Visual evoked potentials during thiopentone-fentanyl-nitrous oxide anaesthesia in humans

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Visual evoked potentials (VEP) during thiopentone-fentanyl-nitrous oxide anaesthesia were studied in 15 healthy patients undergoing non-neurosurgical procedures. The VEP was recorded before and at 1 and 2 min after induction of anaesthesia with 5–6 mg · kg^{-1} of thiopentone. After recording the 1 and 2 min VEPs, anaesthesia was maintained with a fentanyl-nitrous oxide-oxygen combination, and further recordings were made at 5, 10, 15 and 20 min after induction. The 1 and 2 min VEPs showed a marked decrease in the amplitudes. Latencies were increased. The amplitudes gradually returned to the control level at 15 min, while the latencies remained increased throughout the study period. In conclusion, thiopentone should be avoided during the critical period of VEP recording. Once it is given, at least 15 min should elapse before an appropriate interpretation of the VEP can be made. Thiopentone-fentanyl-nitrous oxide anaesthesia slightly increases the latencies of the VEP. These effects should be considered in the interpretation of the VEP when thiopentone-fentanyl-nitrous oxide anaesthesia is used.

Key words
ANAESTHETICS, GASES: nitrous oxide; ANAESTHETICS, INTRAVENOUS: fentanyl, thiopentone; BRAIN: evoked potentials; MONITORING: evoked potentials, visual.

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Evoked potentials (EPs) have been increasingly used to monitor the integrity of the nervous system during surgery. Detection of the early changes in neuronal function will allow corrective measures to be taken in order to prevent permanent damage. Visual evoked potential (VEP) is one of three frequently used EPs. Monitoring of the VEP is done in order to detect injury during procedures involving the visual pathways such as trans-sphenoidal or anterior fossa surgery.[1,2] It has also been used to monitor the central nervous system during cardiopulmonary bypass.[3] The VEP is elicited by flashes coming from light-emitting diodes that are mounted on goggles over the patient's closed eyes. A prominent peak is observed at approximately 100 msec after the stimuli. This peak which is called the P100, is thought to arise in the striated and parastriated visual cortex.[4] A negative peak is also recognized at about 70 msec. The origin of this peak, which is called N70, is not clear. Latencies and amplitudes of the VEP are affected by several factors in addition to surgical manipulation and tissue ischaemia. The VEP is especially vulnerable to anaesthetic agents since it has long latencies of the principal peaks when compared with those of other cortical EPs.[5] Domino *et al.* found that the VEP was enhanced by a low dose, 3 mg · kg^{-1}, and was obliterated by a high dose, 6 mg · kg^{-1}, of thiamylal.[6] Chi *et al.* showed that isoflurane increased the latencies and markedly decreased the amplitudes of the PI (P100) of the VEP.[7] It would be desirable to use anaesthetic agents which affect the VEP least if the VEP is to be monitored during surgery. High-dose fentanyl anaesthesia appears to affect the VEP only minimally.[8] Since thiopentone-fentanyl-nitrous oxide anaesthesia is frequently used in clinical practice, we decided to study its effects on the VEP.

Methods

This study was approved by our Institutional Review Board on human research. Written informed consents were obtained from 15 healthy patients (ASA Physical Status I) undergoing non-neurosurgical procedures. Their

mean age was 33.5 ± 7.9 years while their mean weight was 59.7 ± 10.6 kg. None of the patients had significant neurological or ophthalmological disorders. No premedication was given. As a control, VEP was recorded from the occipital electrode (OZ-CZ) before induction of anaesthesia. Recording variables are described in Table I. Patients were prehydrated with lactated Ringer's solution. Anaesthesia was induced with 0.05 $mg \cdot kg^{-1}$ d-tubocurarine and 5–6 $mg \cdot kg^{-1}$ thiopentone followed by 1.5 $mg \cdot kg^{-1}$ succinylcholine IV. The lungs were ventilated with 100 per cent oxygen by mask in order to maintain end-tidal PCO_2 within 35–40 mmHg. Two VEP recordings were performed to study the effects of a bolus dose of thiopentone (1 and 2 min VEP). Since recording one VEP takes 50–60 seconds, the 1 min VEP recording was begun ten seconds after injection of thiopentone. No additional doses of thiopentone were given throughout the study after induction of anaesthesia. Then, 3–4$\mu g \cdot kg^{-1}$ of fentanyl was given and tracheal intubation was performed. Anaesthesia was maintained with vecuronium, 40 per cent oxygen and 60 per cent nitrous oxide. Subsequent recordings were made at 5, 10 and 15 min after injection of thiopentone. During this period, bolus injections of fentanyl 50–100 μg were given as needed. Following the 15 min VEP recording, a skin incision was made, and 20 min after the injection of thiopentone, another VEP was recorded. The total dose of fentanyl given during the 20-minute study period ranged from 5–6 $\mu g \cdot kg^{-1}$. Blood pressure was measured every minute with a Dinamap automatic blood pressure monitor. Patients whose systolic arterial blood pressure changed by more than ± 25 per cent of the preoperative level were excluded from this study. Body temperature was maintained between 35–37° C. Latencies of N70 and P100 were measured. The vertical distance between N70 and P100 established the amplitude in microvolts. For data analysis, analysis of variance with repeated measures was used. Student-Newman-Keuls tests were used to compare VEPs at different time points. A P value < 0.05 was considered statistically significant.

