

Preoperative Evaluation of the Patient on Steroids

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The stress of anesthesia and major surgery stimulates the hypothalamic-pituitary-adrenal (HPA) axis to increase production of glucocorticoids, primarily cortisol, which is an essential component of the physiologic response to stress. For patients with adrenal insufficiency, who require daily hormone replacement, an increased dose of steroids is used to simulate the expected requirement. However, even patients without pituitary or adrenal disease who have been treated chronically with steroids may be at risk of perioperative adrenal crisis because supraphysiologic doses of glucocorticoids will suppress the HPA axis over time. Thus, the most important perioperative issue in the evaluation and management of the patient on steroids is the need to provide appropriate doses of exogenous glucocorticoids if the HPA axis is unable to respond adequately to stress.

In the 1950's, two case reports described perioperative deaths from presumed adrenal insufficiency in patients whose glucocorticoid therapy had been withdrawn before surgery.^{1,2} These initial cases were the basis for the subsequent practice of "stress dose" perioperative glucocorticoid coverage for patients in whom HPA axis suppression from prior steroid use is suspected. Since "stress dose" coverage has been the standard of care, there are limited data on clinical outcomes without supplementation. In small series of patients, receiving maintenance rather than supplemental steroids, no clear case of clinically significant adrenal insufficiency has been reported.³⁻⁵ Although there are case reports of perioperative adrenal insufficiency in patients who had been on steroids, there is no consensus on the magnitude of the risk for adrenal insufficiency in this setting.⁶⁻⁹

Various diagnostic tests are available to assess the HPA axis.^{10,11} A simple 8 am cortisol level is only helpful to screen for adrenal insufficiency if it is markedly low (≤ 3 mcg/dL) or significantly elevated (≥ 18 to 20 mcg/dL). Intermediate values require dynamic testing such as the ACTH (corticotropin) stimulation test. An inadequate cortisol response to ACTH is expected in primary adrenal insufficiency. Additionally, ACTH stimulation is used to assess suspected chronic hypothalamic-pituitary dysfunction (including suppression by exogenous steroids) because prolonged deficiency of ACTH leads to adrenal gland atrophy. More direct tests of

HPA axis dysfunction, the metyrapone and insulin tolerance tests, are cumbersome, more expensive and potentially dangerous, so they are not used in routine preoperative evaluation of the patient on steroids. A cortisol level that has been drawn during physiologic stress, such as hypotension or fever, may help to diagnose or exclude adrenal insufficiency without imposing additional risk.

There is currently no consensus on the best approach to the ACTH stimulation test, or on the cortisol response that best predicts clinically significant secondary adrenal insufficiency with stress.¹⁰⁻¹⁵ The standard test uses 250 mcg cosyntropin IV or IM, measuring cortisol at baseline and 60 minutes, with plasma cortisol ≥ 20 mcg/dL at either time as a diagnostic cutoff for adequate function.¹⁰ Recently, the sensitivity of the standard test, which uses a supraphysiologic dose of cosyntropin, has been challenged. It may be "normal" in the face of abnormal insulin tolerance or metyrapone results and there are reports of patients with "normal" results who developed clinical adrenal insufficiency during stress.¹⁴ An alternative, the low dose ACTH stimulation test, uses 1 mcg cosyntropin IV, measuring cortisol at baseline and 30 minutes, with plasma cortisol ≥ 18 mcg/dL as a diagnostic cutoff.¹⁰ A seven mcg/dL rise in cortisol has also been used as an indication of a functional HPA axis.¹¹ The low dose ACTH stimulation test has been compared to the standard ACTH stimulation test and to "gold standard" insulin tolerance or metyrapone tests in a number of studies.^{12,13,15} Some critics argue that, depending on the chosen diagnostic cutoff, the two tests are comparable.¹³ There is also concern about reliably delivering the one mcg cosyntropin dose in the clinical setting. The low dose test has not currently replaced the standard test. Given the limited sensitivity (of the standard test in particular) a "normal" ACTH stimulation test result does not preclude the possibility of adrenal insufficiency under major stress.

The most common cause of adrenal insufficiency is the therapeutic use of supraphysiologic doses of steroids, which suppresses hypothalamic CRH and pituitary ACTH production, and leads to adrenal gland atrophy. Numerous studies examine suppression of the HPA axis in relation to steroid dose, duration and delivery route. There is significant individual variation in the dose and duration of therapy that leads to suppression.^{7,16} In general, patients on any dose of steroid for less than three weeks will not have significant suppression. Use of less than 5 mg prednisone daily over any

length of time does not typically cause significant suppression, unless the medication is given at bedtime.⁶ Inhaled or cutaneous steroids, in customary doses, may cause adrenal dysfunction by biochemical testing, but are not likely to put a patient at risk of perioperative adrenal crisis. However, cases of excessive use with Cushing's syndrome and significant HPA suppression have been reported.¹⁷ Patients who have been on more than 20 mg prednisone per day for more than 3 weeks, or patients with clinical features of Cushing's syndrome, are assumed to have functional suppression.⁶ Recovery from HPA axis suppression can take up to 9 to 12 months, so steroid use within the previous year must be considered. For patients with uncertain medication histories, or intermediate dose/duration of steroids, a cosyntropin stimulation test (low or standard dose) can be used to help determine the need for perioperative steroids, or coverage can be given empirically.

