ETOMIDATE AND ADRENOCORTICAL SYNTHESIS IN MAN

SIR,—We read with interest the report on the effects of a bolus dose of etomidate on cortisol and ACTH secretion (Duthie, Fraser and Nimmo, 1985). We cannot, however, accept the conclusion that "a bolus dose of etomidate 0.3 mg kg\(^{-1}\) causes no significant adrenocortical suppression".

Other studies have noted an increase in cortisol secretion which occurs about 1 h after the induction of anaesthesia with thiopentone (Fragen, Shanks and Molteni, 1983; Yeoman et al., 1984; Moore et al., 1985) which was not seen in comparative groups given etomidate for induction. The two studies in patients undergoing "minor" surgical procedures (diagnostic laparoscopy—Fragen, Shanks and Molteni; inguinahernia repair—Yeoman and others) indicated that the cortisol response in the thiopentone groups was decreasing at 3 h after induction. As blood sampling was not performed by Duthie, Fraser and Nimmo between 1 and 4 h after induction, it is hardly surprising that a cortisol stress response was not seen. The prolonged cortisol response reported by Moore and colleagues in patients undergoing abdominal hysterectomy was probably related to the longer duration of surgery and the greater surgical "stress".

In conclusion, we feel that the authors are not justified in their assertion that boluses of etomidate do not cause significant adrenocortical suppression, because they did not sample during the time that a cortisol response would be expected.

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SIR,—I read with interest the paper by Duthie, Fraser and Nimmo (1985). The authors failed to demonstrate significant differences in cortisol, corticosterone or ACTH concentrations when either etomidate or thiopentone was given to induce anaesthesia. They also suggest that the incomplete inhibition of cortisol synthesis was probably compensated for by an increase in ACTH secretion. They did not find a significant increase in ACTH, but it is true that there is a marked variability in ACTH concentrations. However, if their hypothesis is correct (that ACTH compensates for partial inhibition of cortisol synthesis) should not they demonstrate a significant decrease in cortisol concentrations first, since one would expect plasma cortisol concentration to decrease first and then the ACTH concentrations to increase (feedback mechanism)?

Their results, however (no significant difference in cortisol concentrations between etomidate and thiopentone patients), can be explained easily on the basis that their patients had minor or surface surgery.

We do know that etomidate inhibits steroid synthesis (Fry and Griffiths, 1984), but we also know that the type of surgery influences markedly plasma cortisol concentrations (Clarke, Jonhston and Sheridan, 1970). So in some operations, like laparotomy, cortisol is expected to increase as a response to surgical stress. This increase will not occur after etomidate as the drug inhibits the adrenal cortex at the enzyme level. Indeed, Fragn and colleagues (1984) noted, in patients submitted to gynaecological laparotomy, that plasma concentrations of cortisol and aldosterone 1 and 2 h after induction were significantly lower with etomidate than with thiopentone. In contrast, Wagner and White (1984) studied patients who had minor surgery (cervical biopsy) and found similar cortisol and aldosterone concentrations before, during and after operation with either thiopentone or etomidate, but the adrenocortical response to exogenous ACTH stimulation was blunted in the patients receiving etomidate.

Owen and Spence (1984) point out that further similar clinical studies will offer no more than reconfirmation that etomidate suppresses the adrenal cortex.

It appears that the type of surgery accounts for the significant or not significant differences in cortisol concentrations between the etomidate and thiopentone groups reported in the above mentioned studies and not a different degree of inhibition of adrenal cortex by an i.v. bolus injection of etomidate. So an i.v. bolus injection of etomidate produces a "silent" inhibition of the adrenal cortex, but it significantly prevents the response of the adrenal cortex to an "increased stress" such as that caused by major surgery.

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