Anesthesiology
62:626–633, 1985

Effects of Enflurane, Isoflurane, and Nitrous Oxide on Somatosensory Evoked Potentials during Fentanyl Anesthesia

Robert W. McPherson, M.D., Michael Mahla, M.D.,† Robert Johnson, RCPT,‡ Richard J. Traystman, Ph.D.§*

The effects of nitrous oxide, enflurane, and isoflurane on cortical somatosensory evoked potentials (SEPs) were studied in 29 patients undergoing intracranial or spinal operations. Anesthesia was induced with fentanyl (25 μg/kg, iv) plus thiopental (0.5–1.0 mg/kg, iv). In one group of patients (n = 12), nitrous oxide (50%) was compared with enflurane (0.25–1.0%), and in another group (n = 12) nitrous oxide (50%) was compared with isoflurane (0.25–1.0%). In a third group of patients (n = 5) with preexisting neurologic deficits, nitrous oxide (50%) was compared with enflurane (0.25–1.0%). In all three groups, one gas was administered for 30 min, and then the alternate gas was administered for 30 min; then the cycle was repeated for a total of two administrations of each of the two anesthetics. SEPs were determined before and after induction of anesthesia and at the end of each 30-min study period. The latencies and amplitudes of the early cortical components of the upper- and lower-extremity SEP were examined. Induction of anesthesia resulted in increases of latency in both upper- and lower-extremity SEPs without any alteration of amplitude. Nitrous oxide, enflurane, and isoflurane each decreased the amplitude of the upper-extremity SEPs compared with the postinduction value. The amplitude of the upper-extremity SEPs was less during nitrous oxide than with either enflurane or isoflurane. Nitrous oxide decreased the amplitude of lower-extremity SEPs below postinduction value, while enflurane and isoflurane had no effect. Isoflurane and enflurane increased the latency of both upper- and lower-extremity SEPs slightly, while nitrous oxide had no effect. In patients with preexisting neurologic deficits, nitrous oxide decreased amplitude more than enflurane. The authors conclude that during fentanyl-based anesthesia either enflurane or isoflurane (0.25–1.0%) results in less alteration of cortical SEPs than does nitrous oxide (50%), and these concentrations of enflurane or isoflurane are compatible with the generation of waves that are adequate for evaluation. (Key words: Anesthetics, gases: nitrous oxide. Anesthetics, volatile: enflurane; isoflurane. Brain: evoked potentials. Monitoring: evoked potentials.)

CHANGES IN SOMATOSENSORY EVOKED POTENTIALS (SEPs) indicate neurologic dysfunction during spinal cord operations.[1–3] Monitoring of SEPs is also useful in intracranial vascular surgery[4,5] and in the prevention of position related neurologic injury.[6,7] These expanded uses of SEP monitoring require evaluation of anesthetic techniques not containing nitrous oxide, since nitrous oxide may be contraindicated in intracranial operations in which there is a risk of venous air emboli,[8] decreased intracranial compliance,[9,10] and intracranial air.[11] Fentanyl anesthesia with anesthetic gas supplementation is a versatile anesthetic technique, since fentanyl does not adversely affect cerebral compensatory mechanisms such as autoregulation, responses to hypoxia, or changes in Pa_{CO_2},[12] and decreases the MAC of inhalational agents.[13] Additionally, fentanyl may be used as a complete anesthetic with demonstrated hemodynamic stability in both cardiac[14,15] and neurosurgical patients.[16]

The purpose of this study was to compare the effects on SEPs of various anesthetics used to supplement fentanyl-based anesthesia. We compared the effects of nitrous oxide with enflurane and isoflurane on scalp-recorded SEPs.

Methods

This study was approved by the Human Studies Committee of the Johns Hopkins Medical Institutions, and written permission was obtained from each patient prior to the study. Twenty-nine patients undergoing posterior fossa surgery, spinal surgery (cervical or thoracic), or clipping of intracranial aneurysm were studied. Twenty-four patients were without neurologic deficits (excluding cranial nerve deficits), and five had preoperative neurologic deficit (unilateral sensory and motor deficits), the most severe being three-fifths motor strength on the affected side. In one group of patients (group 1, n = 12) the effect of enflurane (0.25–1.0%) was compared with nitrous oxide (50%), and in another group of patients (group 2, n = 12), the effect of isoflurane (0.25–1.0%) was compared with that of nitrous oxide. Within each group, six of the patients received nitrous oxide as the initial anesthetic, and the remaining six patients received the volatile anesthetic (enflurane or isoflurane) initially. In patients with preoperative neurologic deficits (Group 3, n = 5), nitrous oxide (50%) was compared with enflurane (0.25–1.0%). In individual patients, the anesthetic concentration was held constant at a level maintaining hemodynamic stability. Small doses of thiopental (0.25–0.5 mg/kg) were

* Chief, Division of Neuroanesthesia, Assistant Professor of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, Maryland.

