



## Research Article

# Comparison of dexmedetomidine dosing strategies based on Bispectral Index (BIS) and Ramsay Sedation Scale (RSS) in patients undergoing infraumbilical surgeries under spinal anesthesia: A prospective comparative study

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## ABSTRACT

**Objectives and Aim:** This study aimed to evaluate the impact of dexmedetomidine infusion dosage adjustment strategies guided by BIS and RSS on total consumption in patients undergoing infraumbilical surgeries under spinal anesthesia.

**Materials and Method:** Eighty patients aged between 18-70 years, classified as American Society of Anesthesiologists (ASA) I and II, who underwent orthopaedic, urological, and plastic surgery under spinal anesthesia were included. Patients received spinal anesthesia in the lateral position through the L3-4 interval using a median approach. Following the observation of free flow of cerebrospinal fluid, spinal anesthesia was induced with 10 mg (2 ml of 5% hyperbaric bupivacaine) bupivacaine and 25 µg of intrathecal fentanyl. When the sensory block reached the T10 level, all patients were administered a dexmedetomidine loading dose of 1 µg/kg IV over 10 min for sedation, and the maintenance drug infusion dose was titrated to maintain BIS values between 60-80 in the first group and RSS at 3-4 in the second group. Throughout the surgery, hemodynamic variables (heart rate and blood pressure), respiratory parameters (respiratory rate), SpO<sub>2</sub>, sedation scores (BIS and RSS), and drug infusion doses and perioperative complications were recorded. Drug infusion was stopped 5 min before the end of surgery, and the duration of surgery, anesthesia, and total drug consumption were recorded. Statistical analyses were performed, and a p-value of less than 0.05 was considered statistically significant.

**Results:** Desired sedation was achieved by dexmedetomidine administration. A decrease in BIS values and an increase in RSS were observed with the loading dose. In both groups, the heart rate and systolic and diastolic blood pressures were significantly lower at all measurement times than the control values. There was no significant difference in the mean blood pressure between groups B and R ( $p > 0.05$ ). The average blood pressure for B group was  $92 \pm 14.12$  mmHg, while the average blood pressure for R group was  $90 \pm 12.73$  mmHg. There was no statistically significant difference between the two groups in terms of dexmedetomidine infusion doses required to achieve the desired sedation and total drug consumption  $110 \pm 20$  (µg) in B group and  $111 \pm 22$  µg in R group ( $p > 0.05$ ).

**Conclusions:** Dexmedetomidine provides a targeted level of sedation in patients undergoing spinal anesthesia without causing significant respiratory depression. Monitoring sedation depth using the BIS did not change the total drug consumption.

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## 1. Introduction

Regional anesthesia is pivotal in modern surgery, providing key advantages such as maintaining spontaneous breathing, protective reflexes, and extended postoperative pain relief [1]. To maximize these benefits and optimize surgical conditions, sedation is used to ease anxiety and ensure patient comfort. Conscious sedation, the preferred method, reduces awareness while preserving sensory and motor functions, allowing patients to follow commands without remembering the procedure [1]. Striking the perfect balance between analgesia and sedation, particularly during spinal anesthesia, is crucial, as it profoundly influences postoperative outcomes.

Sedation, as a complement to regional anesthesia, not only enhances patient experience by reducing anxiety and ensuring comfort but also contributes to the smooth conduct of the surgery [2]. Among the array of sedatives primarily functioning as  $\gamma$ -aminobutyric acid (GABA) receptor agonists, dexmedetomidine stands out as the preferred choice. Unlike typical sedatives, it operates as an  $\alpha_2$  adrenoceptor agonist, delivering sedative, analgesic, and sympatholytic benefits without causing the respiratory depression that is often a concern with other agents [3]. Tailoring sedation to diverse patient needs and surgical conditions is challenging. Clinically, sedation depth is assessed through clinical observations and objective measures like Bispectral Index (BIS) monitoring, which empirically evaluates hypnotic states.

