NEUROSCIENCES AND NEUROANAESTHESIA

Bispectral index is related to the spread of spinal sensory block in patients with combined spinal and general anaesthesia

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Editor’s key points

- Previous publications described a relationship between the depth of sedation as measured by the bispectral index (BIS) and spinal sensory block height in patients with light to no additional sedation.
- In this study, BIS significantly correlates with the spread of spinal sensory block under conditions of identical predicted effect-site concentration of propofol.

Background. A relationship between the depth of sedation as measured by the bispectral index (BIS) and spinal sensory block height in patients with light to no additional sedation has been described previously. The present study was designed to investigate the hypothesis that BIS values closely correlate with the spread of spinal sensory block in patients deeply sedated with an i.v. target-controlled infusion of propofol.

Methods. Subjects comprised 100 patients aged 20–64 yr and undergoing arthroscopic knee surgery. Patients were given spinal anaesthesia with bupivacaine 0.5% (3 ml). Propofol was administered to achieve a target effect-site concentration of 3.0 µg ml⁻¹. The relationship between the spinal sensory level at 15 min after spinal anaesthesia and BIS values during 1–5, 6–10, 11–15, and 16–20 min time intervals after the estimated effect-site concentration reached 3.0 µg ml⁻¹ was evaluated.

Results. The sensory level of spinal analgesia significantly and strongly correlated with BIS values during each time period after the estimated effect-site concentration remained at 3.0 µg ml⁻¹ (P < 0.0001). The correlation coefficient values were 0.8 during 1–5 min, 0.844 during 6–10 min, 0.801 during 11–15 min, and 0.804 during 16–20 min time periods.

Conclusions. We demonstrated that BIS values significantly correlate with the level of spinal sensory block under deep sedation with propofol. The depth of sedation induced by spinal anaesthesia depends on the spread of spinal sensory block.

Keywords: anaesthesia, depth; anaesthetic techniques, subarachnoid; anaesthetics i.v., propofol; monitoring, bispectral index

Accepted for publication: 19 October 2010

Spinal anaesthesia has been noted to exert sedative effects.1–3 Clinically, patients given high spinal anaesthesia frequently exhibit a decrease in alertness, with drowsiness becoming more frequent and pronounced as the spread of spinal block becomes higher. It has also been reported that the extent of spinal anaesthesia influences the depth of sedation, measured by the bispectral index (BIS) and previously reported to be in the range of 65–75.4–6 However, BIS is sensitive to internal or external circumstances surrounding the patient and can be affected by abrupt arousal, movement, coughing, or noise in patients with light or no additional sedation.7–9 There have not been enough data fully quantifying the relationship between BIS and the spread of spinal block during effect compartmental controlled propofol sedation. The present study aimed at investigating the hypothesis that BIS values closely correlate with the spread of spinal anaesthesia when patients are under deep sedation.

Methods

The study was approved by the Ethics Committee of Nihon University School of Medicine (Ref: 06/0903) and written informed consent was obtained from all patients. Subjects comprised 100 patients aged 20–64 yr [mean age, 37.8 (10.9) yr] with ASA physical status I and with a BMI between 18.5 and 30 who were undergoing elective arthroscopic knee surgery without tourniquets under spinal anaesthesia combined with general anaesthesia with a duration of < 60 min. Exclusion criteria included any history of substance abuse, known allergic disorders, current prescriptions, psychological, cardiovascular, or neurological diseases, regular consumption of alcohol, cigarettes, or both, the use...
of any psychoactive medicines such as benzodiazepines, antidepressants, anticonvulsants, antihistamines, opiates, or recreational drugs during the 10 yr before the day of surgery, and the use of any medicines for common cold including antihistamines during the 3 months before the day of surgery that would be expected to affect the EEG response. The interspaces through which the spinal anaesthetic was administered (L2–3, L3–4, or L4–5) were randomly selected using sealed envelopes. Patients were also randomly allocated by selection of sealed envelopes to tilting the bed upwards, horizontal, or downwards during and for 1 min after receiving spinal anaesthesia. The angle at which the bed was tilted was left to the discretion of the attending anaesthetist to provide an adequate spinal level for the surgery. The aim of the randomization was to produce various levels of spinal anaesthesia.