† Staff Anesthesiologist, Walter Reed Army Medical Center, Washington, D. C.

‡ Critical Care Technician.

§ Associate Professor of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, Maryland.

Received from the Department of Anesthesia and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, Maryland, and the Department of Anesthesiology, Walter Reed Army Medical Center, Washington, D. C. Accepted for publication December 19, 1984.

Address reprint requests to: Dr. McPherson: Department of Anesthesia and Critical Care Medicine, Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, Maryland 21205.

given because of movement or hemodynamic response to stimuli as needed.

One patient required premedication (morphine 6 mg im) because of severe preoperative anxiety. Small amounts of sodium thiopental (50–75 mg, iv) and fentanyl (50–100 μg, iv) were given as necessary during placement of vascular catheters to minimize patient discomfort. Heart rate, mean arterial blood pressure (MABP), central venous pressure (CVP), and end-tidal CO_2 were recorded continuously. Nasopharyngeal temperature was monitored using a YSI® telethermometer (Yellow Springs Instrument Co, Yellow Springs, Ohio). Intracranial pressure was not measured in any patient.

Anesthesia was induced with fentanyl (25 μg/kg, iv) and thiopental (0.5–1.0 mg/kg, iv), followed rapidly by pancuronium (0.15 mg/kg). Following manual hyperventilation for 3–5 min, the patients were intubated, and hyperventilation was continued to maintain arterial CO_2 tension (Pa_{CO_2}) in the range of 25–30 mmHg. Neosynephrine (40 μg/ml) was administered as required to prevent MABP from decreasing more than 10% below preinduction values. Upper- and lower-extremity SEPs were recorded prior to anesthesia induction and after induction, but prior to anesthetic gas administration. The patient then received either nitrous oxide 50% (3 l/min N_2O; 3 l/min O_2) or a volatile anesthetic, (enflurane groups 1 and 3 or isoflurane group 2 in 6 l/min O_2) delivered via a vaporizer designed for the specific anesthetic (Ohio Biomedical). The inspired concentration of enflurane or isoflurane required in individual patients varied between 0.25–1.0% to maintain hemodynamic stability. In each patient, the anesthetic concentration was maintained constant during the study period. The initial anesthetic was continued for 30 min, discontinued, and the alternate anesthetic administered for 30 min. This sequence then repeated, for a total of two administrations of each anesthetic. Additional thiopental (25 mg) was given in response to movement or hemodynamic responses to stimulation. Barbiturate was not given within 10 min of SEP determination. Each patient was interviewed the day following operation to assess memory of intraoperative events.

Somatosensory evoked potentials were measured using a multichannel signal averager (Nicolet Med-80®, Nicolet Biomedical, Madison, Wisconsin). Gold-plated silver-cup electrodes were attached to the scalp 2 cm posterior to C_3 and C_4 for upper-extremity SEP and C_Z for lower-extremity SEP using the international 10–20 electrode system and were designated C_3', C_4', and C_Z', respectively. Electrode impedance was maintained less than 2 kohms. A disposable electrode (impedance 2–3 kohms) was placed at F_{PZ} for reference. A transcutaneous nerve stimulator was used to locate an area near both median nerves and both posterior tibial nerves, which resulted