Although dexmedetomidine offers numerous advantages, its impact on hemodynamics and potential to reduce the consumption of other anesthetic drugs warrant thorough investigation to inform clinical practice [4]. Previous research has highlighted the ability of dexmedetomidine to diminish neuroendocrine and hemodynamic responses to surgery and to reduce the required dosages of co-administered anesthetics, notably during procedures under BIS-guided sedation [5]. Bavullu et al. compared dexmedetomidine and midazolam for sedation during percutaneous drainage of hepatic hydatid cysts and found dexmedetomidine to be effective and well tolerated. Abdullayev et al. demonstrated its efficacy in reducing fentanyl-induced cough, further supporting its versatile application in clinical settings [6,7]. This underscores the necessity for a more comprehensive understanding of the impact of BIS-guided sedation with dexmedetomidine on overall drug consumption, especially within the context of spinal anesthesia, an area that remains relatively underexplored.

In this study, we examined the effects of BIS-monitored sedation with dexmedetomidine on the total consumption of anesthetic agents during spinal anesthesia. By scrutinizing this relationship, we aimed to elucidate the potential for refined sedative practices that promise enhanced patient safety, expedited recovery, and optimized resource utilization.

## 2. Materials and Method

### 2.1. Study design

This prospective, randomized, controlled study received approval from the ethical committee of Kocaeli University Faculty of Medicine (Approval code: 29.09.2011 KAEK 10/7). The research, conducted in the Department of Anesthesiology at Kocaeli University Hospital, spanned from November 2011 to May 2012. The study's adherence to the principles of the Declaration of Helsinki was ensured, and written informed consent was obtained from all participants. The CONSORT checklist for the study is available in Fig. 1.

The study included eighty patients aged 18–70 years who were scheduled for infraumbilical orthopaedic, urological, and plastic surgeries under spinal anesthesia were included in the study. Plastic surgeries included lower limb debridement, and infraumbilical reconstructive surgeries following trauma. Patients were selected from American Society of Anesthesiologists (ASA) risk classification groups I and II. Exclusion criteria encompassed patients with a history of acute or chronic opioid use, coagulation test abnormalities, warfarin use, lumbar vertebral anomaly, those under 18 years of age, advanced lung diseases, severe valvular heart disease or heart failure, neurological diseases, local or systemic infections, known allergy to dexmedetomidine, and those receiving  $\alpha_2$  receptor agonist treatment. Patients who received general anesthesia due to an unsuccessful block, partial block, or block level not reaching T10 were excluded from the study.

### 2.2. Grouping and randomisation

After obtaining written informed consent the patients were randomly divided into two groups of 40 each using the closed envelope method. Group B for Bispectral Index (BIS) monitoring and Group R for Ramsay Sedation Scale (RSS) monitoring. The maintenance dose of dexmedetomidine was titrated between 0.2–0.7  $\mu\text{g}/\text{kg}/\text{hr}$  to maintain a BIS value between 60–80 for Group B, and an RSS score of 3–4 for Group R.

### 2.3. Interventions

A 20G IV cannula was inserted into the back of each patient's hand in the preoperative waiting room. A crystalloid solution infusion at a rate of 10 ml/kg was then started 30 minutes before surgery. In the operating room all patients baseline measurements of systolic, diastolic, and mean arterial blood pressure (SBP, DBP, and MAP), heart rate (HR), peripheral oxygen saturation (SpO<sub>2</sub>), and respiratory rate (RR) were recorded preoperatively. Patients in Group B were monitored using BIS (Aspect A-2000, Aspect Medical Systems, USA). After adhering to aseptic rules, cleaning, and draping the skin, information about each step of the procedure was given to all patients, and spinal anesthesia was performed using a median approach from the L3–4 or L4–5 interval after inject

ing 2 ml of 2% lidocaine (Jetocaine. 20mg/2 ml. Biosel Pharmaceuticals, Istanbul) subcutaneously. A 25G (Braun) spinal needle was inserted into the same interval to access the subarachnoid space and 10 mg of bupivacaine (Marcaine heavy, 15 mg/5 ml. AstraZeneca Pharmaceuticals, Istanbul) and 25µg fentanyl (Fentanyl, Ireland). Patients were positioned supine with the head elevated at 15°. Once the block level reached T10 in the pin-prick test, the surgical procedure initiated. All the patients received a bolus of 1 µg/kg dexmedetomidine (Precedex. 200 µg/ 2 ml, USA) for 10 min, followed by continuous infusion at a rate of 0.6 µg/kg/hr. The maintenance dose of dexmedetomidine was titrated be-

tween 0.2-0.7 µg/kg/hr to maintain a BIS value between 60-80 for Group B, and an RSS score of 3-4 for Group R. In both groups, hemodynamic parameters (SBP, DBP, MAP, and HR), RR, SpO<sub>2</sub>, sedation values (BIS and RSS), and adjusted dexmedetomidine infusion doses according to the level of sedation were recorded every 5 min for the first 30 min, and then every 10 min until the end of surgery. Drug infusion was stopped 5 min before the end of surgery in both groups.