No patients received any premedications. I.V. access was established in a forearm vein before arrival at the operating theatre. The operating theatre was warmed to prevent an increase in EMG activity due to shivering. Standard monitoring devices (Bedside Station, BSS-9800, Nihon Kohden Corporation, Tokyo, Japan) including ECG, non-invasive arterial pressure measurement (NIAP), and arterial oxygen saturation via pulse oximetry (SpO2) were applied and baseline values of vital signs were obtained. All patients received an i.v. colloid solution before initiation of the spinal anaesthesia at a rate of 20 ml kg⁻¹ h⁻¹ and at a rate of 30 ml kg⁻¹ h⁻¹ after spinal injection of the local anaesthetics until completion of data collection to prevent cardiovascular depression. Thereafter, additional hydration was done by administration of a Ringer’s lactate solution according to the discretion of the attending anaesthesiologists. Heart rate, NIAP, and SpO2 were continuously monitored and recorded every 2.5 min using an electronic anaesthesia chart. Before spinal anaesthesia, the BIS electrodes were placed in the fronto-temporal regions as recommended by the manufacturer (Aspect Medical Systems, Norwood, MA, USA) and connected to an EEG monitor (A-2000 ver. 2.1, Aspect Medical Systems) for BIS measurement. Smoothening rate was set at 15 s. To reduce skin/electrode impedance, the skin over the forehead was cleaned with an alcohol-impregnated skin wipe. The attending anaesthesiologists could view BIS and SQI values throughout the study. The BIS values were only considered valid when SOI was above 50%. If SOI was below 50% for 1 min, BIS values for that minute were excluded from data analysis. If SOI was <50% for longer than 20% of the total study period, all data for the patient were excluded from analysis. All data were retrieved from the monitors after completion of each anaesthesia and stored for later analysis.

All anaesthetic procedures were conducted by a board-certified anaesthetist. Once BIS readings were stable, the patient was positioned in the lateral decubitus position with his/her surgical leg dependent. Bed tilting (upwards, horizontal, or downwards) was performed before subarachnoid puncture. Subarachnoid puncture was performed with a 25 G Sprotte needle (Spinocan, B. Braun Melsungen AG, Melsungen, Germany) at the L2–3, L3–4, or L4–5 space. After injection of intradermal local anaesthesia with mepivacaine 1% (2 ml) at the puncture site, plain hyperbaric bupivacaine 0.5% (3 ml) (Marcaine 0.5%, AstraZeneca, Osaka, Japan) (15 mg) was administered into the subarachnoid space. Cerebrospinal fluid aspiration (0.1 ml) was done to confirm correct needle placement before and after spinal drug administration. The bed tilting was maintained until 1 min after administration of the anaesthetic agent, whereafter the patient was turned to the supine position. Sensory block height was evaluated bilaterally using a pinprick test with the sharp tip of a safety pin every 1 min until 15 min after the initiation of the spinal anaesthesia. Bilateral sensory block level was segmentally confirmed to remain at the same level with three consecutive evaluations at 15 min after the administration. Complete motor block of the lower limbs was also confirmed at 15 min after subarachnoid drug administration. If the patients were able to flex either knees or ankles or the sensory block did not extend rostral to the operative site, spinal anaesthesia was readministered and the patient was excluded. Arterial pressure was measured every minute after spinal administration. Hypotension and bradycardia were defined as systolic arterial pressure below 80 mm Hg and heart rate below 45 beats min⁻¹, respectively, according to the definition by Reich and colleagues.¹⁰ If hypotension or bradycardia persisted for more than 1 min, ephedrine or atropine, respectively, was administered i.v. and the patient was excluded from the study since these drugs affect the central nervous system. In addition, all patients had previously been informed that the spread of spinal anaesthesia could reach thoracic or cervical levels due to the bed tilting. If patients complained of any symptoms due to spinal anaesthesia, for example, nausea or dyspnoea, they were scheduled to be immediately sedated and excluded from the study. After checking the adequacy of spinal anaesthesia, a urinary catheter and rectal thermometer was inserted. The rectal temperature was maintained at 36.0–37.0°C using a forced-air warming blanket.

