Sir.—The recent paper by Duthie, Fraser and Nimmo (1985) suggests that the induction of anaesthesia with a single bolus dose of etomidate 0.3 mg kg\(^{-1}\) is not associated with significant depression in cortisol concentration. In support, they cite the data of Sebel, Verghese and Makin (1983), while quoting our data (Sear et al., 1983) to show an effect when the drug is given by continuous infusion for the maintenance of anaesthesia. A re-examination of our data reported elsewhere in three separate studies (Sear et al., 1983; Moore et al., 1985; Sear, Atherden and Edwards, 1985) does not support their argument.

Thirty-five premenopausal women undergoing abdominal hysterectomy were studied. All were premedicated with diazepam 10 mg by mouth 2 h before operation. Anaesthesia was induced in all patients between 08.00 and 10.00 h. Patients were randomly allocated, within the separate studies, to receive one of three anaesthetics:

- **Thiopentone group**: Thiopentone 4 mg kg\(^{-1}\) for induction of anaesthesia, and maintenance with 67% nitrous oxide in oxygen supplemented with 0.5% halothane (n = 14).
- **Etomidate bolus group**: etomidate 0.3 mg kg\(^{-1}\) for induction, and maintenance as in the previous group (n = 10).
- **Etomidate infusion group**: etomidate 0.3 mg kg\(^{-1}\) for induction, and maintenance with an infusion of etomidate 10 \(\mu\)g kg\(^{-1}\) min\(^{-1}\) to supplement 67% nitrous oxide in oxygen (n = 11).

All patients received alcuronium 0.25 mg kg\(^{-1}\) to produce neuromuscular blockade, and fentanyl 3 \(\mu\)g kg\(^{-1}\) for additional analgesia. Blood samples were taken before induction, at the end of surgery, and 4 h after induction; cortisol and glucose concentrations were measured in all patients, and aldosterone concentration in 25 patients. Blood-glucose concentration was measured, as the magnitude of the increase during surgery has been equated with the severity of the surgical trauma (Hall, 1985).

Table I shows blood-glucose concentrations and serum cortisol and aldosterone concentrations in the three groups of patients. There were no significant differences in the glycaemic response between the patients. There were, however, significant differences in the cortisol responses between the groups. At the end of surgery, and at 4 h after induction, the cortisol concentrations were measured in all patients, and aldosterone concentration in 25 patients. Blood-glucose concentration was measured, as the magnitude of the increase during surgery has been equated with the severity of the surgical trauma (Hall, 1985).

<table>
<thead>
<tr>
<th>Glucose (mmol l(^{-1}))</th>
<th>4.89 (0.57)</th>
<th>6.39 (0.98)</th>
<th>7.26 (1.62)</th>
<th>6.01 (1.02)</th>
<th>8.13 (2.11)</th>
<th>7.05 (0.74)</th>
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<tr>
<th>Thalidomide (TP)</th>
<th>4.70 (0.58)</th>
<th>5.01 (0.49)</th>
<th>8.13 (2.11)</th>
<th>7.05 (0.74)</th>
<th>8.13 (2.11)</th>
<th>7.05 (0.74)</th>
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<tr>
<th>Significance between groups</th>
<th>TP vs. EB</th>
<th>PT vs. EB and TP vs. ET</th>
<th>EB vs. ET</th>
<th>All P &lt; 0.001</th>
</tr>
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</table>

On the other hand, the three groups showed a difference in response when the effect on aldosterone secretion was studied. In the thiopentone group, a significant increase occurred both at the end of surgery and at 4 h while in the etomidate groups there was a dose-related inhibition of aldosterone secretion. In the bolus group, there was no increase in hormone concentrations at the end of surgery, but a significant increase by 4 h (P < 0.05). In the infusion group, aldosterone concentrations decreased by the end of surgery (P < 0.01), and were still lower than the preinduction value by 4 h. We also observed a differential effect on aldosterone percursor

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synthesis, 11-deoxycorticosterone concentration being increased in both groups receiving etomidate, but significantly higher in those receiving the single bolus dose (Sear, Atherden and Edwards, 1985). As our previous study showed an effect of infusions of etomidate on 11β-hydroxylation (Moore et al., 1985), this effect on 11-deoxycorticosterone indicated a second, and probably dose-related, inhibition on early pathway synthesis (for example cholesterol side-chain cleavage).