The total amount of dexmedetomidine used was recorded. Perioperative complications such as nausea, vomiting, hypotension, bradycardia and hypoxia documented.

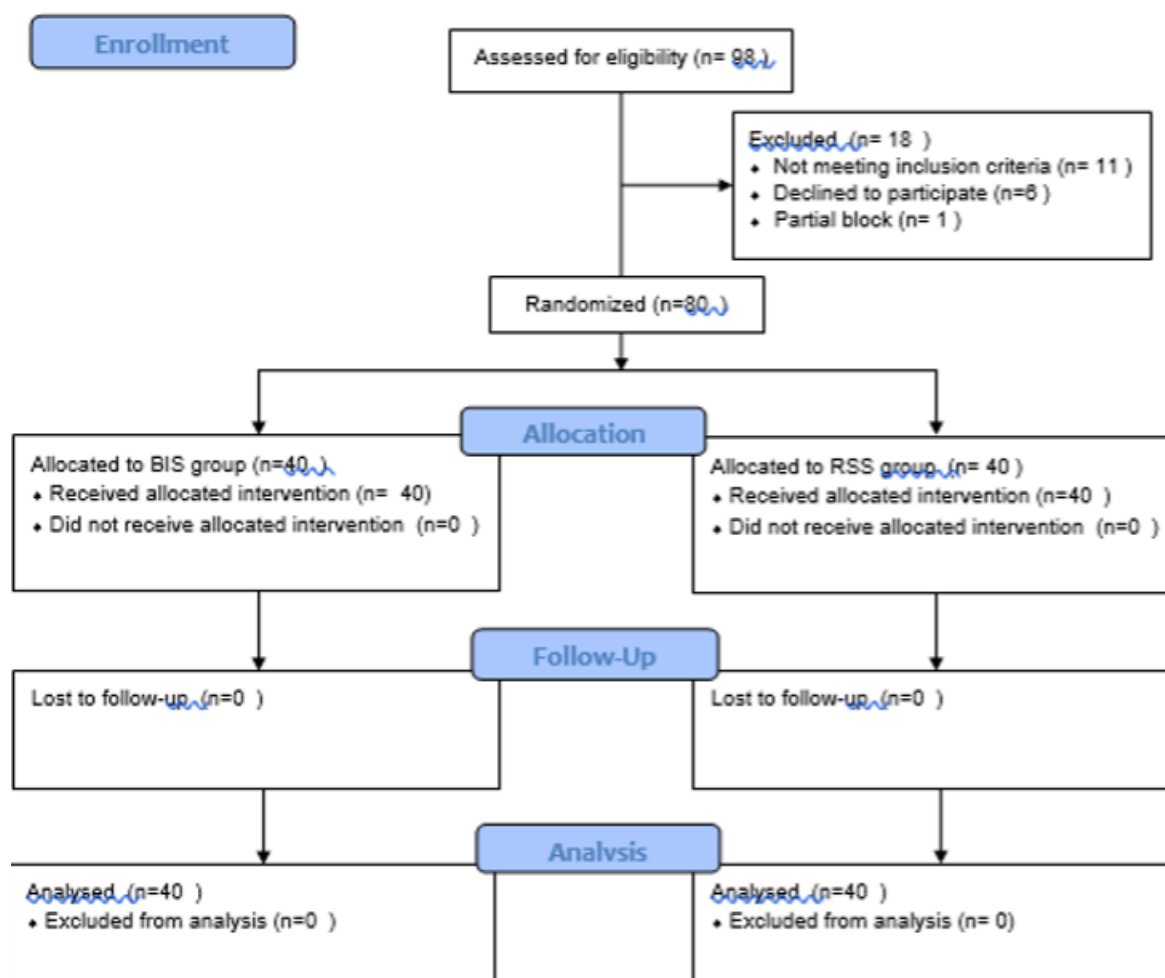


Fig. 1. Flow chart of the study.

