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CONSCIOUS SEDATION WITH MIDAZOLAM AND PROPOFOL CONTROLLED BY AUDITORY EVOKED POTENTIALS INDEX DURING SPINAL ANESTHESIA

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ABSTRACT
The purpose was to arrive adequate doses of midazolam and propofol infusion for sedation during spinal anesthesia, and whether AAI could be an indicator of adequate sedation level. Thirty patients aged 30 to 70 years scheduled for spinal anesthesia were premedicated with midazolam 0.06 mg/kg and atropine 0.01 mg/kg intramuscularly 15 minutes before anesthesia. Spinal anesthesia was performed with 10 mg hyperbaric tetracaine. Midazolam 0.02 mg/kg was intravenously administered and propofol infusion was started at 2.5 mg/kg/h and stopped at the end of surgery. To keep auditory evoked potentials index (AAI) between 40 and 60, propofol infusion dose was up and down by 0.5 mg/kg/h every 5 minutes. The Observer's assessment of alertness/sedation (OAAS) scale was checked every 10 minutes. The discrepancy was judged as AAI outside of 40 to 60 when OAAS scale was 3 or 4. Recovery time was measured as the time from the end of surgery to when OAAS scale became 5. AAI decreased below 40 in 10 minutes after start of sedation. The propofol infusion dose was 1.5 ± 0.75 mg/kg/h. In 180 points measured AAI and OAAS scale simultaneously, 12 points had discrepancy between them. Recovery time was 8.5 ± 2.6 minutes. In conclusion, during spinal anesthesia, after premedication with intramuscular midazolam 0.06 mg/kg, intravenous midazolam 0.02 mg/kg followed by propofol infusion at 1.5 mg/kg/h could provide rapid and adequate sedation. AAI might be useful to keep adequate sedation.

KEYWORDS: Conscious sedation, midazolam, propofol, auditory evoked potentials index.

INTRODUCTION
During spinal anesthesia, many patients want to be sedated. For this purpose, midazolam or propofol are commonly used. Midazolam is a fast-acting benzodiazepine with a short elimination half-life, and it has sedative, anxiolytic, hypnotic, and anterograde amnesic effects.[1] Propofol is an ultrashort-acting intravenous sedative agent, which induces rapid sleep and rapid recovery.[1]

We have already investigated the adequate doses of midazolam[2,3] or propofol[4,5] used for sedation during spinal anesthesia. Combination of midazolam and propofol is more effective than midazolam alone for sedation during endoscopic retrograde cholangiopancreatography in the study by Kim et al.[1] Midazolam prior to propofol decreases injection pain of propofol and co-administration decreases the dose of propofol,[6] which decreases cardiovascular and respiratory depression by propofol.[7] Therefore, midazolam followed by propofol is better than each agent alone for sedation, but there is no study of sedation with these combination during spinal anesthesia. Kim et al.[1] compared bolus midazolam and bolus midazolam with propofol, both intravenous intermittent administration. However, propofol is usually used by infusion for sedation as shown in our previous studies.[4,5] The primary purpose of this study was to investigate adequate doses of midazolam followed by propofol infusion for sedation during spinal anesthesia.

In our previous studies,[2,3,5] we have used sedation scores such as Ramsay score and observer's assessment of alertness/sedation (OAAS) scale to keep adequate sedation levels. Recently, electroencephalic monitors are enthusiastically used to show sedation levels during anesthesia. We showed that auditory evoked potentials (AEP) index (AAI) could distinguish the changes of OAAS scale better than Bispectral index (BIS) during propofol sedation in spinal anesthesia.[4] The second purpose of this study was to investigate whether we could get adequate sedation when we used AAI as an indicator of sedation level.

MATERIALS AND METHODS
After the approval of the ethics committee of the hospital (No.007) and written informed consent from the patients, 30 patients aged 30 to 70 years with ASA physical status I or II scheduled for spinal anesthesia for lower extremity surgery were enrolled. Those who had liver, renal,

mental, neurological, ear, or severe cardiac diseases, who had coagulation disorder, allergy to the agents scheduled to use, or habits of hypnotics or analgesics, and who were obese (body mass index > 30) were excluded from the study.

Midazolam 0.06 mg/kg and atropine 0.01 mg/kg (maximum 0.5 mg) were administered intramuscularly 15 minutes before entering the operation room as routine premedication. In the operating room, an epidural catheter was inserted into L1-2 or L2-3 interspinal space for postoperative analgesia and this was not used during surgery. Then spinal anesthesia was performed at L4-5 interspinal space using 25 gauze spinal needle and 10 mg hyperbaric tetracaine was administered. AAI was monitored by AEP2^{TM} (Danmeter, Odense, Denmark). After anesthesia level was checked by pin prick test and anesthesia level higher than Th12 was obtained, midazolam 0.02 mg/kg was intravenously administered and propofol infusion was started at 2.5 mg/kg/h and stopped at the end of surgery. To keep AAI between 40 and 60, propofol infusion dose was up and down by 0.5 mg/kg/h every 5 minutes. The Observer's assessment of alertness/sedation (OAAS) scale was checked every 10 minutes. The discrepancy was judged as AAI outside of 40 to 60 when OAAS scale was 3 or 4. Recovery time was measured as the time from the end of surgery to when OAAS scale became 5. Memory during sedation was checked on the next morning by asking whether patients remembered to be asked something during surgery. Data were shown as number of patients, mean and range, or mean ± standard deviation.

