

Perioperative Stress Dose Steroids: Is It Really Necessary?

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Perioperative Stress Dose Steroids: Is It Really Necessary? *Jose Enrique L. Garcia, M.D.*

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During conditions of imposed stress (e.g., infection, trauma and surgery), there is a release of “stress” hormones to maintain homeostasis.¹ While the hormones that are released during this stress response include glucagon, epinephrine and growth hormone, cortisol is arguably the most important.¹

A current and widely held concept is that exogenously administered corticosteroids suppress the hypothalamus-pituitary-adrenal (HPA) axis, thereby inhibiting normal endogenous adrenal cortical function and subsequent release of cortisol.² Furthermore, during conditions of stress, failure to increase plasma levels of cortisol can increase the risk of morbidity and/or mortality (i.e., inadequate or “failed” stress response). Although the potential consequences of a failed corticosteroid response are varied (Table 1), the most life-threatening includes refractory hypotension and shock states.

The concept of adrenal hyporesponsiveness during stress situations (i.e., failed stress response) appears to be based on several case reports, published in the 1950s, of intractable and fatal hypotension during or immediately following surgical procedures in patients on preoperative corticosteroids.³⁻⁵

These deaths were attributed to adrenal suppression caused by the preoperative exogenously administered glucocorticoids based upon autopsy findings of adrenal atrophy.⁵ This resulted in recommendations of administration of corticosteroids (i.e., “stress dose” of steroids) during encounters of stress (e.g., perioperative period), which subsequently became a standard of care practice.⁶⁻¹² However, the dose regimens for steroid administration are conflicting and vary significantly (Table 2).

Interestingly, the validity of routine use of a stress dose of corticosteroids has been questioned since the late 1960s.¹³ A study comparing plasma cortisol response after surgical trauma in a control group (i.e., patients not on preoperative steroids) and two groups given chronic glucocorticoids (one group stopped exogenous steroids weeks to a month preoperatively and the other group was currently being treated with exogenous glucocorticoids) did not find endogenous adrenal suppression in patients taking exogenous glucocorticoids.¹⁴

Another study in renal transplant patients receiving prednisone (5-10mg daily) for immunosuppression who had undergone a “stress situation” (e.g., surgery, sepsis, hypertensive crisis or diabetic ketoacidosis) demonstrated a functioning HPA axis based upon serum cortisol and adrenocorticotrophic hormone (ACTH) levels as well as cosyntropin stimulation test.¹⁵ Therefore, these investigators recommended that no additional glucocorticoid administration (i.e., “stress dose”) should be administered other than the daily glucocorticoid dose.

A systematic review of the literature, including both randomized trials as well as cohort trials, concluded that routine administration of stress doses of corticosteroids is not necessary as long as the daily dose of corticosteroid is administered.¹⁶ The authors also suggested that adrenal function testing is not required in these patients, because the test is overly sensitive and does not predict which patients will develop an adrenal crisis.¹⁶

A more recent prospective cohort study, looking at patients with inflammatory bowel disease who were on high-dose corticosteroids but had stopped them within one year before major colorectal surgery, found that avoidance of stress dose steroids did not influence perioperative outcome.¹⁷

A recent Cochrane review found only two randomized control trials assessing stress dose of steroids.¹⁸ These studies reported that endogenously produced steroid combined with exogenous steroid administration (i.e., daily dose) is adequate in the perioperative period. The authors concluded that the recommendations on the use of additional corticosteroids for surgical patients receiving preoperative steroids have not been adequately investigated.

It is suggested that supplementation should be deferred if patients are receiving inhaled or oral steroids, topical glucocorticoids, alternate-day doses of short-acting oral glucocorticoids, daily doses of <5 mg of prednisone or its equivalent.¹⁹ However, evidence for such recommendations is lacking. Also, exogenous glucocorticoid administration should be considered in any patient who has received prior etomidate and develops postoperative hypotension that cannot be explained by other mechanisms, resulting in hypotension that is non-responsive to standard resuscitative fluid administration and/or vasopressor therapy,

which may suggest possible occult adrenal failure. While a recent report suggests that etomidate use does not result in higher mortality rates in the critically ill patient,²⁰ etomidate administration can result in worse outcomes in the intensive care unit (ICU) patient population.^{21,22} Reduced endogenous adrenal cortical production, and systemic release of cortisol by inhibition of the 11 beta and 17 alpha hydroxylase enzyme systems resulting in occult adrenal failure, is considered to be a primary mechanism for the cause of the reported increased mortality rates in these critically ill patients.²¹ In addition, it may be prudent to restrict etomidate use to only those patients who will receive scheduled glucocorticoid treatment as part of their postoperative care.

