

Clinical study of etomidate emulsion combined with remifentanyl in general anesthesia

Digui Weng
Menghua Huang
Runnian Jiang
Rufu Zhan
Chunni Yang

Department of Anesthesiology,
Mindong Hospital Affiliated to Fujian
Medical University, Fuan, Fujian,
People's Republic of China

Background: The aim of this study was to investigate and evaluate the safety, recovery time, and side effects of general anesthesia with different doses of etomidate emulsion combined with remifentanyl.

Methods: One hundred ten patients of American Society of Anesthesiologists class 1 or 2 who underwent gynecological general anesthesia with a 1–3-hour operation time were randomly divided into the following groups: etomidate emulsion group 1 ([E1] $n = 30$); etomidate emulsion group 2 ([E2] $n = 30$); etomidate emulsion group 3 ([E3] $n = 20$); and propofol group ([P group] $n = 30$). For induction of anesthesia, 0.3 mg/kg etomidate emulsion, and the continuous remifentanyl infusion also to induce anesthesia ($0.1\text{--}0.3\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), was applied in all cases. Afterwards, continuous infusion of etomidate emulsion and remifentanyl, respectively (E1: $10\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and $0.1\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; E2: $15\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and $0.2\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; E3: $20\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and $0.2\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), and propofol (P group: $6\text{--}10\text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) were administered. Changes in blood flow kinetics and adverse reactions were noted and compared between the four groups.

Results: Both arterial blood pressure (BP) and heart rate (HR) decreased after induction of anesthesia ($P < 0.05$). Systolic (SBP) and diastolic (DBP) BP changed only slightly, and HRs were slightly infected in E1, E2, and E3. SBP, DBP, and HR during the operation all decreased significantly in P group ($P < 0.05$). Muscle tremor at the time of induction occurred in 13 cases (11.8%). Following etomidate emulsion anesthesia maintenance, postoperative agitation occurred in seven cases (8.75%), lethargy in 20 cases (25%), and vomiting in 19 cases (23.75%). No adverse reactions were found in P group.

Conclusion: Continuous infusion of etomidate emulsion at $10\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{minute}^{-1}$ combined with remifentanyl during anesthesia has the advantages of hemodynamic stability, quick wake-up, and few adverse reactions. Increasing the dose of etomidate emulsion increases the incidence of adverse reactions.

Keywords: etomidate emulsion, remifentanyl, general anesthesia

Introduction

Currently, remifentanyl and propofol is a common combination used in general anesthesia to obtain quick inductions and recoveries, although hemodynamic instability can occur.^{1–4} It has been confirmed that etomidate has little effect on hemodynamics and adrenal cortical inhibition. Corticoid suppression may stop, with recovery of corticoid function within 24 hours.^{1–15} Clinical use of etomidate as an anesthesia induction agent has been approved.^{1–15} Etomidate is a modulator of GABA_A receptors containing $\beta 3$ subunits⁴ and a carboxylated imidazole derivative with anesthetic and amnestic properties. It has no analgesic properties and has been used as an anesthesia induction agent. It has been approved for clinical use as an anesthesia induction agent.^{17–25}

Correspondence: Digui Weng
Department of Anesthesiology, Mindong
Hospital Affiliated to Fujian Medical
University, Fuan, Fujian, 355000,
People's Republic of China
Tel/Fax +86 137 0693 0791
Email wdgmdy813@163.com

Although etomidate, as an inhibitor of cortisol synthesis (11β -hydroxylase), is a preferred anesthetic agent for rapid-sequence intubation in critical illness, its use in critically ill patients may be associated with adrenal dysfunction, an increased rate of adrenal insufficiency, and mortality.^{28,29} Although the use of etomidate combined with remifentanyl, and propofol with remifentanyl, has been researched,³⁰ clinical investigation of etomidate emulsion combined with remifentanyl in maintenance of general anesthesia has not yet been reported, to our knowledge.

The Narcotrend (MonitorTechnik, Bad Bramstedt, Germany) is an electroencephalography (EEG) monitor designed to measure the depth of anesthesia.^{16,17} The Narcotrend software version used in this study includes a dimensionless Narcotrend Index (NI) from 100 (awake) to 0 (electrical silence). The raw EEG signal can be recorded by standard electrocardiogram (ECG) electrodes for single- and double-channel registration.