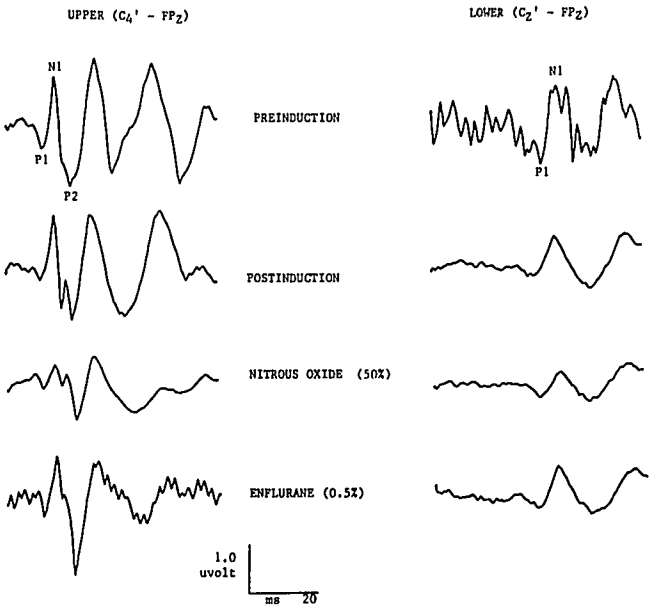

FIG. 1. The upper and lower extremity SEP is shown in one patient from Group 1. A stimulus intensity approximately 3× motor threshold was used for both upper- and lower-extremity SEPs. One hundred twenty-eight stimuli were delivered at a rate of 5.9/s and averaged, and a time period of 80 ms after stimulus was evaluated. In this patient, nitrous oxide (50%) was administered for 30 min and discontinued, and enflurane (0.5% in O_2) was administered for 30 min.

in a distinct digital twitch (motor threshold). This location was marked, and sterile stimulating needle electrodes were placed and the extremities were covered to prevent heat loss. Each extremity was stimulated individually. For upper-extremity SEPs, 128 stimuli were delivered at a rate of 5.9/s (stimulus duration 150 μs) and the responses were amplified and averaged. Stimulus parameters for lower-extremity SEPs were 128 stimuli delivered at a rate of 3.9/s (stimulus duration of 250 μs). A time of 80 ms after stimulus was assessed. Band pass filters of 5–1,500 Hz were used for both extremity SEPs. Preinduction SEPs were determined following vascular catheter insertion and immediately prior to anesthesia induction. A stimulus intensity sufficient to cause a digital twitch (motor threshold) was used in unanesthetized patients. In anesthetized patients, a stimulus intensity approximately 3× motor threshold (19.9 MA) was used for both upper- and lower-extremity SEPs. Replicate waves were obtained for all extremities during each study period, and the waves were stored on magnetic disk for later analysis. Five to 10 min were required for complete data acquisition. High-voltage artifact was rejected automatically by the computer. During periods of frequent use of electrocautery, averaging was halted by the computer operator.

Early waves of each extremity SEPs were evaluated and are shown in figure 1. For the upper extremity this

TABLE 1. Hemodynamic and Temperature Changes during Anesthetic Administration

	Preinduction	Postinduction	Initial N_2O	Initial* Volatile Anesthetic	Second N_2O	Second* Volatile Anesthetic
MABP (mmHg)						
Group 1	100 ± 4	100 ± 6	92 ± 5	93 ± 6	93 ± 5	95 ± 5
Group 2	107 ± 4	111 ± 2	95 ± 4†	102 ± 4	102 ± 6	99 ± 5
Heart rate (beats/min)						
Group 1	86 ± 9	94 ± 9	79 ± 6	76 ± 5	76 ± 5	77 ± 5
Group 2	80 ± 8	84 ± 5	73 ± 4	71 ± 3	68 ± 3†	70 ± 3
Temperature (°C)						
Group 1		36.3 ± 0.1	35.8 ± 0.2†	35.6 ± 0.2†	35.6 ± 0.2†	35.7 ± 0.2†
Group 2		36.1 ± 0.1	35.7 ± 0.2†	35.8 ± 0.2†	35.8 ± 0.3†	35.7 ± 0.2†

Mean ± SEM.
* Group 1 = enflurane; Group 2 = isoflurane.
† $P < 0.05$ compared with postinduction value.

consisted of a positive (P1 about 15 ms), negative (N1 about 20 ms), positive (P2 about 23 ms) complex. In some patients, the positive wave following N1 had a small notch at about 23 ms and a predominant positive wave later. In those patients, the small positive wave was not assessed and the prominent positive wave was used for evaluation. The latency of each wave was defined as the point of maximum voltage deflection, and the latency of the point was determined using the cursor mode of the computer. The amplitude was determined as the voltage difference between the maximum negative deflection of component N1 and the following positive deflection of component P2 (N1P2). Lower extremity SEPs were evaluated in a similar manner. The wave pattern was a small positive (P1 about 35 ms) and a large negative N1 (about 45 ms) (fig. 1). The latency for upper extremity is presented as N1 and P2, and lower extremity is presented as the latency of the first major negative wave (N1). The amplitude of the P1N1 complex was evaluated for the lower extremity. Although P1 of the lower-extremity SEPs probably represents the initial response of the cortex[17] and therefore corresponds to the N1 (negative wave 20 ms after stimulation) of the upper-extremity SEPs thought to be initial response of the cortex,[18] we chose to evaluate N1 latency, since this wave is usually much larger.

