FURTHER EXPERIENCE WITH ETOMIDATE*

C.E. FAMEWO AND C.O. ODUGBESAN

ETOMIDATE is a short-acting non-barbiturate drug for the induction of general anaesthesia. It is a derivative of imidazolecarboxylate and has an ester group which is hydrolysed during metabolism in the liver and blood.¹ In the first 24 hours, approximately 75 per cent of a single dose is excreted by the kidney while about 13 per cent is excreted in the faeces. Etomidate is a hypnotic without any analgesic property. Subsequent to our preliminary report on Etomidate² we have further investigated some aspects of this drug, including the pain on injection, the occurrence of myoclonic movements and the effect of Etomidate on intraocular pressure.

METHOD

A total of 100 patients undergoing minor surgical procedures were studied. There were 45 male and 55 female patients. The youngest patient was ten years of age while the oldest was 65 years.

Premedication

Premedications were given 30 to 60 minutes before induction of anaesthesia with Etomidate. Thirty patients were premedicated with meperidine (Pethidine) and atropine, 30 patients with diazepam (Valium) and atropine, while 40 patients were not premedicated on the ward but received atropine intravenously shortly before induction.

Induction of Anaesthesia

Anaesthesia was induced by intravenous injection of Etomidate in a dose of 0.3 mg/kg body weight. The duration of injection was either 20 seconds or 40 seconds. The site of injection was either the dorsum of the hand or near the antecubital fossa.

Measurements and observations

Before anaesthesia was induced with Etomidate, blood pressure (systolic and diastolic), pulse rate and respiratory rate and depth were

recorded. Intraocular pressure was measured in 40 patients, while the time to verbal contact was noted in 30 patients who were allowed to recover spontaneously from single sleep doses of Etomidate without any other supplement.

RESULTS

Etomidate in the dose used generally gave a fast and smooth induction of anaesthesia. The average time from induction to loss of consciousness was about 16 seconds.

Pain at the site of injection

Of the 34 patients who had the injection site on the dorsum of the hand 14 complained of pain while only four patients out of 30 complained of pain when the injection site was near the antecubital fossa. Narcotic premedication did not influence the incidence of pain.

We subsequently buffered the pH of Etomidate by dissolving the powder in sodium bicarbonate. This increased the pH from 3.9 to 7.9. When this buffered solution was used only three out of the 20 patients who had their injection on the dorsum of the hand complained of pain. None of the 16 patients who received the buffered solution in the larger veins of the antecubital fossa complained of pain during injection (Table I).

Myoclonic movements

A total of 32 out of the 100 patients had myoclonic movements. These were usually transient and self-limiting. The severity of the myoclonic movements were very much reduced when injection of Etomidate was made slowly over 40 seconds rather than over 20 seconds. Neither premedication with diazepam nor pretreatment with pancuronium (0.015 mg/kg body weight) reduced the occurrence of myoclonic movements. *Excessive yawning* was observed in 25 per cent of patients at the time of induction with Etomidate. This, however, posed no problems.

Effect on Cardiovascular and Respiratory Systems

The blood pressure, heart rate and respiratory

*Paper presented at the Canadian Anaesthetists' Society Meeting, June 20-23, 1977.

TABLE I
PAIN DURING INJECTION OF ETOMIDATE

Injection site	Regular solution pH 3.9	Buffered solution pH 7.9
Dorsum of hand	14 of 34 (41.2) (41.2 per cent)	3 of 20 15 per cent
Antecubital fossa	4 of 30 (13.3 per cent)	Nil of 16

TABLE II
ETOMIDATE ANAESTHESIA

	Pre-induction	Post-induction
Mean blood pressure (mm Hg)	126/70	128/70
Mean Heart rate per minute	113	117
Mean respiration rate per minute	22	24

rate were not significantly changed following Etomidate anaesthesia (Table II).

Respiratory depth was generally well sustained. Some patients exhibited increased rate and depth of respiration. A few patients, however, had transient apnoea which did not require controlled ventilation, as spontaneous respiration returned within a few seconds.

Effect on Intraocular Pressure

This was measured in 40 patients using the Schiotz Tonometer with a 5.5 gm weight. Following Etomidate, there was a significant fall in the mean intraocular pressure from 15.52 mm Hg pre-induction to 10.51 mm Hg post-induction³ ($p < 0.001$).

Recovery from Etomidate anaesthesia

Thirty patients were allowed to recover spontaneously from single sleep doses of Etomidate. The mean time to regaining consciousness and verbal contact was 4.5 minutes. Patient acceptability was good and we were impressed by the rapid recovery and the absence of hangover.

