Adrenal failure in the critically ill

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Summary

Three critically ill patients suffered multiple organ failure secondary to sepsis. Despite adequate supportive therapy and appropriate antibiotic cover, they failed to improve and required inappropriate inotrope support. They had not been treated with steroids or other drugs known to suppress adrenal function. Adrenal insufficiency was suspected. A random cortisol concentration and a short synacthen test demonstrated concentrations below the range expected in all three cases. High-dose steroid therapy was commenced with marked improvement in the short-term. However, in each case sepsis eventually caused death. (Br. J. Anaesth. 1998; 81: 468–470).

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In the past, steroids were used in the treatment of many disorders commonly seen in the intensive care unit (ICU). The inflammatory nature of these disorders and the known anti-inflammatory effect of steroids made these drugs an obvious therapeutic choice in critically ill patients. However, the results of the use of steroids in humans have been disappointing. As a result of these studies, corticosteroids are not recommended for the management of severe sepsis, including septic shock and adult respiratory distress syndrome.1

However, it is important to remember that a small number of patients develop adrenal insufficiency in severe illness and require steroid replacement. Adrenal failure in the critically ill may be difficult to recognize as the syndrome is often masked by other causes of hypotension and organ failure.2 Weakness, fatigue, weight loss and hypotension, the traditional symptoms of adrenal insufficiency, occur in most ICU patients and are therefore of little value in making the diagnosis. The metabolic upset that occurs in critically ill patients with multiple organ dysfunction also renders the classical electrolyte abnormalities seen in adrenal failure meaningless. A less recognized indicator of adrenal insufficiency is resistance to beta-adrenoceptor stimulation.3

We present three cases of adrenal insufficiency. In each case suspicion of adrenal failure was raised only when an inappropriate amount of inotropic support was required.

Case reports

PATIENT NO. 1

A 75-yr-old male presented to a district hospital with abdominal pain and distension. His past medical history included a diagnosis of Felty’s syndrome and chronic renal impairment. Felty’s syndrome consists of rheumatoid arthritis, splenomegaly and neutropenia, leading to repeated infections and weight loss. The patient had never been treated with steroids. He was transferred to our tertiary referral centre for further management. Two days of conservative management resulted in no improvement. Laparotomy was performed and splenectomy was required for a ruptured spleen. His initial postoperative course was uneventful. However, he deteriorated on day 6 with a generalised sepsis requiring respiratory and haemodynamic support. Repeat laparotomy was performed; a necrotic appendix was removed and a transverse loop colostomy made. His sepsis resolved and he was weaned from inotropes. Two days later he again required increasing amounts of epinephrine to a maximum dose of 100 μg kg⁻¹ min⁻¹, despite no definite focus of sepsis being identified and remaining apyrexial.

The possibility of adrenal insufficiency was raised and a short synacthen test was performed. It revealed a baseline serum cortisol concentration of 0.01 μmol litre⁻¹, increasing to 0.16 μmol litre⁻¹ after administration of ACTH. These concentrations were well below those expected in a critically ill patient and steroids were commenced (hydrocortisone 100 mg qds). Within hours, inotropic requirements were reduced markedly and subsequently discontinued. However, his condition deteriorated again over the next few days and the patient died of massive colonic haemorrhage.

PATIENT NO. 2

A 61-yr-old woman with a 12-yr history of polymyositis was admitted for elective plasma exchange therapy to alleviate worsening weakness of her neck, arms and muscles of swallowing. She had been receiving maintenance therapy of cyclophosphamide 50 mg daily (an alkylating agent) and had never been treated with steroids.

Her hospital stay was complicated by chest infection and the organism Klebsiella pneumoniae was isolated. Initial management with antibiotics and CPAP via a face mask was unsuccessful and she required tracheal intubation and artificial ventilation. Inotropic therapy was commenced and titrated to maintain an adequate mean arterial pressure as
evidence of septic shock developed. Her requirements for epinephrine reached 80 µg kg⁻¹ min⁻¹. She progressively developed multiple organ failure, including renal failure, requiring continuous veno-venous haemofiltration (CVVHDF). Within 72 h the septic shock had improved but she still required epinephrine 10 µg kg⁻¹ min⁻¹ to maintain adequate mean arterial pressure.