Data are presented as mean ± SEM in text and figures. Analysis of variance (ANOVA) for repeated measures was used to assess changes related to anesthetic gas administration for each extremity within each group. A two-way analysis of variance was used to compare awake values between groups 1 and 2 and to compare preinduction and postinduction values. If ANOVA demonstrated significance ($P < 0.05$), a Duncan's multiple range test then was used to determine values that were different.

Results

Satisfactory data were obtained prior to induction of anesthesia in all neurologically normal patients for upper-extremity SEPs and for 15 of 24 patients for lower-extremity SEPs. Preinduction data were incomplete in patients with preoperative deficits due to discomfort or excessive muscle artifact. Following induction of anesthesia, reproducible waveforms were obtained in all patients for both upper- and lower-extremity SEPs. To ensure that the order of gas administration was not important either on hemodynamic or evoked potential parameters assessed, ANOVA was used to compare the subgroups (N_2O first and anesthetic gas first) within both Group 1 and Group 2. There was no difference in either Groups 1 and 2 between patients who received N_2O initially and those who received a volatile anesthetic initially and the data were combined. Three patients (normal preoperative examination) had intraoperative changes in SEPs, and all three had transient hemiparesis postoperatively without permanent sequelae.

MABP and heart rate were similar in Groups 1 and 2 prior to anesthesia induction and during all five study periods. Statistically significant but clinically unimportant differences occasionally were noted. Nasopharyngeal temperature decreased to 36.3 ± 0.1° C at the time of postinduction data determination and stabilized at 35.7 ± 0.2° C during the remaining study periods and was similar in the two groups (table 1).

Figure 1 shows the effect of two anesthetics on ipsilateral upper- and lower-extremity SEPs in a patient from Group 1 in which enflurane (0.5%) was compared with nitrous oxide (50%). The specific parts of the waves evaluated for both upper- and lower-extremity SEPs are labeled. The smaller amplitude of both upper- and lower-extremity SEPs during nitrous oxide compared to enflurane can be seen.

Figure 2 shows the effect of nitrous oxide and enflurane on upper-extremity SEPs in a patient from Group 3 (neurologically abnormal). This patient had a preoperative left hemiparesis. Nitrous oxide depressed the left upper-extremity SEPs to the extent that monitoring was difficult, while enflurane was less depressing. The patients with preoperative hemiparesis generally had

