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# The Use of Etomidate in the Management of Severe Head Injury

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**Abstract.** The effects of continuous and supplementary bolus dose administration of etomidate have been investigated in ten artificially ventilated patients in traumatic coma. Continuous infusion of etomidate (5 – 25 μg/kg/min) proved to be a practical and safe means of sedating these patients and appeared to control moderately elevated ICP. Additional bolus doses of etomidate (0.2 mg/kg) always reduced acutely elevated ICP (>20 mmHg), which fell by a mean of 33%. However, MAP usually fell, and occasionally serious hypotension occurred. Of a total of 61 bolus dose administrations which were analysed, CPP rose on 40 occasions, fell on 19 and was unchanged twice. There was a weak correlation between the control level of ICP and the magnitude of the fall in ICP in response to the bolus dose of etomidate ($r = 0.51$, $p < 0.001$). Bolus doses of etomidate given just before noxious stimulation, for example chest physiotherapy, prevented or limited the expected rise in ICP (with bolus mean change in ICP = $-2.7 \pm 6.9$ mmHg, without bolus mean change in ICP = $+7.0 \pm 6.4$ mmHg). Again MAP tended to fall following the bolus dose. Overall CPP tended to fall slightly following stimulation whether or not a bolus dose was administered ($-3.2 \pm 11.1$ mmHg and $-4.9 \pm 11.5$ mmHg respectively). However, when the bolus of etomidate was not given, occasional dramatic and dangerous rises in ICP were seen, in spite of the infusion, during which CPP fell to critical levels. This very rarely occurred when the bolus had been given. Furthermore, serious episodes of hypotension in response to etomidate administration appeared to occur mainly in patients who were relatively hypovolaemic.

**Key words:** Head injuries – Critical care – Etomidate

The intensive care management of patients with severe head injury is directed towards prevention of secondary cerebral damage caused by neuronal ischaemia/hypoxia. Treatment is therefore aimed at controlling raised intra-cranial pressure (ICP), maintaining arterial blood pressure (BP) and ensuring adequate oxygenation.

Adequate sedation of these patients is essential in order to avoid hypertension and rises in ICP in response to coughing, movement and resisting the ventilator. The rise in ICP is usually greater than the increase in mean arterial pressure (MAP) so that, generally, cerebral perfusion pressure (CPP) falls. Patients are particularly at risk when stimulated, for example by chest physiotherapy [8]. Traditionally, intermittent intravenous administration of analgesics, muscle relaxants and sedatives has been employed, with the risk of unexpected arousal, often in response to stimulation, causing dangerous rises in ICP. Clearly the uninterrupted, controllable sedation provided by a continuous intravenous infusion would be preferable, supplemented if necessary by bolus doses prior to noxious stimulation. A relatively short-acting and non-cumulative agent is required since this allows neurological assessment and early weaning from IPPV.

It is known that many intravenous anaesthetic agents reduce ICP [4, 6, 12 – 14, 16, 22 – 26, 28] and cerebral blood flow (CBF) [10, 17, 19, 20], probably in response to a reduction in cerebral metabolic demand [17, 19, 20]. It has also been shown that both thiopentone and althesin can limit the rise in ICP which occurs in response to physiotherapy [15]. A major disadvantage of many intravenous agents is that they may depress the cardiovascular system, thereby reducing MAP and thus CPP [14, 22 – 25]. This is particularly true of the barbiturates [14, 22 – 24], the effects of which are also cumulative. Althesin has the added disadvantage of a relatively

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high incidence of adverse reactions [2] and concern has been expressed as to the likely effects of continuous intravenous administration of the solubilising agent Cremophor EL in large doses for long periods of time. Etomidate, a carboxylated imidazole derivate, is an intravenous anaesthetic agent which causes minimal cardiovascular depression [9, 11], is rapidly inactivated, non-cumulative [13], does not release histamine [5] and is now available as a concentrated solution in alcohol. It has also been shown to reduce CBF [10, 19] and ICP [4, 6, 16, 22–24].

We have investigated the effects of continuous and supplemetary bolus dose administration of etomidate in patients being artificially ventilated following severe head injury. The purpose of the study was to determine whether:

1. A continuous moderate dose infusion of etomidate would provide safe, adequate sedation and control ICP in artificially ventilated patients with severe head injuries,
2. additional bolus doses of etomidate would reduce acutely raised ICP, without jeopardising CCP and
3. additional bolus doses of etomidate would prevent, or limit, surges in ICP in response to noxious stimuli, without jeopardising CPP.