DISCUSSION

Etomidate rapidly produces sleep like thiopentone but without the depression of the cardiovascular and respiratory systems often seen with thiopentone. This observation agrees with other published studies.⁴⁻⁶ These are desirable features

of Etomidate as an induction agent. The occurrence of pain during Etomidate induction, however, is undesirable to the patient and certainly not pleasing to the anaesthetist. Analgesic premedication did not reduce the occurrence of pain. The acidic pH of Etomidate solution is probably responsible, at least in part, for the occurrence of pain during Etomidate injection because the buffered solution with pH 7.9 noticeably reduced the occurrence and severity of the pain. The use of a big vein for injection also reduced the occurrence of pain, probably by a dilutional effect. Gooding and Corssen in their study⁶ similarly observed the absence of pain in patients who had Etomidate injection in the antecubital veins.

The other major side effect of Etomidate is the occurrence of myoclonic movements. Although undesirable they were no more distressing than the sometimes marked suxamethonium-induced fasciculations. Unlike the latter, however, pretreatment with a small dose of a non-depolarizing muscle relaxant (pancuronium 0.015 mg/kg) did not influence the occurrence of myoclonic movements.

Etomidate decreases intraocular pressure similar to the effect of thiopentone. This makes Etomidate a safe anaesthetic agent in situations where an increase in intraocular pressure is undesirable. The reduction in intraocular pressure was rather surprising in view of the occurrence of myoclonic movements involving the facial muscles in many of these patients.

SUMMARY

We report our further anaesthetic experience with Etomidate in 100 patients. The cardiovascular and respiratory systems were not significantly affected but intraocular pressure was reduced. The occurrence of pain during injection of Etomidate was unaffected by analgesic premedication but was reduced by using a solution buffered to a higher pH and by choosing a big vein for injection. The myoclonic movements often seen with Etomidate anaesthesia were transient and have so far not created any major problem; they were reduced by a slower speed of injection but unaffected by diazepam premedication or pre-treatment with low dose of a non-depolarizing muscle relaxant (pancuronium). Etomidate is a satisfactory alternative to thiopentone in situations where depression of the cardiovascular and respiratory systems are undesirable or where barbiturates are otherwise contraindicated and is a useful addition to the induction agents in our anaesthetic practice.

RÉSUMÉ

Nous présentons un rapport sur la poursuite de nos travaux sur l'Etomidate. Cent malades ont été soumis à l'étude.

Les systèmes respiratoires et cardiovasculaires sont peu affectés par cet agent. La pression intra-oculaire est abaissée.

La douleur à l'injection de l'Etomidate n'est pas modifiée par l'emploi d'une prémédication incorporant un analgésique; cependant, elle est moindre si l'on utilise une solution tamponnée de façon à élever le pH et si l'on choisit une grosse veine comme site d'injection.

Les mouvements myocloniques observés fréquemment avec cet agent ont été transitoires et n'ont causé aucun problème majeur. Ils étaient

diminués si l'injection était faite lentement; l'administration préalable de diazepam ou d'un curarisant à faible dose (Pancuronium) ne les prévenait pas.

L'Etomidate représente une alternative satisfaisante au thiopentone lorsque l'on doit éviter une dépression cardiovasculaire ou dans le cas de contre-indication à l'emploi de barbituriques. Nous considérons cet agent comme une addition utile à notre pratique anesthésique.

ACKNOWLEDGEMENT

We thank Professor S.A. Oduntan, Department of Anaesthesia, University of Ibadan for his support and useful suggestions during the study. Etomidate was supplied by Johnson & Johnson, Nigeria Ltd. (representing Janssen Pharmaceutica of Belgium).

REFERENCES

1. REMAMAN, R.S. & JANSSEN, P.A.J. Experimental pharmacology of Etomidate. Beerssen, Belgium, Janssen Pharmaceutica (1974).
2. FAMEWO, C.E. & ODUGBESAN, C.O. Clinical trial of Etomidate: preliminary observations on a new non-barbiturate induction agent. *Canad. Anaesth. Soc. J.* 24: 35-38 (1977).
3. FAMEWO, C.E., ODUGBESAN, C.O., & OSUNTOKUN, O.O. Effect of Etomidate on intraocular pressure. *Canad. Anaesth. Soc. J.* 24: 712-716 (1977).
4. MORGAN, M., LUMBAY, J., & WHITWAM, J. Etomidate, a new water soluble non-barbiturate intravenous induction agent. *Lancet* 9955-9956 (1975).
5. DOENICKE, A., GABANYI, D., LEMCHE, H., & SCHURK-BULCHIM. Circulatory behaviour and myocardial function after administration of three short I.V. hypnotics-etomidate, propanidid, and methothexital. *Anaesthesist* 23: 108-115 (1974).
6. GOODING, J.M. & CORSEN, D.G. Etomidate, an ultra-short-acting non-barbiturate agent for anaesthesia induction. *Anaesthesia and Analgesia Current Researches* 55: 286-289 (1976).