Level of consciousness affects the excitability of spinal motor neurones during propofol sedation in humans

M. Kakinohana* and K. Sugahara

Department of Anesthesiology, Faculty of Medicine, University of the Ryukyus, Okinawa, Japan

*Corresponding author: Department of Anesthesiology, Faculty of Medicine, University of the Ryukyus, 207 Uehara, Nishihara, Okinawa, 903-0125, Japan. E-mail: mnb-shk@ryukyu.ne.jp

Background. To investigate the relationship between the depression of spinal motor neuronal excitability and the sedative level induced by propofol infusion, we simultaneously analysed the suppressive effect of propofol on the F wave and the sedative level during propofol infusion.

Methods. After spinal anaesthesia, sedation was achieved using a propofol target-controlled infusion (TCI) system to achieve a score of 4 on the Wilson sedation scale. The excitability of spinal motor neurones was determined by measuring the left median nerve F wave. F-wave persistence and the F/M ratio were recorded at pre-sedation as the control, during sedation, at arousal by mild physical stimulation and at post-sedation.

Results. Wilson sedation scores increased significantly corresponding to the increase in the target propofol concentration (Cpt), and a Cpt-producing Wilson sedation scale 4 ranged between 1.2 and 1.8 μg ml⁻¹. The F-wave persistence and F/M ratio before propofol infusion were 80.7 (8.6)% and 9.5 (3.9)%, respectively. At Wilson sedation scale 4, F-wave persistence and F/M ratio were 17.6 (12.8)% (0–37.5%) and 4.3 (4.1)%, and, at return of consciousness by mild physical stimulation, significantly increased to 71.3 (7.9)% and 10.0 (5.0)%, respectively.

Conclusion. We demonstrated that the excitability of spinal motor neurones was suppressed during sedation by propofol TCI, but this suppressive effect vanished at return of consciousness by mild physical stimulation even at a constant Cpt. Our data suggested that the effect of propofol on the excitability of spinal motor neurones might be affected by consciousness level rather than propofol Cpt in humans.

Keywords: anaesthetics i.v., propofol; complications, spinal motor neuronal excitability; F wave

Accepted for publication: February 24, 2006

Recent studies suggest that the spinal cord is as important as the brain as the site of anaesthetic action. Especially, the depression of spinal motor neurones by volatile anaesthetics appears to be associated with surgical immobility in humans. Some reports have recommended the analysis of the F wave to monitor surgical immobility in humans. A human study of F-wave analysis showed that propofol 2 mg kg⁻¹ administered i.v., but not ketamine 1 mg kg⁻¹ i.v. or fentanyl 5 μg kg⁻¹ i.v., decreased F-wave persistence, suggesting that propofol can reduce the excitability of spinal motor neurones. Our previous study has shown that propofol predictably suppresses the excitability of spinal motor neurones in a concentration-dependent manner. Interestingly, in that investigation we sometimes observed that F-wave persistence, which was decreased by propofol infusion by a target-controlled infusion (TCI) system at a sedative level, increased abruptly upon arousal even at constant predicted plasma concentrations of propofol (Cpt). According to this observation, we speculated that the suppressive effect of propofol on the excitability of spinal motor neurones might be caused not only by the direct spinal action of propofol, but also partly by the reduction of facilitation or enhancement of inhibitory supra-spinal input. To our knowledge, no investigation of the relationship between the depression of spinal motor neuronal excitability and the sedative level induced by propofol infusion has been reported. In this study we simultaneously analysed the suppressive effect of propofol on the F wave and the...
sedative level [Wilson sedation scale and bispectral index (BIS) values] in order to investigate the differences between spinal or supra-spinal contributions to the reduction of spinal motor neuronal excitability.

Materials and methods
The research protocol was approved by the Department of Anaesthesia and written informed consent was obtained from study participants. Subjects were 10 adult patients aged 41–61 yr [50.8 (7.2) yr, mean (SD)] who were classified as ASA physical status I and who underwent elective surgery under spinal anaesthesia combined with i.v. administration of propofol for intraoperative sedation. Patients with any history of neuromuscular disease, use of central nervous system-acting medication, or diabetes mellitus were excluded.

Premedication consisted of atropine 0.5 mg given i.m. 30 min before the spinal anaesthesia. On arrival in the operating room, all patients were monitored with continuous ECG, heart rate determination, non-invasive blood pressure measurement and pulse oximetry. I.V. access was established in a forearm vein. After baseline values were recorded, spinal anaesthesia was administered with the patient in the lateral decubitus position. Local anaesthesia with lidocaine 1% to the skin and plain hyperbaric dibucaine 0.24% (2.0–2.2 ml) was injected at the third or fourth lumbar interspace through a 25 gauge Whitacre needle. The patient was immediately returned to the supine horizontal position. The extent of dermatomal analgesia by pinprick and cold sensitivity was assessed every 5 min until sensory blockade was confirmed. After confirming an adequate anaesthesia level for the operative procedure, analysis for the excitability of spinal motor neurones was started.

