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Evaluation of the relationship between sedation methods and postoperative delirium in geriatric patients operated with spinal anesthesia

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ABSTRACT

Aims: With the rapidly aging population, the geriatric patient population is increasing, requiring a careful approach in anesthesia management. The comorbidities commonly seen in these patients often direct anesthetists towards regional anesthesia techniques; however, the adverse effects of certain sedative agents used during regional anesthesia on cognitive functions can create uncertainty about which agent should be preferred. In this context, our study aims to evaluate the effects of dexmedetomidine and remifentanil, administered for sedation in geriatric patients undergoing spinal anesthesia, on postoperative delirium.

Methods: This prospective observational clinical study was conducted after obtaining ethical approval in patients aged 65 and older classified as American Society of Anesthesiologists (ASA) I-II-III who were planned for lower extremity surgery with spinal anesthesia. All patients underwent preoperative confusion assessment method (CAM) testing, and the cases were divided into two groups: dexmedetomidine group (group D, n=38) and remifentanil group (group R, n=38). After the completion of the surgery, sedation was discontinued, and the follow-up of the cases was maintained in the postoperative care unit until the modified Aldrete score reached 9. On the postoperative 24th hour, 72nd hour, and 30th day, the CAM test was repeated by the researcher who conducted the initial test.

Results: No significant difference was found in postoperative delirium between the two different sedation protocols in the geriatric population ($p>0.05$). A statistically significant decrease in simultaneous mean arterial pressure (MAP) values was observed in group D patients at intraoperative 90, 105, 120, and 135 minutes ($p<0.05$).

Conclusion: The effects of using dexmedetomidine and remifentanil as sedative agents in geriatric patients are similar regarding the frequency of postoperative delirium.

Keywords: Postoperative delirium, spinal anesthesia, sedation

INTRODUCTION

The rapid increase in the elderly population has led to a significant increase in the number of surgeries performed among geriatric patients.[1] In geriatric patients, age-related physiological and pharmacodynamic changes lead to increased sensitivity to anesthesia, which may affect mortality and morbidity depending on the choice and dosage of anesthesia.[2-4] The frequent comorbidities in these patients lead anesthesiologists to prefer regional anesthesia methods, particularly spinal anesthesia.[2] For patients receiving regional anesthesia, sedation plays a crucial role in maintaining patient comfort during both the intraoperative and postoperative periods.[2] There is still uncertainty regarding the choice of sedative agent.[2,5-7]

Dexmedetomidine, frequently preferred in geriatric patients, stands out due to its potential to provide analgesia and anxiolysis without the risk of respiratory depression. Additionally, α2-agonists positively impact cardiovascular stability and attenuate the physiological response to surgical stress.[5] Dexmedetomidine is known to offer better control over sedation depth in geriatric patients compared to benzodiazepines and is linked to fewer complications.[6] On the other hand, its short duration of action and rapid metabolism make remifentanil another suitable agent for sedation in geriatric patients.[7] Depending on the sedative agent to be used, one of the most common complications, especially in geriatric patients, is postoperative cognitive dysfunction (PCD).[1,2] The effects of dexmedetomidine and remifentanil in terms of PCD in geriatric patients remain unclear in the literature.[2,5-7]

The most prevalent form of PCD is delirium.[2,8] Delirium is characterized by acute daily fluctuations and impairments in attention and memory.[8] Moreover, delirium has been identified as a risk factor for dementia in aging individuals.[9] Postoperative delirium (POD) is a condition that impairs recovery, prolongs hospital stays, escalates healthcare costs, and contributes to increased morbidity and mortality, particularly in elderly patients.[8] The confusion assessment

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method (CAM), widely utilized for diagnosis, demonstrates high sensitivity and specificity.[10]

In light of this information, the primary outcome of the study was defined as the effect of two commonly used sedative agents, dexmedetomidine and remifentanil, on cognitive functions in geriatric patients undergoing surgery under spinal anesthesia. The secondary outcomes were defined as the effects of these agents on mean arterial pressure and heart rate.

