EFFECT OF THIOPENTONE ON MOTOR EVOKED POTENTIALS INDUCED BY TRANSCRANIAL MAGNETIC STIMULATION IN HUMANS

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SUMMARY

We have studied the effect of repeated doses of thiopentone on motor evoked potentials (MEP) after transcranial magnetic stimulation in 13 patients. Thiopentone was administered i.v. in an initial dose of 2 mg kg⁻¹, followed by repeated doses (1 mg kg⁻¹ every 3 min) until the appearance of burst suppression on the EEG. The total dose administered was mean 10.7 (SD 2.6) mg kg⁻¹. The magnetic coil was placed over the MEP scalp stimulation region and evoked electromyographic responses were recorded from the contralateral abductor pollicis brevis. After an initial dose of thiopentone, reproducible MEP responses were recorded in all patients, but amplitudes were reduced to 42.8% of baseline values. Further administration of repeated doses of thiopentone produced a dose-dependent decrease in success rate of MEP recordings and a significant reduction in MEP amplitude (P < 0.01). Latency did not change significantly, although there was a tendency to increase. During burst suppression on the EEG, MEP was not recorded successfully in all patients. We conclude that MEP recording during the administration of thiopentone is feasible only at a minimum dose, with a marked reduction in MEP amplitude.

KEY WORDS

Anaesthetics, intravenous; thiopentone. Brain, electroencephalography, evoked potentials.

Transcranial electrical and magnetic stimulation to produce motor evoked potentials (MEP) has been advocated to assess the functional integrity of motor pathways during anaesthesia [1–3]. High voltage electrical stimuli are assumed to excite the pyramidal cells directly beneath their cell bodies, whereas magnetic stimuli probably excite the descending motor pathways transsynaptically [4,5]. Both techniques make it possible to evoke motor responses in various muscles of the upper and lower limbs and of the face. However, anaesthetic agents may interfere with the reproducibility of such responses and limit the usefulness of this technique [3,6–8]. Thiopentone is a commonly used anaesthetic agent which reduces cerebral blood volume and may protect the brain in large doses. Patients with severe head injury, increased intracranial pressure, brain swelling and massive cerebral ischaemia have been treated with large doses of barbiturate [9–11]. In such patients, it is crucial to assess the descending pathways in addition to ascending pathways, using somatosensory evoked potentials (SEP).

Several authors have demonstrated the effects of thiopentone on SEP and MEP [7,8,12–16], but there are no data on the minimum dose of thiopentone for successful recording of MEP during high-dose barbiturate therapy. Therefore, we have evaluated the effect of thiopentone on MEP induced by transcranial magnetic stimulation.

PATIENTS AND METHODS

The study was approved by the Ethics Committee of Osaka Neurological Institute and informed consent was obtained from each patient. We studied 13 patients (mean age 40.2 yr (range 19–65 yr), ASA I–II; nine women) undergoing elective surgery. All patients were free from motor dysfunction and had normal MEP responses at the preoperative examination. Patients with liver dysfunction or heart disease were excluded. Each patient was premedicated i.m. with atropine 0.5 mg and famotidine 20 mg 30 min before induction of anaesthesia. An i.v. catheter was inserted and the overnight fluid deficit was replaced with glucose-free lactated Ringer’s solution. Routine monitoring included ECG, automated oscillotonometry, pulse oximeter, temperature and end-tidal carbon dioxide measurements.

The motor cortex and cervical region (7th cervical vertebra) were stimulated with a magnetic stimulator (SMN-1100, Nihon Kohden, Japan), consisting of a capacitor and a flat coil (i.d. 10.5 cm; o.d. 17 cm). A large current (7500 A) passes through the coil after discharge of the capacitor (1500 μF). A large current (7500 A) passes through the coil after discharge of the capacitor (1500 μF). The strength of the magnetic fields varies according to the electric...
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FIG. 1. Changes in mean arterial pressure and heart rate during administration of repeated doses of thiopentone (mean, SD). C = Control; B = burst.

current, which is controlled by the voltage of the discharge current of the capacitor. The maximum magnetic field of 0.4 Tesla was obtained with an output voltage of 1000 V (= 7500 A) about 166 μs after the onset of discharge. Magnetic stimulation was given with a stimulus intensity of 900 V for the motor cortex and 600 V for the cervical region. MEP were recorded with surface electrodes placed over the abductor pollicis brevis muscle. Signals were amplified and recorded with the restricted filter setting of 20–3000 Hz, using a conventional electromyographic recording system (Neuromatic 2000C, Dantec, Denmark). MEP amplitude was measured as the vertical distance between two successive peaks and onset latency was measured on the MEP of shortest latency. EEG was recorded using a Neurofax (Nihon Kohden, Japan). Gold cup electrodes were placed according to the international 10–20 system at F3, F4, P3, P4, O1, O2, references to linked earlobes. A time constant of 0.3 s and a high-pass filter of 120 Hz were used. Electrode impedances were matched within 1 kΩ.

After duplicate baseline recordings of MEP were obtained, thiopentone was given i.v. in an initial dose of 2 mg kg⁻¹, followed by repeated doses (1 mg kg⁻¹) every 3 min until the appearance of burst suppression on the EEG. Each dose was given over 10 s. MEP induced by transcranial magnetic stimulation were recorded 2 min after the injection of each dose of thiopentone. MEP induced by magnetic stimulation of the cervical region were recorded before and after administration of the total doses required for appearance of burst suppression. At 1-min intervals during the study, arterial pressure and heart rate were recorded and methoxamine was administered if necessary for maintenance of arterial pressure. Ventilation was assisted manually using a facemask with 100% oxygen to maintain an end-tidal carbon dioxide partial pressure of 4.6–5.3 kPa. All patients had a rectal temperature > 36.5°C. At the conclusion of the study, the patients were given vecuronium 8 mg i.v. and the trachea was intubated.