Accordingly, in this study, we aimed to investigate the effects of different doses of etomidate emulsion combined with remifentanyl on general anesthesia duration and, using the Narcotrend, to evaluate side effects of etomidate emulsion and improve postoperative morbidity and mortality.

Materials and methods

Patient selection

The investigation protocol conformed to ethical guidelines as set forth in the Declaration of Mindong Hospital Affiliated to Fujian Medical University, Fujian Province, People's Republic of China, after receiving approval for the investigation by the Human Subjects Review Committee and the Research Ethics Board of Mindong Hospital Affiliated to Fujian Medical University, and informed consent was obtained from each patient. One hundred ten patients scheduled for gynecologic surgery of 1–3 hours, of American Society of Anesthesiologists class 1 or 2, and aged 20 to 60 years, were enrolled in this study. Patients with anemia, shock, metabolic diseases, electrolyte disorder, or emulsion allergies were excluded, as were: pregnant women; patients abusing hormones or narcotic analgesic drugs; those with predicted or current airway difficulties; those with any cardiac, liver, pulmonary, or renal diseases; and those taking diuretics or any other medication known to interfere with the investigation parameters.

Patients were randomized via sealed-envelope assignment into four groups: etomidate emulsion group 1 ([E1] $n = 30$), etomidate emulsion group 2 ([E2] $n = 30$),

etomidate emulsion group 3 ([E3] $n = 20$), and propofol group ([P group] $n = 30$). Etomidate emulsion and midazolam were obtained from Xuzhou Enhua Zhiyao Limited Company (Xuzhou, People's Republic of China). Propofol was purchased from Fresenius Kabi (Bad Homburg, Germany). Vecuronium, remifentanyl, and fentanyl were obtained from Yichang Humanwell Pharmaceutical Co., Ltd. (Yichang, People's Republic of China). Flurbiprofen was purchased from Beijing Tide Pharmaceutical Co., Ltd (Beijing, People's Republic of China).

Anesthesia technique

All patients fasted for more than 8 hours before surgery and did not receive any premedication. All patients were monitored in the operating room using blood pressure (BP), ECG, blood-oxygen saturation (SPO_2), and Narcotrend instruments. Fifteen minutes before induction of anesthesia, 5 mL/kg balance liquid (physiological saline) was intravenously injected. Five minutes before tracheal intubation, 0.05 mg/kg midazolam was intravenously infused; 3 minutes before tracheal intubation, 3–4 $\mu\text{g/kg}$ fentanyl was intravenously injected; 2 minutes before tracheal intubation, 0.1 mg/kg vecuronium was intravenously injected; and 0.5 minutes before tracheal intubation, 0.3 mg/kg etomidate emulsion was intravenously injected. After full muscle relaxation, endotracheal intubation was carried out and intermittent positive pressure ventilation was established using a Datex-Ohmeda Aestiva[®]/5 (GE Healthcare, Little Chalfont, UK). One hundred percent oxygen was used at the rate of 1 L/minute. Ventilator settings ($V_T = 8\text{--}10$ mL/kg and respiratory rate (RR) = 12 times/min) were adjusted to maintain (end-tidal carbon dioxide) P_{ETCO_2} between 30–40 mmHg.

Anesthesia was induced with a 0.3 mg/kg etomidate emulsion bolus and a remifentanyl $0.1\text{--}0.3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{minute}^{-1}$ continuous infusion, then maintained by continuous infusion of etomidate emulsion. Depending on the group, the anesthesia was maintained by propofol infusion (P group: $6\text{--}10 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) or three different constant rate infusions of etomidate emulsion and remifentanyl (E1: $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and $0.1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E2: $15 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and $0.2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E3: $20 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and $0.3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, respectively). Intermittent bolus injections of vecuronium were used to maintain full muscle relaxation.

Thirty minutes before the end of surgery, 0.1 mg fentanyl and 50 mg flurbiprofen were administered intravenously and vecuronium infusion was stopped. Five minutes before the end of operation, 3 mg granisetron

was administrated by intravenous injection. When the surgery was complete, remifentanyl, etomidate emulsion, and propofol infusion were stopped. When spontaneous respiration was recovered, neostigmine was used to reverse residual muscle relaxation. When the NI was maintained at phases D and E, we adjusted the dose of remifentanyl (ie, infusion rate $0.1\text{--}0.3\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) to control hemodynamic changes. Awakening was considered as the moment when the patient opened their eyes after being called by their name. Analysis of extubation indications was divided into four grades: cough and swallowing reflex complete recovery; basic consciousness complete recovery and opening of the eyes when the name was called; $V_T > 6\ \text{mL/kg}$, $\text{RR} = 12\text{--}30$ times/minutes, muscle strength recovered time of flight (TOF) of ballistic $> 75\%$, and head elevation for more than 2 seconds; and BP, heart rate (HR), and ECG at normal levels.