#### 2.4. Outcomes measurements

The primary outcome of this study was total consumption of dexmedetomidine.

Secondary outcomes included:

- The level of sedation achieved: Measured by BIS and RSS
- Hemodynamic stability: Heart rate and blood pressure
- Respiratory parameters: Respiratory rate and SpO<sub>2</sub>
- Incidence of perioperative complications such as nausea, vomiting, hypotension (a decrease in MAP below 60 mmHg or Systolic Arterial Blood Pressure (SAB) <

90 mmHg, or a reduction of more than 20% from the initial SBP, DBP, and MAP values), bradycardia (HR less than 50 beats per minute), and hypoxia (SpO<sub>2</sub> < 90%) were defined.

#### 2.5. Sample size and statistical analysis

Based on a similar study in the literature, a sample size of 40 patients per group was determined through power analysis, indicating that this number would be sufficient to detect a clinically significant difference in sedative drug consumption with a power of 80% and a significance level of 0.05 [8].

Statistical evaluation was performed using SPSS (version 16.0; IBM Corp., Armonk NY, USA). The conformity of data within each group to a normal distribution was determined using the Shapiro-Wilk test. Continuous variables were compared between groups using the Student's t-test for variables following a normal distribution and the Mann-Whitney U test for those that did not. Comparisons of SBP, HR, MAP, and DBP within the same group against control values were assessed using the Wilcoxon test. Throughout all tests, a p-value of less than 0.05 was considered statistically significant.

### 3. Results

In total, 98 patients were assessed for eligibility. Of these, 18 patients were excluded for various reasons, including not meeting the inclusion criteria (11 patients), declining to participate (6 patients), and other reasons (1 patient). The remaining 80 patients were randomized into two groups, with 40 patients each allocated to the BIS and 40 patients to the RSS monitoring groups as visually represented in the CONSORT Flow diagram (Fig. 1). Both groups received allocated interventions. None of the patients in either group failed to receive any inter-

vention. Follow-up was completed without loss or discontinuation in either group. Consequently, 40 patients in each group were included in the final analysis.

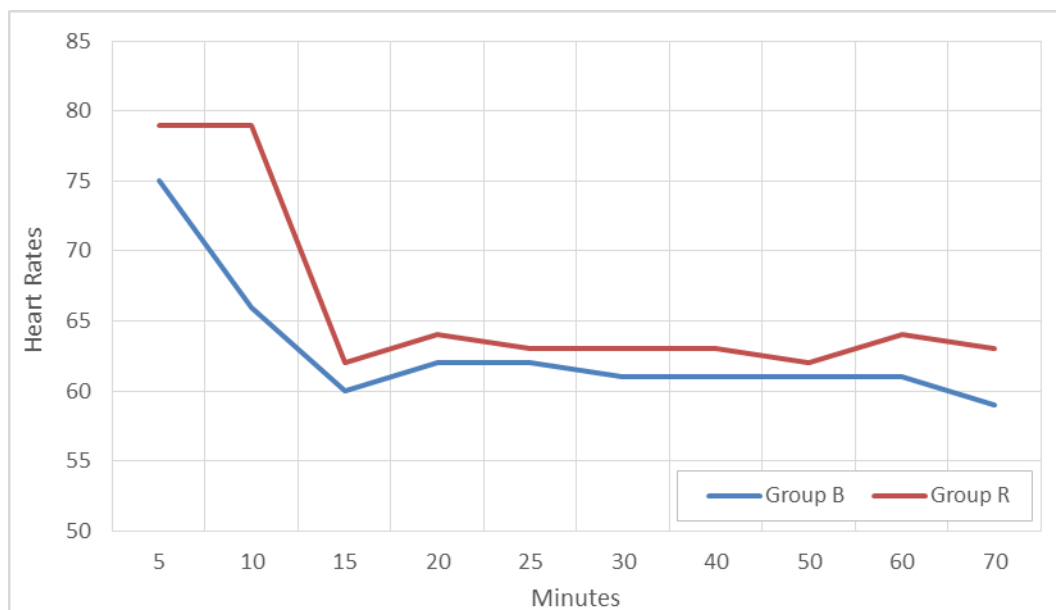
The surgical procedures performed on the study participants were well distributed between the two groups. In Group B (consisting of 40 patients), 24 underwent urological surgeries, while both plastic and orthopaedic surgeries were performed in 8 patients each. Similarly, in Group R (40 patients), 25 underwent urological surgeries, 9 underwent plastic surgeries, and 6 underwent orthopaedic surgeries.