Results

Satisfactory recordings of the VEPs were obtained in all patients studied. Two patients were excluded from the study because their systolic blood pressures were altered more than ± 25 per cent of the preoperative level. Three patients showed visible muscular fasciculations after succinylcholine administration; however, the VEP did not appear to be altered by this. The remaining patients showed no visible fasciculations. Typical VEP recordings at different time points from a patient are illustrated in the Figure. Means and standard deviations of latencies and amplitudes are shown in Table II. One minute after

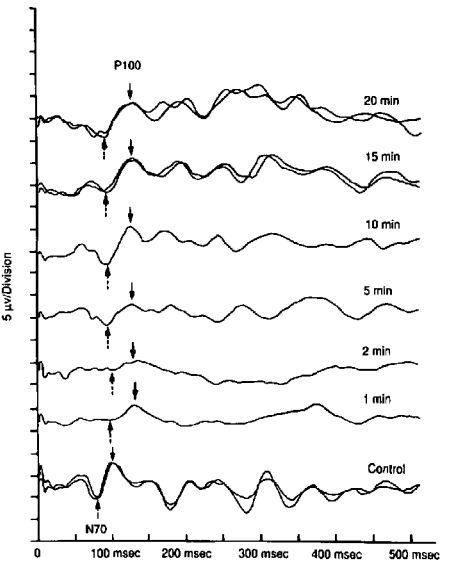

FIGURE The VEP recording from a patient at different time points after 6 $mg \cdot kg^{-1}$ of thiopentone and during fentanyl-nitrous oxide anaesthesia. The amplitudes of VEP recovered to baseline around 10–15 min after injection of thiopentone. The latencies remained increased throughout the study period.

injection of thiopentone (1 min VEP), the latency of N70 increased from 75.5 ± 9.4 msec to 92.2 ± 16.5 msec and that of P100, from 106.7 ± 16.0 msec to 124.8 ± 16.8 msec. Latencies remained significantly increased during the remainder of the study period when compared with control. There were no significant differences in the latencies of recordings at different time points after induction of anaesthesia. The amplitude of the 1 min VEP decreased markedly from 10.04 ± 4.35 μV to 4.56 ± 4.11 μV. There was a gradual recovery in amplitude as time passed. Finally at 15 and 20 minutes after induction, there were no significant decreases in amplitude when compared with the control. During this study, there were no reports of patients experiencing discomfort or injuries.

Discussion

Recording of EP is affected by many factors other than anaesthetic agents. Premedication was eliminated. Since hypothermia increases the latency of VEP, the temperature was kept within a narrow range.[10] Fluctuation of end-tidal CO_2 was minimized by utilizing controlled ventilation to avoid its effects on EP.[11] Arterial blood pressure was maintained within ± 25 per cent of the

TABLE I Recording variables of the VEP

Stimulus	Binocular flash from LED arrays on goggles placed over patients' closed eyes
Duration	10 msec
Frequency	1.9 Hz
Electrodes	Chlorided silver disc electrodes
Channel*	Oz-Cz
Ground	Mastoid
Impedance	Less than 3000 ohm
Sensitivity	100 μV full scale
Sweep Time	500 msec
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.[9]

preoperative level.[12] To avoid the effects of surgical stimulation, recordings were made before surgery commenced except for the 20 min VEP recording which was made after skin incision.

After injection of thiopentone, the latency of the VEP increased significantly and the amplitude decreased markedly. These findings appear to be the immediate effects of thiopentone. Domino *et al.* described similar effects on the VEP when a high dose, 6 $mg \cdot kg^{-1}$, of thiamylal was used.[6] Return of the amplitude to the control level 15 min after induction of anaesthesia suggests dissipation of the effects of thiopentone. This observation corresponds approximately to the clinical effects of thiopentone. Except for the first two-minute period when VEPs were recorded to check the effect of the bolus dose of thiopentone, the increased latency before 15 min of the study period could be caused by the combined effects of thiopentone, fentanyl and nitrous oxide. After 15 min, the latency could have remained increased predominantly due to the effects of fentanyl and nitrous oxide even though the effects of surgical incision could not be ruled out.