Antiemetics were administered intravenously if patients experienced nausea or vomiting. All patients were prohibited administration of corticosteroids during and 24 hours after the operation. Postoperative analgesia was also prohibited.

Assessment of variables

The maximum and minimum systolic BP (SBP), diastolic BP (DBP), and HR values were continuously monitored in the hospital operating room immediately before surgery, before tracheal intubation, at the time of skin incision, and during the operation. The amount of drug injected was monitored. Durations of anesthesia, surgery, wake-up, and extubation were recorded. Side effects were observed and recorded during induction of general anesthesia, postoperatively, and at follow-up visits. The same surgical team performed all procedures on the investigation patients.

Statistical analysis

All statistical analysis was performed with SPSS 13.0. software (IBM Corporation, Armonk, NY, USA). Data were presented as mean \pm standard deviation. Analysis of variance (ANOVA) was used to test the significance of the differences

between two groups. Data were considered significantly different at the level of $P < 0.05$ and very significantly different at the level of $P < 0.01$.

Results

There were no significant differences between the four patient groups with regards to the demographic characteristics age, height, body weight, anesthetic duration, and operation duration (Table 1). No complications were observed, and no patient required blood transfusion during the overall investigation period.

As shown in Table 2, the SBP, DBP, and HR of the four groups decreased before tracheal intubation versus in hospital operating rooms pre-surgery ($P < 0.05$). The SBP and HR of P group patients and the SBP of E3 patients reduced at the time of skin incision (both $P < 0.05$). The SBP, DBP, and HR of P group patients decreased during the operation ($P < 0.05$ or $P < 0.01$). The SBP and DBP of E1, E2, and E3 patients decreased during the operation ($P < 0.05$), but their HRs showed no significant difference. The intraoperative SBP and HRs of P group patients decreased compared with skin incision ($P < 0.05$). The intraoperative SBP of E3 patients decreased compared with skin incision ($P < 0.05$). The maximum and minimum values of intraoperative SBP, DBP, and HR in P group decreased compared with skin incision ($P < 0.05$ or $P < 0.01$). The maximum and minimum values of intraoperative SBP, DBP, and HR in E2 and E3 showed no significant difference from skin incision ($P < 0.05$ or $P < 0.01$).

As Table 3 shows, the remifentanyl dose significantly decreased, comparing E1 to P group ($P < 0.05$), while E2 and E3 showed no significant difference. Durations of wake-up and extubation in E3 were prolonged ($P < 0.01$); E2 and P group showed no significant difference.

As Table 4 shows, of the groups receiving etomidate emulsion maintenance, 13 patients (11.8%) showed myoclonus during the induction of anesthesia; seven patients (8.75%) experienced postoperative agitation; 20 patients (25%) experienced postoperative sleepiness; and 19 patients (23.75%) experienced

Table 1 Demographic characteristics of the four groups (mean \pm SD)

Group	Patients, n	Age, years	Height, cm	Body weight, kg	Anesthetic duration, minutes	Operation duration, minutes
E1	30	38.45 ± 7.27	157.12 ± 9.15	60.12 ± 6.68	90.12 ± 18.56	79.83 ± 19.41
E2	30	37.03 ± 6.63	155.64 ± 8.22	57.47 ± 7.48	92.36 ± 16.57	81.35 ± 16.38
E3	20	39.73 ± 5.47	158.37 ± 7.45	58.36 ± 9.09	92.76 ± 17.09	83.45 ± 15.29
P	30	37.54 ± 7.17	158.14 ± 6.75	59.39 ± 8.35	90.36 ± 16.73	80.07 ± 16.32

Notes: Etomidate emulsion and remifentanyl, respectively: E1, $10\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and $0.1\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; E2, $15\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and $0.2\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; E3, $20\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and $0.2\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. Propofol: P, $6\text{--}10\ \text{mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$.

Abbreviation: SD, standard deviation.

