Title: ADRENAL CORTICAL SUPPRESSION AFTER ETOMIDATE INDUCTION

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Induction. Etomidate, a carboxylated imidazole, has been used for anesthetic induction by i.v. bolus injection and for prolonged sedation of intensive care patients by i.v. infusion Long term infusion of etomidate was associated with increased mortality in critically ill multiple trauma patients (1), possibly due to an effect on the adrenal cortex. A study to compare the effects of etomidate and thiopental induction on adrenal cortical and other stress hormones was undertaken.

Methods. Ten healthy patients, age 25-49 yrs, who were scheduled for gynecologic laparotomy participated in this institutionally approved study after giving informed consent. Using a random number table, they were assigned to receive either thiopental, 4 mg/kg, (group T) or etomidate, 0.35 mg/kg (group E) for induction of anesthesia (N=5 with each drug). An i.v. infusion was started in an antecubital vein and from this site undiluted blood samples were collected for hormone and etomidate measurements. Anesthesia was induced with fentanyl, 100 μg, and the assigned drug. Tracheal intubation followed succinylcholine, 1 mg/kg. Surgical relaxation was provided by d-tubocurarine, 3-9 mg. Patients were ventilated with a 50:50 mixture of N_2O and O_2 to which enflurane, 1-2% was added. Venous blood samples were drawn into iced syringes 30 min. before and just prior to induction, then at 0.5,1,2,3,4,5, 8,12, and 24 hours after induction. Samples were packed in ice, then plasma separated in a refrigerated centrifuge and frozen at -30°C for later hormone and drug level measurements. Cortisol, aldosterone and ACTH were measured by RIA and radioenzymatic methods were used to measure epinephrine, norepinephrine and dopamine. Etomidate concentrations for five hours after induction were measured with HPLC. All results are expressed as mean±SD. Within group comparisons of cortisol and aldosterone were made with ANOVA for repeated measures followed by Bonferroni paired t-test. The relationship between the two adrenocorticoids were made with analysis of covariance. Other within and between group comparisons were made with appropriate nonparametric tests. P<0.01 was considered significant.

Results. Both groups were similar in age (T=33.5±5,E=33±10 yrs), weight (T=61±12,E=64±15 kg) and operation time (T=142±69,E=177±90 min). The amounts of the i.v. and inhalation anesthesia were similar for each group. Plasma cortisol and aldosterone concentrations are shown before and after thiopental (fig.1) and etomidate (fig.2). After thiopental, significant increases above preinjection values are seen from hours 2-5 for cortisol and from hours 1-4 for aldosterone. After etomidate, the only significant increase in cortisol occurred 12 hours later and no significant increases in aldosterone occurred. Significant between group differences in cortisol and aldosterone occurred from the 1st thru the 5th hour after injection. In both groups the plasma concentration of cortisol and aldosterone seemed to rise and fall together or change little. During the same period, no between group differences in ACTH, epinephrine, norepinephrine or dopamine occurred, ACTH levels often rose above normal values during hours 1-8 after etomidate injection. Plasma concentrations of etomidate followed a normal concentration-time profile. Plasma catacholamine concentrations after both hypnotics varied within and above the normal range during the five hours that cortisol and aldosterone levels were suppressed after etomidate.

figure 1

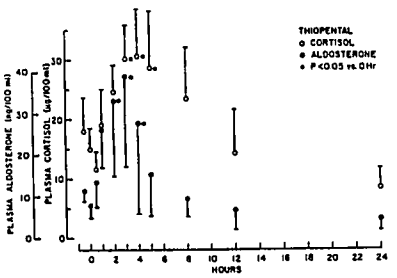
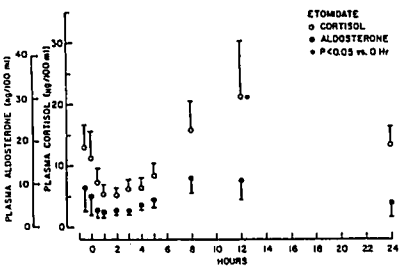


figure 2



Discussion. The doses of anesthetic agents used in this study, other than the induction agents, previously have been shown not to suppress stress hormones. The attenuation by etomidate of both cortisol and aldosterone response to surgical stress in the presence of normal or increased ACTH, suggests that etomidate is acting at the adrenal cortex. This may be the result of the inhibiting the release or interfering with the synthesis of these hormones. Because cortisol and aldosterone levels do not fall befow the lower limit of normal and the suppressive effects of etomidate diminish after the fifth hour, the possible adverse effects of the temporary adrenocortical suppression of a single etomidate dose remain speculative.

Reference.
1. Ledingham I McA, Finlay WEI, Watt I, McKee JI. Etomidate and adrenocortical function. Lancet i: 1434,1983