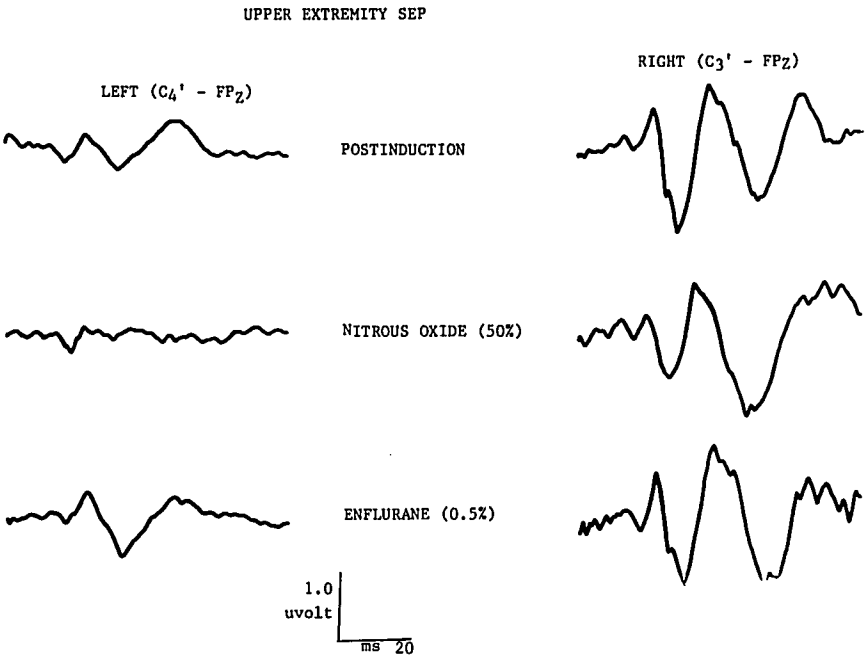

FIG. 2. The effect of enflurane and N_2O on upper-extremity SEP in a patient with preoperative left hemiparesis is shown. Each anesthetic was administered for 30 min. One hundred twenty-eight stimuli were delivered at a rate of 5.9/s and averaged.

asymmetry of SEPs with abnormalities consistent with preoperative deficits.

Table 2 shows the effect of the anesthetics (nitrous oxide, enflurane, isoflurane) on amplitude during the study periods. In Group 1, both nitrous oxide and enflurane decreased the amplitude of the upper-extremity SEPs with the depression being less with enflurane than with nitrous oxide. Nitrous oxide, but not enflurane, decreased the amplitude of the lower-extremity SEPs. In Group 2, both nitrous oxide and isoflurane decreased the upper-extremity SEPs' amplitude, but the decrease was greater with nitrous oxide. Nitrous oxide decreased

TABLE 2. SEP Amplitude during Anesthetic Gas Administration

	Preinduction	Postinduction	Initial N_2O	Initial* Volatile Anesthetic	Second N_2O	Second* Volatile Anesthetic
Group 1 (n = 12)						
Upper extremity (μV)						
Left	2.2 ± 0.3	2.6 ± 0.3	1.1 ± 0.2†	1.8 ± 0.3†‡	1.2 ± 0.3†	2.3 ± 0.6‡
Right	2.0 ± 0.3	3.3 ± 0.3§	1.2 ± 0.2†	2.3 ± 0.2†‡	1.2 ± 0.2†	1.8 ± 0.3†‡
Lower extremity (μV)						
Left	1.5 ± 0.1	1.8 ± 0.4	1.0 ± 0.2†	1.8 ± 0.4†	1.0 ± 0.3†	1.8 ± 0.3‡
Right	1.3 ± 0.1	2.0 ± 0.4	1.1 ± 0.4†	1.5 ± 0.4†‡	1.1 ± 0.3†	1.7 ± 0.4‡
Group 2 (n = 12)						
Upper extremity (μV)						
Left	2.0 ± 0.3	1.9 ± 0.3	1.1 ± 0.2	1.6 ± 0.2†‡	1.0 ± 0.1†	1.5 ± 0.2†‡
Right	2.7 ± 0.4	2.8 ± 0.5§	1.5 ± 0.2†	2.1 ± 0.3†‡	1.3 ± 0.2†	2.1 ± 0.4†‡
Lower extremity (μV)						
Left	1.8 ± 0.3	1.7 ± 0.2	1.1 ± 0.1†	1.7 ± 0.2‡	1.2 ± 0.1†	1.7 ± 0.2‡
Right	1.9 ± 0.5	1.8 ± 0.3	1.1 ± 0.2†	1.8 ± 0.4‡	1.1 ± 0.2†	1.6 ± 0.3‡
Group 3 (n = 5)						
Upper extremity (μV)						
Left		1.5 ± 0.5	0.9 ± 0.2†	1.1 ± 0.4	0.9 ± 0.3†	1.4 ± 0.3
Right		2.1 ± 0.4§	1.0 ± 0.2†	1.9 ± 0.4	1.0 ± 0.2†	1.7 ± 0.5
Lower extremity (μV)						
Left		1.1 ± 0.2	1.0 ± 0.3	0.7 ± 0.2	0.8 ± 0.3	0.8 ± 0.4
Right		1.9 ± 0.8	1.1 ± 0.3	0.8 ± 0.1	1.2 ± 0.4	1.2 ± 0.3

Mean ± SEM.
* Groups 1 and 3 = enflurane; Group 2 = isoflurane.
† $P < 0.05$ compared with postinduction.
‡ $P < 0.05$ compared with N_2O (50%).
§ Different from contralateral side.

