Challenge Journal of Perioperative Medicine

Research Article

How does intravenous ondansetron affect motor and sensory block in spinal anesthesia administered with intrathecal levobupivacaine? A prospective randomized controlled study

Mustafa Felat Ataman [a,*], Husnu Suslu [b], Leyla Saidoglu [c]

[a] *Department of Anesthesiology and Reanimation, Bolu İzzet Baysal State Hospital, Bolu, Türkiye*
[b] *Department of Algology, Maltepe University, İstanbul, Türkiye*
[c] *Anesthesiology and Reanimation, Specialist Doctor (Retired), İstanbul, Türkiye*

ABSTRACT

Background: Spinal anesthesia is commonly performed in surgical procedures, and ondansetron, frequently used as an antiemetic, is often administered to manage postoperative nausea and vomiting. Given their frequent co-administration, we sought to investigate the potential effects of intravenous ondansetron on the block characteristics of spinal anesthesia performed with levobupivacaine.

Materials and Method: In this prospective, randomized controlled study, forty patients were divided into two groups: Group L (spinal anesthesia with levobupivacaine) and Group OL (spinal anesthesia with levobupivacaine plus intravenous ondansetron).

Results: Our findings showed that while motor block duration was similar between the groups ($p>0.05$), sensory block duration was significantly shorter in the ondansetron group ($p<0.05$). There were no significant differences in patient demographics or hemodynamic parameters between the groups ($p>0.05$).

Conclusions: The shortened sensory block with ondansetron administration may be clinically undesirable as it could limit the intended duration of anesthesia. We recommend administering ondansetron at the end of surgery to avoid this effect. Further studies are required to confirm these findings and clarify the mechanisms involved.

ARTICLE INFO

Article history:
Received 30 June 2024
Revised 24 September 2024
Accepted 21 October 2024

Keywords:
Spinal anesthesia
Levobupivacaine
Ondansetron
Motor block
Sensory block

1. Introduction

Neuraxial anesthesia stands as the foremost technique among regional anesthesia methods employed as primary anesthetic approaches and should be regarded as one of the fundamental skills of an anesthesiologist [1,2]. Spinal anesthesia (SA), the most frequently employed neuraxial technique, aims to provide effective anesthesia while ensuring that the selected local anesthetic and positioning align with the nature and duration of the surgical procedure. To achieve this, various agents with differing durations of action are available, and the objectives of anesthesia can be predicted through appropriate patient positioning [3].

The primary objective of researchers in the field of SA has been to achieve effective and long-lasting postoperative analgesia by extending the duration of sensory block while minimizing the extension of motor block duration spinal anesthesia [4]. This dual objective is crucial for enhancing patient comfort and facilitating early mobilization after surgical procedures. In recent years, numerous studies have focused on this aspect of spinal anesthesia. To achieve this goal, a wide range of techniques and methodologies have been investigated, with the ma-

* *Corresponding author*. E-mail address: drfelat78@hotmail.com (M. F. Ataman)
ISSN: 2980-292X / DOI: https://doi.org/10.20528/cjpm.2024.03.005

jority of these approaches concentrating on the addition of intrathecal adjuvants and systemically administered agents to the medications [5–7]. These adjuvants are intended to enhance the analgesic properties of the local anesthetics used in spinal anesthesia, thereby providing a more favorable balance between sensory and motor block durations.

Ondansetron is a 5-Hydroxytryptamine type 3 (5-HT3) serotonin antagonist and is commonly used as an antiemetic in perioperative medicine. However, hypotheses have been proposed that intravenous ondansetron administration in patients undergoing surgery with spinal anesthesia may provide more stable hemodynamics in addition to its antiemetic effect [8]. On the other hand, the effects of intravenous ondansetron on the block characteristics in spinal anesthesia procedures performed with bupivacaine, one of the most commonly used local anesthetics, have been investigated; however, conflicting findings have been observed [9,10]. No study has yet been reported that specifically examines the effects of intravenous ondansetron on sensory and motor block characteristics, as well as hemodynamic variables, in spinal anesthesia performed with levobupivacaine, highlighting a gap in the current literature regarding this combination.