Patients were sedated with i.v. administration of propofol after confirmation of the level of the sensory block. All patients received plasma target-controlled infusion using the Diprifusor syringe pump (TERUMO Inc., Tokyo, Japan).

General anaesthesia was induced with i.v. propofol and vecuronium after preoxygenation. The target plasma concentration of propofol was initially set at 6.0 μg ml⁻¹. After loss of consciousness and confirmation of the absence of a difficult airway, vecuronium bromide was administered i.v. at a dose of 1 mg kg⁻¹ to facilitate the insertion of a laryngeal mask airway (LMA) and controlled ventilation of the lungs. No further doses of vecuronium were administered. The LMA was inserted 2.5 min after the administration of propofol, and the plasma target concentration of propofol was subsequently reduced to 3.0 μg ml⁻¹. If LMA insertion could not be successfully completed at the first attempt, the target concentration of propofol was maintained at 6.0 μg ml⁻¹ until successful insertion was achieved and the patient was excluded. The patient’s lungs were ventilated...
with an oxygen and air (1:2) mixture, maintaining normocapnia and $\text{SpO}_2$, above 98% using a respiratory frequency of 10 bpm and an inspiration to expiration ratio of 1:1.5. BIS values over the 20 min period after propofol plasma effect-site concentration equilibration at 3.0 $\mu$g ml$^{-1}$ were recorded for further analysis.

If the BIS value was above 65 for more than 30 s or above 60 for more than 3 min, the attending anaesthesiologists could increase or add anaesthetics and the patient was excluded from analysis.\textsuperscript{11,12} The patients remained unstimulated during data collection; surgery commenced after completion of data collection. All patients who participated in this study were interviewed on postoperative day 1 to inquire about intraoperative awareness.

**Data analysis**

Data analysis was performed by a blinded investigator. The maximum height of the sensory block on both sides was averaged and expressed as the spinal thoracic level. The spinal thoracic level of anaesthesia is expressed from 0.0 to 12.0, in which 0.0, 1.0, and 2.0 correspond to C8, Th1, and Th2, respectively. BIS values at 20 min after the effect-site concentration of propofol reached and remained at 3.0 $\mu$g ml$^{-1}$ were divided into 1–5, 6–10, 11–15, and 16–20 min periods and mean BIS values were calculated separately for each of these periods. Correlation was evaluated between spinal thoracic levels at 15 min after spinal anaesthesia and the corresponding BIS values at the same time. Correlation was also evaluated between spinal thoracic levels at 15 min after spinal anaesthesia and the averaged BIS values for the periods 1–5, 6–10, 11–15, and 16–20 min after the effect-site concentration equilibration at 3.0 $\mu$g ml$^{-1}$. Statistical analysis was performed by Spearman’s rank correlation coefficient by rank test to evaluate the correlation between the spinal thoracic level and the BIS value. Data were expressed as mean (standard deviation).

**Results**

Six of the 100 patients were excluded. Four were excluded because of the use of ephedrine or atropine to treat hypotension or bradycardia (two patients each). One patient was excluded from analysis because of unsuccessful LMA insertion at the first attempt. One patient was excluded because of poor SQI. The remaining 94 patients (male/female, 59/35) completed the study without missing data nor adverse events. The height and weight were 166.3 (8.7) cm and 66.3 (11.3) kg, respectively [BMI, 23.9 (3.2)].