## Method

Ten consecutive patients (eight male, two female; age range 3–37 years) admitted to the intensive care unit (ICU) with severe head injuries (Glasgow coma score <8) were studied. Five patients had intracranial haematomas evacuated: there were one intracerebral, one extradural, two subdurals and one combined intracerebral and subdural. Of the remaining patients three had diffuse swelling, one had oedema predominantly affecting the left hemisphere and the other had diffuse cerebral damage and a normal CAT scan.

### *Monitoring*

A teflon catheter of appropriate size was introduced into a radial artery to allow continuous blood pressure recording and frequent sampling of arterial blood. The central venous pressure (CVP) was measured using a teflon cannula inserted via the right internal jugular vein. Bell and Howell type 4/327/I pressure transducers were used for both measurements (Simonsen and Weel Ltd).

ICP was monitored using a subdural pressure transducer, which was calibrated prior to insertion, the zero of which could be checked in situ as required (Gaeltec Ltd, Dunvegan, Isle of Skye) [7].

The EEG was continuously monitored using three scalp needle electrodes connected to a cerebral function monitor (Par Medex Ltd) and full conventional EEGs were performed at intervals.

ICP, BP, CVP and cerebral function were continuously recorded on a Devices M19 4 channel chart recorder with three 3559 transducer amplifiers for the pressure measurements. CPP was calculated and displayed digitally.

### *Treatment*

Intermittent positive pressure ventilation was adjusted to achieve an arterial $PCO_2$ of between 3.3 and 4.7 kPa (25–35 mmHg) and supplemental oxygen was used to ensure that arterial blood was fully saturated with oxygen. Intravenous opiates (usually phenoperidine 1–2 mg) were given at regular intervals to provide analgesia. In some cases it was necessary to administer pancuronium 2–4 mg intravenously in order to prevent the patient resisting the ventilator.

Every attempt was made to ensure that cerebral perfusion pressure remained greater than 60 mmHg.

Diuretics were used only when the ICP rose consistently above 20–25 mmHg. Initially mannitol (0.3 g/kg) was given intravenously not more often than every 6 h. All except one patient received mannitol at some time during their hospital admission, although only five required repeated administration of this agent. If on any occasion the raised ICP failed to respond to mannitol, this was discontinued and 20 mg of frusemide was given intravenously, followed by six hourly intravenous acetazolamide 250 mg. Crystalloid fluid intake was restricted to 5% dextrose (1 ml/kg/h) unless special circumstances required modification of this regime.

Prophylactic anti-convulsant therapy consisted of intramuscular phenobarbitone eight hourly (60 mg in adults, 5 mg/kg for children), if necessary supplemented with phenytoin.

On arrival in the ICU a continuous intravenous infusion of etomidate was started via a central venous line. The concentrated preparation of etomidate in alcohol (125 mg in 2 ml) was diluted to 50 ml and administered using an infusion pump (IMED 927). The initial rate of the infusion was 5 μg/kg/min. If necessary this was then adjusted to provide a clinically satisfactory level of background sedation and to control ICP. The infusion rate varied from 5 to 25 μg/kg/min.

Before undertaking essential stimulating procedures (e.g. chest physiotherapy, endotracheal suction, turning the patient, insertion of intravascular catheters) an intravenous bolus dose of etomidate (0.2 mg/kg) was administered. The procedure was timed to commence approximately one minute after the bolus injection.

Acute, severe elevations of ICP were also treated with bolus doses of etomidate (0.2 mg/kg). If further rises in ICP occurred the bolus dose was followed by the administration of diuretics and/or increasing the rate of the etomidate infusion up to a maximum of 25 μg/kg/min.

All events, procedures and drug treatment were noted on the 4 channel chart recording which was then analysed retrospectively. Recordings were obtained for as long as the patient was being artificially ventilated (up to 7 days). The changes in mean arterial blood pressure (MAP), ICP and CPP during procedures preceded by a bolus injection of etomidate were compared with the changes occurring in response to a similar procedure when the bolus dose had been accidentally omitted. Comparisons were only made between consecutive events when the baseline ICPs were similar. Consequently only a few observations were obtained for each patient except in those who were ventilated for long periods. The changes in MAP, ICP and CPP when a bolus dose of etomidate was administered to control an acute rise in ICP were also noted.