Why are our results different from those of Duthie and colleagues? It may relate to the magnitude of the surgical stress, a uniform induction time avoiding diurnal variations in hormone concentrations, or a sex difference (all Duthie's patients being male). In our studies, 15 of the patients receiving etomidate had cortisol concentrations at the end of surgery below the normal laboratory limits of 280–690 nmol l⁻¹⁻¹. Although our previous study (Moore et al., 1985) showed a significant and comparable increase in ACTH concentration in patients receiving either thiopentone or etomidate by infusion, the results presented here do not agree with the view of Duthie and colleagues that the effect of a bolus dose of etomidate is to cause partial inhibition of the 11β-hydroxylase enzyme without significant adrenocortical suppression.

J. Sear

REFERENCES


SIR,—Thank you for allowing us the opportunity to reply to the letters of Drs Fassoulaki, Sear, and Byrne and Yeoman.

The response of cortisol to adrenocorticotropic hormone (ACTH) is rapid and concentrations of the two hormones quickly attain equilibrium. Therefore, differential changes in concentration of the type suggested by Dr Fassoulaki would not have been apparent in the sampling regimen we used. Also, our regimen would not detect changes occurring only at 3 h after induction of anaesthesia.

It is difficult to make a quantitative comparison of the surgical "stress" imposed on our patients and those of Dr Sear, since plasma ACTH concentrations were variable in ours and not reported in theirs. However, the much higher plasma cortisol concentrations after surgery reported by Dr Sear suggest that the differences between the reports may be explained by differences in surgical "stress".

The locus of action of etomidate is not in dispute. We presented unequivocal evidence of an inhibition of 11β-hydroxylase activity and allude in our discussion to other studies which suggest that etomidate may have additional effects earlier in the steroid biosynthetic pathway. These effects would not have been apparent from the assays we performed, but have been detailed elsewhere (Vanden Bossche et al., 1984).

D. J. R. DUTHIE
Sheffield

REFERENCES


INTRATHECAL MORPHINE AND MULTIPLE FRACTURED RIBS

SIR,—Intrathecal morphine has been used extensively to provide pain relief both in the postoperative period, and in patients with cancer. It has not, however, to date been used in the treatment of thoracic injuries.

This case report illustrates the satisfactory use of intrathecal morphine in a patient with thoracic as well as abdominal injuries.

A 63-year-old woman was admitted to Casualty after falling down the stairs at home. She had a ruptured stomach, and multiple fractured ribs on her left side, with a flail segment. There were no other associated injuries, and she was not severely shocked. Following initial resuscitation in Casualty, and surgical repair of her ruptured stomach in theatre, the trachea was extubated and the patient was transferred to the intensive care unit with a urinary catheter, an arterial cannula, a central venous catheter, and peripheral venous cannula in position. On arrival in the intensive care unit she was haemodynamically stable. Fluid restriction was used, humidified oxygen was administered by a face mask, and arrangements were made with the physiotherapy department for intensive chest physiotherapy. It was decided to use intrathecal morphine as the method of pain relief instead of intercostal nerve block, extradural morphine, or extradural bupivacaine.

Lumbar puncture was performed under strict aseptic conditions, with the patient in the lateral position. L3-4 and L4-5 spaces were chosen on alternate days. Following identification of the subarachnoid space with a 25-gauge spinal needle, 1 mg (1 ml) of preservative-free morphine was injected with physiological saline 4 ml through a bacterial filter. Following injection, the patient was kept supine for at least 1 h, and her respiratory and cardiovascular systems were monitored.

The patient experienced excellent pain relief throughout the 7-day period. Onset of analgesia usually took 15–20 min, and was complete in 45–60 min. The quality of the pain relief was such that the ends of the fractured ribs could be moved against each other without any discomfort whatsoever. The patient was able to cough, take deep breaths, and tolerate frequent vigorous chest physiotherapy. She was able to sit out of bed quite soon after her operation, and was ambulant at a very early stage.

Her cardiovascular and respiratory systems remained relatively stable (table I), her respiratory rate varying between