Intensive insulin therapy for septic shock patients does not show survival benefit

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Treating adults with septic shock with intensive insulin therapy to counter elevated blood glucose levels associated with corticosteroid therapy did not result in a reduced risk of in-hospital death, compared to patients who received conventional insulin therapy, according to a study in the January 27 issue of *JAMA*. The researchers also found that adding a 2nd corticosteroid to treatment did not significantly reduce the risk of death within the hospital.

Septic shock is a major complication of infectious diseases, with a mortality rate of 60 percent within a short period, according to background information in the article. Corticosteroids are used in the treatment of septic shock and may provide a survival benefit, but their use is associated with hyperglycemia.

Djillali Annane, M.D., of the Hôpital Raymond Poincaré, Garches, France, and colleagues with the Corticosteroids and Intensive Insulin Therapy for Septic Shock (COIITSS) trial examined whether normalization of blood glucose levels with intensive insulin treatment would improve outcomes for adults with septic shock treated with hydrocortisone. Also, the researchers analyzed the benefit of adding the corticosteroid fludrocortisone to hydrocortisone therapy. The randomized trial, which included 509 adults with septic shock who had received hydrocortisone treatment, was conducted from Jan. 2006 to Jan. 2009 in 11 intensive care units in France.

Patients were randomly assigned to 1 of 4 groups: continuous intravenous insulin infusion with hydrocortisone alone; continuous intravenous insulin infusion with hydrocortisone plus fludrocortisone; conventional insulin therapy with hydrocortisone alone; or conventional insulin therapy with intravenous hydrocortisone plus fludrocortisone. Hydrocortisone was administered every 6 hours, and fludrocortisone was administered once a day for 7 days.

The researchers found that at hospital discharge, 117 of 255 patients (45.9 percent) treated with intensive insulin therapy died and 109 of 254 patients (42.9 percent) treated with conventional insulin therapy died. No significant difference existed between treatment groups for any of the secondary outcome measures, such as the median (midpoint) number of days that surviving patients spent in the ICU in the intensive insulin group (10) vs. for those in the conventional insulin group (9); the median length of stay in the hospital for the intensive insulin group (24 days) vs. those in the conventional insulin group (22 days); the median vasopressor-free (drug or other agent that is used to help raise blood pressure) days for each group was four; and the median mechanical ventilation-free days was 10 for the experimental group vs. 13 days for the control group. Patients treated with intensive insulin experienced significantly more episodes of severe hypoglycemia than those in the conventional treatment group.

Regarding the outcomes of adding fludrocortisone to therapy, at hospital discharge, 42.9 percent of the patients in the fludrocortisone-treated group died and 45.8 percent of patients in the conventional insulin therapy group died. "No significant difference in overall mortality existed between the fludrocortisone-treated patients and the controls," the authors write. "Nor did significant differences exist between the two groups for the survivors' ICU and hospital lengths of stay, for the number of vasopressor-free days, and for mechanical ventilation-free days."

"The current study showed no evidence to support a strategy of intensive insulin therapy aimed at maintaining blood glucose levels in the range of 80 to 110 mg/dL for treating septic shock with corticosteroids," they write. "The current data do not support the routine use of oral fludrocortisone in addition to hydrocortisone when physicians decide to introduce corticosteroids in the management of a patient with septic shock."

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