TABLE 3. SEP Latency during Anesthetic Gas Administration

	Preinduction	Postinduction	Initial N_2O	Initial* Volatile Anesthetic	Second N_2O	Second* Volatile Anesthetic
Group 1						
Upper extremity latency (ms)						
N1 Left	20.1 ± 0.5	20.8 ± 0.4	20.9 ± 0.4	21.2 ± 0.6	20.8 ± 0.5	21.1 ± 0.6
Right	20.3 ± 0.5§	20.9 ± 0.5	20.8 ± 0.5	21.9 ± 0.6†‡	20.8 ± 0.4	21.4 ± 0.5†‡
P2 Left	24.6 ± 0.9§	26.6 ± 1.0§	25.7 ± 0.8§	26.9 ± 1.1§	26.0 ± 0.8§	27.2 ± 0.9§
Right	24.9 ± 1.0§	27.0 ± 0.8§	26.9 ± 1.0§	28.0 ± 1.0§	26.9 ± 1.0§	27.6 ± 1.2§
Lower extremity latency N1 (ms)						
Left	44.8 ± 2.7	44.3 ± 1.8	44.6 ± 2.0	45.4 ± 2.0	43.2 ± 1.7	43.6 ± 1.6
Right	43.8 ± 2.6	44.5 ± 1.8	45.1 ± 1.9	45.7 ± 1.8	43.6 ± 1.8	43.6 ± 1.6
Group 2						
Upper extremity latency (ms)						
N1 Left	18.9 ± 0.5	19.4 ± 0.4	19.4 ± 0.4	20.1 ± 0.4†‡	19.1 ± 0.5	19.8 ± 0.5‡
Right	19.1 ± 0.5	19.9 ± 0.5	19.9 ± 0.5	20.5 ± 0.4†‡	19.6 ± 0.5	20.3 ± 0.5†‡
P2 Left	23.1 ± 0.5	23.1 ± 0.5	22.8 ± 0.8	24.0 ± 0.6†‡	23.3 ± 0.6	24.2 ± 0.8†‡
Right	22.6 ± 0.8	23.1 ± 0.8	23.2 ± 0.9	23.9 ± 0.7†‡	23.1 ± 0.8	24.0 ± 0.9†‡
Lower extremity latency (ms)						
Left	46.8 ± 0.4	47.6 ± 1.1	47.7 ± 1.0	49.2 ± 0.7†	47.2 ± 0.9	48.6 ± 0.8
Right	45.1 ± 1.0	46.8 ± 0.7	48.1 ± 0.9†	48.3 ± 0.7†	47.8 ± 0.7†	48.6 ± 0.8†
Group 3						
Upper extremity latency (ms)						
N1 Left		22.5 ± 1.8‡	23.0 ± 2.3	22.8 ± 1.9	22.3 ± 2.0	23.1 ± 2.1
Right		22.0 ± 1.6	22.0 ± 1.7	22.7 ± 1.6	21.7 ± 1.7	21.9 ± 1.9
P2 Left		31.0 ± 3.2‡	30.1 ± 4.2	30.4 ± 3.8	30.1 ± 4.1	30.9 ± 4.0
Right		28.6 ± 3.0‡	27.3 ± 2.2	29.4 ± 3.1	27.0 ± 2.5	28.7 ± 3.5
Lower extremity latency (ms)						
Left		56.9 ± 2.0¶	58.0 ± 2.1	55.0 ± 3.5	54.9 ± 1.2	53.7 ± 1.8
Right		51.7 ± 3.5¶**	52.3 ± 4.4	55.0 ± 4.4	48.9 ± 2.4	50.7 ± 2.7

Mean ± SEM.
* Group 1 and 3 = enflurane; Group 2 = isoflurane.
† $P < 0.05$ compared with postinduction.
‡ $P < 0.05$ compared with N_2O (50%).
§ $P < 0.05$ compared with Group 2.
¶ $P < 0.05$ compared with Groups 1 and 2.
** $P < 0.05$ compared with contralateral side.

the amplitude of the lower-extremity SEPs, while isoflurane had no effect. Amplitude of the right upper-extremity SEPs was greater in all three groups immediately following induction, and this tendency continued during all periods. This may be a result of suboptimal electrode placement, as the arterial catheter was placed in the left radial artery and prevented optimal placement of the stimulating electrode near the left median nerve.