The data for the changes in mean ICP represent the maximum observed change from the immediately preceding level. If during any period of noxious stimulation the ICP fell, but then subsequently rose, the figure noted is the maximum rise in pressure which occurred. The MAP was calculated according to the formula MAP = diastolic pressure + 1/3 (systolic-diastolic pressure). The changes in MAP represent the maximum change, except if a fall was followed by an increase in pressure the maximum decrease was used to calculate CPP. CPP was calculated as the difference between the MAP and the mean ICP. CVP was invariably low and it was not therefore necessary to take it into account when calculating CPP.

## Results

The continuous infusion of etomidate provided clinically satisfactory sedation for these patients and no complications attributable to this agent were seen. Provided that the circulating volume was maintained cardiovascular depression was not a problem. Thrombophlebitis was avoided by infusing the drug via a central vein and abnormal muscle movements were not troublesome. In these comatose patients it was not possible to make an accurate assessment of neurological recovery time following cessation of the infusion. However in three patients analysis of the CFM trace revealed that following a bolus dose of etomidate the mean time to maximum CFM depression was 3.1 ± 2.0 min ($n$ = 99) and that the mean time for recovery of the CFM to its previous level was 18.8 ± 8.9 min ($n$ = 101) (Fig. 1). Furthermore resumption of spontaneous respiration was usually possible without discontinuing the infusion and this al-

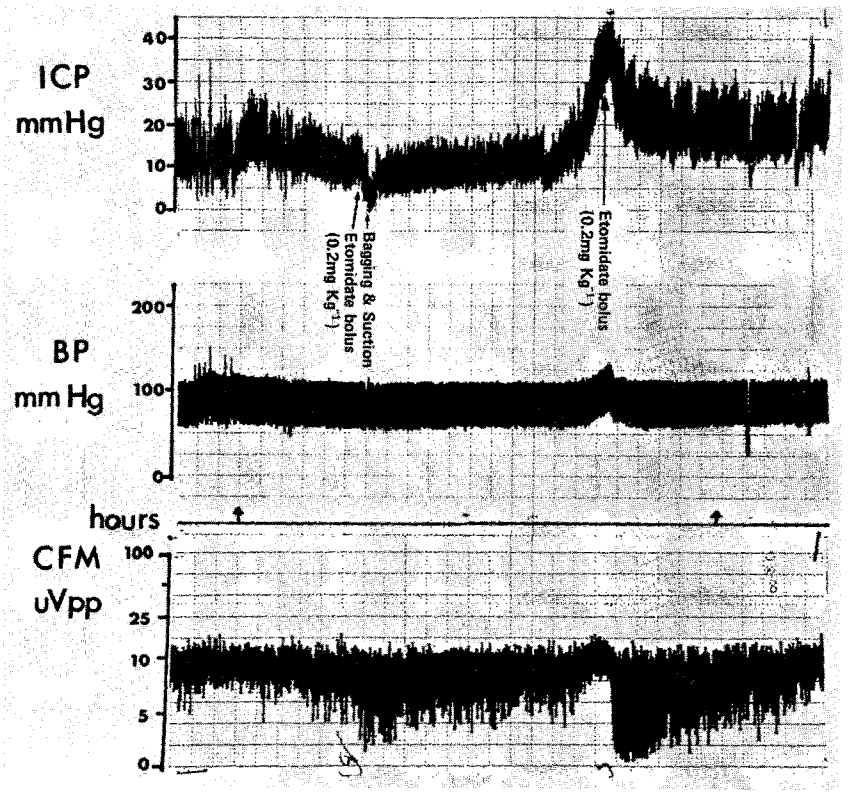



**Fig. 1.** Effect of bolus dose of etomidate 10 mg on ICP, MAP and CFM. Note the effect on the lower margin of the CFM trace which is depressed to near zero, whilst the upper margin is little affected; this picture is equivalent to a burst suppression pattern on the EEG

lowed continuing control of the ICP during weaning from IPPV.

In most cases increasing the rate of the infusion successfully controlled moderately elevated ICP, but two of the ten patients in this study (one with a subdural, the other with combined intracerebral and subdural haematomas) were admitted to the unit with ICPs >35 mmHg, which continued to rise progressively despite aggressive management, including increasing the rate of the infusion to 25 μg/kg/min, and the administration of diuretics. These patients are not, therefore, included in the studies of the effects of bolus dose administration.

