201. Hydrocortisone infusion after induction with etomidate in major surgery: failure to abolish the postoperative ACTH increase


It has been well documented that a single induction dose of etomidate (et) blocks adrenocortical 11β-hydroxylase activity for several hours, leading to decreased cortisol (F) levels and exaggerated plasma ACTH compared to thiopentone [1]. The clinical relevance of adrenocortical blockade is still uncertain. Only limited data are available on the time course in major surgery.

The aim of our study therefore was to analyse the effect of glucocorticoid supplementation on hormonal and anaesthetic parameters in patients undergoing major surgery after induction with et. 20 consecutive patients undergoing colorectal resection were randomly allocated to hydrocortisone (100 mg as continuous infusion over 10 hours) or placebo (5% glucose). Induction was performed with et (0.26 mg/kg) and fentanyl. Blood samples for ACTH and cortisol were taken prior to and 1, 2, 3, 4, 5, 6, 9, 12, 18 and 24 hours after induction. ACTH was measured by a highly specific two-site immunoradiometric assay. F was determined by RIA. Et alone led to a decrease in serum F with a nadir at 2 hours (7.9 ± 1.1 μg/dl) followed by an exaggerated F increase beginning after 6 hours and persisting against the normal daily rhythm until the 24th hour (29.2 ± 2.5 vs. 12.1 ± 1.2 μg/dl). Plasma ACTH peaked after 6 hours (566 ± 76 pg/ml) when surgery was completed, followed by a slow decline to the normal range after 24 hours (Fig. 1). Continuous hydrocortisone supplementation led to a high increase of serum F reaching a plateau at 2 hours (44–55 μg/dl). After hydrocortisone application was stopped serum F gradually fell but remained high after 24 hours. Despite supranormal serum F concentrations plasma ACTH increased significantly and reached a maximum of 288 ± 77 pg/ml at 6 hours (p < 0.02, Fig. 1). Our results show that the initial blockade of the adrenal cortex by et is followed by rapid recovery after 6 hours. Interestingly, F concentrations higher than those achieved by maximum exogenous ACTH stimulation were unable to suppress plasma ACTH values which were higher in the postoperative period than those seen in normals after stimulation with CRF, vaso¬pression or hypoglycaemia.

Conclusions: 1. The initial blockade of the adrenals by et is followed after 6 hours by a period of high adrenocortical secretory activity which lasts until the following day. 2. Maximum ACTH
stimulation does not occur during surgery but in the early postoperative period. 3. The very high ACTH increase in the placebo group cannot be explained by steroid feedback alone, as high ACTH concentrations were also seen after hydrocortisone supplementation. 4. The precise mechanism of ACTH increase in the presence of high F levels remains to be elucidated.

References


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202. Pharmacokinetics of dexamethasone in depressed patients during the dexamethasone suppression test (DST)

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Several disturbances of the pituitary-adrenocortical system in psychiatric patients have recently been identified, including increased cortisol production and resistance of plasma corticosteroid concentrations to the suppressive action of dexamethasone. The latter abnormality has received considerable attention as a diagnostic aid in depressive patients and as a tool for monitoring their adequate drug treatment. Several technical factors have now been identified which may invalidate a DST result. We have recently reported that nonsuppressed cortisol levels are frequently associated with low plasma