The excitability of spinal motor neurones was determined by measuring the left median nerve F wave. A baseline F wave was evoked with supramaximal (10–16 mA) electrical stimuli (duration of 0.1 ms) and recorded using Neuropack Σ™ (Nihon Koden Inc., Tokyo, Japan). Two surface recording electrodes were placed 4–5 cm apart over the abductor pollicis brevis muscle. Supramaximal stimuli of a 0.1 ms duration were applied percutaneously to the median nerve at the wrist joint at a stimulation rate of 0.5 Hz. To distinguish F waves from background noise, we accepted only appropriately timed (25–35 ms after electrical stimuli) deflections from baseline with an amplitude of at least 50 μV. The filter setting was set at 100–1500 Hz to remove background noise. F-wave persistence (number of measurable F waves divided by the number of electrical stimuli) was determined offline from a series of 16 stimuli delivered at an interstimulus interval of 2 s. The F/M ratio (mean amplitude of F wave divided by M wave amplitude) also was calculated.

After BIS monitoring (Aspect A-2000™; Aspect Medical Systems, Newton, MA, USA) was established, all patients received a computer-controlled infusion of propofol by a propofol TCI pump (TERUMO Inc., Tokyo, Japan) computer that was loaded with three-compartment propofol pharmacokinetic data. TCI was used to rapidly reach and maintain the target sedation level (Wilson sedation scale 4) (Table 1). Oxygen, 4 litre min⁻¹ was given for at least 10 min before recording the F wave and end-tidal CO₂ through a face mask was monitored continuously during the entire recording period. Blood pressure was supported to maintain mean arterial pressure values of no less than 75% of pre-sedation values using i.v. infusion of lactated Ringer’s solution.

After BIS and F wave were recorded pre-sedation as the control, sedation was achieved using the propofol TCI system. At first, propofol infusion was started at a Cpt of 0.5 μg ml⁻¹. Then, the Cpt was increased stepwise with 0.1 μg ml⁻¹ every 3 min until the sedation level reached a Wilson sedation scale 4. Once this occurred, the Cpt at this point remained constant for the entire study in each patient. F waves and BIS were recorded as sedative values at 15 min and 1 h after Wilson sedation scale reached 4. After recording sedation values, one anaesthetist (M.K) with more than 10 yr experience tugged the patient’s right earlobe slightly with verbal commands, for example, ‘open your eyes, please’ so that the patient became conscious. At the return of consciousness F waves were also recorded (first recordings). A second recording was made 1 h after the first recording using the same protocol. At the end of surgery, the propofol infusion was stopped and the patient was transferred to the post-anaesthetic care unit. BIS and F waves were also recorded 30 min after admission to post-anaesthetic care unit.

The average BIS values, F-wave persistence and F/M ratios were calculated. For statistical analysis of the BIS values, F-wave persistence and F/M ratio; the Dunnett’s test was used for ANOVA before and after propofol infusion. Probability values less than 0.05 were considered significant.

Results
The peak level of sensory block was lower than T10 bilaterally in all patients. Blood pressure changes >25% of baseline were observed in two patients during the study, which were recovered by i.v. infusion of lactated Ringer’s solution. At a Cpt of 0.5 μg ml⁻¹, no patient showed a change in consciousness. However, Wilson sedation scores increased.

Table 1 Wilson sedation scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fully awake and oriented</td>
</tr>
<tr>
<td>2</td>
<td>Drowsy</td>
</tr>
<tr>
<td>3</td>
<td>Eyes closed but rousable to command</td>
</tr>
<tr>
<td>4</td>
<td>Eyes closed but rousable to mild physical stimulation (earlobe tug)</td>
</tr>
<tr>
<td>5</td>
<td>Eyes closed but unrousable to mild physical stimulation</td>
</tr>
</tbody>
</table>
significantly corresponding to an increase in Cpt, and a Cpt-producing Wilson sedation scale 4 ranged between 1.2 and 1.8 μg ml⁻¹ (Fig. 1). Mean BIS value was 97.3 (1.3) before sedation. Although, at Wilson sedation scale 4, the mean BIS values at the first and second recording decreased significantly to 71.3 (3.6) and 74.4 (2.7), respectively. BIS abruptly increased to 91.9 (3.3) and 89.8 (4.9), respectively; by return to consciousness through mild physical stimulation. F-wave persistence and the F/M ratio before propofol infusion were 80.7 (8.6)% and 9.5 (3.9)% [mean (SD)], respectively. At Wilson sedation scale 4, F-wave persistence and the F/M ratio in the first recording were 17.6 (12.8)% (0–37.5%) and 4.3 (4.1)%, and at return of consciousness through mild physical stimulation, significantly increased to 71.3 (7.9)% and 10.0 (5.0)%, respectively. Data for F-wave persistence and F/M ratio in the second recordings were consistent with those in the first recordings (Figs 2 and 3).