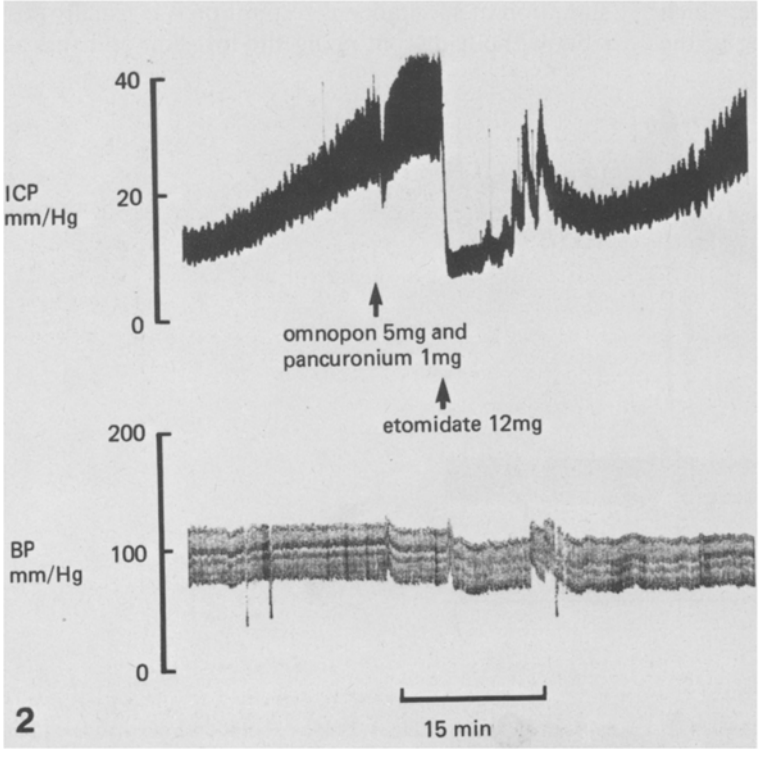
Six patients received bolus doses of etomidate (0.2 mg/kg) to control acute rises in ICP to 20 mmHg or higher (Table 1). In all cases the bolus dose successfully reduced the elevated ICP, with a mean fall for all patients of 9.4 ± 6.2 mmHg (33%) (Figs. 2 and 3). However, usually MAP also fell (Fig. 2), and occasionally serious hypotension occurred. Overall MAP fell by a mean of 6.7 ± 7.7 mmHg so that mean CPP rose on average by 2.9 ± 7.8 mmHg. Of the total of 61 bolus dose administrations, CPP rose on 40 occasions, fell on 19 and was unchanged twice. In general changes in CPP were small and on only four occasions did CPP fall by >10 mmHg. Following the bolus of etomidate CPP was less than 40 mmHg on nine occasions (in all cases CPP was <46 mmHg prior to the bolus dose) and less than 30 mmHg only twice (in these cases CPP was <32 mmHg before bolus dose administration).

**Table 1.** The effect of a bolus dose of etomidate on ICP, MAP and CPP [$\bar{x}$ (SD)] in patients with acutely elevated ICP

| Patient | Control ICP (mmHg) | ΔICP (mmHg) | ΔMAP (mmHg) | ΔCPP (mmHg) | *n* |
|---|---|---|---|---|---|
| 1 | 27.3 (5.5) | −5 (4.0) | −9.3 (4.6) | −4.3 (2.3) | 3 |
| 2 | 32.4 (5.5) | −13.6 (6.6) | −9.8 (9.3) | 3.8 (8.7) | 17 |
| 3 | 25.3 (4.0) | −13.7 (5.8) | −4.4 (4.4) | 9.3 (6.7) | 12 |
| 4 | 26.4 (2.7) | −6.4 (2.8) | −18.2 (10.2) | −10.0 (4.9) | 5 |
| 5 | 31.0 (0) | −3.0 (0) | −7.0 (0) | −4.0 (0) | 1 |
| 6 | 27.2 (4.5) | −5.6 (3.1) | −2.7 (3.3) | 2.8 (3.5) | 23 |
| Total | 28.3 (5.2) | −9.4 (6.2) | −6.7 (7.7) | 2.9 (7.8) | 61 |

There was a weak correlation ($r = 0.51$, $p < 0.001$) between the control level of ICP and the magnitude of the change in ICP in response to the bolus dose of etomidate (Fig. 4). There was, however, no correlation between the control level of ICP, or CPP, and the change in CPP.

