



How to modify steroid replacement in patients with adrenal failure undergoing surgery, and why

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Surgical stress activates the hypothalamus-pituitary adrenal axis (HPA) and increases adrenal secretion of cortisol. In patients with adrenal failure who are facing surgery, the dosage modification of replacement steroids must avoid both under- and over-replacement.

A recent systematic review and meta-analysis provides data, which help predict the physiologic increase of cortisol associated with surgery (1). The authors reviewed all the studies published between 1990 and 2016, including at least 5 patients, and with at least one measurement of serum cortisol during the procedure and up to 10 days later. After elimination of neurosurgical studies requiring use of steroids, 71 studies, for a total of 2953 patients, were included.

The results show that the cortisol response increases with the invasiveness of the intervention, from minimally invasive surgery (grade 1, e.g. inguinal hernia repair) to moderately-to-highly invasive surgery (grade 2, e.g. cholecystectomy, and grade 3, e.g. coronary artery by-pass graft):

- In the **perioperative period**: grade 1 procedures are not associated with a cortisol peak, while grade 2 and 3 are associated with cortisol serum levels above the upper normal range for up to one week after the operation, particularly in women and the elderly.
- Within the **first 24 hours from surgery**: cortisol serum levels, in comparison to healthy controls, increase 2 times in patients undergoing surgery grade 1, 4 times in patients undergoing surgery grade 2, and 3.5 times in patients undergoing grade 3 surgery.
- **Characteristics of the intervention**: laparoscopic surgery and epidural anesthesia stimulate a lower cortisol response than, respectively, open surgery and general anesthesia. Length of the procedure and use of etomidate (an anesthetic agent which may inhibit cortisol biosynthesis) were not correlated with the cortisol response.

Discussion

This study provides food for thought, and useful clinical data. It does however have some **limits**, namely:

- Heterogeneity of the studies included
- Lack of standardization of cortisol assays used for measurement
- Evaluation limited to total cortisol and not its free fraction.

In patients with adrenal failure, replacement dosage must be increased in the preparation to surgery and during the intervention, and use of hydrocortisone must be favored.

The rise in cortisol levels depends on the severity of the intervention (in line with the suggestions of the Endocrine Society) but also on age and sex of the patient, surgical approach and type of anesthesia. The elderly, women, and patients undergoing “open” surgery under general anesthetics seem to require higher doses of steroids. The difference between men and women could be result from the raised level of cortisol-binding globulin promoted by female hormones, without difference in free hormone (2). Finally, patients undergoing surgery type 2 or 3 may require an increase in steroid dosage up to one week following the procedure.

References

1. Prete A, Yan Q, Al-Tarrah K, et al. The cortisol stress response induced by surgery: a systematic review and meta-analysis. *Clin Endocrinol (Oxf)* [2018, 89: 554-67](#).
2. Qureshi AC, Bahri A, Breen LA, et al. The influence of the route of oestrogen administration on serum levels of cortisol-binding globulin and total cortisol. *Clin Endocrinol (Oxf)* [2007, 66: 632-5](#).