Table 3 shows wave latency during the study periods. In Group 1, slight and variable increases in latency of upper-extremity SEPs occurred with enflurane administration. Lower-extremity SEPs' latency was not altered by either N_2O or enflurane. In Group 2, isoflurane slightly increased the latency of upper-extremity SEPs N1 and P2, whereas nitrous oxide had no effect. Likewise, isoflurane increased lower-extremity latency, while N_2O had no effect.

Discussion

Our results demonstrate that fentanyl–enflurane–oxygen and fentanyl–isoflurane–oxygen allow generation of adequate SEPs, while nitrous oxide supplementation of fentanyl depresses SEP amplitude more than supplementation with either enflurane or isoflurane. Although relatively low concentrations of enflurane and isoflurane were used (0.25–1.0%), there was not a single incidence of postoperative recall, despite the absence of amnestic agents such as diazepam or scopolamine, indicating an acceptable anesthetic level with this technique. We have shown that the choice of anesthetic supplementation during fentanyl-based anesthesia affects SEPs waveforms and that larger and presumably easier-to-evaluate waveforms are generated during either enflurane or isoflurane than during nitrous oxide. In patients with very small

SEPs, choice of an anesthetic technique avoiding nitrous oxide would provide a greater possibility of generating SEPs adequate for clinical monitoring. Additionally, changes in SEPs occurring with addition or removal of nitrous oxide tends to interfere with the monitoring because the changes must be distinguished from those due to intraoperative neurologic injury.

The waveforms developed prior to induction of anesthesia in the present study are similar to those reported previously. Specifically, the latency of the upper-extremity negative wave (N1) prior to induction reported here is in general agreement with those previously studied in unanesthetized patients.[18-21] Likewise, the latency of the prominent negative wave of the lower extremity is similar to that previously published.[17] Induction of anesthesia included administration of both anesthetic agents and neuromuscular blocking agents. The necessity of immediate hyperventilation in patients in this study prevented assessment of induction agents (fentanyl and thiopental) on SEPs prior to administration of neuromuscular blocking agents. The presence of a muscular response to stimulation affects the primary cortical response (N_2O–P23 complex), and hence the effect of the neuromuscular blocking agent directly might affect the cortical response by preventing muscle twitch.[22]

Intraoperative monitoring of SEPs presumes that the monitor demonstrates changes rapidly enough to prevent injury, is specific for neurologic insult, and does not interfere with currently acceptable standards of care. Appropriate anesthetic technique for patients with neurologic disease must provide stable anesthesia, be flexible enough to handle major problems (*e.g.*, air emboli), and allow rapid awakening for postoperative neurologic examination. Likewise, the anesthetic technique should allow rapid generation and evaluation of SEPs. We demonstrated that nitrous oxide (50%) has a greater depressant effect than either enflurane or isoflurane (0.25–1.0%) on SEP waveforms monitored intraoperatively, and this is at variance with the suggested anesthetic technique in a recent review of the subject.[23] The results of this study are supported by animal studies by others concerning the effects of enflurane and isoflurane on SEPs.[24,25] The controversy may relate to the specific anesthetic technique used.

Since all three anesthetics used (nitrous oxide, enflurane, isoflurane) decreased the size of the scalp-recorded SEPs, the optimal anesthetic for monitoring of SEPs might be a pure fentanyl anesthetic technique. However, difficult awakening may occur at the end of the operation, and a prolonged narcotic antagonist infusion (naloxone) may be necessary to maintain arousal and normal ventilation.[16] Bolus injection of fentanyl for anesthesia induction was chosen for several reasons. The amount of supplementary anesthetic would be minimized prior to the time of dural decompression due to a decrease in MAC by fentanyl,[13] and the serum level of fentanyl would decline slowly over the course of the study (120 min).[13,26,27] Half of each group of patients received N_2O initially, and the other half received the volatile anesthetic initially; and two sets of anesthetic administrations were studied so that the effect of a declining fentanyl level should not be an explanation for the differential depression seen with N_2O compared with either enflurane or isoflurane. Intravenous supplementation was required in a minority of patients receiving either N_2O or the volatile anesthetic, and the amounts given were similar in each group. Additionally, a greater depressant effect by N_2O was seen in each patient, regardless of occurrence of barbiturate supplementation.

