia developed in nearly 28% of patients who received isotonic fluids.[28] Surgical admissions and certain admitting diagnoses also appear to have a strong impact on developing hyponatremia. A recent meta-analysis of 10 randomized controlled trials demonstrated a significantly higher risk of both hyponatremia (Na $<$ 136) and severe hyponatremia (Na $<$ 130), when hypotonic fluids were administered.[29] While fluid volume and clinical volume status at admission may contribute to dysnatremia, there is increasing evidence supporting the use of isotonic fluids for post-surgical and trauma patients.

Stress hyperglycemia and the use of insulin

Stress hyperglycemia is a relatively common occurrence in critically ill children. Through multiple mechanisms at the cellular level, the overall effect is increased blood glucose concentrations to provide an easily available fuel source for vital organs. While especially useful in the acute phase of illness when metabolic demand is higher, persistence of stress hyperglycemia may eventually become harmful.[30]

Several studies have demonstrated an association with hyperglycemia and mortality in critically ill children.[31–42] This association has been demonstrated in several different patient populations within the PICU, namely patients with severe burns, trauma including traumatic brain injury, septic shock, and post-cardiac surgery. While these studies have demonstrated strong associations between hyperglycemia and critical care outcomes, no direct causal relationship has been elucidated. Rather, hyperglycemia induced by physiologic stress appears to be a marker of severe illness, which can ultimately lead to increased infectious complications and even mortality.

In 2001, the first randomized controlled trial in critically ill adult surgical patients demonstrated a significant decrease in mortality in patients receiving insulin therapy to achieve a glucose levels between 80 and 110 mg/dL.[43] Despite some controversy in duplicating these results in different population groups, as well as the significant risk of iatrogenic hypoglycemia, there was intense interest in expanding these findings into the care of critically ill children.

Vlasselaers et al. attempted to examine this relationship in a largely post-cardiac surgical cohort in a randomized study evaluating intensive insulin therapy vs. conventional therapy. They demonstrated decreased mortality and infections with tight glycemic control, but the rate of hypoglycemia was 25% in the intensive insulin group compared to 1% in the conventional group.[44] Attempts to replicate these findings have been less successful.

Macrae et al.[45] recently published results of a multicenter randomized controlled trial examining tight glycemic control with insulin therapy in pediatric patients admitted to the PICU. Thirteen sites participated, with 1369 children randomized to receive either tight glycemic control or conventional management. No difference was found in the primary outcome between the 2 groups: ventilator-free days alive within 30 days of trial entry. The groups were also similar in their risk of infection, length of stay, and mortality. However, a lower proportion of renal replacement therapy was noted in the tight glycemic control arm, as well as a higher proportion of hypoglycemia. In non-cardiac surgical patients, there was a decrease in average costs at 12 months in the tight glycemic control arm. While there was no apparent clinical outcome benefit attributable to the tight glycemic control arm, there still remained a significant risk of iatrogenic hypoglycemia.

The balance between preventing the harmful effects of hyperglycemia to the physiologically stressed infant or child with the potential risk of iatrogenic hypoglycemia has decreased enthusiasm for tight glycemic control with intensive insulin therapy. Currently, there are no consensus recommendations, and the practitioner is left to determine the best course of action with regard to insulin therapy in response to stress hyperglycemia. Additional study is needed to identify an improved method to monitor and reduce the harm of hyperglycemia while decreasing the risk of inducing potentially devastating hypoglycemia.

Enteral nutrition in critically ill children

Optimal nutritional support is a fundamental goal in the care of critically ill children; however, the optimal timing and best way to achieve this goal remains relatively controversial. Parenteral nutrition has obvious benefits in critically ill children, as it does not need to be interrupted for procedures or rely on gut motility. However, it has significant risks related to central venous access, infection rates, as well as interference with electrolyte and glucose homeostasis. In adult critically ill patients, enteral nutrition has been associated with decreased infectious complications and length of stay when compared with parenteral nutrition.[46–48] There may also be physiologic benefits with decreased expression of cytokines, such as IL-6, in patients that receive enteral nutrition.[49] Consequently, enteral nutrition has been promoted by consensus-based guidelines in both adult and pediatric intensive care units.[50] But when should enteral nutrition be initiated and is there a preferred method of delivery in critically ill children?

When possible, the enteral route has become the preferred route for administration of nutrition in critically ill children. There