The demographic characteristics and surgical and sedation durations of the 80 enrolled patients did not differ significantly between groups ( $p > 0.05$ ). The average infusion dose required to achieve the targeted level of sedation in Group B was  $0.44 \pm 0.15 \mu\text{g}/\text{kg}/\text{h}$ , in Group R it was slightly lower at  $0.39 \pm 0.14 \mu\text{g}/\text{kg}/\text{h}$ ; however, not statistically significant ( $p > 0.05$ ). The total drug consumption was also similar between the groups ( $p > 0.05$ ) (Table 1).

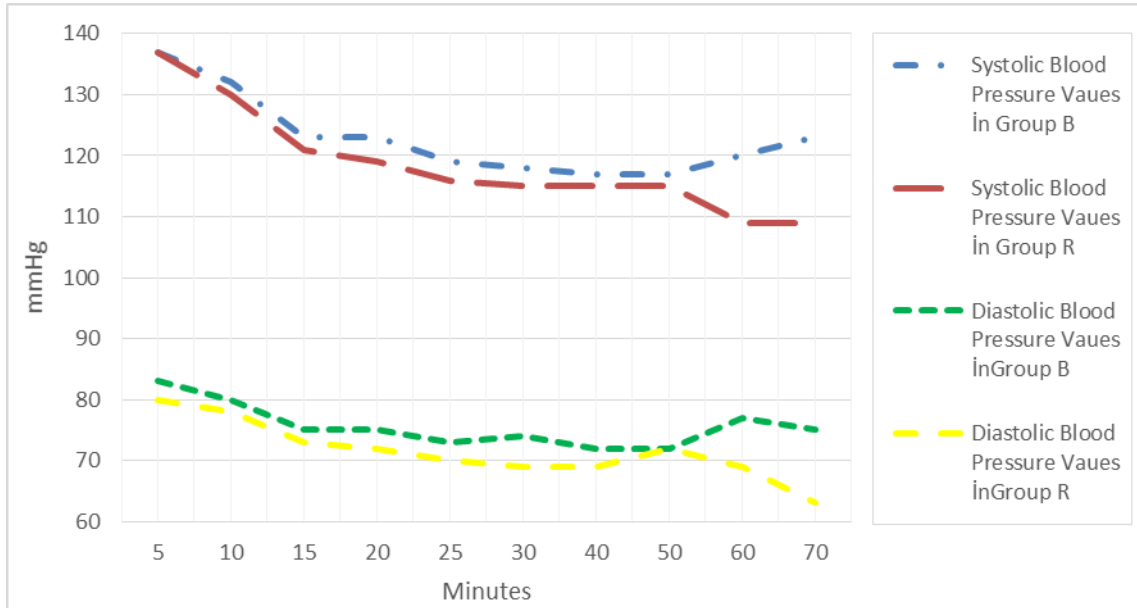
Intragroup comparisons revealed a significant decrease in heart rate (Fig. 2). SBP and DBP (Fig. 3) at various measurement times compared to control values ( $p < 0.05$ ). No significant differences were detected between the groups at the same time points ( $p > 0.05$ ).

**Table 1.** Demographic and intraoperative characteristics of patients undergoing sedation.

Variable	Group B (n=40)	Group R (n=40)	p-value
Age (years)	47.77 $\pm$ 15.38	44.57 $\pm$ 15.31	0.35
BMI (kg/m <sup>2</sup> )	26.67 $\pm$ 4.45	27.30 $\pm$ 4.35	0.52
Gender (F/M)	10/30	11/29	0.18
Drug infusion duration (min)	58.5 $\pm$ 11.8	60.3 $\pm$ 15.1	0.53
Surgical duration (min)	68.5 $\pm$ 11.8	70.38 $\pm$ 15.1	0.90
Drug quantity consumed ( $\mu\text{g}$ )	110 $\pm$ 20	111 $\pm$ 22	0.80



**Fig. 2.** Comparative heart rates in Group B and Group R throughout anesthesia.



**Fig. 3.** Comparative distribution of systolic and diastolic blood pressure values in Group B and Group R throughout anesthesia.