Table 2 shows the effect of stimulating procedures on ICP, MAP and CPP with and without a bolus



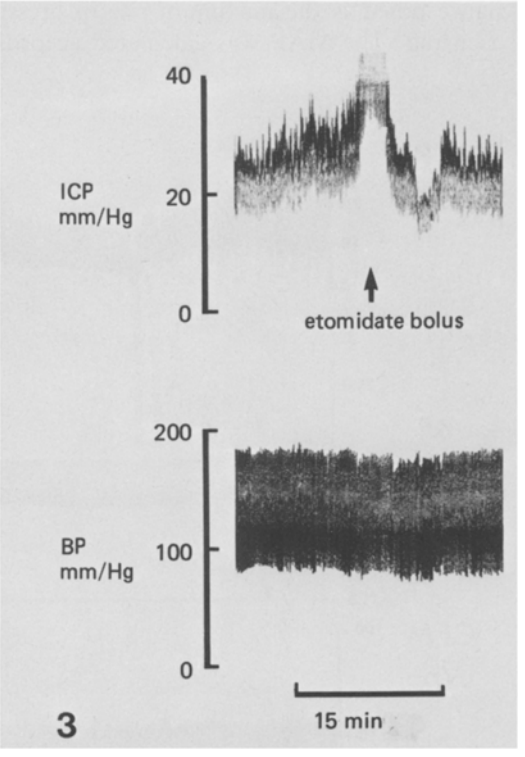




**Fig. 2.** Transient effect of omnopon and pancuronium and of etomidate in a patient with progressive rise in ICP. Notice the small fall in MAP following the bolus of etomidate

**Fig. 3.** A bolus dose of etomidate reduces elevated ICP with only a minimal effect on MAP

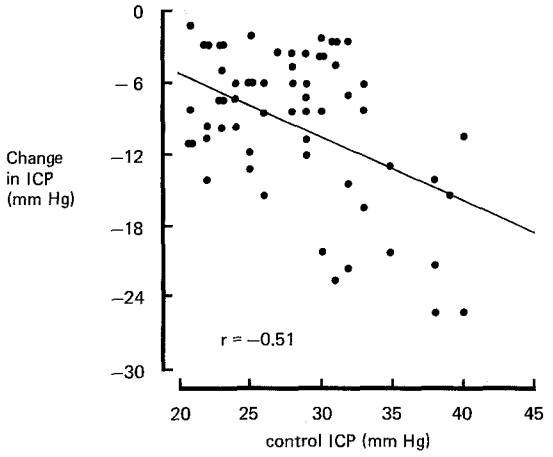



**Fig. 4.** The change in ICP following a bolus dose of etomidate (0.2 mg $kg^{-1}$) plotted against the ICP immediately prior to bolus dose administration. The regression line is also shown

dose of etomidate. Bolus doses of etomidate prevented, or limited, rises in ICP in response to noxious stimulation (Fig. 5) and in six of the patients mean ICP actually fell when stimulation was preceded by a bolus dose (Fig. 6). Overall mean ICP fell slightly ($-2.7 \pm 6.9$ mmHg) following stimulation preceded by a bolus of etomidate, whereas without the bolus dose it rose by $7 \pm 6.4$ mmHg in response to stimuli. Analysis of variance showed that there was no significant difference between the baseline ICPs in the two groups ($0.05 < p < 0.1$), but that the change in ICP in response to stimulation was significantly different ($p < 0.001$) with and without the bolus dose.

MAP also fell following the bolus dose, whereas stimulation without a bolus caused a rise in MAP. Analysis of variance showed that the initial blood pressures were comparable, and that the response to noxious stimulation was significantly different ($p < 0.001$) with and without preliminary bolus injection of etomidate.

CPP tended to fall slightly overall whether or not a bolus dose was administered (mean $-3.2 \pm 11.1$ mmHg and $-4.9 \pm 11.5$ mmHg respectively). Analysis of variance confirmed that there was no significant difference between either the control level of CPP, or the change in CPP between the two groups.

## Discussion

Autopsy of patients dying after severe head injury has demonstrated that more than 80% have pathological evidence of raised ICP and areas of ischaemic cerebral damage [1]. Prevention of this secondary cerebral damage is based on the maintenance of an adequate CPP by controlling ICP and maintaining an adequate MAP.

Techniques currently employed to control ICP include artificial ventilation, the administration of osmotically active agents, diuretics and, in some centres, steroids. However, many of these are of unproven benefit and all may be associated with undesirable side effects.

The use of intravenous anaesthetic agents to control ICP is therefore attractive, either as an alternative or as a supplement to some of these techniques. A continuous infusion of such drugs is also a convenient method of providing a constant and predictable level of sedation. Furthermore it is possible that, particularly in high doses, the reduction in cerebral metabolic demand both at rest and in response to stimulation, together with the control of any seizure discharge, may help to protect the brain from secondary ischaemic damage.