Table 2 Hemodynamics of the four groups before and after anesthetization (mean \pm SD)

Parameter	Group	Patients, n	Before treatment	Before intubation	Skin incision	Maximum intraoperative	Minimum intraoperative
SBP (mmHg)	E1	30	123.4 \pm 12.7	103.8 \pm 10.6*	118.9 \pm 10.3	124.5 \pm 10.5	108.7 \pm 9.5*
	E2	30	121.5 \pm 10.6	101.3 \pm 9.0*	116.2 \pm 9.5	123.3 \pm 9.3	106.3 \pm 9.0*
	E3	20	121.9 \pm 10.2	103.3 \pm 8.6*	106.3 \pm 9.6* ^Δ	122.5 \pm 10.5	106.5 \pm 8.7*
	P	30	121.4 \pm 10.3	101.4 \pm 9.4*	103.6 \pm 9.3* ^Δ	109.3 \pm 9.0* ^Δ	93.9 \pm 8.6 ^{▽,Δ}
DBP (mmHg)	E1	30	74.2 \pm 10.6	66.8 \pm 9.4*	71.9 \pm 9.9	76.3 \pm 9.8	65.4 \pm 9.8*
	E2	30	72.6 \pm 7.2	65.3 \pm 8.4*	71.5 \pm 9.2	74.6 \pm 9.0	63.6 \pm 8.3*
	E3	20	72.4 \pm 6.1	63.0 \pm 8.5*	72.8 \pm 8.0	73.5 \pm 7.8	61.3 \pm 7.4*
	P	30	72.3 \pm 9.0	63.4 \pm 9.9*	70.6 \pm 9.1	66.6 \pm 8.5* ^Δ	55.3 \pm 8.8* ^Δ
HR (counts/min)	E1	30	79.1 \pm 8.9	67.5 \pm 9.8*	76.4 \pm 10.5	83.5 \pm 9.9	75.3 \pm 9.5
	E2	30	81.7 \pm 10.6	69.6 \pm 9.3*	79.3 \pm 11.6	84.1 \pm 10.5	76.4 \pm 10.2
	E3	20	79.2 \pm 8.8	66.5 \pm 9.6*	75.2 \pm 12.5	80.1 \pm 10.6	74.9 \pm 9.6
	P	30	79.4 \pm 10.1	69.4 \pm 9.9*	66.3 \pm 9.4* ^Δ	71.3 \pm 9.3* ^Δ	59.1 \pm 9.2 ^{▽,Δ}

Notes: Etomidate emulsion and remifentanyl, respectively: E1, 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.1 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E2, 15 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E3, 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Propofol: P, 6–10 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. * $P < 0.05$, vs before treatment; $^{\nabla}P < 0.01$, vs before treatment; $^{\Delta}P < 0.05$, vs E1.

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; SD, standard deviation.

postoperative vomiting. These side effect incidences were related to the amount of etomidate emulsion administered. There were no side effects among P group patients during the investigation. No patient showed adrenal hypofunction in renal function tests (detecting the levels of creatinine, blood urea nitrogen, and uric acid) at the return visit.

Discussion

Although etomidate combined with remifentanyl has more favorable effects than propofol with remifentanyl during the monitoring of transcranial motor evoked potentials under comparable bispectral index (BIS) levels, the safety, recovery time, and side effects of general anesthesia with different doses of etomidate emulsion combined with remifentanyl have not yet been fully investigated.³⁰ The single intravenous injection of etomidate emulsion to induce anesthesia is often 0.2–0.6 mg/kg, and then the rate for general anesthesia maintenance is generally 5–20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{minute}^{-1}$.¹⁶ BIS levels of patients may maintain the level of anesthesia desired when etomidate emulsion is continuously bolus-infused at the rate of 10–15 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.²⁰

Table 3 Remifentanyl dose and awakening and extubation durations (mean \pm SD)

Group	Patients, n	Remifentanyl (mg)	Awakening, minutes	Extubation, minutes
E1	30	0.96 \pm 0.31	12.3 \pm 5.7	18.6 \pm 9.1
E2	30	1.01 \pm 0.26	12.8 \pm 6.5	17.9 \pm 8.2
E3	20	1.04 \pm 0.24	22.6 \pm 9.1 ^Δ	27.3 \pm 14.4 ^Δ
P	30	0.81 \pm 0.15*	11.6 \pm 5.4	17.5 \pm 8.3

Notes: Etomidate emulsion and remifentanyl, respectively: E1, 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.1 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E2, 15 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E3, 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Propofol: P, 6–10 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. * $P < 0.05$, vs E1; $^{\Delta}P < 0.01$, vs E1.