Throughout anesthesia, the RR per minute did not demonstrate any significant variation within or between the groups ( $p > 0.05$ ). Although there was a statistically significant difference in the SpO<sub>2</sub> values between the groups at 15. minute ( $p = 0.03$ ), 30. minute ( $p = 0.03$ ), and 40. minute ( $p = 0.04$ ), no clinically significant difference was detected. In both groups, desatura-

tion was not observed during the operation or anesthesia period.

Throughout anesthesia, there was no statistically significant difference between the groups regarding the dexmedetomidine infusion dose required to achieve adequate sedation, and the total amount of drug consumed was found ( $p > 0.05$ ) (Table 2).

**Table 2.** Comparison of dexmedetomidine infusion doses for Group B and Group R.

Time	Group B (mean ± SD)	Group R (mean ± SD)	p-value
Inf. dose T5	0.5 ± 0.1	0.5 ± 0.1	0.38
Inf. dose T10	0.5 ± 0.2	0.4 ± 0.1	0.20
Inf. dose T15	0.5 ± 0.2	0.4 ± 0.1	0.12
Inf. dose T20	0.5 ± 0.2	0.4 ± 0.2	0.05
Inf. dose T25	0.5 ± 0.2	0.4 ± 0.2	0.14
Inf. dose T30	0.4 ± 0.2	0.5 ± 0.1	0.56
Inf. dose T40	0.4 ± 0.2	0.3 ± 0.2	0.65
Inf. dose T50	0.3 ± 0.3	0.2 ± 0.2	0.06
Inf. dose T60	0.2 ± 0.3	0.2 ± 0.2	0.56
Inf. dose T70	0.5 ± 0.4	0.2 ± 0.3	0.22
Inf. dose T80	0.5 ± 0.3	0.2 ± 0.2	0.21
Average Inf. Dose (µg-1.kg-1.hr-1)	0.44 ± 0.15	0.39 ± 0.14	0.14
Drug quantity consumed (µg)	110 ± 20	111 ± 22	0.80

µg-1.kg-1.hr-1: The Average drug infusion dose; SD: standard deviation; Group B: The group monitored with BIS for sedation; Group R: The group monitored with RSS for sedation; p: Student’s t-test.

Complication rates were similar between the two groups. Hypotension was observed in four patients, with two being treated with fluid therapy and the other two receiving intravenous ephedrine in Group B. Hypotension occurred in three patients, where the blood pressure of one patient was normalized with fluid therapy, and two patients were administered intravenous ephedrine in Group R. Bradycardia developed in 11 patients in Group B and in 10 patients in Group R, with heart rates returning to normal levels after intravenous atropine administration. Nausea was observed in 3 patients from each group, which resolved without the need for any medication. No significant difference was found in the amounts of atropine and ephedrine used between the two groups ( $p>0.05$ ).

#### 4. Discussion

Our study demonstrated that the use of BIS monitoring in patients undergoing spinal anesthesia with dexmedetomidine did not significantly alter the total drug consumption compared with traditional RSS monitoring.

Dexmedetomidine is a preferred sedative in anesthesia practices due to its short half-life, analgesic properties, and minimal respiratory suppression. Dexmedetomidine is considered a potential sedative option due to its favorable sedative profile. Nonetheless, its application is constrained by its propensity to reduce heart rate and arterial blood pressure, which is of particular concern given cardiac complications such as bradyarrhythmias [9]. In our study, dexmedetomidine decreased heart rate and cardiac output in a dose-dependent manner, which is consistent with the findings of Başar et al. [10] and Shehabi et al. [11]. It is important to note that a study by Beloel et al. reported five cases of severe bradycardia in patients receiving dexmedetomidine, which led to the premature termination of their trial. In our study, although bradycardia was observed, it was managed effectively with atropine and did not lead to premature termination. This highlights the need for careful monitoring and management of hemodynamic parameters when using dexmedetomidine, particularly in patients with underlying cardiovascular conditions [12]. Dexmedetomidine's hypotensive effects have been exploited to blunt the sympathetic response during general anesthesia and facilitate controlled hypotension perioperatively [10,13]. Similar to our study, Wang et al. [14] added evidence supporting the hemodynamic stability provided by dexmedetomidine, which is beneficial for reducing surgical bleeding and providing a better operative field.