It is now well established that etomidate reduces CBF and ICP both in normal individuals and in patients with intracranial pathology [4, 6, 10, 16, 19, 22–24]. Renou et al. showed that etomidate reduced both cerebral oxygen consumption and regional cere-

**Table 2.** Change in ICP, MAP and CPP [$\bar{x}$ (SD)] in response to stimulating procedures with and without a bolus dose of etomidate (0.2 mg/kg)

| Patient | With bolus of etomidate | | | Without bolus of etomidate | | | |
|---|---|---|---|---|---|---|---|
| | ΔICP (mmHg) | ΔMAP (mmHg) | ΔCPP (mmHg) | ΔICP (mmHg) | ΔMAP (mmHg) | ΔCPP (mmHg) | *n* |
| 1 | −4.0 (2.3) | −5.8 (4.2) | −1.8 (4.0) | +3.2 (1.7) | −2.0 (7.7) | −1.2 (8.0) | 6 |
| 2 | +6.7 (2.3) | −14.6 (6.8) | −21.3 (6.6) | +14.4 (7.5) | −1.1 (4.0) | −15.6 (7.0) | 7 |
| 3 | −11.5 (7.2) | −6.0 (6.3) | +5.4 (10.8) | +12.0 (7.3) | +1.7 (12.3) | −10.3 (12.3) | 15 |
| 4 | −3.2 (2.7) | −17.5 (6.9) | −14.3 (8.4) | +6.5 (3.4) | +2.5 (12.1) | −4.0 (9.9) | 6 |
| 5 | −3.6 (2.9) | −6.3 (6.6) | −2.6 (4.8) | +0.75 (1.6) | −5.3 (6.8) | −6.0 (6.8) | 8 |
| 6 | −4.3 (4.0) | −2.9 (4.1) | +1.4 (5.9) | +6.3 (5.5) | +6.3 (5.3) | 0.0 (5.3) | 8 |
| 7 | −0.2 (5.5) | −0.6 (6.9) | −0.4 (10.2) | +6.0 (5.8) | +3.4 (12.8) | −2.6 (13.7) | 18 |
| 8 | +1.7 (3.3) | −4.7 (7.9) | −6.3 (7.2) | +4.7 (1.7) | +4.8 (13.4) | +0.08 (12.3) | 12 |
| Total | −2.7 (6.9) | −5.9 (8.0) | −3.2 (11.1) | +7.0 (6.4) | +2.1 (10.9) | −4.9 (11.5) | 80 |