Spinal anaesthesia was successfully performed in all the patients. Both sufficient spinal sensory block for surgery and complete motor block of the lower limbs were obtained in all the patients. No patients complained of severe or moderate symptoms due to the spinal anaesthesia. The consumption of propofol adjusted to body weight from the start of induction till the time when the effect-site concentration reached 3.0 $\mu$g ml$^{-1}$ was approximately equal among patients. The consumption of propofol was 3.47 (0.02), 4.14 (0.02), 4.78 (0.02), 5.39 (0.02), and 5.99 (0.02) mg kg$^{-1}$, respectively, at 0, 5, 10, 15, and 20 min after the effect-site concentration reached 3.0 $\mu$g ml$^{-1}$. The mean time interval from the time when the target effect-site concentration was reduced and set at 3.0 $\mu$g ml$^{-1}$ to the time when the concentration reached 3.0 $\mu$g ml$^{-1}$ was 11 min and 15 s. No patients reported awareness during general anaesthesia at the postoperative interviews on the day of surgery or on postoperative day 1.

Data from one representative patient are presented in Figure 1 as an example. The mean BIS values for this patient were 37.6 during 1–5 min, 39.0 during 6–10 min, 40.0 during 11–15 min, and 36.8 during 16–20 min time interval after the effect-site concentration of propofol reached and remained at 3.0 $\mu$g ml$^{-1}$.

Mean baseline BIS values on admission to the operating theatre were 97.4 (0.5). Mean BIS values at 15 min after spinal bupivacaine administration were 97.1 (0.8). The spinal thoracic level did not significantly correlate with the BIS value at 15 min after spinal anaesthesia (Fig. 2). The correlation coefficient for this time was 0.135 ($P=0.195$). Spinal

![Fig 1 BIS values of one representative patient during 1–20 min after the effect-site concentration of propofol reached and remained 3.0 $\mu$g ml$^{-1}$.

![Fig 2 Scattergram showing the relationship between the spinal thoracic level of spinal sensory blockade and BIS values at 15 min after the spinal administration of bupivacaine. The correlation coefficient for this time was 0.135 ($P=0.195$). Spinal anaesthesia itself did not cause any significant decreases in BIS values at 15 min after spinal anaesthesia.](https://academic.oup.com/bja/article-abstract/106/2/202/243955)
anaesthesia itself did not cause any significant decreases in BIS values at 15 min after spinal anaesthesia.

The relationship between spinal thoracic levels of sensory block and BIS values after propofol administration is illustrated in Figure 3A–D. The correlation coefficients between spinal thoracic levels at 15 min after spinal anaesthesia and BIS values were 0.800, 0.848, 0.804, and 0.801, respectively, between 1 and 5, 6 and 10, 11 and 15, and 16 and 20 min after the estimated effect-site concentration of propofol attained a constant level of 3.0 μg ml⁻¹ (P<0.001 for each value).

**Discussion**

The present study demonstrates that BIS significantly correlates with the spread of spinal sensory block under conditions of identical predicted effect-site concentration of propofol. We conducted this study under deep sedation because the BIS value may be affected by arousal, movement, cough, or noise under light or no sedation. Our results suggest that depth of sedation with propofol is influenced by the height of the spinal sensory block at 15 min after spinal anaesthesia.

The proposed mechanisms of the sedative effects induced by spinal anaesthesia include systemic general anaesthetic effects of absorbed local anaesthetics, rostral spread of the local anaesthetics through cerebrospinal fluid with direct actions on the brain, and decreased facilitatory sensory input to the reticular activating system due to loss of proprioceptive inputs from skin, muscles, or joints. However, no previous studies have demonstrated that the sedative effect is due to the spread of spinal anaesthesia or to the dose of intrathecally administered local anaesthetics. The present study revealed that the local anaesthetics delivered to the brain after systemic absorption into the circulation is not the only cause of the decrease in BIS values because the dose of bupivacaine was identical in all patients in this study. The depth of sedation induced by spinal anaesthesia depends on the extent of spinal sensory block.