METHODS

Ethics

This is a prospective observational clinical study conducted in accordance with the principles of the Declaration of Helsinki, following the approval of the Ankara Bilkent City Hospital Ethics Committee (Date: 27.04.2022, Decision No: E2-22-1760) and after obtaining informed consent from the patients. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Subject Selection, Inclusion and Exclusion Criteria

The study included patients aged 65 and older who underwent elective lower extremity surgery under spinal anesthesia and were classified as ASA I-III according to the American Society of Anesthesiologists (ASA) classification.

Exclusion criteria included obesity (body-mass index >35 kg/m^2), history of dementia, contraindications to spinal anesthesia, emergency surgeries, history of substance abuse, psychiatric disorders, severe cardiac disease, central nervous system diseases, renal and/or hepatic dysfunction, bleeding diathesis, need for premedication, preoperative CAM test positivity, glasgow coma score below 14, and patients unable to cooperate postoperatively (e.g., mental retardation, communication barriers).

Intervention and Randomization

As part of the study, all patients underwent fasting following a standard protocol. The demographic characteristics of the patients were recorded preoperatively in the ward. Intraoperatively, surgical duration, heart rate, and mean arterial pressure (MAP) were recorded.

Patients were randomized into two groups using a computerized randomization program (www.randomization.com). In the dexmedetomidine group (group D), an initial bolus of dexmedetomidine was administered at 0.5 mcg/kg over 10 minutes, followed by a continuous infusion at 0.2 mcg/kg/hour. In the remifentanil group (group R), an initial bolus of remifentanil was administered at 0.1 mcg/kg/hour over 5 minutes, followed by a continuous infusion at 0.05 mcg/kg/hour. Infusion doses were adjusted to maintain the BIS value between 65 and 85 and the Richmond agitation-sedation scale (RASS) between -1 and -3.[4,5] A respiratory rate ≤8, SpO_2 <95, heart rate <40, and systolic blood pressure <80 mmHg were defined as endpoints. When these thresholds were reached, the sedation dose was reduced regardless of the BIS value. The maximum dose did not exceed 1.4 µg/kg/h in the dexmedetomidine group (group D, n=38) and 10 µg/kg/h in the remifentanil group (group R, n=38).

Anesthesia Management

Patients were transferred to the operating room for routine preoperative preparation and standard monitoring, including electrocardiography (ECG), peripheral oxygen saturation (SpO_2), noninvasive blood pressure (NIBP), and bispectral index (BIS®, A 2000™ Bispectral Index®, Aspect Medical Systems). Intravenous access was established, and hydration was maintained with an infusion of isotonic sodium chloride solution at 10 ml/kg per hour. Spinal anesthesia was performed in all patients by administering 2-2.2 ml of 0.5% hyperbaric bupivacaine into the subarachnoid space using a 25-gauge spinal needle at the L3-L4 or L4-L5 intervertebral space while in the sitting position. Patients were positioned supine with a 30-degree head elevation. Sensory block was evaluated using a pinprick test with a hypodermic needle, while motor block was assessed using the modified Bromage scale. Sedation was initiated in patients with a sensory block at T10 or above. All patients received oxygen at 3 L/min via a face mask throughout the procedure. A decrease of 20% or more in mean arterial pressure from baseline was defined as hypotension, and in such cases, a 250 ml fluid infusion and 5 mg of ephedrine were administered. All patients were provided with active warming measures to prevent hypothermia throughout the procedure.

Measurements and Outcome Parameters

Demographic characteristics and intraoperative data of the patients were recorded. Blood pressure, respiratory rate, sedation scores, and BIS values were assessed preoperatively, after spinal anesthesia, and at 15-minute intervals throughout the procedure.

After completion of surgery, patients were monitored in the postoperative care unit until the modified Aldrete score reached 9, following discontinuation of sedation. Cognitive function was assessed using CAM on the first preoperative day and at 0, 24, 72 hours, and 30 days postoperatively.[9,10] Patients were evaluated in their wards at 24 and 72 hours postoperatively, while all study participants were assessed via telephone on the 30th day.

Statistical Analysis

Power analysis was conducted using the G*power 3.1.9.7 (Franz Faul, Universität Kiel, Germany) statistical software. The analysis yielded a power of 92% with group D (n=38, -1.44±0.57) and group R (n=38, -0.96±0.66), with α=0.05 and an effect size (d) of 0.78.