The patients studied differ from previously studied groups in whom SEPs have been monitored for scoliosis repair[1-3] in that the period of risk (distraction) was predictable and heavy premedication was not contraindicated. The lack of premedication in the present study undoubtedly contributed to difficulty in obtaining preanesthesia data in some patients in this study. Patient discomfort, hemodynamic responses to stimulation, and excessive muscle artifact in response to stimulation prevented generation of acceptable data prior to anesthesia induction in some patients. Induction of anesthesia removed all these obstacles, and thus we considered the postinduction data as control for comparison of anesthetics. The absence of preinduction data in individual patients is of consequence only if the induction of anesthesia has detrimental effects on neurologic function. Neither fentanyl[12] or thiopental[28] adversely alters cerebral hemodynamics, so that in the absence of a decrease in cerebral perfusion pressure, neurologic function would be expected to be unchanged. None of the patients in Groups 1 or 2 were symptomatic from increased intracranial pressure and blood pressure, and presumably cerebral perfusion pressure was maintained near induction value during all study periods.

Preoperative neurologic abnormalities and the associated abnormalities of SEPs waveform create a particularly difficult situation. The waveforms frequently are difficult to evaluate because of decreases in amplitude and abnormalities of latency (fig. 2). Also, the lesion contributing to both neurologic injury and abnormal SEPs are likely to be involved in the surgical field and to be at risk of further injury. We have included patients who had preoperative neurologic abnormalities, and at least the first anesthetic comparison in the study was concluded prior to obvious causes of neurologic change such as brain retraction; hence the changes in SEPs reflect only drug-related changes. In patients with abnormally small SEP waves, nitrous oxide decreased the wave amplitude to near the lower limits of resolution,

which could make rapid diagnosis of intraoperative changes more difficult (fig. 2).

The accuracy and speed of determination of latency of SEPs is dependent upon the size and distinctiveness of the waveform. Disruptive influences (electrocautery) frequently occur during times of interest so that an anesthetic technique that allows large waves to be generated quickly is desirable. Data analysis in this study was performed off-line so that unlimited time was available for accurate analysis. The analysis of extremely small waveforms was aided by the replicate waveforms obtained during the study. The time requirement for replication of waves and evaluation presents obvious clinical difficulty during incidences of possible alterations in neurologic function related to reversible events such as retraction of neural tissue, since definite therapy may not be initiated as quickly as possible.

Early waveforms of SEPs were chosen for analysis because they are recognized easily in awake patients, and during anesthesia those waves appear after only a few stimuli are averaged so that electrophysiologic changes can be appreciated quickly. Clinical decisions based on changes in SEPs require verification by repeating the SEPs and evaluation of the contralateral side to rule out systemic effects in addition to appropriate equipment checks. The stimulus parameters used allowed generation of individual waves in approximately 45 s. Although different stimulus parameters may allow more precise localization of dysfunction within the neural axis, wave generation may require as long as 8–10 min.[29] The shorter wave generation time seems more appropriate for intraoperative monitoring where the patient serves as his own control.

This study was performed during the early part of neurologic procedures and the length of each study period was chosen so that comparison between anesthetics could be made prior to progression of surgery to the point of risk to neurologic tissue. The use of two comparisons of N_2O with the volatile anesthetic over 120 min tends to decrease both the effect of declining effect of the induction agents (fentanyl and thiopental) and the recent onset of hyperventilation. The uptake and excretion of nitrous oxide would be expected to be near steady state after 30 min of administration or 30 min after discontinuation.[30] Likewise, isoflurane reaches a near steady state after 30 min of inhalation and excretion after a short period of administration (30 min).[31] The uptake and excretion of enflurane is similar to isoflurane.

In conclusion, we have demonstrated that induction of anesthesia with fentanyl and thiopental causes small changes in the scalp-recorded SEP. In addition, we have shown that during fentanyl-based anesthesia, volatile anesthetics (enflurane and isoflurane, 0.25–1.0%) depress the SEP amplitude less than nitrous oxide (50%) in patients with and without preexisting neurologic deficits. Thus, in situations in which the size of SEP waves are important for clinical monitoring, low concentrations of enflurane and isoflurane (0.25–0.75%) offer better conditions for monitoring than 50% nitrous oxide.

The efforts of Renee Craig in preparation of this manuscript are greatly appreciated. The assistance of Joanne Backofen, M.D., also is acknowledged.

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