

# Supplemental Steroids in the Operating Room: A Review of the Literature

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## Abstract

An universally accepted clinical use of corticosteroids is the replacement in deficiency states. In addition, corticosteroids have been used in various diseases for the anti-inflammatory effects these drugs exhibit. The use of steroids remain still controversial in most situations outside of a deficiency state.

As a result of two case reports from the 1950's<sup>1, 2</sup>, the assumption has been made that regular administration of exogenous glucocorticoids, such as prednisone, will result in suppression of the hypothalamic-pituitary-adrenal axis. Most clinicians believe that patients treated with glucocorticoids who have exposure to highly stressful events such as surgery will need supplemental doses of steroids during the intraoperative period. As a result of the hypothalamic-pituitary-adrenal axis suppression, patients will have an inadequate supply of endogenous glucocorticoids to meet the demands of operative stress. The adrenal insufficiency which may develop can result in cardiovascular collapse.

Recent reports suggests that the recommendation for supplemental steroids is based on correlations from clinical case reports rather than from prospective, randomized, controlled studies<sup>3, 4</sup>. These reports suggests that clinical suppression of the hypothalamic-pituitary-adrenal axis is uncommon and glucocorticoid levels required for surgery are less than previously thought<sup>3, 5, 6</sup>.

As administration of glucocorticoids is not without adverse effects, the supplemental doses should be rationalized. Possible adverse effects from corticosteroids include: delayed wound healing, increased susceptibility to infections, gastric ulcerations, catabolic effects on skin, muscle, bone and connective tissue and electrolyte disturbances.

This article will review current research regarding the administration of supplemental steroids in the perioperative

period. A summary of recent studies will be reviewed and a general consensus about the use of supplemental steroids will be given.

A variety of methods have been utilized to determine if the current accepted regimen of supplemental steroids for surgical stress is necessary. These methods consists of clinical data such as vital sign measurements and the assessment of serum levels of various circulating hormones.

Kehlet et al.<sup>7</sup> suggests that the plasma concentration of cortisol is not the primary determinant of blood pressure in the glucocorticoid treated patient during and after surgery. This study utilized hypotension as the parameter to measure clinical adrenocortical insufficiency. The conclusion was that acute, stress-induced adrenocortical insufficiency must be infrequent. Also, other factors should be considered when the adrenocortical response is absent in glucocorticoid treated patients. Some of the other possibilities for hypotension in glucocorticoid treated patients are: 1) the fact that many of these patients are in a general catabolic state and suffer from anemia and hypoproteinemia, caused partly from the glucocorticoids themselves and partly from the underlying disease and 2) the underlying disease process that causes these patients to be less resistant to exogenous stress.

Symreng et al.<sup>8</sup> showed that lower doses of supplemental steroids are adequate to cover surgical stress and even these may be unnecessary. A corticotropin stimulation test was used for this study with measured levels of plasma cortisol and aldosterone. They found that the vast majority of patients receiving long term steroid replacement had a normal response to corticotropin stimulation. Patients with normal corticotropin stimulation response who had been treated with steroids preoperatively were not given any supplemental steroids on the day of the operation. Patients

with a decreased response to the stimulation received a low dose regimen of 25 mg of hydrocortisone at induction of anesthesia, followed by a continuous infusion of 100 mg over 24 hours. There was no evidence of circulatory insufficiency in any group.

Udelsman et al. <sup>9</sup> tested monkeys which had been adrenalectomized and were receiving glucocorticoid replacement therapy. This study concluded that supraphysiologic doses of glucocorticoids provided no advantage over normal physiologic levels of the hormones. They did suggest that patients with potential for adrenal insufficiency receive at least a physiologic dose of replacement steroids before surgery. This study concluded that the glucocorticoid doses equivalent to the daily unstressed cortisol production rate are sufficient for normal homeostatic mechanisms to occur during surgery.

Schlaghecke et al. <sup>5</sup> studied 279 patients who received daily doses of steroids in an attempt to determine the degree of suppression of pituitary-adrenal function. The pituitary-adrenal response to the administration of exogenous corticotropin-releasing factor (CRH) was measured. This group determined that pituitary-adrenal function in patients receiving glucocorticoids cannot be adequately estimated on the basis of dose or duration of therapy. A stimulation test may be necessary if termination of therapy is planned to prevent overlooking impaired pituitary-adrenal function.

Friedman et al. <sup>3</sup> looked at a group of patients having orthopedic surgery to determine if supplemental steroids were necessary for the operation. The suggestion was made that the biochemical changes which result from the long-term administration of glucocorticoids may be clinically and physiologically unimportant. In this study clinical data such as the presence of hypotension, myalgia, arthralgia, ileus and fever was noted. Lab data consisting of serum sodium levels, eosinophil count and 24 hour urine free-cortisol levels were determined both pre-operatively and at non-stress post-operative periods. The levels of 24 hour urine samples showed all patients had endogenous adreno-cortical function. When this finding was considered with the clinical outcome, the determination was made that these patients had adequate adrenocortical function to undergo surgery without supplemental steroids. The orthopedic procedures are simplified if supplemental steroids can be avoided, due to decreased complications and cost.