RESULTS

A total of 86 patients were evaluated in this study, and 82 patients who met the inclusion criteria were randomly assigned into two groups (n=41 per group). In the dexmedetomidine group (group D), two patients were excluded due to the need for general anesthesia following a change in the surgical procedure, and one patient was lost to follow-up postoperatively. Similarly, in the remifentanil group (group R), one patient was excluded due to the need for general anesthesia following a change in the surgical procedure, and two patients were lost to follow-up postoperatively. Consequently, the study was completed with a total of 76 patients: 38 in group D and 38 in group R (Figure).

No significant differences were observed between the groups regarding age, gender, height, weight, BMI, ASA score, education level, surgical duration (minutes), and hospital stay (days) (p>0.05) (Table 1).

In the comparison of primary and secondary outcomes between the two groups, no statistically significant difference

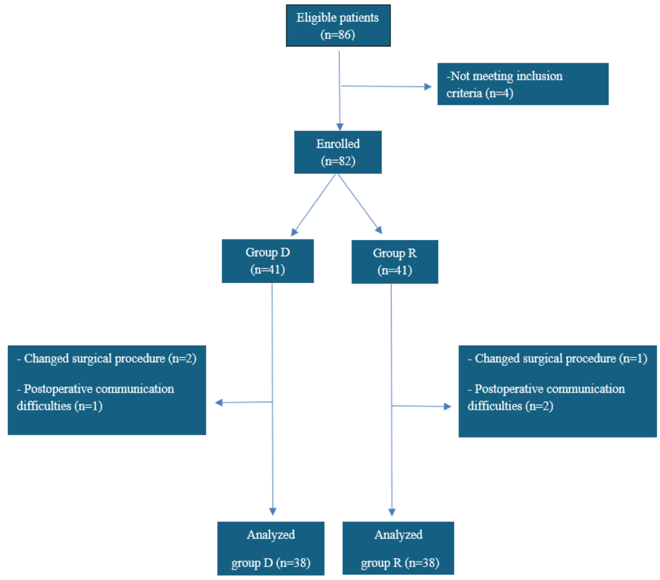

Figure. Consort flow chart

Table 1. Comparison of demographic data, hospital stay, and surgical duration between groups

	Group D (n=38)	Group R (n=38)	p
Sex			
Female	31 (81.6%)	29 (76.3%)	0.778
Male	7 (18.4%)	9 (23.7%)	
Age (years)	69.9±4.4	71.8±5.5	0.110
Height (cm)	158.7±6.8	159.1±6.9	0.789
Wieght (kg)	82.5±12.8	78.7±9.6	0.145
BMI (kg/m²)	32.9±5.6	31.2±4.5	0.156
Educational level			
Illiterate	7 (18.4%)	5 (13.2%)	0.444
Primary school	19 (50.0%)	22 (57.9%)	
Middle school	6 (15.8%)	5 (13.2%)	
High school	5 (13.2%)	2 (5.3%)	
College or higher	1 (2.6%)	4 (10.5%)	
ASA			
I	-	-	
II	28 (73.7%)	35 (92.2%)	0.0676
III	10 (26.3%)	3 (7.8%)	
Hospital stay (days)	5.92±3.66	5.39±2.58	0.471
Surgical duration (min)	103.0±30.9	94.5±29.7	0.223

Data are presented as mean±SD, number (%) or (n), BMI: Body-mass index, ASA: American Society of Anesthesiologists, SD: Standard deviation

was observed in simultaneous CAM scores, which represent the primary outcome (p>0.05) (Table 2).

Regarding the secondary outcomes, no significant differences were found between the groups in simultaneous heart rate (HR) measurements at any time point during the intraoperative period (p>0.05) (Table 2). Similarly, no statistically significant differences were observed in simultaneous MAP values at 15, 30, 45, 60, 75, 150, and 165 minutes intraoperatively (p>0.05). However, significant differences in MAP were found at 90, 105, 120, and 135 minutes (p<0.05), with lower MAP values consistently observed in group D during these time points (p<0.05) (Table 3).