This study examines the effects of intravenous ondansetron on sensory and motor block characteristics and hemodynamic variables in patients receiving spinal anesthesia with levobupivacaine. By addressing conflicting findings in the literature, this research aims to clarify the potential benefits of ondansetron administration in this context. The primary outcome of this study was defined as the duration of the sensory and motor block achieved with spinal anesthesia. By evaluating this critical parameter, we aim to provide a detailed understanding of the efficacy of intravenous ondansetron in modulating block characteristics. Additionally, secondary outcomes were identified to include the time to onset of the block and hemodynamic changes during the procedure. These secondary measures are crucial for assessing not only the effectiveness of ondansetron in enhancing anesthetic quality but also its potential impact on patient stability and safety throughout the perioperative period.

2. Materials and Methods

This prospective, randomized controlled study was conducted at Dr. Lütfi Kırdar Kartal Education and Research Hospital between February and September 2010, following ethics committee approval. Written informed consent was obtained from all patients, and the study adhered to the principles outlined in the Declaration of Helsinki and the CONSORT statement for reporting randomized trials. A total of 40 patients, aged 25 to 77 years, classified as ASA (American Society of Anesthesiologists) I-III and scheduled for elective hip and lower extremity surgeries, were included. Patients with ASA IV or higher, peripheral neuropathy, neuromuscular disorders, substance abuse, chronic pain treatment, those receiving α2 agonists or Ca^2+ channel blockers, obese patients (BMI>30), hypersensitivity to local anesthetics, scoliosis, previous lumbar surgery, coagulopathy, and infection were excluded.

Patients were randomized into two groups using sealed envelopes. Group L (n=20) received 4 ml of 0.9% isotonic NaCl intravenously 15 minutes before intrathecal injection. Group OL (n=20) received 8 mg/4 ml of ondansetron intravenously 15 minutes before intrathecal injection. Spinal anesthesia was administered with 2 ml of 10 mg levobupivacaine.

Standard monitoring (ECG, heart rate, blood pressure, peripheral oxygen saturation) was performed. Sensory block was assessed using the "pin-prick" test at 2-minute intervals until loss of sensation at the T10 dermatome. Motor block was evaluated using the Bromage scale every 2 minutes, with the onset of motor block defined as Bromage score 2–3. The presence and level of sensory and motor block were checked every 15 minutes to determine the time to recover from the blocks.

Bromage Scale:
0: No paralysis, full flexion of hip and knee.
1: Only knee and foot movement, unable to lift leg.
2: No knee movement, only foot movement.
3: Complete paralysis, no movement of ankle or toes.

3. Statistical Analyses

Statistical analysis was performed using NCSS 2007 software. Descriptive statistics (mean, standard deviation) were employed alongside Friedman's test for repeated measures, Kruskal-Wallis test for intergroup comparisons, Dunn's multiple comparison test for subgroup analysis, and Mann-Whitney U test for paired comparisons. Chi-square and Fisher's exact tests were used for categorical variables. Statistical significance was set at $p<0.05$ with a 95% confidence interval.

4. Results

A total of 44 patients were evaluated for the study. However, 2 patients declined spinal anesthesia, and 2 others were excluded due to their expected surgical duration exceeding 2.5 hours. Ultimately, 40 patients were included in the analysis, with 20 patients in each group. Group L consisted of patients who received spinal anesthesia with levobupivacaine, while Group OL included those who received spinal anesthesia with levobupivacaine plus systemic ondansetron (Fig. 1). There were no significant differences between the groups regarding descriptive parameters such as age, gender, height, weight, and ASA classification ($p>0.05$) (Table 1).

No significant statistical differences were observed between the groups in terms of non-invasive blood pressure (systolic, diastolic, and mean), heart rate, and oxygen saturation, both before spinal anesthesia and at multiple time points following intrathecal injection (1, 3, 5, 10, 15, 20, 30, 40, 60 minutes) as well as during the initial post-operative recovery room measurements ($p>0.05$ for all parameters at all-time intervals).

