

## ORIGINAL RESEARCH

## REGIONAL ANESTHESIA

# Relationship between the patient state index and sedation scale during dexmedetomidine sedation during spinal anesthesia

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## Abstract

**Background & Objectives:** Dexmedetomidine, a highly selective  $\alpha$ -2 adrenoceptor agonist, is a widely used sedative during spinal anesthesia. Indices devised using processed electroencephalographic monitors are useful for identifying the level of sedation without disturbing the patient. However, we lack studies on the relationship between the patient state index (PSI) and dexmedetomidine sedation. We investigated the relationship between the PSI and sedation scale during dexmedetomidine sedation in patients undergoing spinal anesthesia.

**Methodology:** This study entailed a review of the anesthetic records of patients who underwent dexmedetomidine sedation under SEDLine™ monitoring. After intrathecal injection, dexmedetomidine 1  $\mu$ g/kg was injected intravenously over 10 min, followed by maintenance infusion at 0.4  $\mu$ g/kg/h for 50 min. The PSI, mean blood pressure, heart rate, and oxygen saturation were recorded at regular intervals. The patients' 'Observer's Assessment of Alertness/Sedation' (OAA/S) scores were measured repeatedly until deep sedation (OAA/S  $\leq$  2) was achieved. The Spearman test was used to evaluate the correlation between the PSI value and OAA/S score. The cut-off PSI value for identifying OAA/S scores  $\leq$  2 was calculated using receiver operating characteristic curve analysis.

**Results:** The PSI values corresponding to OAA/S scores of 5, 4, 3, 2, and 1 during dexmedetomidine sedation were  $86.56 \pm 10.45$ ,  $76.90 \pm 13.99$ ,  $68.16 \pm 16.18$ ,  $61.48 \pm 15.26$ , and  $55.67 \pm 16.75$ , respectively ( $P < 0.001$ ). The Spearman correlation coefficient for the PSI and OAA/S scores was 0.6228 ( $P < 0.001$ ). The cut-off value of PSI for OAA/S scores  $\leq$  2 was 76. The mean blood pressure and heart rate decreased significantly compared to baseline and 60 min after continuous dexmedetomidine infusion ( $P < 0.001$ ).

**Conclusion:** The patient state index decreased with the progression of dexmedetomidine sedation. Patient state index assessment could prove useful for evaluating the depth of sedation without distressing the patients.

**Abbreviations:** BIS: Bispectral index; Dex: Dexmedetomidine; EEG: Electroencephalography; OAA/S: 'Observer's Assessment of Alertness/Sedation'; PSI: Patient state index; SA: Spinal anesthesia

**Key words:** Conscious Sedation; Dexmedetomidine; Electroencephalography

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## 1. Introduction

Dexmedetomidine (Dex), a highly selective  $\alpha$ -2 adrenoceptor agonist, has been widely used as a

sedative for patients undergoing spinal anesthesia (SA). Dex is a useful and attractive sedative with great potential for application in several clinical situations. Dex induces a lower degree of respiratory depression compared to other sedatives such as propofol or

midazolam.<sup>1</sup> A high level of sensory blockade and deep sedation are often required during surgery under SA. Dex can prolong the level of sensory and motor blockade of SA and provide moderate to deep sedation.<sup>2</sup> Serious adverse complications can occur if the depth of sedation is too great. The loading dose of Dex induces a transient elevation in blood pressure (BP) and a reflexive decline in the heart rate (HR), especially in the healthy young patients.<sup>3</sup> Therefore, examination of the depth of sedation is essential for the safety of procedural sedation.

Several sedation scales are typically used to determine the level of sedation in the clinical setting. The ‘Observer’s Assessment of Alertness/Sedation’ (OAA/S) score is a useful tool for determining the status of sedation (Table 1)<sup>4</sup> and is frequently used in our hospital. The OAA/S score is reliable and valid, as demonstrated by the respective high correlation between the two raters and high correlations between the OAA/S score and other standard tests.<sup>4</sup> However, these instruments provide discontinuous and subjective evaluation and can disturb patient sedation.

