Visual evoked potentials during etomidate administration in humans

Oak Za Chi MD, Jaya Subramoni MD, Dale Jasaitis MS

The effects of etomidate on visual evoked potentials (VEP) were studied in 22 patients undergoing gynaecological procedures. They were divided into two groups: the etomidate group (12 patients) and the fentanyl-N_2O-etomidate group (ten patients). In the etomidate group, etomidate 0.3 mg · kg^{-1} was given as a bolus injection during induction of anaesthesia which was followed by an infusion of etomidate 0.05 mg · kg^{-1} · min^{-1}. No significant changes were observed in the amplitudes of P100 or N70. Latencies of the P60, N70, and P100 were slightly increased. In the fentanyl-N_2O-etomidate group, a bolus injection of 0.3 mg · kg^{-1} of etomidate was given during anaesthesia with 3–4 μg · kg^{-1} of fentanyl and 60 per cent nitrous oxide. The amplitude of the P100 was significantly decreased and the latencies of the P60 and N70 were signficantly increased. In conclusion, interpretation of the VEP during etomidate administration alone was not hard to perform but, when given together with fentanyl-nitrous oxide anaesthesia, the VEP was affected significantly making its interpretation difficult.

Nous avons évalué les effets de l'étomidate sur les potentiels évoqués visuels (PEV) lors de 22 interventions gynécologiques. Aux douze patients du groupe étomidate, nous avons injecté un bolus de 0,3 mg · kg^{-1} suivi d'une perfusion de 0,05 mg · kg^{-1} d'étomidate, sans observer d'autre effet qu'une légère augmentation des périodes de latence de P60, N70 et P100 alors que les amplitudes de N70 et de P100 ne changeaient pas. En sus de 60 pour cent de protoxyde d'azote et de 3–4 μg · kg^{-1} de fentanyl, on injectait aux dix autres patients, un bolus de 0,3 mg · kg^{-1} d'étomidate, ce qui amenait une diminution significative de l'amplitude de P100 et une augmentation significative des périodes de latence de P60 et de N70. Donc, l'interprétation des PEV est facile sous anesthésie à l'étomidate employé seul mais elle se complique si on ajoute du protoxyde d'azote et du fentanyl au régime anesthésique.

Key words
ANAESTHETICS, INTRAVENOUS: etomidate;
BRAIN: evoked potentials;
MONITORING: evoked potentials, visual.

From the Department of Anesthesia, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School-Robert Wood Johnson University Hospital, New Brunswick, New Jersey.

Address correspondence to: Dr. O.Z. Chi, Department of Anesthesia, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, One Robert Wood Johnson Place, CN-19, New Brunswick, New Jersey 08903-0019.

Etomidate is one of the anaesthetic induction agents which has gained popularity for its minimal cardiovascular and respiratory depressant effects when compared with other agents. It does not appear to release histamine.[1-3] It decreases cerebral metabolic rate, cerebral blood flow, and intracranial pressure. These characteristics are beneficial in neurosurgical procedures.[4,5]

Evoked potentials (EPs), which are used in monitoring the integrity of the nervous system during various operations, are frequently affected by anaesthetic agents. In spite of their vulnerability to various factors during surgery, visual evoked potentials (VEP) have been used to monitor the integrity of the visual pathways during neurosurgical procedures[6,7] and the function of the central nervous system during cardiopulmonary bypass since disturbance of visual function is one of the most common complications following cardiovascular surgery.[8-10]

A VEF is elicited by flashes from light-emitting diodes attached to a pair of goggles which are placed over the patient's closed eyes. Several positive and negative peaks are observed at various times after the stimuli. Some frequently recognized peaks are P60, N70, and P100. Of these, P100 is relatively stable and the most useful clinically. Other peaks are more vulnerable and have too much variation to be considered clinically important. The P100, which is observed at approximately 100 msec after the stimuli, is thought to arise in the striated and parastriated visual cortex.[11] The origins of the other peaks are not known.