Individuals with known adrenal insufficiency due to hypothalamic, pituitary or adrenal disease will require perioperative supplemental glucocorticoids. Those with adrenal gland dysfunction require continuation of the mineralocorticoid replacement.¹⁸ A patient with unrecognized adrenal insufficiency is at risk of adrenal crisis when subjected to the stress of anesthesia and surgery. The diagnosis may be missed because the presenting symptoms of adrenal insufficiency (weakness, fatigue, anorexia, nausea) are quite nonspecific.¹⁰ While routine preoperative testing of the HPA axis is not justified by the prevalence of adrenal insufficiency, a cosyntropin stimulation test should be considered in patients with suggestive symptoms who are at high risk of hypothalamic, pituitary or adrenal disease. Hypothalamic or pituitary dysfunction should be considered in patients with tumor, prior brain irradiation, or infiltrative diseases such as sarcoidosis. Primary adrenal insufficiency is more common in patients with tuberculosis, AIDS, and autoimmune endocrine syndromes.¹⁰

Perioperative management of adrenal insufficiency is based on the anticipated glucocorticoid requirements for a given level of stress. Doses that have historically been given as "stress coverage" are often excessive when compared to studies of perioperative corticosteroid production by healthy patients.^{7,8,18} Maximal cortisol secretion is about 300 mg in the 24 hours following surgery. More typically, secretion is 75 to 150 mg in 24 hours following major surgery, and less for minor procedures. Although short term, high dose steroids are generally well tolerated, excess glucocorticoids could play a role in

impaired wound healing, increased blood glucose or increased susceptibility to infection in the perioperative setting. Thus, adjusting steroid supplementation to the estimated level of physiologic stress is now routine, with doses ranging from simple maintenance of baseline medication for minor procedures to 300 mg hydrocortisone over 24 hours for major surgery and severe postoperative complications.^{7,8,18}

Patients with adrenal insufficiency are at risk of adrenal crisis during emergency surgery if their endocrine status is unknown.¹⁹ Patient and family education and the use of medical identification are essential safeguards. Patients may be provided with prefilled dexamethasone (4 mg) syringes for IM self-administration while seeking care for severe stress or trauma.

Currently, there is not evidence to support a single, definitive approach concerning the preoperative evaluation and perioperative management of the patient on steroids. The degree of risk for perioperative adrenal insufficiency, the optimal diagnostic test(s) for adrenal function, and the appropriate doses of perioperative steroid coverage are somewhat controversial. Preoperative consultation should include a clinical assessment of the patient's risk for adrenal insufficiency under stress, based on underlying diseases and the prior use of therapeutic glucocorticoids. When uncertainty exists, options include preoperative testing with an ACTH stimulation test or empiric glucocorticoid supplementation. Perioperative steroid doses should be based on the degree of physiologic stress and can be tapered rapidly with recovery. Even with a "normal" ACTH stimulation test, adrenal insufficiency should be considered in the surgical patient with unexplained or refractory hypotension.

Summary of Recommendations:

- Identify patients at risk for perioperative adrenal crisis:
- Known adrenal insufficiency
- Nonspecific symptoms and high-risk for HPA axis disease
- Prior steroid therapy – more than 5 mg prednisone daily for more than three weeks in the preceding year
- Presume adrenal suppression in patients on more than 20 mg prednisone for three weeks in the preceding year or in patients with Cushingoid features.

- Consider ACTH stimulation test when HPA function is uncertain due to intermediate steroid dose (5 to 20 mg prednisone) or unclear medication history:
 - Standard test uses 250 mcg cosyntropin IV or IM to achieve a cortisol level \geq 20 mcg/dL at baseline or 60 minutes.
 - Low dose test uses 1 mcg cosyntropin IV to achieve a cortisol level \geq 18 mcg/dL at baseline or 30 minutes. The low dose is more physiologic, but not proven to better predict clinical outcomes.
 - Provide glucocorticoid coverage in anticipation of steroid requirements:
 - For major surgery, 100 mg hydrocortisone IV before induction of anesthesia, and 100 mg IV or continuous infusion q 8 hrs for 24 hours.
 - For moderately stressful procedures, 100 mg hydrocortisone single IV dose, or 50 mg q 12 hrs for 24 hours.
 - For minor procedures under local anesthesia, maintenance steroid dose adequate.
 - Taper rapidly (50% per day) to maintenance dose; adjust taper based on clinical assessment of stress if there are postoperative complications.
 - Prepare patients with known adrenal insufficiency for unforeseen surgery:
 - Patient education and medical identification
 - Syringes with 4 mg dexamethasone for patient's IM use
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