**Table 1. Observer’s Assessment of Alertness/Sedation Scale**

1	Does not respond to mild prodding or shaking
2	Responds to mild prodding or shaking
3	Responds only after name is spoken loudly or repeatedly
4	Lethargic response to name spoken in normal tone
5	Responds readily to name spoken in normal tone

Assessing the level of sedation using processed electroencephalographic (EEG) monitors, as an alternative to sedation scales, can enhance the quality of sedation. Processed EEG monitors do not disturb patient sedation and provide intuitive indices. Several processed EEG monitors are available for clinical use, including the bispectral index (BIS), patient state index (PSI), and entropy.<sup>5</sup> The BIS and PSI are widely used quantitative parameters for evaluating the depth of sedation in our institution.

Since these monitors function via different mechanisms, the indices derived from them may be different, whereas the same sedatives are used in the clinical setting. Several studies have investigated the relationship between the BIS and the sedatives.<sup>6–8</sup> However, to the best of our knowledge, studies on the relationship between the PSI and Dex sedation are lacking.

Therefore, we evaluated the relationship between the PSI and OAA/S scores during Dex sedation as the primary objective of this study. The secondary objective included the performance of the PSI in identifying the OAA/S score.

## 2. Methodology

This single-center retrospective study was performed at a university hospital between July 2015 and October 2015. We reviewed patients who underwent monitoring of the PSI value using SEDLine™. This study was conducted in accordance with the ‘Strengthening the Reporting of Observational Studies in Epidemiology’ guidelines and the ‘Declaration of Helsinki’. The study was approved by the Institutional Review Board of Hospital (IRB No.: 2021-08-045). The requirement for written informed consent was waived off, owing to the retrospective design of the study.

The study included 45 patients with an ASA physical status of 1 to 3, who were planned to undergo urologic surgery under SA, with an estimated operative time of 60 min. The exclusion criteria were severe obstructive lung disease, diagnosis of cerebrovascular disease, use of medication altering the central nervous system, history of allergy to Dex or heavy bupivacaine, and patients with contraindications to SA.

No premedication was administered. Patients underwent electrocardiography, invasive or non-invasive BP, pulse oximetry, and SEDLine™ monitoring. BP measurements were performed using a noninvasive BP cuff or invasive arterial BP monitoring based on clinical judgement. Before SA, patients were administered crystalloid fluid (6 mL/kg) intravenously. Patients were placed in the lateral decubitus position with a spinal tap at the L3/4 or L4/5 intervertebral space using the midline approach. Spinal anesthesia was induced using 0.5% heavy bupivacaine 10–12 mg (Marcaine® Spinal Heavy; Astra, Sodertalje, Sweden) with a 25-gauge spinal needle. Dex administration was initiated 5 min after intrathecal bupivacaine injection. Patients were administered Dex 1 µg/kg intravenously for 10 min, followed by maintenance infusion of Dex 0.4 µg/kg/h for 50 min. Dex administration was discontinued when the surgeon started the skin suture. The values of PSI, mean blood pressure (MBP), HR, and oxygen saturation were recorded at regular intervals as follows: time-0 (baseline), SA (spinal anesthesia; intrathecal injection of bupivacaine), LO-0 (loading dose of Dex), IF-0 (initiation of Dex infusion), and then after every 10 min. The OAA/S scores were measured repeatedly until deep sedation (OAA/S score ≤ 2) was achieved. The patients were shifted to the post-anesthetic care unit (PACU), where they stayed for

**Table 2. Demographic characteristics of the patients**

Variables	Values
Sex (Male/Female)	29/14
ASA (1/2/3)	10/29/4
Age (y)	56.3 ± 15.3
Height (cm)	164.8 ± 9.7
Weight (kg)	66.7 ± 13.2
Level of lumbar puncture (L3-4/L4-5)	10/33
Maximum sensory blockade level	T 6.9 ± 1.5

Values are presented as counts and mean ± standard deviation.

