Impact of Stress-Induced Diabetes on Outcomes in Severely Burned Children

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BACKGROUND: Post-burn hyperglycemia leads to graft failure, multiple organ failure, and death. A hyperinsulinemic-euglycemic clamp is used to keep serum glucose between 60 and 110 mg/dL. Because of frequent hypoglycemic episodes, a less-stringent sliding scale insulin protocol is used to maintain serum glucose levels between 80 and 160 mg/dL after elevations >180 mg/dL.

STUDY DESIGN: We randomized pediatric patients with massive burns into 2 groups, patients receiving sliding scale insulin to lower blood glucose levels (n = 145) and those receiving no insulin (n = 98), to determine the differences in morbidity and mortality. Patients 0 to 18 years old with burns covering ≥30% of the total body surface area and not randomized to receive anabolic agents were included in this study. End points included glucose levels, infections, resting energy expenditure, lean body mass, bone mineral content, fat mass, muscle strength, and serum inflammatory cytokines, hormones, and liver enzymes.

RESULTS: Maximal glucose levels occurred within 6 days of burn injury. Blood glucose levels were age dependent, with older children requiring more insulin ($p < 0.05$). Daily maximum and daily minimum, but not 6 AM, glucose levels were significantly different based on treatment group ($p < 0.05$). Insulin significantly increased resting energy expenditure and improved bone mineral content ($p < 0.05$). Each additional wound infection increased incidence of hyperglycemia ($p = 0.004$). There was no mortality in patients not receiving insulin, only in patients who received insulin ($p < 0.004$). Muscle strength was increased in patients receiving insulin ($p < 0.05$).

CONCLUSIONS: Burn-induced hyperglycemia develops in a subset of severely burned children. Length of stay was reduced in the no insulin group, and there were no deaths in this group. Administration of insulin positively impacted bone mineral content and muscle strength, but increased resting energy expenditure, hypoglycemic episodes, and mortality. New glucose-lowering strategies might be needed. (J Am Coll Surg 2014;218:783–796. © 2014 by the American College of Surgeons)

Worldwide, >10 million people were burned in 2009, with >381,000 burn injuries reported in the United States alone.[1] A hypermetabolic response develops in patients with burns on ≥30% of total body surface area (TBSA), which is characterized by a catecholamine and corticosteroid surge, catabolism, lipolysis, immune suppression, inflammation, insulin resistance, and hyperglycemia.[2,3] Inadequate protein synthesis occurring alongside elevated protein breakdown results in the loss of lean body mass.[4] The catabolic response is not limited to muscle, as shown by concurrent reductions in fat mass and bone mineral content (BMC).[5] These changes in body composition lead to alterations in glucose homeostasis.[6] Hyperglycemia occurs alongside an increased rate of glucose appearance[7];

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Drs Finnerty, Ali, and Herndon contributed equally to this work.

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Abbreviations and Acronyms

BMC = bone mineral content
IL = interleukin
REE = resting energy expenditure
TBSA = total body surface area

reduced glucose extraction from the blood by tissue, especially muscle[8]; and insulin resistance.[9,10] In hyperglycemic burn patients, more infections, greater catabolism, substantial skin graft loss, and higher mortality are reported.[11] Although many of the sequelae related to poor glucose control occur acutely, perturbations in glucose metabolism can persist up to 3 years after the initial burn insult, indicating long-term alterations in glucose homeostasis.[6] Adequate glucose control is necessary for improving patient outcomes. The current standard of care for managing hyperglycemia in severely burned patients is to administer insulin. We have demonstrated that intensive insulin therapy for tight glycemic control can be beneficial in severely burned children, with associated improvements in lean body mass, reductions in infections and sepsis, and decreased prevalence of multiple organ failure.[12] Patients receiving intensive insulin therapy did experience considerably more mild and severe hypoglycemic episodes compared with control patients, however.

The implementation of tight glycemic control protocols for critically ill patients has become controversial after Van Den Berghe and colleagues' report that outcomes in critically ill patients were improved with intensive insulin.[13] Additional studies have shown increased morbidity and mortality in patients receiving intensive insulin.[14-17]As even a single episode of hypoglycemia is independently associated with increased mortality in critically ill patients,[18] the ranges for glycemic-control protocols have been expanded recently, per the recent American College of Physicians' recommendation that glucose levels be maintained between 140 and 200 mg/dL in all ICU patients to avoid hypoglycemic episodes.[19]

Currently, our standard of practice is to administer insulin when blood glucose levels exceed 180 mg/dL

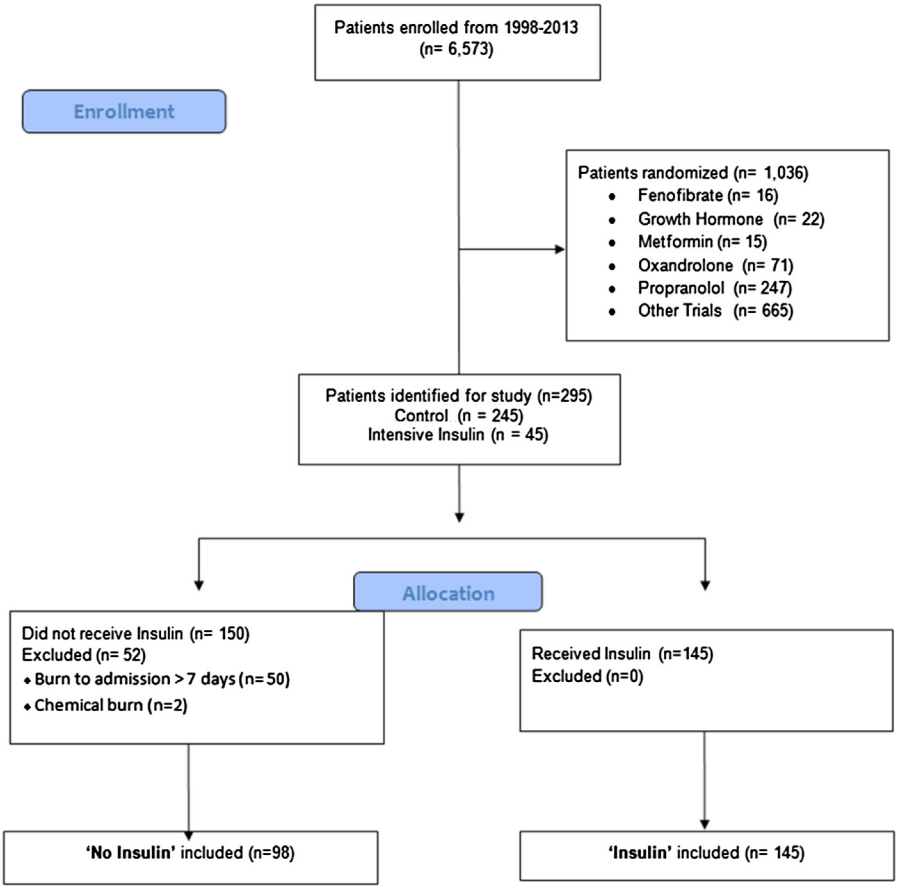

Figure 1. CONSORT diagram.