Adrenal Insufficiency

Adrenal Insufficiency in Acute Severe Illness

The normal adrenal response to acute illness or stress is an increase in production of cortisol, which has important protective effects. Unfortunately, this needed increase may be lacking in some persons because of exogenous use of corticosteroids that suppress native cortisol production, or dysfunction in the hypothalamic-pituitary-adrenal (HPA) axis seen in some cases of severe illness. Cooper and Stewart reviewed the risk factors for adrenal insufficiency, clinical factors that should raise suspicion for inadequate adrenal function, and treatment with exogenous steroids for deficient patients. Among the disease states that have been associated with HPA dysfunction are pituitary infarction, adrenal insufficiency caused by tumor invasion or infection, head injury, and sepsis. Human immunodeficiency virus (HIV) infection may affect the HPA axis in a number of deleterious ways. Both opportunistic agents and their drug treatment can lead to adrenal insufficiency, which occurs commonly in critically ill patients with HIV infection.

Native cortisol production is enzymatically inhibited by the anesthetic agent etomidate and the antifungal medication ketoconazole. Exogenous use of corticosteroids can suppress the HPA axis with as little as 7.5 mg of prednisone/prednisolone or 0.75 mg of dexamethasone daily for more than three weeks. This suppression may last for months after the exogenous steroid is stopped.

The clinical factors that manifest in adrenal insufficiency are somewhat nonspecific and may easily be missed. Classic features of Addisonian crisis include nausea, vomiting, diarrhea, abdominal pain, and delirium, but these are often present for other reasons in critically ill patients. Physical examination findings of adrenal hypofunction include postural hypotension, tachycardia, and fever. Increased skin pigmentation may occur with longstanding adrenal insufficiency. Of

the laboratory findings seen with inadequate adrenal function, hypoglycemia and eosinophilia are important to remember, because they are less likely to be occur in other disease states. Hyponatremia and hyperkalemia typically occur but may be masked by fluid and electrolyte replacement.

The authors note that it is difficult to define a normal cortisol level for an ill patient, as values can fluctuate widely depending on the type and severity of illness. Nonetheless, they propose 15 mcg per dL (414 nmol per L) of serum cortisol as a threshold below which adrenal insufficiency is likely, and 34 mcg per dL (938 nmol per L) as the upper cutoff where adrenal hypofunction is unlikely. Additional information may be gained in unclear cases by administering a corticotropin stimulation test. A rise in serum cortisol of less than 9 mcg per dL (250 nmol per L) after stimulation supports the likelihood of inadequate adrenal function.

Treatment of adrenal insufficiency in a critically ill patient is typically accomplished with 50 mg of hydrocortisone given via an intravenous or intramuscular route every six hours. A large study of empiric use of supplemental steroids in patients with septic shock showed reduced mortality and time spent on vasopressors. Mineralocorticoid replacement (50 mcg fludrocortisone daily) was given in addition to the hydrocortisone supplement in these patients.

The authors caution that supraphysiologic high-dose steroid replacement has not been shown to improve outcomes in critically ill patients and may actually be harmful. Long-term supplemental steroids may be needed in some patients when HPA axis dysfunction persists after the severe illness has passed.