ASA: American Society of Anesthesiologists

30 min. Patients were discharged from the PACU when the modified Aldrete score was  $\geq 9$ .

Hypotension (BP 20% less than the baseline MBP) was treated with intravenous ephedrine 5 mg or phenylephrine 50 µg, based on the clinical judgement. Hypertension (BP 20% greater than the baseline MBP) was treated with intravenous nicardipine 0.5 mg, based on the clinician's decision. Bradycardia (HR < 45 bpm) was treated with intravenous atropine 0.5 mg. The incidence of hypoxia (oxygen saturation < 93%) was also recorded.<sup>9</sup>

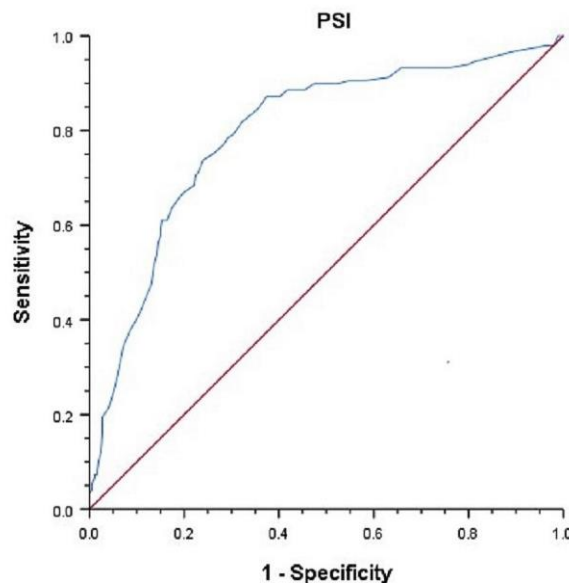
### Statistical analysis

All statistical analyses were performed using the SPSS software (version 25.0; SPSS Inc., Chicago, IL, USA). The correlation of the PSI value with the OAA/S score was determined using the Spearman test. The cut-off value of PSI for OAA/S scores  $\leq 2$  was obtained using receiver operating characteristic curve analysis. Continuous data were expressed as the mean ± SD. A generalized linear mixed model was used for the hemodynamic variables via post-hoc Bonferroni comparison. Statistical significance was set at  $P < 0.05$ .

## 3. Results

Forty-five patients were included in this study. Two patients were excluded because of contraindications to SA. Finally, 43 patients were included in the analysis. The demographic characteristics are described in Table 2.

The PSI values corresponding to OAA/S scores of 5, 4, 3, 2, and 1 were  $86.56 \pm 10.45$ ,  $76.90 \pm 13.99$ ,  $68.16 \pm 16.18$ ,  $61.48 \pm 15.26$ , and  $55.67 \pm 16.75$ , respectively ( $P < 0.001$ ). The changes in the PSI values showed a



**Figure 1: Area under the curve and receiver operating characteristic curve of PSI**

significant correlation with the changes in the OAA/S score ( $r = 0.6228$ ,  $P < 0.001$ ).

The area under the curve and receiver operating characteristic curve of PSI showing the ability of PSI to discriminate between OAA/S scores  $\leq 2$  and OAA/S scores  $> 2$  are presented in Figure 1. A PSI value of 76 identified an OAA/S score  $\leq 2$  (sensitivity 87.2%; specificity 63%).

The changes in MBP, HR, and PSI values over time are shown in Table 3. The MBP, HR, and PSI declined significantly compared to those at baseline (time 0) and 60 min after the initiation of Dex (IF-60) infusion ( $P < 0.001$ ). Hypertension, hypotension, and bradycardia occurred in 5 (11.6%), 6 (13.9%), and 9 (20.9%) patients, respectively. The oxygen saturation did not decrease during Dex sedation.

## 4. Discussion

The PSI value decreased significantly as Dex sedation deepened, without the incidence of any serious hemodynamic adverse events. Thus, the PSI value can provide useful information regarding the depth of Dex sedation without disturbing the patient's sleep during SA.

