Hyperglycemia Requiring Insulin Among Pediatric Patients Diagnosed With Hemophagocytic Lymphohistiocytosis

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Describe role of Submitting/Presenting Trainee in this project (limit 150 words): Assisted in literature review, chart review and data collection, and writing abstract.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening disorder marked by massive cytokine release due to macrophage and T-cell activation. Hallmarks of the diagnosis include fever, splenomegaly, cytopenias, hypertriglyceridemia, hypofibrinogemia, and elevations in ferritin and soluble IL-2 receptor. Given HLH is associated with critical illness, elevation in inflammatory markers, and treated with glucocorticoids, the development of hyperglycemia during its course is not unexpected. However, detailed descriptions of the severity of hyperglycemia and strategies in insulin management among HLH patients are lacking. We describe 10 years' experience at a single tertiary pediatric health center with HLH patients who developed insulin dependent hyperglycemia.

Objectives: To describe the demographics, clinical and laboratory findings, treatment regimens, and outcomes for children with HLH treated with insulin due to hyperglycemia.

Study Design: Retrospective chart review from 2010 through 2019 of youth 0 to 21 years of age who required insulin therapy during or shortly after a hospitalization where they were diagnosed with HLH using established criteria. Descriptive statistics were used to characterize the population of interest.

Results: Of 30 patients diagnosed with HLH, 33% (n=10) required insulin therapy. Half (n=5) were female and half (n=5) male. The mean age was 8.4 years (7.8 months - 17 years). The majority (80%) were non-Hispanic white. Mean BMI at admission was 53rd percentile (5th - 87th percentile). Max serum glucose ranged from 267 to 725 mg/dL (mean 421 mg/dL). Marked inflammation was present (max CRP 2.6 - 44.9 mg/dL, max ferritin 1,091 - 90,219 ng/mL). All were treated with dexamethasone, doses ranging from 5 to 11 mg/m2/day and duration from 2 to 70 days. Most (90%) received parenteral nutrition (PN) with a mean max GIR of 8 mg/kg/min (SD=2.7). Intravenous infusions of regular insulin were used in 80% of patients, though 2 patients were later transitioned to long and short acting subcutaneous insulin. Mean duration of IV insulin therapy was 9.5 days (2-24 days); however, 2 patients died while on IV insulin therapy. The majority (70%) needed insulin within 5 days of starting steroids. Two patients (20%) were treated with subcutaneous insulin only (no IV). Only 1 patient was discharged home on insulin therapy. Mean hospital stay was 60 days (10-202 days). Mortality was 50% (n=5).

Conclusions: One-third of pediatric HLH patients required insulin during their hospitalization for severe hyperglycemia likely secondary to multiple factors including glucocorticoid use, parenteral nutrition, inflammation, and severe illness. Insulin is typically started within 5 days of initiating steroid therapy, limited to IV infusions, and often is not needed by the time of discharge. Risk of mortality is very high.