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Hydrocortisone therapy in septic shock

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Keywords

Adrenocorticotrophic hormone, cortisol, hydrocortisone, sepsis, septic shock, shock

Comments

This study aids our understanding of the pathophysiology behind the improvement in vascular reactivity with hydrocortisone therapy in vasopressor-dependent septic shock and confirms that cortisol levels are raised in patients with septic shock. Furthermore, the reduction in vasopressor support with hydrocortisone therapy was comparable to previous studies (see Additional information). The peak cortisol levels following hydrocortisone therapy emphasise that this therapy is supraphysiological (at least in the early stages), and it may be that smaller doses of hydrocortisone would be sufficient. The decline in cortisol levels over time, despite a constant infusion, suggest that hydrocortisone metabolism changes during the course of therapy, as other work (see Additional information) has shown that cortisol production is not suppressed by steroids in septic shock. It may be that its half-life is prolonged in the early stages of septic shock. Finally, it appears that patients with an 'inadequate' endogenous cortisol production during septic shock, benefit the most through hydrocortisone infusions, although the exact mechanism is unclear. It does not appear to be a consequence of previously suggested reductions in acute phase reactants, since inflammatory mediators in this study were similar in patients with an 'inadequate' and 'adequate' cortisol production. Larger multicentre studies are awaited to determine whether this beneficial effect on haemodynamics can translate into a reduction in mortality.

Introduction

Mortality from septic shock remains > 50% despite improvements in supportive therapies. Consequently, research has focused on understanding and modifying the pathogenesis of septic shock, and steroid therapy has featured prominently in this context. Historically it has been inferred that the use of high dose steroids in septic shock may be harmful, despite experimental data showing that steroids improve vascular reactivity in sepsis. More recently, randomised controlled trials have confirmed the beneficial effects of steroids on haemodynamics in patients with septic shock in the ICU. This study explored the pharmacological and pathophysiological basis for this phenomenon in more detail.

Methods

- . Prospective, observational study in 20 medical intensive care patients with vasopressor-dependent septic shock receiving continuous hydrocortisone therapy (10 mg/h)
- . Short corticotrophin test performed on all patients prior to commencement of hydrocortisone infusion, followed by serial plasma cortisol estimations
- . Hydrocortisone infusion continued for 7 days followed by dosage reduction and cessation of therapy by day 10

Results

- . Cortisol production was 'adequate' in nine patients (defined by cortisol rise > 200 nmol/l following synacthen or pre-synacthen cortisol > 1000 nmol/l) and 'inadequate' in the remaining 11.
- . Cortisol levels in patients with 'inadequate' cortisol production were significantly lower on day 1 following initiation of hydrocortisone infusion, but there were no differences between the groups on subsequent days.
- . The rate of reduction of vasopressor (noradrenaline) therapy was significantly greater in the 'inadequate' group (85% reduction versus 50% reduction on day 2), and these patients were also free of vasopressor support significantly earlier than the 'adequate' cortisol production group.
- . There were no differences in survival or course of inflammatory mediators (C-reactive protein, procalcitonin, leukocyte count) between the two groups.

Additional information

Accompanying editorial in same issue

Briegel J: **Hydrocortisone and the reduction of vasopressors in septic shock: therapy or only chart cosmetics?** *Intensive Care Med* 2000, 26:1723-1726.

Related papers

Bollaert P, Charpentier C, Levy B, Debouverie M, Audibert G, Larcan A: **Reversal of late septic shock with supraphysiologic doses of hydrocortisone.** *Crit Care Med* 1998, 26:645-650.

Briegel J, Forst H, Haller M, Schelling G, Kilger E, Kuprat G, Hemmer B, Hummel T, Lenhart A, Heyduck M, Stoll C, Peter K: **Stress doses of hydrocortisone reverse hyperdynamic septic shock: a prospective, randomized, double blind, single center study.** *Crit Care Med* 1999, **27**:723-732.

Perrot D, Bonneton A, Dechaud H, Motin J, Pugeat M: **Hypercortisolism in septic shock is not suppressible by dexamethasone infusion.** *Crit Care Med* 1993, **21**:396-401.

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1. Oppert M, Reinicke A, Graf K-J, Barckow D, Frei U, Eckardt K-U: Plasma cortisol levels before and during low dose hydrocortisone therapy and their relationship to hemodynamic improvements in patients with septic shock. *Intensive Care Med.* 2001, **26**: 1747-1755.