Abbreviation: SD, standard deviation.

The dosage of 0.3 mg/kg was used for inducing anesthesia by intravenous injection in this study. We found that arterial BP and HR declined slightly, but the two parameters rapidly recovered after tracheal intubation to the levels found, preoperatively, after skin incision (E1 and E2), although SBP of E3 patients remained at low levels. This was possibly because etomidate emulsion was used for inducing anesthesia and then a large dosage of etomidate emulsion was infused for the maintenance of anesthesia, which was concerned with the resulting of deep anesthesia by a large amount of etomidate emulsion administered. SBP and DBP of E1, E2, and E3 patients did not change. HRs changed slightly during the maintenance of anesthesia. SBP, DBP, and HRs of P group patients decreased from the beginning of skin incision. These results show that hemodynamics may be more stable with etomidate emulsion (at 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) in anesthesia maintenance than with propofol. A large dosage of etomidate emulsion (20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) was also used for anesthesia maintenance in this study, and produced a transient effect on SBP and almost the same effect on DBP and HR. Etomidate emulsion showed anesthetic and amnestic properties, but no analgesic properties.

Remifentanyl was used as an ultra-short-acting synthetic opioid analgesic drug. The two drugs, Remifentanyl in combination with etomidate emulsion, worked rapidly, with a short half-time in vivo. We designed our study for the use of different dosages of etomidate emulsion combined with remifentanyl in the maintenance of general anesthesia. BP, ECG, SPO₂, and depth of anesthesia were monitored in all patients in the operating theater with a Narcotrend EEG device.

The amount of remifentanyl administered can be adjusted to maintain hemodynamic stability when the NI is maintained at phase D or E. The results show that, when the dosage

Table 4 Incidence of adverse effects in the four groups

Group	Patients, n	Myoclonus, n (%)	Restlessness, n (%)	Sleepiness, n (%)	Vomiting, n (%)
E1	30	3 (10)	1 (3.4)	2 (6.7)	2 (6.7)
E2	30	4 (13.2)	2 (6.8)	5 (16.5)*	9 (30) ^Δ
E3	20	3 (15)*	4 (20)*	13 (65) ^Δ	8 (40) ^Δ
P	30	3 (10)	0	0	0

Notes: Etomidate emulsion and remifentanyl, respectively: E1, 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.1 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E2, 15 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; E3, 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 0.2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Propofol: P, 6–10 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. * $P < 0.05$, vs E1; ^Δ $P < 0.01$, vs E1.

of etomidate emulsion used for anesthesia maintenance was 10–20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{minute}^{-1}$, NI could be maintained at phase D or E and the hemodynamics remain stable. The dosage (6–10 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) of remifentanyl in the P group was less than the etomidate emulsion dose in E1–E3 (10–20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). These results show that remifentanyl should be added up to the dosage of etomidate emulsion in anesthesia maintenance.

Awakening and extubation times were slightly prolonged when a single etomidate emulsion was used in anesthesia maintenance, but the difference was not significant.^{17–19} The study results show that awakening and extubation times were 12 minutes and 18 minutes, respectively, with etomidate emulsion at 10–15 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{minute}^{-1}$ combined with remifentanyl, which was used for maintenance of general anesthesia and administered at equal dosage to P group. When the dosage of etomidate emulsion for maintenance of general anesthesia was increased (20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), the awakening and extubation times were prolonged.

Myoclonus is a frequent complication with etomidate emulsion induction in anesthesia maintenance, but the complications may interfere with anesthetics and analgesics.²⁰ We adopted the sequence of midazolam, fentanyl, vecuronium, and etomidate emulsion according to their pharmacokinetic characteristics in inducing anesthesia and in anesthesia maintenance. The incidence of myoclonus was 11.8%, equal to the findings of a previous study²⁰ and below those of other reports (25%).^{26,27} The results show that the incidences of postoperative agitation, sleepiness, and vomiting were 8.15%, 25%, and 23.75%, respectively, and were higher than in P group. The incidences of postoperative agitation, sleepiness, and vomiting increased with increased etomidate emulsion dosages. The incidence of side effects was lower with the low dosage of etomidate emulsion (10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). When the dosage was increased, the incidence of postoperative agitation also increased, and quality of recovery from anesthesia decreased. The incidence of vomiting also increased with increasing etomidate emulsion dosage. This was possibly because the etomidate emulsion

affected transient adrenal cortical inhibition, but this needs to be confirmed in future studies. Adrenal hypofunction was not found in any patient in postoperative return visits when etomidate emulsion had been continuously infused during anesthesia for 1–3 hours.