Since the effects of etomidate on visual evoked potentials are not known, we decided to investigate the

TABLE I Variables used in recording the VEP

Stimulation	
Mode	– Binocular flash stimulation
Source	– LED arrays on opaque binocular goggles placed over closed eyes
Duration	– 10 msec
Rate	– 1.9 Hz
Recording	
Electrodes	– Chlorided silver disc electrodes affixed with collodion
Montage*	– 02-A1 or 01-A2
Ground	– FPz
Filters	– 1–100 Hz
Sensitivity	– 100 μV full scale
Sweep time	– 250 msec
Impedance	– <3000 ohm
Repetition	– 100

Nicolet Pathfinder I (Nicolet Biomedical Instruments, Madison, WI) was used to record the VEP.
*The 10-20 international system of electrode placement was used 13.

effects of etomidate on VEPs in humans. We also investigated how etomidate modified the VEP changes induced by fentanyl-nitrous oxide anaesthesia, which usually causes only a slight increase in the latency without affecting the amplitude of the VEPs.[12]

Methods

This study was approved by our Institutional Review Board. Twenty-two consenting patients undergoing gynaecological procedures were studied. They were divided into two groups: the etomidate group (12 patients) and the fentanyl-N_2O-etomidate group (ten patients). The mean age and mean weight in the etomidate group were 30.7 ± 5.2 (yr ± SD) and 63.0 ± 7.7 (kg ± SD) respectively. In the fentanyl-N_2O group, they were 33.0 ± 4.6 (yr ± SD) and 69.3 ± 13.2 (kg ± SD) respectively. None of the patients in either group had significant neurological or ophthalmological disorders. No patient received premedications. In the operating room, goggles equipped with LED were applied over the patient's closed eyes. The recording variables are described in Table I.[13] Blood pressure was monitored with a Dinamap automatic blood pressure measuring device, while the ECG was monitored continuously. A Nellcor pulse oximeter sensor was applied on the index finger in order to monitor continuously arterial oxygen saturation. A Stat-Temp temperature sensor was applied on the patient's forehead. End-tidal carbon dioxide was monitored with a SARA Cap Plus multiple gas analyzer. Prior to induction of anaesthesia, the first VEP was recorded as a control.

In the etomidate group, vecuronium 1 mg was given as pretreatment. Then, anaesthesia was induced with a bolus injection of etomidate 0.3 $mg \cdot kg^{-1}$, which was followed by a continuous infusion of etomidate 0.05 $mg \cdot kg^{-1} \cdot min^{-1}$. Immediately after the bolus injection, vecuronium 0.12 $mg \cdot kg^{-1}$ was administered to diminish any visible myoclonic movements. During induction, the lungs were manually ventilated with a mask to maintain end-tidal CO_2 within 35–40 mmHg. Ten seconds after the bolus injection, a recording of the VEP was started. One VEP recording was performed every minute for three minutes. Etomidate infusion was continued during VEP recordings. Tracheal intubation was delayed until VEP recordings were completed.

In the fentanyl-N_2O-etomidate group, anaesthesia was induced with 3–4 $mg \cdot kg^{-1}$ of thiopentone and 0.12 $mg \cdot kg^{-1}$ of vecuronium. After tracheal intubation, fentanyl 3–4 $\mu g \cdot kg^{-1}$ and 60 per cent N_2O were administered. No additional fentanyl was given until the VEP recordings were completed. Fifteen minutes after induction, a baseline VEP was recorded which was followed by the administration of a bolus injection of etomidate 0.3 $mg \cdot kg^{-1}$. Ten seconds after the etomidate administration, VEP recordings were started and the first recording was completed in approximately one minute. Subsequent recordings were performed at two, four and six minutes after the etomidate administration. Skin incision was delayed until the VEP recordings were completed.

From the VEP recordings, the first prominent positive, the first prominent negative, and the second prominent positive peaks were identified. These were designated P60, N70, and P100, respectively. Latencies of P60, N70, and P100 were measured. The amplitude of N70 was measured as the vertical distance between the peaks of P60 and N70, while the amplitude of P100 was measured as the vertical distance between the peaks of N70 and P100.

For data analysis, analysis of variance with repeated measures and the Student-Newman-Keuls multiple comparison test were performed. A P value <0.05 was considered statistically significant.

Results

Blood pressure and heart rate were stable during the study period. Satisfactory VEP recordings were obtained from all the patients studied. However, in two patients in each group, there was no recognizable P60, and they were excluded from the statistical analysis involving P60.

In the etomidate group, administration of etomidate increased the latencies of P60, N70, and P100 slightly at various time points. On the other hand, the amplitudes of N70 (P60-N70) and P100 (N70-P100) were not changed significantly (Table II). A typical VEP recording during induction of anaesthesia from a patient in the etomidate group is shown in Figure 1.