Given the paucity of supporting clinical evidence, we may be needlessly subjecting patients to the risks of high-dose steroids based on the current and defensive strategy of perioperative supplementation with no actual benefit.^{13,16} In addition to the known systemic side effects, additional steroid doses can increase the risk of acute side effects, which can influence surgical outcomes, especially in supra-physiologic doses – namely hyperglycemia, hypertension, fluid retention and an increased risk of infection.^{13, 16, 23} With significant controversial publications, one is confronted with several clinical questions. How should patients on long-term steroids be treated perioperatively? Should a stress dose of steroids be administered in all patients who have received chronic steroids regardless of remote use? If not, who should receive a stress dose and how much? Also, when should a patient who was previously on steroids be considered to have been devoid of risks of adrenal suppression?

Several investigators have demonstrated that the cortisol response is variable and determined by the type of surgical procedure.^{24,25} Thus, patients undergoing minor surgery may not induce a stress response, while patients undergoing major surgical procedures may have a significant increase in plasma cortisol concentrations.^{26,27} Therefore, while we wait for further evidence, our current practice could be based upon more restraint by administering stress of steroids based upon the type of surgical procedure (Table 3).

In summary, stress dose steroid administration remains controversial. With lack of evidence of benefits and concerns of potential adverse effects of stress dose of steroids, it would be prudent to follow a more conservative and less aggressive approach.

Table 1: Signs of Adrenal Crisis

Modified from UpToDate 2013 (reference 6)

Dehydration, hypotension or shock out of proportion to severity of current illness

Nausea and vomiting with a history of weight loss and anorexia

Abdominal pain (“acute abdomen”)

Unexplained hypoglycemia

Unexplained fever

Hyponatremia, hyperkalemia, azotemia, hypercalcemia or eosinophilia

Hyperpigmentation or vitiligo

Other autoimmune endocrine deficiencies (hypothyroidism or gonadal failure)

Table 2: Recommendations for Stress Dose of Steroids in Anesthesiology Textbooks (references 9-12)

Source Text	Recommendations
Clinical Anesthesiology (8)	Hydrocortisone 100mg every 8 h the evening before or on morning of surgery. For diabetics, give 25 mg hydrocortisone at induction followed by a 100 mg infusion for 24 hours.
Clinical Anesthesia (9)	Hydrocortisone 200-300 mg/70 kg body weight in divided doses on the day of surgery (higher doses for patients undergoing more extensive surgical procedures)
Principles and	Usual maintenance dose of steroid perioperatively with symptomatic

Practice of Anesthesiology (10)	<p>management as needed.</p> <p>OR</p> <p>Stress dose of steroids based on the degree of perioperative stress. Minor surgical stress (e.g. inguinal herniorrhaphy), a single dose of hydrocortisone 25 mg the day of surgery. Moderate stress (e.g. open cholecystectomy, lower extremity vascular procedure, total joint replacement, segmental colectomy, hysterectomy), hydrocortisone 50-75 mg for 1-2 days, and resume usual dose thereafter. Major surgical stress (e.g. Whipple procedure, esophagogastrectomy, total colectomy, cardiopulmonary bypass), hydrocortisone 100-150 mg for 2-3 days, and resume usual dose thereafter.</p>
Anesthesia and Co-Existing Disease (11)	<p>Similar dosing recommendations from Principles and Practice of Anesthesiology but divergent in recommending a tapered steroid dose over a 1-2 days period instead of resuming the usual dose. Also, no steroid supplementation necessary for superficial surgical and dental procedures/biopsies.</p>
Miller's Anesthesia (12)	<p>Minor surgical procedures, hydrocortisone 100 mg/day/70 kg body weight followed by tapering in 25% increments until baseline steroid dose. Maximum stresses, hydrocortisone 200 mg/day/70 kg body weight followed by tapering in 25% increments until baseline steroid dose.</p>

Table 3: Recommendations for corticosteroid coverage for surgery in patients taking exogenous corticosteroids are as follows (Modified from UpToDate, reference 6)

Minor surgical procedures: Morning steroid dose, but no supplementation necessary.

Moderate surgical procedures (e.g., lower extremity revascularization, total joint replacement): Morning steroid dose, plus supplementation with hydrocortisone 50 mg I.V., intraoperatively, and 25 mg every 8 hours for 24 hours. Resume routine dose thereafter.

Major surgical procedures (e.g., cardiothoracic surgery, major abdominal surgery): Morning steroid dose, plus supplementation with hydrocortisone 100 mg I.V., intraoperatively, and 50 mg every 8 hours for 24 hours. Taper dose by half per day to maintenance level.

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