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Editorial
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# Hyperglycemia in Critically Ill Children: When to Treat?

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## Editorial

Hyperglycemia is a common problem among critically ill pediatric patients that is associated with significant morbidity and mortality. Hyperglycemia has several effects which are regarded as potentially pathogenic. It induces a pro-inflammatory state and increased oxidative stress. In addition, hyperglycemia has a pro-thrombotic effect and reduces endothelial nitric oxide level, decreasing organ perfusion [1].

Stress hyperglycemia is attributed to insulin resistance caused by high levels of counter-regulatory hormones, cytokines, oxidative stress, and drugs like steroids and catecholamine [1] although suppression of insulin secretion due to elevated levels of pro-inflammatory cytokines may partially underlie hyperglycemia in children with meningococcal sepsis [2].

A peak serum glucose level >178mg/dL was shown to be associated with a higher mortality among children with septic shock [3]. Hyperglycemia was also associated with a longer duration of Pediatric Intensive Care Unit (PICU) stay [4]. Among children ventilated for meningococcal sepsis, peak blood glucose was shown to be negatively correlated with ventilator-free days at 30 days and to be significantly higher among the patients who developed nosocomial infection or required inotropic support or renal replacement therapy [5].

These findings suggest that tight glycemic control may be of benefit for critically ill children. However, it is also quite possible that hyperglycemia is merely an epiphenomenon. Consequently, randomized controlled trials (RCT) were badly needed.

In adults, several RCT and meta-analyses [6-7] have concluded that intensive insulin therapy for tight glycemic control in medical and surgical patients did not significantly reduce mortality. Furthermore, the NICE-SUGAR trial [8] showed increased mortality with tight glycemic control. A consistent finding in these studies was the high incidence of hypoglycemia with intensive insulin therapy. The "surviving sepsis campaign" strongly recommends starting insulin infusion in adult patients only if two consecutive blood glucose levels are >180mg/dL rather than targeting an upper level of ≤110mg/dL as previously recommended [9].

In pediatric patients, several RCT have been performed. One study demonstrated a shorter length of PICU stay, a lower level of the inflammatory marker C-reactive protein, and a decreased mortality rate among infants and children managed by intensive insulin therapy [10]. However, a meta-analysis of pediatric RCT revealed that, compared with conventional glycemic control, tight glycemic control was not associated with a significant reduction in 30-day mortality or health care-associated infections [11]. On the other hand, tight glycemic control was associated with a higher incidence of hypoglycemia. Moreover, a recent meta-analysis [12] of 6 pediatric RCT revealed that tight glycemic control decreased the need for dialysis but was not associated with a reduction in hospital mortality, sepsis, or seizures. Furthermore, tight glycemic control increased the incidence of hypoglycemia.

With regard to the issue of hypoglycemia, reassuring findings have been reported by an RCT which found that brief hypoglycemia resulting from tight glycemic control was not associated with poor neurocognitive outcome 4 years after PICU admission [13].

Overall, available evidence from pediatric and adult studies generally points to a lack of beneficial effect from tight glycemic control in addition to a significant risk of hypoglycemia. It seems prudent prudent to keep glucose level in critically ill children below an upper target level of 180mg/dL.

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