RESULTS

Patients were 49 (31 – 62, range) years, 18 male and 12 female, 63 (45 – 74) kg in body weight and 162 (143 – 178) cm in height. Duration of surgery was 96 (65 – 140) minutes. Anesthesia level was Th6 (Th4 – Th10).

AAI decreased below 40 in 10 minutes after start of sedation, and it was kept almost between 40 and 60 during the study (Figure 1). The final propofol infusion dose was 1.5 ± 0.75 mg/kg/h (Figure 2). At 60 minutes after start of propofol infusion, OAAS scale was 3 or 4 in all patients (Table 1). In 180 points measured AAI and OAAS scale simultaneously, 12 points had discrepancy between AAI and OAAS scale (Table 1). Three patients remembered that they were asked something during sedation. Recovery time was 8.5 ± 2.6 minutes. Blood pressure and heart rate decreased during sedation, but no treatment was necessary.

Table 1: OAAS scale.

Time (min)	10	20	30	40	50	60
OAAS 2	15	6	2	4	2	0
OAAS 3	12	21	20	24	22	26
OAAS 4	3	3	8	1	4	4
OAAS 5	0	0	0	1	2	0
Discrepancy	2	1	3	4	2	0

Number of patients are shown. Discrepancy: outside of AAI 40 – 60 with OAAS 3-4.

OAAS: Observer's assessment of alertness/sedation, AAI: auditory evoked potentials index.

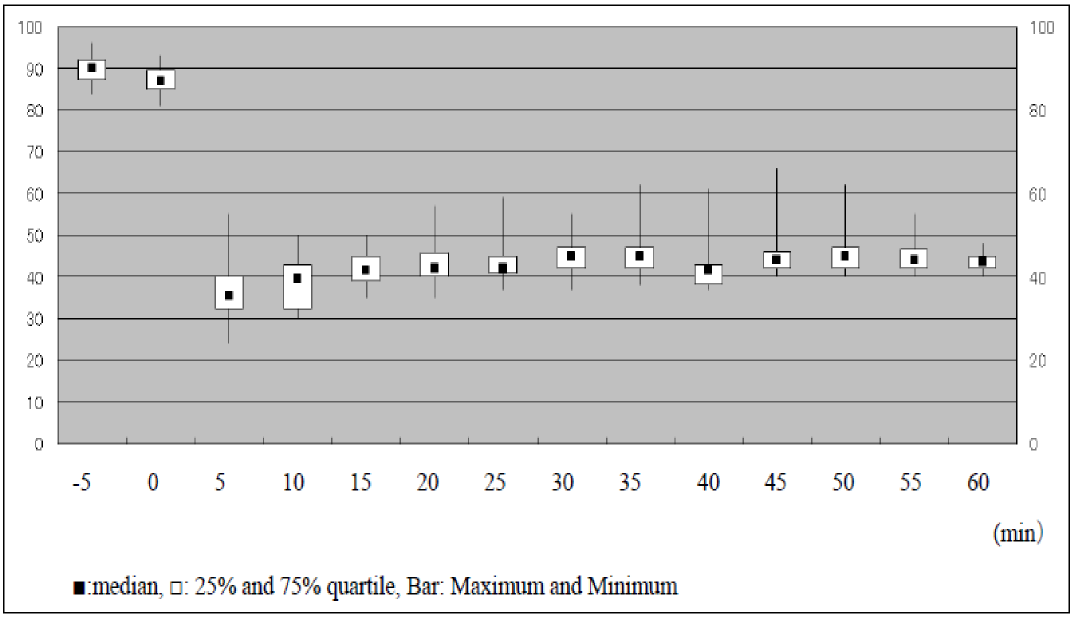

Figure 1. Auditory evoked potentials index

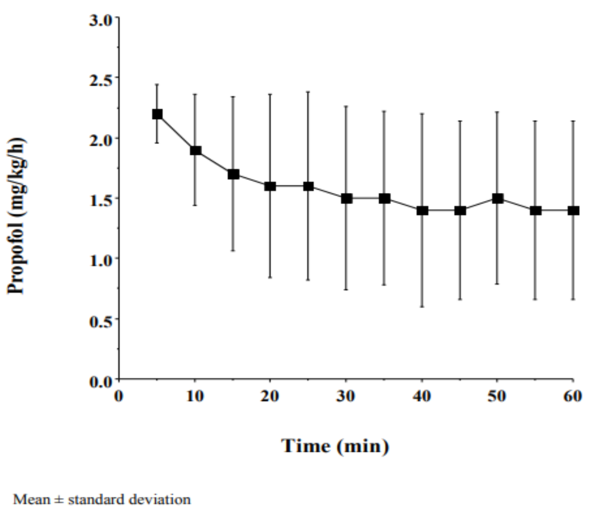

Figure 2. Infusion dose of propofol

DISCUSSION

To provide adequate sedation with AAI between 40 and 60 during spinal anesthesia after premedication with intramuscular midazolam 0.06 mg/kg, intravenous bolus midazolam 0.02 mg/kg followed by propofol infusion at 1.5 mg/kg/h might be the choice. Only some discrepancies were observed between AAI and OAAS scale.