There are several studies examining the effects of the different levels of spinal anaesthesia on BIS values in patients with light to no sedation. Our results are consistent with these studies, suggesting that a higher spinal anaesthesia deepens the level of depth of sedation, mirrored by the BIS, compared with a lower spinal anaesthesia. However, in these previous studies, the differential spread of spinal anaesthesia was produced by different doses or baricity of the local anaesthetic. Our study demonstrated that the sedative effect of spinal block produced by equal dose of the same anaesthetic was dependent on the level.
of spinal sensory block at 15 min after spinal anaesthesia when the estimated effect-site concentration of propofol remained at 3.0 μg ml⁻¹. In contrast to our findings, Toprak and colleagues reported that the requirements of sedatives were decreased by spinal anaesthesia, although this decrease did not significantly correlate with the level of the spinal sensory block. In Toprak and colleagues' study, spinal anaesthesia was administered with 10 and 17.5 mg of hyperbaric bupivacaine and the obtained mean anaesthetic levels were close to each other, at Th7 and Th9, in the two groups compared. The proximity of the anaesthetic levels could explain the difference between their results and ours. From their study, it appears that it is the dose of spinally administered local anaesthetics that affects the sedative effect induced by spinal anaesthesia. Conversely, the present study revealed that the sedative effect, mirrored by BIS values, is dependent on the height of spinal sensory block at 15 min after spinal anaesthesia, when the dose and baricity of the local anaesthetic for spinal anaesthesia remain unchanged.

The spinal thoracic level did not significantly correlate with BIS values before sedation at 15 min after spinal anaesthesia in our study. It has been reported that spinal anaesthesia alone leads to a significant decrease in BIS values in patients and healthy volunteers. In Pollock and colleagues' study, the volunteers were placed in a darkened room with soft music to measure BIS values before and after spinal anaesthesia. In contrast, our patients were undergoing surgery in a well-lit operating theatre, were free to communicate with medical staff, and were spoken to by the anaesthetist to assess the height of spinal block every minute, which would have repeatedly stimulated the patients. It is possible that those stimuli may have counteracted the sedative effects of spinal anaesthesia before the induction of general anaesthesia in our study. Furthermore, it was reported that the sedative effect induced by spinal anaesthesia starts to appear at 15 or 20 min after spinal anaesthesia. Thus, evaluation of the effect of spinal anaesthesia on the depth of sedation at 15 min after spinal anaesthesia might have been too early. These two factors might explain why there was no correlation between BIS values and the level of spinal anaesthesia at 15 min after spinal anaesthesia.

There are a few limitations to the present study. First, the attending anaesthetist was not blinded to the study; however, the level of spinal anaesthesia was determined before data collection and analysis. The bias of the attending anaesthetist could not have affected the BIS values because the data collection was automatically made from the monitor recording system. Secondly, 15 min may not be long enough for the local anaesthetic to cease its maximal rostral spread after spinal anaesthesia. Hence, the spinal level at 15 min post-spinal administration is not likely to be the same as that during the later periods after propofol administration. In our study, correlation was evaluated between the spinal level at 15 min after spinal administration and BIS values during the fixed time periods after patients were sedated with propofol. However, according to our study protocol, the time period from administration of spinal anaesthesia to setting up the concentration of TCI was approximately equal in all the patients. The consumption of propofol from the induction of anaesthesia to the periods evaluated was also approximately equal among patients, when adjusted for body weight. Therefore, the calculated BIS value during each period can be evaluated for comparison with the spinal sensory level at 15 min after spinal administration.

The present study demonstrated that BIS values significantly correlate with the level of spinal block assessed at 15 min after spinal anaesthesia under deep sedation with propofol in young and middle-aged patients. The depth of sedation induced by spinal anaesthesia is influenced by the spread of spinal sensory block.

Conflict of interest
None declared.

Funding
This study was supported by departmental and institutional funding only.

References