Conclusion

Etomidate emulsion combined with remifentanyl was used for the maintenance of general anesthesia and the hemodynamics kept stable. Etomidate emulsion at the dosage of 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{minute}^{-1}$ combined with remifentanyl in maintenance of general anesthesia led to few side effects and rapid awakening. The amount of etomidate emulsion used in the maintenance of general anesthesia should be increased with larger doses of remifentanyl. The etomidate emulsion combined with remifentanyl demonstrates benefit-to-risk balance: remifentanyl prevents the hemodynamic reflex response to tracheal intubation and surgical stimulation, while, in combination with etomidate emulsion, reducing side effects associated with etomidate emulsion and improving postoperative morbidity and mortality.

Acknowledgment

This study was supported by the Science and Technology Plan Project of Linde City, Fujian Province (200941).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Ball C, Westhorpe R. Intravenous induction agents: etomidate. *Anaesth Intensive Care*. 2002;30:405.
2. Pagel PS, Hettrick DA, Kersten JR, Lowe D, Warltier DC. Propofol, but not thiopentone or etomidate, enhances isoflurane-induced coronary vasodilatation in dogs. *Can J Anaesth*. 1998;45(8):809–817.
3. Lopatka CW, Muzi M, Ebert TJ. Propofol but not etomidate, reduces desflurane-mediated sympathetic activation in humans. *Can J Anaesth*. 1999;46(4):342–347.
4. Wagner RL, White PF. Etomidate inhibits ad renocortical function in surgical patients. *Anesthesiology*. 1984;61:647–651.
5. Gepts E. Pharmacokinetic concepts for TCI anaesthesia. *Anaesthesia*. 1998;(53 Suppl 1):4–12.