In the fentanyl-N_2O-etomidate group, the latencies of P60, N70, and P100 were significantly increased after the

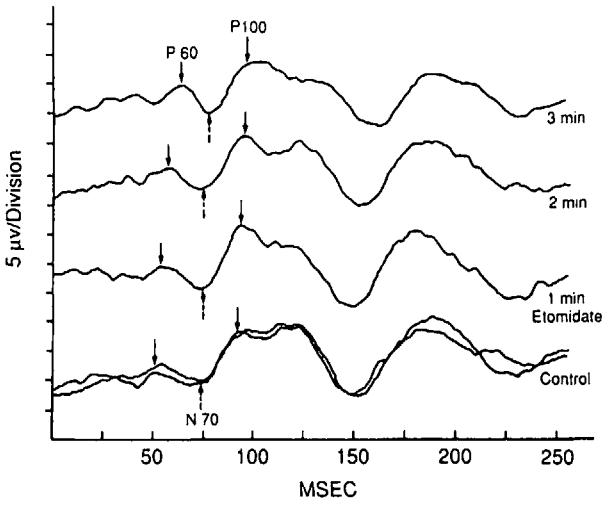

FIGURE 1 A typical VEP recording during induction of anaesthesia with a bolus injection of etomidate 0.3 $mg \cdot kg^{-1}$ followed by infusion of etomidate 0.05 $mg \cdot kg^{-1} \cdot min^{-1}$ from a patient in the etomidate group. Time represents minutes after the etomidate injection.

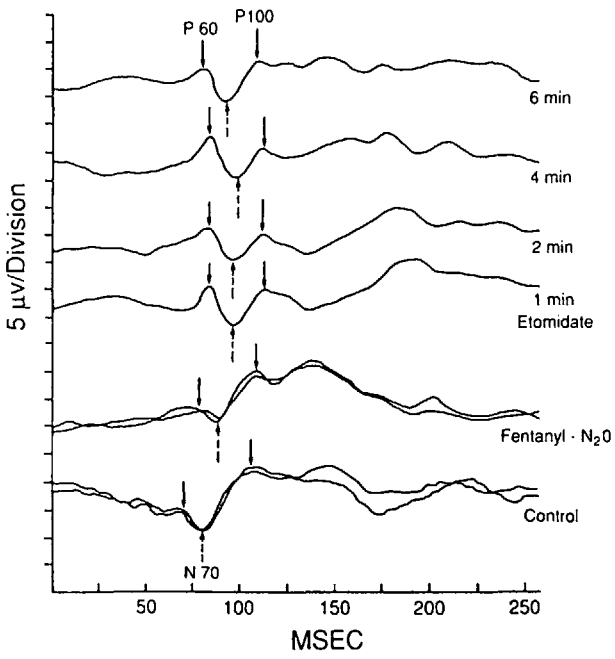

FIGURE 2 A typical VEP recording after a bolus administration of etomidate 0.3 $mg \cdot kg^{-1}$ from a patient in the fentanyl-N_2O-etomidate group. Time represents minutes after the etomidate injection.

administration of fentanyl and nitrous oxide. The amplitudes showed no statistically significant changes. Administration of etomidate during fentanyl-N_2O anaesthesia further increased the latencies of P60 and N70 significantly at every time point. However, the latency of P100 showed no statistically significant increase. The amplitude of P100 (N70-P100) was significantly decreased after the etomidate administration. Even though it was statistically insignificant, the amplitude of N70 (P60-N70) seemed to increase (Table III). A typical VEP recording after the etomidate administration from a patient in the fentanyl-N_2O-etomidate group is shown in Figure 2.

Discussion

Factors other than anaesthetic agents can affect VEP recording. Hypothermia increases the latency of the VEP as described by Russ *et al.* and others.[14,15] In our study, the temperature was maintained within a narrow range. Since CO_2 tension may affect EPs, ventilation was controlled to keep the end-tidal CO_2 within the normal range.[16] Premedication was eliminated. During our study, blood pressure was stable and no intervention was needed.[17] In order to eliminate the effects of surgical stimuli, all VEP recordings were performed before surgical incisions were made.[18]

In our study, induction of anaesthesia with etomidate by itself did not signficantly affect the amplitude of P100. This is in contrast to the marked increase of the cortical SSEP found by other researchers. Several authors noted

TABLE II Latencies and amplitudes of the VEP in the etomidate group. Time represents minutes after etomidate injection

	Latency (msec ± SD)			*Amplitude (µV ± SD)*	
	P60 (n = 10)	*N70 (n = 12)*	*P100 (n = 12)*	*P60-N70 (n = 10)*	*N70-P100 (n = 12)*
Control	61.5 ± 10.1	77.0 ± 8.4	105.3 ± 11.6	4.90 ± 2.96	11.83 ± 4.29
1 min	66.6 ± 10.4	81.9 ± 8.6*	107.5 ± 8.2	6.92 ± 2.61	11.04 ± 5.50
2 min	68.0 ± 9.5*	82.8 ± 10.2*	110.3 ± 13.1	6.73 ± 4.27	11.71 ± 6.94
3 min	69.3 ± 10.5*	83.4 ± 10.0*	112.3 ± 12.3*	6.08 ± 3.97	11.06 ± 6.39
P	<0.05	<0.005	<0.05	NS	NS

NS: Statistically non-significant.
*Significantly different from control.