TABLE II Latencies and amplitudes of the VEP at control and at different time points after 5–6 $mg \cdot kg^{-1}$ thiopentone

	Latency (msec)		*Amplitude (μV)*
	N70 *Mean ± SD* *(n = 13)*	*P100* *Mean ± SD* *(n = 13)*	*Mean ± SD* *(n = 13)*
Control	75.5 ± 9.4	106.7 ± 16.0	10.04 ± 4.35
1 min	92.2 ± 16.5*	124.8 ± 16.8*	4.56 ± 4.11*
2 min	93.5 ± 10.9*	124.2 ± 17.6*	4.53 ± 4.22*
5 min	94.8 ± 11.0*	125.8 ± 19.3*	5.29 ± 4.09*
10 min	91.8 ± 15.8*	123.5 ± 17.8*	7.06 ± 3.68*
15 min	88.9 ± 13.9*	122.5 ± 20.8*	8.23 ± 4.56
20 min	92.7 ± 13.6*	127.0 ± 17.9*	9.52 ± 4.87
P	$P < 0.0005$	$P < 0.0005$	$P < 0.0005$
Significance	S	S	S

S = Statistically significant.
*Compared with control, the difference is statistically significant.

Narcotic anaesthesia is frequently recommended when EPs are monitored. Ideally, pure narcotic anaesthesia would be the best agent to minimize the effects of the anaesthesia on the VEP. In the clinical setting, however, thiopentone is frequently used for induction of anaesthesia and nitrous oxide is added to narcotics for various reasons. Our study was restrained by clinical practice. In order to define the effects of each anaesthetic agent or the combined effects of several, further study will be needed utilizing dose-response curves.

Compared with the effects of isoflurane on the VEP, which showed marked decrease in amplitude (−65.3 per cent at 1 MAC),[7] fentanyl-nitrous oxide anaesthesia in our study did not affect the amplitude significantly after the effects of thiopentone had dissipated. This makes the interpretation of the VEP somewhat easier during fentanyl-nitrous oxide anaesthesia than during isoflurane anaesthesia which tends to obliterate the peaks and valleys of the VEP.

Previously, Chi *et al.* showed that a high dose of fentanyl, 60 $\mu g \cdot kg^{-1}$, slightly decreased the amplitude of the VEP without affecting the latency.[8] Sebel *et al.* demonstrated that increased concentrations of nitrous oxide increased the latency and decreased the amplitude of the VEP.[13] In our study, fentanyl-nitrous oxide anaesthesia increased the latency with no significant changes in the amplitude. Apparently, the effects of fentanyl and nitrous oxide on the VEP are not simply additive. In a study of somatosensory evoked potentials, Koht *et al.* showed that the additive effects of fentanyl and nitrous oxide vary according to the induction agents.[14] In our study, induction of anaesthesia with thiopentone may have changed the effects of fentanyl and nitrous oxide on the VEP.

In conclusion, thiopentone increases the latency and decreases the amplitude of the VEP after a bolus dose of thiopentone. At about 15 min, the amplitude of the VEP seems to recover to the control level. Thiopentone should be avoided during the critical period of VEP recording. Once it is given, at least 15 min have to elapse before a meaningful recording of the VEP can be made. Thiopentone-fentanyl-nitrous oxide anaesthesia slightly increases the latency of the VEP. This effect should be taken into account when VEP is monitored during anaesthesia.

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Résumé

Nous avons enregistré les potentiels évoqués visuels (PEV) de 15 patients anesthésiés au thiopental-fentanyl-protoxyde d'azote pendant une intervention non neurochirurgicale. Les mesures avaient lieu une et deux minutes après l'injection de 5–6 $mg \cdot kg^{-1}$ de thiopental puis sous fentanyl et protoxyde d'azote 5, 10, 15 et 20 minutes après l'induction. A une et deux minutes, les PEV avaient une période de latence prolongée et une amplitude réduite. Cette dernière revint progressivement à la normale au bout de 15 minutes mais la période de latence demeura allongée jusqu'à la fin de l'étude. Ainsi, le thiopental interfère avec l'interprétation des PEV et cet effet dure au moins 15 minutes. L'anesthésie au thiopental-fentanyl-protoxyde d'azote prolonge aussi légèrement la période de latence des PEV. On devra tenir compte de ces effets dans l'interprétation des PEV.