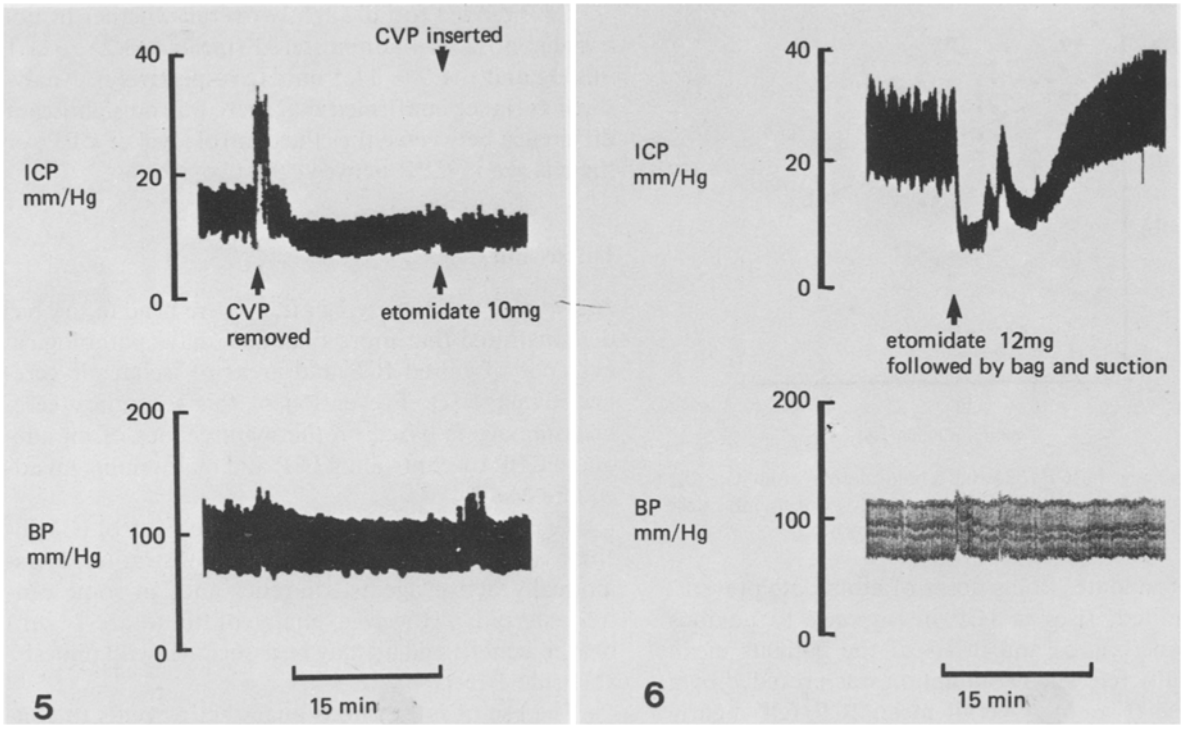



**Fig. 5.** The effect of noxious stimulation with and without prior administration of a bolus of etomidate

**Fig. 6.** The protective effect of a bolus dose of etomidate administered prior to manual hyperventilation and suction. Note the stability of MAP

bral blood flow in patients undergoing carotid angiography. Furthermore cerebrovascular reactivity to carbon dioxide was maintained [19]. Reductions in ICP in response to bolus doses of etomidate have been demonstrated both in patients with space occupying lesions [4, 15] and in those in traumatic coma [23]. Moss et al. found a mean fall in ICP of 6.8 mmHg (41.5%) in response to etomidate 0.2 mg/kg IV in 10 anaesthetised patients with intracranial pathology and a mean baseline ICP of 16.4 mmHg [16]. This is similar to the fall in ICP demonstrated by Cunitz et al. in neurosurgical patients with hydrocephalus or space occupying lesions [4]. They showed that induction of anaesthesia with etomidate 0.15 mg/kg reduced the mean baseline ICP of 15.4 mmHg to 10.8 mmHg. We have found that in a group of ventilated head injury patients bolus doses of etomidate 0.2 mg/kg reduced more substantially elevated ICP (mean baseline ICP 28.3 mmHg) by a mean of 9.4 mmHg (33%). This can be compared with a 26% fall in ICP found by Schulte am Esch in a group of intensive care patients with primarily elevated ICP (mean ICP = 27 ± 11.7 mmHg) including some with severe head injury, given boluses of etomidate of 0.3 mg/kg [23].

Unfortunately, although most intravenous anaesthetic agents will reduce ICP there is always the danger of cardiovascular depression and a fall in MAP which may reduce CPP. Various workers have demonstrated minimal cardiovascular effects when etomidate is used as an induction agent in man [9, 11, 21], although Prakash et al. have demonstrated a dose dependent depression of cardiac output, arterial pressure and left ventricular dp/dt max when etomidate infusions were administered to pigs [18]. These effects were relatively minor at a dose equivalent to that required for surgical anaesthesia, but cardiovascular depression might be anticipated in patients given higher doses of etomidate.

In our study of patients in traumatic coma with significant intracranial hypertension MAP fell by 6.7 mmHg and overall CPP increased slightly with etomidate. However, in 30% of instances CPP fell following the bolus dose administration, and in three of the six patients CPP tended to be reduced by etomidate. Furthermore the number of observations was greater in those who responded favourably to bolus dose administration (52:9). On the other hand, changes in CPP were generally small and falls of >10 mmHg occurred on only four occasions. Following

bolus dose administration CPP was less than 40 mmHg on nine occasions and less than 30 mmHg twice. On five of these CPP was already <40 mmHg prior to administration of etomidate. The critical level of perfusion pressure is not known but Brierley et al. [3] have shown that in Rhesus monkeys brain damage only occurred when CPP was <25 mmHg for >15 min. Schulte am Esch et al. found that in a group of intensive care patients with primarily elevated ICP, including some in traumatic coma, boluses of etomidate induced a transient fall in MAP by a mean of 8.0% (8.5 mmHg). However, ICP also fell by a mean of 26% so that overall CPP was unchanged [23]. In a later study in patients with severe brain injury the same group of workers confirmed the minimal effect of etomidate on MAP and CPP [24]. Moss et al. have also demonstrated a small decrease in MAP in anaesthetised neurosurgical patients given etomidate, and on average CPP fell slightly. In their study CPP increased in 50% and decreased in 50%, but always remained adequate [16].