Data were analysed using a one-way analysis of variance (ANOVA) with repeated measures and Tukey’s post hoc test. Statistical significance was assumed at P < 0.05.

RESULTS

In all patients, we obtained distinct baseline MEP induced by transcranial magnetic stimulation. Latencies and amplitudes were 21.1 (0.5) ms and
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1069.4 (968.0) μV, respectively. The total dose of thiopentone administered was 10.7 (2.6) mg kg⁻¹. Mean arterial pressure and heart rate did not change significantly during the study (fig. 1).

Figure 2 shows MEP recordings before and during the administration of thiopentone and figures 3 and 4 show the success rate of MEP recordings and changes in MEP amplitudes during administration of thiopentone. After an initial dose of thiopentone 2 mg kg⁻¹, reproducible MEP responses were recorded in all patients, but amplitudes were reduced to 42.8% (range 0.75–85%) (P < 0.01). With thiopentone 3 mg kg⁻¹, MEP responses were obtained in nine of 13 patients and amplitudes ranged from 7.5 to 57% (average 24.4%) (P < 0.01) of the baseline values. With thiopentone 4 mg kg⁻¹, MEP responses were obtained in eight patients, with amplitudes reduced to 16.4% (P < 0.01). MEP response was obtained until a total dose of thiopentone 9 mg kg⁻¹ had been given to one patient. No MEP were obtained during burst suppression of the EEG.

There were no significant changes in MEP latency during administration of thiopentone (fig. 5).

Amplitudes and latencies of MEP induced by magnetic stimulation of the cervical region did not change significantly after administration of thiopentone (amplitude 740.8 (712.1) μV before and 710.3 (702.8) μV after thiopentone; latency 12.2 (1.0) ms before and 12.3 (0.8) ms after thiopentone) (fig. 6).

DISCUSSION

Our results showed that MEP responses induced by transcranial magnetic stimulation were obtained during administration of thiopentone 2 mg kg⁻¹ with a marked reduction in MEP amplitudes. Further administration of repeated doses of thiopentone induced a dose-dependent decrease in the success rate of recording MEP and MEP amplitudes. MEP latencies did not change significantly, although there was a trend to increase. The amplitudes and latencies of MEP induced by magnetic stimulation of the cervical region did not change significantly during administration of thiopentone.

The results of our study are consistent with
Wollmen [20] demonstrated that EEG changes in MEP responses 2 min after administration of each dose of thiopentone were evident 2 min later and had occurred during a 3-min period when the drug was administered. Moffat and Serpico [12] demonstrated that a bolus of thiopentone 4 mg kg⁻¹ induced a significant increase in latency with a decrease in amplitude of the early cortical response to median nerve stimulation. Abrahamian and colleagues [13] recorded the cortical response to median nerve stimulation in surgical patients and observed that incremental administration of thiopentone 6–8 mg kg⁻¹ occasionally produced increases in the latency of the primary specific complex. Drummond, Todd and U [14] demonstrated that the administration of a dose of thiopentone in excess of twice that required to produce EEG isoelectricity caused dose-related increases in latency, with significant reductions in amplitudes of the cortical primary specific complex.

The mechanism of the effect of thiopentone on MEP induced by transcranial magnetic stimulation is not clear; however, it may be related to the inhibitory action of thiopentone on synaptic transmission in the central nervous system. Magnetic fields induced for MEP recordings presumably activate preferentially the transsynaptically-mediated cortical motoneurones, producing mainly indirect (I) waves [5].

We observed great variability in the doses of thiopentone which affected monitoring of MEP. The causes are not clear, but several possible explanations may be advanced. Great variability in amplitudes of MEP have been reported between subjects [1] and this may have influenced our results. The concentration of thiopentone at sites of action in the brain may vary markedly between subjects and several authors have observed the great variability in the dose of thiopentone required to produce suppression [17,18].

One possible criticism of our study is the use of repeated doses of thiopentone. In a preliminary study, we administered thiopentone 4 mg kg⁻¹, but we could not record MEP in some patients. Therefore, we chose to use repeated doses with an initial dose of 2 mg kg⁻¹ to identify the minimum for successful recordings of MEP. After a single i.v. dose of thiopentone, unconsciousness occurs after 10–20 s and the depth of anaesthesia may increase for up to 40 s and then decrease progressively until consciousness returns in 20–30 min [19]. Moffat and Wollmen [20] demonstrated that EEG changes occurred during a 3-min period when the drug was administered, were evident 2 min later and had disappeared by 5–10 min after the administration of thiopentone was completed. Therefore, we measured MEP responses 2 min after administration of each dose of thiopentone at 3-min intervals. However, the effects of thiopentone on MEP may differ according to whether a fixed dose of thiopentone is administered in the form of a bolus or by several increments.

The magnetic stimulator used in the present study has a maximum magnetic field of 0.4 Tesla, which is somewhat less than that of other stimulators [1] and may influence the results obtained in the present study. A greater magnetic field may increase the success rate of recording MEP.

REFERENCES