Table 2. Comparison of CAM scores between groups

CAM	Group D (n=38)	Group R (n=38)	p
Postop 0. hour	0.00±0.00	0.00±0.00	1.000[a]
No delirium	38 (100.0%)	38 (100.0%)	1.000[b]
Postop 24 hours	0.05±0.23	0.00±0.00	0.160[a]
No delirium	36 (94.7%)	38 (100.0%)	0.493[b]
Delirium present	2 (5.3%)	--	
Postop 72 hours	0.03±0.16	0.00±0.00	0.324[a]
No delirium	37 (97.4%)	38 (100.0%)	1.000[b]
Delirium present	1 (2.6%)	--	
Postop 30 days	0.00±0.00	0.03±0.16	0.324[a]
No delirium	38 (100.0%)	37 (97.4%)	1.000[b]
Delirium present	--	1 (2.6%)	

CAM: Confusion assessment method, a: Independent samples T test (mean±SD), b: Chi-square test n (%), SD: Standard deviation

Table 3. Comparison of heart rate and MAP between groups

	Time (n/n)	Group D (n=38)	Group R (n=38)	p
MAP (mmHg)	15th min (38/38)	109.6±10.1	106.4±15.8	0.302
	30th min (38/38)	94.0±14.9	91.9±11.3	0.479
	45th min (38/38)	87.1±13.0	86.0±13.2	0.721
	60th min (38/38)	82.9±14.0	84.7±13.9	0.567
	75th min (37/35)	80.2±12.1	84.5±16.4	0.207
	90th min (34/29)	78.8±13.2	88.2±15.9	0.013
	105th min (30/18)	79.4±14.6	93.3±15.2	0.003
	120th min (19/14)	77.3±11.2	96.1±15.9	0.000
	135th min (10/8)	75.4±9.0	94.1±16.4	0.015
	150th min (4/3)	81.8±12.4	92.0±17.8	0.406
	165th min (3/2)	75.0±6.2	99.0±31.1	0.469
	180th min (3/0)	73.0±10.8	--	--
	195th min (1/0)	82.0±0.0	--	--
HR (bpm)	15th min (38/38)	81.6±15.4	79.5±13.4	0.532
	30th min (38/38)	72.9±15.5	75.1±13.0	0.513
	45th min (38/38)	63.7±13.2	68.9±14.0	0.103
	60th min (38/38)	62.6±11.4	68.0±12.7	0.055
	75th min (37/35)	62.7±11.5	67.1±10.0	0.085
	90th min (34/29)	62.4±10.9	67.0±10.7	0.103
	105th min (30/18)	63.1±10.9	65.6±9.4	0.422
	120th min (19/14)	63.3±9.8	66.3±10.1	0.403
	135th min (10/8)	67.4±9.9	65.0±11.0	0.632
	150th min (4/3)	74.0±9.4	63.0±14.8	0.278
	165th min (3/2)	69.7±10.0	72.0±19.8	0.867
	180th min (3/0)	71.0±12.3	--	--
	195th min (1/0)	59.0±0.0	--	--

Data are presented as mean±SD, number (%) or (n), MAP: Mean arterial pressure, HR: Heart rate

DISCUSSION

This study investigates the effects of sedation strategies on postoperative delirium in geriatric patients undergoing elective surgery under spinal anesthesia. The findings indicate no significant difference in the incidence of postoperative delirium between the dexmedetomidine and remifentanil groups. Delirium was observed in 5.2% of patients in the dexmedetomidine group and 2.6% in the remifentanil group. Furthermore, MAP values were lower in the dexmedetomidine group at 90, 105, 120, and 135 minutes.

Postoperative delirium is associated with both patient-related and surgery-related risk factors. Advanced age is recognized as the most significant risk factor for postoperative delirium.[11] With aging, organ function declines, and alterations occur in the metabolism and excretion of anesthetic agents.[11] Male sex has also been identified as a predisposing factor for postoperative delirium, a view supported by numerous studies.[11,12] Major and emergency surgical procedures have been associated with a higher incidence of delirium compared to minor and elective surgeries, and the risk of delirium increases with prolonged surgical duration.[13] An extended hospital stay has also been identified as a risk factor for delirium.[13] A meta-analysis by Yang et al.,[13] including 10,053 patients, identified factors associated with delirium following orthopedic surgeries in geriatric patients, with hospital stay duration being one of them. In our study, no significant differences were observed regarding predisposing risk factors for postoperative delirium.