Comfortable sedation is a crucial aspect of patient satisfaction during SA. Adverse effects are more likely to occur with the deepening of the level of sedation; therefore, it is mandatory to measure the depth of sedation using processed EEG monitors or sedation scales.<sup>10</sup> Several sedation scales have long been used in the clinical setting. The Ramsay Sedation Scale was

**Table 3. Mean blood pressure, heart rate, and patient state index value during dexmedetomidine sedation**

Time to record	MBP (mmHg)	HR (beats/min)	PSI value
0	95.77 ± 14.89	74.56 ± 13.03	93.19 ± 3.17
SA	95.37 ± 13.62	73.51 ± 14.02	91.52 ± 4.66
LO0	92.12 ± 12.71	72.14 ± 13.75	88.95 ± 7.07
IF0	96.10 ± 15.19	58.05 ± 11.14 <sup>†</sup>	75.21 ± 15.86 <sup>††</sup>
IF10	93.32 ± 13.47	56.88 ± 10.40 <sup>†</sup>	63.00 ± 16.95 <sup>†</sup>
IF20	88.02 ± 13.98 <sup>††</sup>	57.19 ± 9.75 <sup>†</sup>	56.00 ± 16.80 <sup>††</sup>
IF30	85.92 ± 13.08 <sup>††</sup>	57.56 ± 10.65 <sup>††</sup>	58.67 ± 16.26 <sup>††</sup>
IF40	82.77 ± 13.88 <sup>††</sup>	56.10 ± 8.46 <sup>††</sup>	64.37 ± 19.80 <sup>††</sup>
IF50	81.81 ± 12.41 <sup>††</sup>	54.92 ± 9.84 <sup>††</sup>	66.91 ± 21.21 <sup>††</sup>
IF60	77.83 ± 9.69 <sup>†††</sup>	54.22 ± 11.83 <sup>††</sup>	59.08 ± 27.16 <sup>††</sup>

Data are presented as mean ± standard deviation. \* $P < 0.001$  compared with the baseline reading (Time 0). <sup>†</sup> $P < 0.001$  compared to SA. Time 0, baseline; SA, spinal anesthesia; LO0, loading dose at start of DEX infusion; IF0, initiation of DEX infusion; IF10, 10 min after initiation of DEX infusion; IF20, 20 min after initiation of DEX infusion; IF30, 30 min after initiation of DEX infusion; IF40, 40 min after initiation of DEX infusion; IF50, 50 min after initiation of DEX infusion; IF60, 60 min after initiation of DEX infusion, MBP, mean blood pressure; HR, heart rate; PSI, patient state index

developed in 1974 and is commonly used in intensive care units (ICUs).<sup>11</sup> The OAA/S is a sedation scale developed to assess the severity of sedation and analgesia in ambulatory surgery and explain the pharmacology of benzodiazepines.<sup>12</sup> The Richmond Agitation Sedation Scale, which was developed in a collaborative effort with practitioners in the intensive care unit, possesses high reliability and validity.<sup>13</sup> This score is significantly correlated with the BIS value during Dex sedation ( $r = 0.900$ ;  $P = 0.0001$ ) in the ICU.<sup>14</sup>

Dex is a widely used sedative during SA. The binding of Dex to the  $\alpha_2$  receptors hyperpolarizes the locus coeruleus neurons, limiting norepinephrine release.<sup>15</sup> The loss of inhibitory input from the locus coeruleus results in sedation due to the activation of the inhibitory pathways from the pre-optic area to the arousal centers. The activation of inhibitory input from the preoptic area is postulated to be an essential component in the initiation of non-rapid eye movement sleep.<sup>15</sup> The EEG signatures of Dex are composed of a combination of

slow-delta oscillations with spindles, i.e., 9–15 Hz oscillations that occur in bursts of 1–2 s.<sup>15</sup> The median BIS values at OAA/S scores of 1, 2, 3, 4, and 5 during Dex sedation were 95, 62, 45.5, 39.5, and 24.5, respectively.<sup>16</sup> During target-controlled infusion of Dex, the mean values of the BIS were 93.98, 71.50, 61.15, 48.11, and 40, 23 at modified OAA/S scores of 5, 4, 3, 2, and 1, respectively.<sup>5</sup> Thus, the calculated cut-

off BIS value for an OAA/S score of  $\leq 2$  was lower than the PSI value in our study.<sup>16</sup> A previous study reported that PSI values were approximately 70 when patients were under light sedation induced by Dex,<sup>17</sup> which is similar to our result. The PSI value was approximately 70 when the OAA/S scores were 3 and 4 (light sedation).