TABLE III Latencies and amplitudes of the VEP in the fentanyl – N_2O – etomidate group. Time represents minutes after etomidate injection

	Latency (msec ± SD)			*Amplitude (μV ± SD)*	
	P60 (n = 8)	*N70 (n = 10)*	*P100 (n = 10)*	*P60-N70 (n = 8)*	*N70-P100 (n = 10)*
Control	60.8 ± 10.8	71.4 ± 13.7	100.0 ± 18.4	3.58 ± 2.05	12.17 ± 6.06
Fent-N_2O	68.6 ± 5.0*	79.7 ± 8.2*	108.8 ± 10.3*	3.04 ± 2.11	11.62 ± 4.50
1 min	78.2 ± 14.0*†	90.5 ± 18.5*†	112.8 ± 18.9*	4.94 ± 4.09	8.22 ± 7.14
2 min	79.9 ± 13.5*†	91.3 ± 19.0*†	111.4 ± 20.1*	4.44 ± 2.13	6.18 ± 5.20*†
4 min	79.6 ± 13.8*†	91.9 ± 19.4*†	113.9 ± 21.6*	5.48 ± 2.85	6.74 ± 4.26*
6 min	79.3 ± 15.0*†	91.6 ± 17.6*†	114.5 ± 19.5*	4.95 ± 2.50	9.06 ± 4.51
P	<0.0005	<0.0005	<0.005	NS	<0.01

Fent-N_2O: after fentanyl-nitrous oxide anaesthesia was started and before etomidate was given.
NS: Statistically non-significant.
*Significantly different from control.
†Significantly different from fent-N_2O.

that 0.3–0.4 mg·kg^{-1} of etomidate given intravenously markedly increased the amplitude of N20-P23 in the cortical portion of the somatosensory evoked potentials (SSEP) in humans.[19,20] The latencies of N20 and P23 were only slightly increased. Ebner *et al.* also found that the amplitudes of the parietal P25 and the frontal N30 of the SSEP were markedly increased by the intravenous administration of etomidate.[21] These findings were similar to those observed in patients with cortical myoclonus who did not receive any anaesthesia. They suggested that there was a separation of relatively stable (P14, N20, P22) and modifiable (P25, N30) components of the SSEP in the sensory motor cortex. These modifiable components were characterized by their enhancement in conditions of cortical myoclonus and during etomidate administration in neurologically normal patients. They were abolished during the ictal period which was provoked by an electroconvulsive shock. It was speculated that a similar neurophysiological mechanism could be responsible for the alteration of the SSEP during etomidate administration and during myoclonic movements. Halliday compared SSEP and VEP in a large series of patients with progressive myoclonic epilepsy.[22] He noted large SSEP appearing in the contralateral Rolandic area. Measurement of VEP revealed large early (50–60 msec) components. The degree of enhancement of the amplitudes was much greater in SSEP (4.53 times of the control) than in VEP (1.69 times of the control). Our study also suggests that etomidate has less effects on VEP than cortical SSEP.

In our study, the amplitude of N70 (P60-N70) tended to increase after administration of etomidate in both groups even though these changes were statistically not significant. This finding may be a resemblance to the enhancement of early components of the VEP in myoclonic epilepsy in Halliday's study.[22] The origin and significance of the P60 and N70 of the VEP are not known. These components of the VEP exhibit much variation and are difficult to interpret. Further exploration will be needed in order to establish a meaningful interpretation of the P60 and N70.

Administration of etomidate during fentanyl-N_2O anaesthesia did not increase the amplitude of P100. Rather, it was decreased after the etomidate injection. This is in contrast to the findings of Sloan *et al.* who showed that the amplitude of the cortical SSEP was increased when etomidate was added to alfentanil-midazolam anaesthesia.[23] Further, they suggested that enhanced SSEP with etomidate might be useful in interpreting changes of EPs caused by surgical manipulation. Our findings from the fentanyl-N_2O-etomidate group are very similar to those of Thornton. He found that etomidate, when added to 70 per cent nitrous oxide, increased the latency and decreased the amplitude of early cortical auditory evoked potentials.[24] Obviously, the effects of etomidate on cortical evoked potentials are different from one modality of the EPs to the other.

In conclusion, interpretation of the VEP during etomidate administration alone may not be hard to perform. However, when given together with fentanyl-nitrous oxide anaesthesia, the VEP was affected significantly making its interpretation difficult.

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