Variable Dosing Strategies of Hydrocortisone in Intensive Care Unit Septic Shock Patients (HYDRO-SS Study)

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Abstract
Background/Purpose:
Despite adequate fluid resuscitation in sepsis, patients can have persistent hypotension leading to the requirement of vasopressor therapy. In septic shock, the dysregulated immune response can cause a relative adrenal insufficiency, requiring the need for treatment with corticosteroids.
There are several trials published to date evaluating benefits of corticosteroids in patients with septic shock. The CORTICUS study concluded hydrocortisone 50 mg every six hours versus placebo did not improve survival or reversal of septic shock, but those who received hydrocortisone did achieve shock reversal earlier compared to placebo. The HYPRESS and ADRENAL trial found the use of hydrocortisone therapy as a continuous infusion for five days in severe sepsis patients did not reduce the risk of septic shock and did not lower 90-day mortality, respectively. Bonnin et al found hydrocortisone 50 mg every 6 hours compared to hydrocortisone 100 mg every 8 hours had similar rates of shock reversal in septic shock patients, and hydrocortisone 100 mg every 8 hours may reduce the rates of shock recurrence and need for additional vasopressor therapy.
Though the results of these studies are inconclusive, the 2021 Surviving Sepsis Campaign (SSC) recommends intravenous hydrocortisone at a dose of 200 mg per day if adequate fluid resuscitation and vasopressor therapy is unable to restore hemodynamic stability. In comparison, the 2017 Guidelines for the Diagnosis and Management of Critical Illness-Related Corticosteroid Insufficiency (CIRCI) support doses of hydrocortisone up to 400 mg/day for greater than or equal to 3 days.
Based on the current guidelines and studies, there is a lack of clear consensus on the ideal dosing strategy for patients in septic shock
Objective: The primary objective was to determine the effect of variable hydrocortisone dosing strategies on discontinuation of vasoactive agent(s) in intensive care unit patients. Secondary objectives included duration of mechanical ventilation, ICU length of stay, 28-day mortality, and adverse events from hydrocortisone therapy.
Methods: This was a retrospective, multi-center study analyzing hydrocortisone 100 mg IV every eight hours versus hydrocortisone 50 mg IV every six hours initiated within 48 hours of septic shock diagnosis. Patients with pre-existing diagnoses requiring daily steroid use, receiving both doses of hydrocortisone, or alternate corticosteroids were excluded. Chi-squared, Fisher-exact test, and Student T-tests were performed for descriptive statistics. Cox proportional hazards regression model analyses and Kaplan-Meier event rate estimates were conducted for the primary outcome analysis. Cox proportional regression model and logistic regression model were performed for secondary outcomes.
Results: 107 patients were included, 76 in the hydrocortisone 50 mg every 6 hours group and 31 in the hydrocortisone 100 mg every 8 hours group. After controlling for confounders via Cox proportional hazards regression, a statistically significant difference in time to vasopressor discontinuation in the hydrocortisone 100 mg every 8 hours group (1.61 HR [0.99-2.61], p=0.05) compared to hydrocortisone 50 mg every 6 hours group was identified. There were no statistically significant differences found in

mortality (p=0.18), ICU length of stay (p=0.38), duration of mechanical ventilation (p=0.68), or adverse effects (p=0.94) between the two groups.
Conclusion: The use of hydrocortisone 100 mg every 8 hours strategy could provide a benefit in early vasopressor discontinuation rates and warrants further evaluation.