The incidence of postoperative delirium following orthopedic surgery ranges from 5% to 61%; this variation is influenced by predisposing risk factors and the choice of sedative agents.[2,5-7] In our study, the incidence of postoperative delirium was 3.9%, which is below the reported average in the literature. These findings suggest that both sedative agents evaluated may be safe regarding postoperative delirium.

In a randomized controlled trial by Shin et al.,[2] intraoperative dexmedetomidine and propofol sedation were compared in patients over 65 years undergoing lower extremity surgery under spinal anesthesia. The incidence of postoperative delirium was lower in patients receiving dexmedetomidine sedation. A retrospective study by Park et al.,[14] including 1045 patients, yielded similar results, demonstrating that dexmedetomidine sedation led to a lower incidence of postoperative delirium compared to propofol in elderly patients. Maldonado et al.[15] compared sedation with propofol, dexmedetomidine, and midazolam, reporting a delirium incidence of 50% in the propofol and midazolam groups, whereas it was only 3% in the dexmedetomidine group. Poorzamany et al.[16] concluded that dexmedetomidine was more reliable than remifentanil for sedation in cataract surgery. However, this study included patients aged 40 to 70. Moreover, the number of studies comparing postoperative delirium incidence between dexmedetomidine and remifentanil in geriatric patients remains limited in the literature. In our study, postoperative delirium occurred in 5.2% of geriatric patients in the dexmedetomidine group and 2.6% in the remifentanil group. These findings suggest that both agents may effectively reduce the incidence of postoperative delirium in geriatric patients.

Although hypotension is commonly observed during sedation in spinal anesthesia, sufficient studies on its impact on postoperative delirium are lacking, and findings in the literature appear contradictory. In a retrospective study, Maheshwari et al.[17] linked intraoperative and postoperative hypotension to delirium, suggesting that preventing hypotension may play a crucial role in reducing its incidence. Conversely, Wang et al.[18] reported that both excessively high and low mean arterial pressure increase the risk of postoperative delirium. However, Hirsch et al.[19] reported that neither moderate nor profound hypotension was associated with delirium in their study. Similarly, in the large-scale ISPOCD1 study, Moller et al.[20] found no association between hypotension and postoperative delirium. In our study, intraoperative MAP was significantly lower in group D patients at 90, 105, 120, and 135 minutes; however, no significant difference was observed throughout the remainder of the operation. Despite lower blood pressure, hypotension was prevented in both groups, with intervention applied if mean arterial pressure decreased by 20% or more from baseline. In this context, beyond utilizing studies linking hypotension to delirium, we prioritized maintaining stable hemodynamic management while considering the frailty of our patient population.

In a study by Jo et al.[21] comparing dexmedetomidine and midazolam sedation under BIS monitoring, the bradycardic effect of dexmedetomidine was highlighted. Similarly, Yıldırım et al.[22] compared remifentanil and dexmedetomidine for sedation in spinal anesthesia among patients aged 20 to 60. Bradycardia was not observed in either group. While remifentanil provided more stable hemodynamics, caution is required regarding its respiratory depressant effect. In our study, there was no significant difference in heart rate between the two groups. No cases of respiratory depression were observed in the remifentanil sedation group. Thus, both sedation agents appear to be safe regarding bradycardia and respiratory complications at the doses used in our study. Do et al.[23] highlighted the association between low social support and postoperative delirium.

Limitations

This study has several limitations. One important factor that may be overlooked in the evaluation of delirium in geriatric patients is social support. Although a relative accompanies the patient during surgery, geriatric patients living alone may experience significant stress due to concerns about future isolation and reduced functionality without a caregiver. Another limitation was the inability to assess postoperative mobilization duration. Early mobilization is known to reduce the risk of delirium; however, in our study, postoperative mobilization could not be tracked due to insufficient patient documentation in orthopedic units.

CONCLUSION

Our study demonstrates that dexmedetomidine and remifentanil administration in geriatric patients under spinal anesthesia result in similar postoperative delirium incidence rates. These findings suggest that both sedation methods can be safely and effectively utilized.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Bilkent City Hospital Ethics Committee (Date: 27.04.2022, Decision No: E2-22-1760).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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