MÆDICA - a Journal of Clinical Medicine

JOURNAL CLUB

Corticosteroids in septic shock: no survival benefit in CORTICUS trial

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Severe sepsis and its most severe complication – septic shock – represent a major cause of mortality and morbidity worldwide. The incidence of the septic shock has been rising, and a death rate of 33 to 61% has been reported in the placebo groups of many trials. The use of corticosteroids as an adjunctive therapy has been controversial for decades.

Many studies did not confirm a survival benefit after a short course of high-dose corticosteroids and suggested an increase in mortality caused by superinfections. Studies that used lower doses of hydrocortisone for longer durations mentioned earlier reversal of shock and improved survival.

This study – Corticosteroid Therapy of Septic Shock (CORTICUS) – evaluated the efficacy and safety of low-dose hydrocortisone therapy in a broad population of patients with septic shock – in particular, patients who had had a response to a corticotropin test, in whom a benefit was unproven.

In the trial – multicenter, randomized, double-blind, placebo-controlled – the authors assigned 251 patients to receive 50 mg of intravenous hydrocortisone and 248 patients to receive placebo every 6 hours for 5 days; the dose was then tapered during a 6-day period.

The primary objective was the rate of death at 28 days in patients who did not have a response to corticotropin. Secondary objectives were the rates of death at 28 days in patients who had a response to corticotropin and in all patients, the rates of death in the ICU and in the hospital, the rates of death at 1 year after randomization, a reversal of organ system failure (including shock), and the duration of the stay in the ICU and the hospital.

Of the 499 patients in the study, 46.7% did not have a response to corticotropin (125 in the hydrocortisone group and 108 in the placebo group). At 28 days, there was no significant difference in mortality between patients in the two study groups who did not have a response to corticotropin (39.2% in the hydrocortisone group and 36.1% in the placebo group, P=0.69) or between those who had a response to corticotropin (28.8% in the hydrocortisone group and 28.7% in the placebo group, P=1.00). In the hydrocortisone group, shock was reversed more quickly than in the placebo group. However, there were more episodes of superinfection, including new sepsis and septic shock. The proportion of patients in whom reversal of shock was achieved was similar in the two groups.

The use of hydrocortisone did not decrease mortality in a general population of patients with septic shock, even though the drug hastened reversal of shock. This lack of improvement may be related to an increased incidence of superinfection and new septic episodes. No benefit was seen in a subgroup of patients who had had no response to corticotropin, as was shown previously for patients with severe septic shock.

In conclusion, hydrocortisone cannot be recommended as general adjuvant therapy for septic shock (vasopressor responsive), and the test with corticotropin cannot be promoted to determine which patients should receive hydrocortisone therapy.

Comment on the paper:
Sprung CL, Annane D, Keh D, et al., for the CORTICUS Study Group – Hydrocortisone Therapy for Patients with Septic Shock. *N Engl J Med* 2008; 358(2):111-124