Given the inotrope requirements, the possibility of adrenal insufficiency was raised. A short synacthen test was performed which revealed a random cortisol concentration of 0.245 µmol litre⁻¹ and a post-synacthen concentration of 0.454 µmol litre⁻¹. This was felt to be an inadequate response for a stressed patient. She was commenced on hydrocortisone 100 mg qds. Within 2 h, her inotropic requirements were reduced to 5 µg kg⁻¹ min⁻¹. They were reduced further overnight and discontinued the following day. She continued to improve on maintenance steroid therapy. A further episode of sepsis 2 weeks later was treated unsuccessfully and she died on day 21 of her ICU stay.

PATIENT NO. 3
A 52-yr-old man presented to our accident and emergency department with a 3-day history of progressively worsening respiratory distress associated with mild wheeze, pleuritic pain, haemoptysis and intermittent sweats. He also gave a history of influenza for the preceding 2 weeks. Broad-spectrum antibiotics were commenced to cover a community acquired infection. He was treated with flucloxacinil, cefotaxime, erythromycin and gentamycin. CPAP via a face mask was used to improve gas exchange. He deteriorated and required tracheal intubation, artificial ventilation and inotropic support. Epinephrine was titrated to maintain mean arterial pressure greater than 60 mm Hg. He rapidly developed multiple organ failure and required CVVHDF.

His critical condition was felt to be secondary to septic shock but the possibility of adrenal failure was suggested because of the high requirements for epinephrine (100 µg kg⁻¹ min⁻¹). A short synacthen test was performed. The basal cortisol concentration was 0.17 µmol litre⁻¹ and post-ACTH 0.18 µmol litre⁻¹. He was commenced on hydrocortisone 100 mg qds. For 72 h the inotropic demand was reduced greatly and the dose of epinephrine was reduced to 20 µg kg⁻¹ min⁻¹. Despite maximum cardiovascular and respiratory support he failed to improve. He died on day 21 in the ICU from multiple organ failure.

Discussion
Absolute adrenal insufficiency occurs uncommonly in the general ICU population but in certain subgroups the risk of developing adrenal insufficiency is significant. Several studies have reviewed the incidence of adrenal failure in the critically ill patient. It ranges from 6.25% to 75% depending on the population tested. Patients who are not responding to standard therapy should be suspected of adrenal insufficiency.

In patients with septic shock, serum cortisol concentrations are usually increased compared with those in unstressed, healthy individuals. Cortisol plays an important role in the ability to respond to stress. There is a decreased rate of cortisol clearance from the body and reduced binding of cortisol to transcortin, resulting in an increase in circulating free cortisol concentration in acute illness. Thus critically ill patients generally show hypercortisolism. The benefit of this increase is thought to be maintenance of intravascular volume.

There is a small group of patients in whom adrenal hyporesponsiveness is a feature. The aetiology of this relative insufficiency is complex. “Stressed” adrenal glands are more susceptible to haemorrhage and adrenal vein thrombosis. Failure of such patients to respond to therapy such as antibiotics, prompt and aggressive fluid management and, if possible, removal of an infective focus should arouse suspicion of adrenocortical insufficiency. Because of the extremely wide range of plasma cortisol concentrations seen in ICU patients, caution is needed when applying normal values for plasma cortisol to acutely hospitalized patients. High basal cortisol concentrations in septic shock may still indicate relative adrenal insufficiency. On the basis of a recent study of plasma cortisol concentrations in patients with sepsis or trauma, a plasma cortisol value of more than 0.7 µmol litre⁻¹ in a patient requiring intensive care rules out adrenal insufficiency, but a safe lower cut-off value is unknown.

An inadequate response to ACTH may identify patients who would benefit from corticosteroid therapy. A short ACTH stimulation test, known as the synacthen test, using a single i.v. dose of cosyntropin 250 µg is recommended. An adequate response is defined as an increase in plasma cortisol concentration of greater than 0.25 µmol litre⁻¹ and a peak concentration of 0.7 µmol litre⁻¹. An inadequate response warrants immediate high dose cortisol therapy. Hydrocortisone 100 mg qds is the recommended dose for pharmacological treatment in these patients.

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References