Propofol and midazolam were the first-choice sedatives during SA before the introduction of Dex in our country. Propofol acts as a direct gamma-aminobutyric acid A (GABA<sub>A</sub>) agonist.<sup>18</sup> Propofol-induced loss of consciousness is characterized by an increase in the delta power (0.5–4 Hz) and the appearance of highly coherent frontal alpha power mediated by thalamocortical

feedback mechanisms.<sup>19</sup> Propofol enables a deeper state of unconsciousness by inducing slow large-amplitude oscillations that produce prolonged neuronal silence.<sup>19</sup> Slow delta and alpha oscillations are markers of propofol-induced unconsciousness.<sup>15</sup> The median BIS values at OAA/S scores of 1, 2, 3, 4, and 5 during propofol sedation were 95.5, 78, 67, 57, and 34, respectively.<sup>19</sup> The median PSI values at modified OAA/S scores of 0, 1, 2, 3, 4, and 5 during propofol infusion were 87, 66, 55, 44, 34, and 26, respectively.<sup>20</sup> The BIS value in the midazolam group was significantly higher than that in the propofol and Dex groups.<sup>21</sup> The PSI value in the Dex-midazolam group was higher than that in the Dex-only group in elderly patients undergoing SA.<sup>17</sup> Midazolam acts as a positive allosteric modulator of GABA<sub>A</sub> receptors.<sup>12</sup> This GABAergic effect causes sedation; however, benzodiazepines can lead to paradoxical excitation at low doses. On EEG, benzodiazepines cause an increase in power within the beta frequency band (12–25 Hz) and a decrease in the activity of the alpha band (8–12 Hz).<sup>12</sup>

The calculated index of the processed EEG monitors can be significantly different at the same depth of anesthesia, depending on the anesthetic agent.<sup>16</sup> The BIS and PSI algorithms are not the same. The BIS utilizes an algorithm based on power spectral analysis, bispectral analysis, and burst suppression data,<sup>22</sup> whereas PSI uses a proprietary algorithm to analyze raw EEG signals.<sup>20</sup> The methods included in the



algorithm, estimated time delay, and index calculation are all different for each processed EEG monitor.<sup>23</sup>

## 5. Limitations

This study has several limitations. First, this retrospective observational study was performed over a short duration of surgery. Further prospective studies in various surgical settings are required to validate our findings. Second, SA can reduce PSI values and OAA/S scores because of the reduction in afferent input to the reticular activating system.<sup>24</sup> Third, it is difficult to devise a reliable method for evaluating intermediate levels of sedation. Patients older than 55 y showed a significantly weaker correlation between the PSI and OAA/S scores than those aged 55 y or younger. The distribution of clinical sedation scores varied from unconscious to alert within the range of 61 to 80 for the BIS and PSI.<sup>25</sup> However, sedation monitoring using processed EEG monitors, such as PSI, is widely used, despite numerous limitations. Clinicians should know the characteristics and EEG features of each anesthetic.

## 6. Conclusion

The Patient State Index value was correlated with the 'Observer's Assessment of Alertness/Sedation' score during dexmedetomidine sedation and may be advantageous for monitoring the sedation status. Thus, the Patient State Index, along with the clinical sedation scale, may prove useful in assessing the depth of hypnosis of a patient during sedation with dexmedetomidine.

## 7. Data availability

The numeric data generated during this study are available with the author.

## 8. Declaration

This study was presented as an e-poster presentation at KoreaAnesthesia 2021.

## 9. Acknowledgments

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## 10. Conflicts of interest

The author declares no conflict of interest.

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