Because of the shape of the cerebral compliance curve, the response to administration of bolus doses of intravenous anaesthetic agents will clearly depend on the degree of pre-existing intracranial compression. As might have been anticipated we have shown that the higher the initial ICP the greater the response to etomidate (Fig. 4). Moss et al. also found a correlation between the control level of ICP and the magnitude of the fall in ICP in response to etomidate administration ($r = 0.624$), although they had insufficient numbers to demonstrate statistical significance [16]. Furthermore the magnitude of the fall in MAP in response to bolus dose administration may depend partly on the pre-treatment cardiovascular status including the circulating blood volume. These variables must therefore be considered when comparing the results of such studies and in particular the changes in CPP.

The administration of a bolus dose of etomidate would therefore appear to be a convenient and effective way of lowering ICP in head injured patients as well as in those with intracranial hypertension due to space occupying lesions. However in some instances MAP may also fall sufficiently to reduce CPP, although serious reductions in CPP are unusual.

Moss and his colleagues have previously reported that both althesin and thiopentone can prevent the rises in ICP which are known to occur in response to chest physiotherapy and that this was achieved without significant arterial hypotension [15]. We have confirmed that bolus doses of etomidate will prevent, or limit, the expected rise in ICP in response to noxious stimulation and that CPP is usually well maintained. Occasionally significant falls in MAP occurred, particularly in the first two patients studied, and sometimes this led to potentially serious reductions in CPP. However in the first patient marked falls in CPP also occurred when the bolus dose was omitted. We feel that significant hypotension in response to etomidate usually only occurs in relatively hypovolaemic patients and can be at least partially prevented by more aggressive replacement of the circulating volume with colloids. Indeed once we became aware of the importance of this, large falls in MAP were rare and when they did occur rapid expansion of the circulating volume was undertaken. Even without prior administration of etomidate ICP sometimes remained unaltered in the face of noxious stimulation, and sometimes MAP fell slightly. Overall CPP tended to fall slightly whether the bolus was administered or not and it might be argued, therefore, that the danger of unpredictable hypotension and falls in CPP might outweigh the advantages of bolus dose administration. However when the etomidate was omitted, occasional dramatic and dangerous rises in ICP (>10 mmHg) were seen during which CPP fell to critical levels. This almost never occurred when the bolus had been given. White and his colleagues, on the other hand, were unable to demonstrate a protective effect of either thiopentone of lignocaine in unparalysed, comatose head injury patients [27]. In the study by Moss and his colleagues [15], muscle relaxants were administered immediately prior to stimulation, whilst our patients were paralysed as necessary. This suggests that a degree of muscle relaxation is required if bolus doses of intravenous anaesthetic agents are to achieve a protective effect.

The onset of action of etomidate in reducing ICP is rapid, but its effect is relatively short-lived. In our study using boluses of 0.2 mg/kg of etomidate, the maximum fall in ICP usually occurred within 60 s, and the effect seemed to last for between 10 and 20 min. This may be related to our initial CFM findings in three of the patients in whom the mean time to maximum CFM depression was 3.1 ± 2.0 min, while the CFM returned to baseline in 18.8 ± 8.9 min (Fig. 1). This time course is similar to that described by Schulte am Esch et al. [23] who used boluses of etomidate of 0.3 mg/kg and showed that the maximum fall in ICP occurred at 3 min and that ICP returned towards baseline within 20 min. Moss et al. [16] used the same dose of etomidate as was used in this study (0.2 mg/kg) and found that ICP had returned to baseline levels within 10 min in only two of ten patients studied. In our patients the protective effect of boluses of etomidate in relation to noxious stimulation appeared to last for between 5 and 15 min (Fig. 6). Consequently the timing of the bolus dose in relation to stimulating procedures is crucial and it may be

necessary to administer repeated doses during prolonged procedures.

In conclusion, we have found a continuous infusion of etomidate to be a practical and safe means of sedating ventilated head injury patients and we feel that such an infusion helps to control moderately elevated ICP. However in two patients with severe intracranial hypertension, unresponsive to other measures, infusing etomidate at up to 25 μg/kg/min was ineffective. Bolus doses of etomidate both reduce acutely elevated ICP and prevent or limit the rise in ICP in response to noxious stimulation. Provided circulating volume is adequate, CPP is usually unchanged, although occasionally severe hypotension, which can be unexpected, may jeopardise perfusion pressure.

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