Chernow et al. <sup>4</sup> examined the hormonal response to graded surgical stress. Surgical stress was graded by three groups:

1) minimal stress such as a hernia repair. 2) moderate stress such as a cholecystectomy. 3) severe stress such as a colectomy. Plasma catecholamine levels, cortisol and serum angiotensin converting enzyme(ACE) levels were analyzed. The surgically-induced hormonal changes were characterized by increases in cortisol, epinephrine, norepinephrine and a decrease in serum ACE levels. Group 1 showed no significant hormonal changes induced by surgery. Groups 2 and 3 showed changes at one hour and occasionally twenty-four hours. This study concluded: that hormonal changes reflect the degree of surgical stress; hormonal changes are transient, lasting no longer than twenty-four hours if surgery is uncomplicated; and hormonal responses to minimal surgical stress are negligible.

Claussen et al. <sup>10</sup> presented three case studies in which profound nonhemorrhagic shock developed in one postoperative and two trauma patients. They suggested that acute adrenal insufficiency may present as shock after postoperative stress or trauma, with the hemodynamics mimicking septic shock. This article suggested that the cosyntropin stimulation test was the best test for evaluation of adrenal function in critically ill patients. Two patients in this case study showed dramatic improvement when exogenous doses of steroids were administered.

Dorin et al. <sup>11</sup> examined high output circulatory failure in patients with acute adrenal insufficiency. The patients involved demonstrated hypotension, low systemic vascular resistance, high cardiac output (>7 liters) and were on dopamine at doses of 10ug/kg/min or greater. The clinical condition improved with the administration of glucocorticoids. The conclusion was that adrenal insufficiency is a cause of high output circulatory failure.

Sampson et al. <sup>12</sup> attempted to establish a test of adrenal function for patients previously treated with steroids and are having surgery. They concluded that the corticotropin test correlated with the plasma-cortisol levels which were obtained during the operation. The authors suggested that unnecessary administration of steroids during surgery could increase the incidence of infection and it should be determined which patients need steroid cover and only administer to those patients. The patients who showed a satisfactory response to the corticotrophin test were operated on without steroid cover and without mishap. The patients with an unsatisfactory response collapsed during the operation without steroid cover.

Udelsman et al. <sup>13</sup> raised the question that anesthetic events

such as reversal, extubation and recovery may be the stressors that contribute to death, not surgical stress. Levels of plasma corticotrophin-releasing hormone (CRH), ACTH, cortisol, norepinephrine, epinephrine and renin activity were measured. The periods of reversal, extubation and early recovery showed marked increases in plasma ACTH, cortisol and epinephrine, not the actual surgical procedure itself. These observations raise further questions about the issue of steroid coverage. Is the stressful event surgery or anesthesia?

Salem et al.<sup>14</sup> reassessed the issue of perioperative glucocorticoid coverage 42 years after the problem was initially revealed. The authors felt that the current clinical and experimental evidence support the concept that the accepted perioperative coverage is excessive and based on anecdotal information. They proposed new recommendations which concern the amount and duration of glucocorticoid coverage based on the data collected. These include: 1) preoperative dose of glucocorticoid coverage taken by the patient should be considered. 2) the preoperative duration of glucocorticoid administration is a factor. 3) the nature and anticipated length of the surgery should be taken into consideration.

### SUMMARY

Based on the review of the literature, it is clear that this issue requires further studies. Most of the data suggest that the current regimen of supplemental steroid administration for surgical procedures is excessive and should be modified. The data indicate that adrenal cortical insufficiency in patients receiving exogenous steroids is a very serious problem and should be considered such. The use of test to measure the adrenocortical response to stress have good results. In the days of cost-conscious health care, the price of such testing will have to be evaluated, while weighing the risks and benefits of such tests. In addition, in our days of "same day admit surgery" and increasing outpatient surgery it might not always be possible to perform preoperative testing. The costs of the administration of the supplemental steroids must also be considered in the future.

As general consensus we think that supplemental steroids should be given perioperatively in patients receiving chronic steroid medication despite mentioned side effects and additional costs. As recommended by Salem et al.<sup>14</sup> one should consider 1) the preoperative dose of glucocorticoid coverage taken by the patient, 2) the preoperative duration of glucocorticoid administration, and 3) the nature and

anticipated length of the surgery. We recommend that the patient should take his daily dosage of steroids up to and including the day of surgery. In addition, a dose of 25 to 100 mg of hydrocortisone equivalent (according to the magnitude of expected surgical stress) should be administered to the patient during surgery. The administered dose should be reduced over the following 24 (to 48) hours until the initial dosage is reached. Until there is better data suggesting a favorable risk/benefit ratio using smaller doses of perioperative steroid coverage we are convinced that this type of regimen is in the best interest for our patients.

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