We used AAI not BIS as the primary indicator of sedation. AAI indicates the response to auditory stimulation, i.e. the degree to which the brain can be excited from its suppression by anesthetics.[8] AAI and OAAS scale showed significant positive correlation during sedation with midazolam and alfentanil in gastrointestinal endoscopy.[9] The AAI could keep adequate sedation levels than Ramsay sedation scale in propofol sedation during bronchoscopy.[10] It is reported that correlation coefficient between BIS and OAAS scales was better than that between AAI and OAAS scales in sedation using midazolam with propofol during colonoscopy.[11] However, linear regression analysis and the coefficients of Spearman's rank correlation with OAAS scale for AAI were greater than BIS in sedation with propofol or midazolam.[12] AAI was better than BIS to discriminate transition from anesthesia and return of consciousness.[13,14] AAI but not BIS could discriminate slight changes of consciousness during light sedation with propofol infusion in spinal anesthesia.[4]

AAI can monitor sedation with midazolam, but BIS cannot.[15,16] Therefore, we used AAI not the BIS. AAI could provide less patient movement and better sedation than OAAS scale during target-controlled infusion (TCI) of propofol.[17] Thus, it is better to use AAI than OAAS scale to provide adequate sedation in spinal anesthesia because patient movement sometimes interrupts surgery.

We chose AAI between 40 and 60 as an indicator of adequate sedation. The reliability of AAI increases as sedation deepens.[9] The transition of loss of response occurred at a mean AAI of 46.[18] AAI > 60 indicated fully awake or minimally sedated, 40 to 60 were light to moderate sedation, 25 to 40 showed deep sedation, and 15 to 25 were in surgical anesthesia.[19] Therefore, we used AAI 40 to 60. AAI lacks linearity at both very low and high levels of propofol sedation with almost on-off behavior for wakefulness and hypnosis.[20] However, our target sedation levels were light to moderate sedation, in the range of linearity. AAI 42 to 54 corresponded well to OAAS scale 3.[9] Our results were consistent with their reports.

We administered midazolam as a premedication. In the present study, initial dose of midazolam and propofol were employed from our previous studies where midazolam was used as a premedication.[2-5] Therefore, midazolam was administered as a premedication in the present study. In addition, intramuscular premedication of midazolam decreased propofol dose inducing sedation,[21] which decreases hemodynamic changes by propofol.[22,23] Midazolam and propofol were synergistic at induction of anesthesia and reduced 25 to 50% of each dose.[6] Combination of midazolam and propofol increased free plasma concentration of midazolam about 20%, which could decrease dose of midazolam, while free plasma concentration of propofol did not increase.[24] Sedation with propofol and midazolam decreased required propofol dose, but recovery from sedation became slower than sedation with propofol alone,[25] while Taylor et al. showed that midazolam and propofol induced more rapid recovery than propofol alone.[26] The present study did not compare combination with singlea gent, but recovery time of 8.5 minutes, which was shorter than the study by Seifert et al.,[25] and it might have no problems.

After premedication with intramuscular midazolam 0.06 mg/kg, intravenous midazolam 0.02 mg/kg induced adequate sedation in spinal anesthesia.[3] When midazolam was used as continuous infusion, midazolam 0.6 mg/kg/h for 1.6 minutes followed by 0.15 mg/kg/h induced rapid sedation and kept Ramsay score 4 with stable hemodynamics and respiration.[2] To keep OAAS scale at 3 or 4, mean propofol infusion dose was 2.18 to 2.35 mg/kg/h after premedication with midazolam.[4] In our another study,[5] after premedication with midazolam, propofol infusion starting at 10 mg/kg/h, decreasing to 5 mg/kg/h after 1 minute, and 2.5 mg/kg/h after another minute induced rapid onset of sedation and kept OAAS scale 3 or 4.[5] When midazolam and propofol were used together after premedication with intramuscular midazolam 0.06 mg/kg, intravenous bolus midazolam 0.02 mg/kg followed by propofol infusion at 1.5 mg/kg/h could induce adequate sedation rapidly in the present study. That decreased propofol infusion dose than our previous study with propofol alone.[4,5]

CONCLUSION

During spinal anesthesia, premedication with intramuscular midazolam 0.06 mg/kg 15 minutes before anesthesia and intravenous bolus midazolam 0.02 mg/kg followed by propofol infusion at 1.5 mg/kg/h could provide rapid and adequate sedation. AAI might be useful to keep adequate sedation.

Conflict of interest: The author has no conflict of interest.

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