6. Chen W, Shen Y, Yu B. The changes of plasma glucose and cortisol during induction of anesthesia with propofol or etomidate. *J Clin Anesthesiol. (Chinese)*. 2000;16(2):79–80. Available from: <http://www.shvoong.com/medicine-and-health/1611180-changes-plasma-glucose-cortisol-induction/>. Accessed July 31, 2013.
7. Cicero M, Graneto J. Etomidate for procedural sedation in the elderly: a retrospective comparison between age groups. *Am J Emerg Med*. 2011;29(9):1111–1116.
8. Diaz-Guzman E, Mireles-Cabodevila E, Heresi GA, Bauer SR, Arroliga AC. A comparison of methohexital versus etomidate for endotracheal intubation of critically ill patients. *Am J Crit Care*. 2010;19(1):48–54.
9. Seymour VA, Curmi JP, Howitt SM, Casarotto MG, Laver DR, Tierney ML. Selective modulation of different GABAA receptor isoforms by diazepam and etomidate in hippocampal neurons. *Int J Biochem Cell Biol*. 2012;44(9):1491–1500.
10. Chan CM, Mitchell AL, Shorr AF. Etomidate is associated with mortality and adrenal insufficiency in sepsis: a meta-analysis*. *Crit Care Med*. 2012;40(11):2945–2953.
11. de la Grandville B, Arroyo D, Walder B. Etomidate for critically ill patients. Con: do you really want to weaken the frail? *Eur J Anaesthesiol*. 2012;29(11):511–514.
12. Banh KV, James S, Hendey GW, Snowden B, Kaups K. Single-dose etomidate for intubation in the trauma patient. *J Emerg Med*. 2012;43(5):e277–e282.
13. Warner KJ, Cuschieri J, Jurkovich GJ, Bulger EM. Single-dose etomidate for rapid sequence intubation may impact outcome after severe injury. *J Trauma*. 2009;67(1):45–50.
14. Hildreth AN, Mejia VA, Maxwell RA, Smith PW, Dart BW, Barker DE. Adrenal suppression following a single dose of etomidate for rapid sequence induction: a prospective randomized study. *J Trauma*. 2008;65(3):573–579.
15. Zuckerbraun NS, Pitetti RD, Herr SM, Roth KR, Gaines BA, King C. Use of etomidate as an induction agent for rapid sequence intubation in a pediatric emergency department. *Acad Emerg Med*. 2006;13(6):602–609.
16. Moody EJ, Knauer CS, Granj AR, Strakhovava M, Skolnick P. Distinct structural requirements for direct and indirect actions of the anaesthetic etomidate at GABA(A) receptors. *Toxicol Lett*. 1998;100–101:209–215.
17. Giese JL, Stanley TH. Etomidate: a new intravenous anesthetic induction agent. *Pharmacotherapy*. 1983;3(5):251–258.
18. Schaeuble J, Heidegger T, Gerig HJ, Ulrich B, Schnider TW. Comparison of etomidate and propofol for fiberoptic intubation as part of an airway management algorithm: a prospective, randomized, double-blind study. *Eur J Anaesthesiol*. 2005;22(10):762–767. [sic]
19. Zed PJ, Abu-Laban RB, Harrison DW. Intubating conditions and hemodynamic effects of etomidate for rapid sequence intubation in the emergency department: an observational cohort study. *Acad Emerg Med*. 2006;13:378–383.
20. Zhou J, Wang P, Lei W. Etomidate clinical observation for abdominal surgery under general anesthesia. *J Clin Anesthesiol. (Chinese)*. 2011;27(4):385–387. Available from: <http://www.cnki.net/KCMS/detail/detail.aspx?QueryID=36&CurRec=33&dbcode=CJFQ&dbname=CJFD1112&filename=LCMZ201104034&urlid=&yx=&uid=WEEvREcwSIJHSlDdTtGJhYIMyYVVPcmFOVWRvWTJRUFOL0QzMFDxK3o5N01yNXlscLZRZ3ZKblJ2TmcRDBJMG==&v=MDI4-NjVMbWZWT1Z2RnkvbU3ck5LUzdHZEExHNEg5RE1xNDIHWUISOGVYMUxleFITN0RoMVQzcVRyV00xRnJDVVI=>. Accessed July 31, 2013.
21. Kreuer S, Wilhelm W. The Narcotrend monitor. *Best Pract Res Clin Anaesthesiol*. 2006;20:111–119.
22. Kreuer S, Bruhn J, Stracke C, et al. Narcotrend or bispectral index monitoring during desflurane-remifentanyl anesthesia: a comparison with a standard practice protocol. *Anesth Analg*. 2005;101:427–434.
23. Wilhelm W, Kreuer S, Larsen R; Narcotrend-Studiengruppe. Narcotrend EEG monitoring during total intravenous anaesthesia in 4.630 patients. *Anaesthesist*. 2002;51:980–988. German. [sic]
24. Kreuer S, Wilhelm W, Grundmann U, Larsen R, Bruhn J. Narcotrend index versus bispectral index as electroencephalogram measures of anesthetic drug effect during propofol anesthesia. *Anesth Analg*. 2004;98:692–697.
25. Liu J, Li J, Deng X. Feasibility of TCI etomidate for total intravenous anesthesia. *J Clin Anesthesiol*. 2009;25(5):389–391. Chinese.
26. Doenicke AW, Roizen MF, Kugler J, Kroll H, Foss J, Ostwald P. Reducing myoclonus after etomidate. *Anesthesiology*. 1999;90:113–119.
27. Hueter L, Schwarzkopf K, Simon M, Bredle D, Fritz H. Pretreatment with sufentanil reduces myoclonus after etomidate. *Acta Anaesthesiol Scand*. 2003;47:482–484.
28. Albert SG, Ariyan S, Rather A. The effect of etomidate on adrenal function in critical illness: a systematic review. *Intensive Care Med*. 2011;37(6):901–910.
29. Cherfan AJ, Arabi YM, Al-Dorzi HM, Kenny LP. Advantages and disadvantages of etomidate use for intubation of patients with sepsis. *Pharmacotherapy*. 2012;32(5):475–482.
30. Liu HY, Zeng HY, Cheng H, Wang MR, Qiao H, Han RQ. Comparison of the effects of etomidate and propofol combined with remifentanyl and guided by comparable BIS on transcranial electrical motor-evoked potentials during spinal surgery. *J Neurosurg Anesthesiol*. 2012;24:133–138.

Drug Design, Development and Therapy

Publish your work in this journal

Drug Design, Development and Therapy is an international, peer-reviewed open-access journal that spans the spectrum of drug design and development through to clinical applications. Clinical outcomes, patient safety, and programs for the development and effective, safe, and sustained use of medicines are a feature of the journal, which

Submit your manuscript here: <http://www.dovepress.com/drug-design-development-and-therapy-journal>

Dovepress

has also been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.