Dexmedetomidine's profile as a sedative is notably marked by its low risk of respiratory depression, a finding our study corroborates. In agreement with these observations, our research suggests that dexmedetomidine does not significantly impair respiratory function [15]. Conversely, Shehabi et al. observed an elevated incidence of adverse events in a cohort receiving dexmedetomidine compared to those receiving standard care in a large-scale study evaluating early sedation effects in critically ill patients [16]. Although we reported no res-

piratory symptoms, we observed minor and self-closing side effects (nausea) after dexmedetomidine administration.

The influence of BIS monitoring on anesthetic usage has been the subject of extensive studies [17]. It was observed that dexmedetomidine could decrease the need for propofol and remifentanyl when using bispectral index-guided closed-loop anesthesia for monitoring [18]. Turkmen et al. reported that the Richmond Agitation-Sedation Scale (RASS) levels were in substantial agreement with BIS readings during dexmedetomidine-induced sedation in mechanically ventilated critically ill patients [19]. BIS monitoring of dexmedetomidine use has been reported to benefit from reducing agent consumption during mechanical ventilation in critically ill patients [14]. Importantly, the dosage of dexmedetomidine used was not affected by this monitoring method. In our investigation, applying BIS to oversee sedation levels did not lead to a notable change in overall sedative consumption compared to RSS. These results are consistent with those of Luginbüh et al. [20], who also reported no significant impact on the time taken for patients to emerge from sedation, although BIS monitoring was associated with reduced anesthetic requirements.

BIS monitoring has been extensively studied since 1996, some studies have suggested its utility in preventing both over and under-sedation [18]. Our research indicates that in patients undergoing spinal anesthesia with dexmedetomidine sedation, BIS monitoring did not significantly affect total drug consumption or reduce perioperative complications or recovery time. This underscores the need for a nuanced approach to monitoring and titration of sedation, integrating clinical judgment with objective measures such as BIS. Future research should continue to explore the multifaceted dynamics of sedation management to enhance patient safety and optimize anesthesia practices.

The interpretation of the findings of this study has several limitations. First, the investigation was conducted with a relatively small sample size, which may not provide a broad representation of the population undergoing spinal anesthesia. This limits the generalizability of our results, and further studies with larger cohorts are necessary to validate our findings. Another limitation is the single-center nature of the study, which introduces potential biases related to specific anesthetic practices and patient populations. Multi-center studies would be beneficial to confirm the applicability of these results across different clinical settings and patient demographics. Additionally, while BIS monitoring has proven to be a useful tool for assessing sedation depth, it is not without its challenges. The accuracy of BIS monitoring can be affected by various factors, including electrical interference and patient movement, which were not controlled for in this study. Hence, the reliability of BIS readings as the sole indicator of sedation depth is questionable. Our study did not include patients with significant comorbidities, such as ASA classification III or above. This selection criterion excluded a segment of the patient population that might respond differently to dexmedetomidine, thereby limiting the scope of the study's applicability.

The lack of a placebo or control group not receiving BIS monitoring is another limitation that restricts the ability to draw definitive conclusions about the efficacy of BIS monitoring over standard practice or no monitoring at all. Future studies addressing these limitations are necessary to provide a more comprehensive understanding of the impact of BIS monitoring on drug consumption and recovery during sedation with dexmedetomidine during spinal anesthesia.

## 5. Conclusions

Dexmedetomidine effectively achieves sedation during spinal anesthesia without significant respiratory depression. However, BIS monitoring did not reduce drug consumption compared to RSS monitoring. While BIS monitoring is valuable for sedation assessment, its impact on dexmedetomidine's efficacy in spinal anesthesia appears limited. Clinical decisions should consider both monitoring methods and patient-specific factors. Future research could explore integrating BIS monitoring with other sedatives in various surgical contexts to optimize sedation practices and patient safety.

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### Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this manuscript.

### Author Contributions

All of the authors made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; were involved in drafting the manuscript or revising it critically for important intellectual content; and gave final approval of the version to be published.

### Data Availability

The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.

### Ethics Approval and Consent to Participate

This study was approved by the ethics committee of Kocaeli University Faculty of Medicine (Approval code: 29.09.2011 KA EK 10/7). All methods were performed in accordance with relevant guidelines and regulations.

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