Propofol infusion was stopped at the end of surgery and the patient became gradually alert over a period of about 20 min. At about 30 min after cessation of the propofol infusion, BIS value, F-wave persistence and the F/M ratio returned to pre-sedation values.

Discussion

Results of this study show that both the F/M ratio and the persistence decreased during propofol sedation compared with pre-sedation values, but returned to pre-sedation levels upon arousal by mild physical stimulation even at a constant propofol Cpt. These data indicate that the excitability of spinal motor neurones might be predominantly affected by the consciousness level rather than the propofol Cpt.

In this study, the peak level of sensory block in all patients is lower than T10. According to published data in the literature, F-wave persistence in upper extremities of normal adults is reported to be varied between 69.8 and 84.8%; these data are consistent with our data in this study. Therefore, it is unlikely that intrathecal local anaesthetics, in this study, can affect the excitability of spinal motor neurons in the cervical level.

The excitability of spinal motor neurones is dependent on the balance between excitatory and inhibitory pathways, which are mediated by spinal and supra-spinal systems. The former consists of the monosynaptic reflex circuit (dynamic gamma motor neuron), Ia inhibitory interneurones and Renshaw cells. The latter includes the descending fibre...
spinal motor neurones, in our study, 10 overlapped most of the response curve between propofol and the excitability of spinal motor neurones, it is demonstrated that, after the spinal shock stage, F-wave persistence and amplitude are significantly decreased on the paretic side.15 16 After acute spinal cord injury, 50% of the patients showed a complete F-wave loss of median and ulnar nerves during the initial course of the injury.17 Also, the existence of noradrenergic neurones projecting to the spinal motor neurones was shown in the locus coeruleus and the depression of these neurones in the locus coeruleus depressed the excitability of spinal motor neurones in humans.18 In addition, Ichikawa and Yokota19 demonstrated that F waves could disappear in normal subjects during sleep. These findings suggested that a signal from the supra-spinal level, including the reticular formation, through the descending tract fibre to the spinal cord is likely to affect the excitability of spinal motor neurones.

We demonstrated a reduction in the excitability of spinal motor neurones by propofol by its subanaesthetic concentrations in humans.10 In using an isolated spinal cord in vitro preparation from rats, however, Matute and colleagues20 showed that propofol could reduce the motor neuronal action potential wind-up in response to repetitive activation of nociceptive afferents in a concentration-dependent manner; whereas propofol was able to reduce motor neuronal action potential firing to only 50% of control within the anaesthetic concentration ranges. From these results, they speculated that the reduction of spinal motor neuronal excitability by subanaesthetic concentrations of propofol, in our previous study,10 was probably attributable to the depression of the descending facilitating signals rather than to a direct action of propofol on spinal motor neurones, which is consistent with our present data.

Results from our previous study,10 using the same protocol as in this study, suggested that propofol can suppress the excitability of spinal motor neurones in a Cpt-dependent manner with a plasma propofol concentration producing 50% inhibition from baseline of 1.05 μg ml⁻¹. In humans, Shafer and colleagues21 showed that the blood propofol concentration at which 50% of patients were awake was 1.07 μg ml⁻¹. It is of interest that the concentration–response curve between propofol and the excitability of spinal motor neurones, in our study,10 overlapped most of that between blood propofol concentration and awakening from propofol anaesthesia. According to comparisons of these data and findings from this study, we could also speculate that propofol at the spinal level by itself might show a much weaker inhibitory effect on the excitability of spinal motor neurones than expected. Also, the additional inhibition of propofol at Cpt higher than 1 μg ml⁻¹ might be attributed to a depression in the descending facilitating signals rather than to a direct action of propofol on motor neurones. This speculation is consistent with that of Matute and colleagues.20

In conclusion, we demonstrated that the excitability of spinal motor neurones was suppressed during sedation by TCI of propofol when analysing F-wave persistence and the F/M ratio, but this suppressive effect vanished at return of consciousness by mild physical stimulation even when the Cpt remained constant. Our data suggested that the effect of propofol on the excitability of spinal motor neurones might be affected by the consciousness level rather than the propofol Cpt in humans.

Acknowledgement

Financial support in part by Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan (No. 16591551, 17591479) is gratefully acknowledged.

References

1 Antognini JF, Schwartz K. Exaggerated anesthetic requirements in the preferentially anesthetized brain. Anesthesiology 1993; 79: 1244–9
4 King BS, Rampil IJ. Anesthetic depression of spinal motor neurons may contribute to lack of movement in response to noxious stimuli. Anesthesiology 1994; 81: 1484–92
5 Rampil IJ, King BS. Volatile anesthetics depress spinal motor neurons. Anesthesiology 1996; 85: 129–34
15 Drory VE, Neufeld MY, Korczyn AD. F-wave characteristics following acute and chronic upper motor neuron lesions. Electromyogr Clin Neurophysiol 1993; 33: 441–6

745