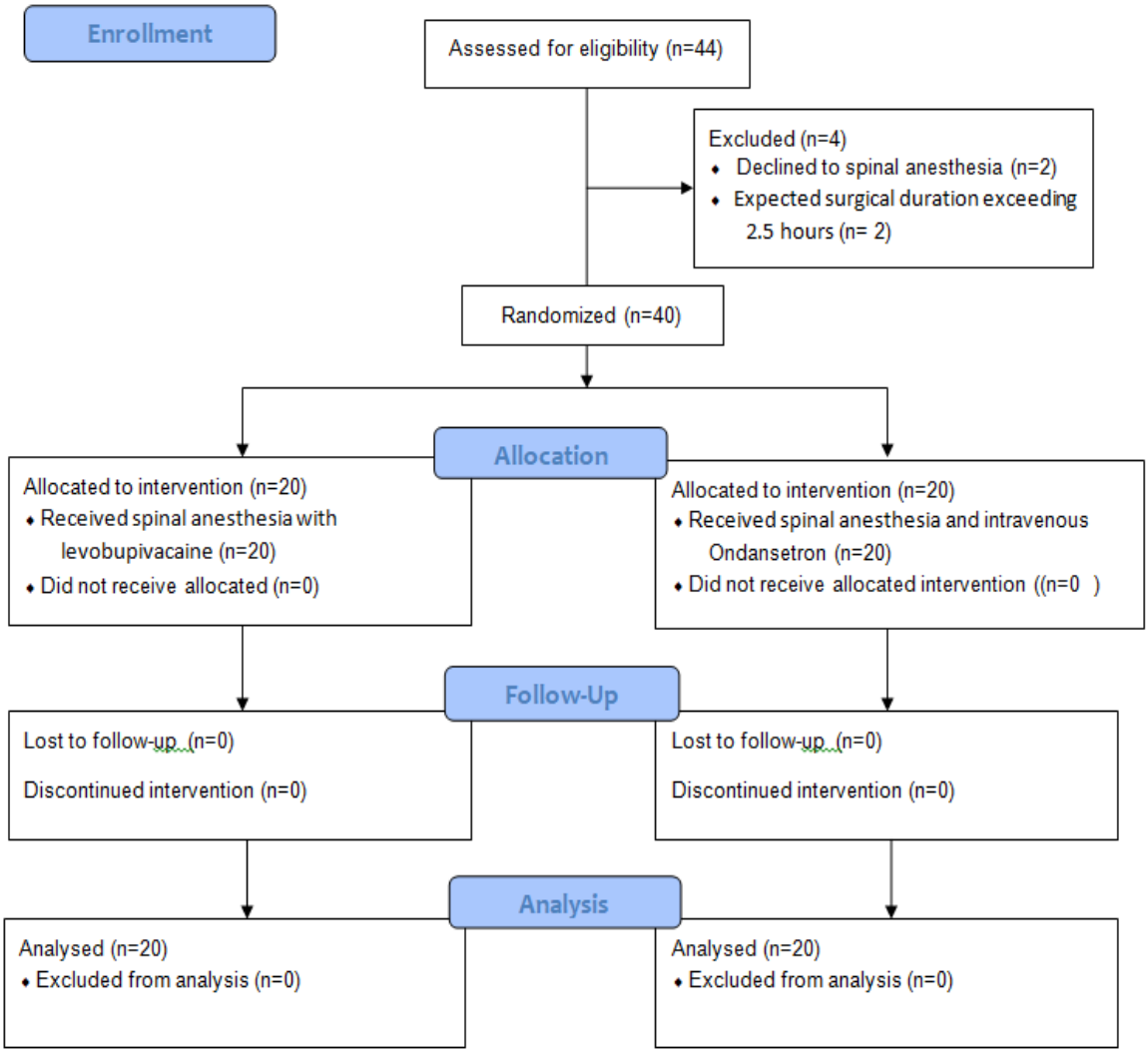

Fig. 1. Flow diagram of the study.

Table 1. Demographics of patients and comparisons.

	Group L	Group OL	p value
Age (years)	53.95 ± 15.32	49 ± 17.44	0.346
Weight (kg)	74.4 ± 14.34	74.85 ± 9.57	0.908
Height (cm)	171 ± 9.35	173.8 ± 9.51	0.354
Gender (F/M)	7/13	9/11	0.519
ASA (I/II/III)	7/8/5	10/8/2	0.404

ASA refers to the American Society of Anesthesiologists classification. Gender is represented as Female (F) and Male (M). Data are presented as mean ± standard deviation (SD) or as the number of patients.

While the onset times for motor and sensory blocks were similar between the two groups, the regression and termination times for motor blocks were also comparable ($p<0.05$). However, the regression and termination times for sensory blocks were shorter in the ondansetron group ($p<0.001$, $p<0.001$, respectively). No statistically significant differences were observed in the distributions of nausea, agitation, hypotension, hypertension, arrhythmia, bradycardia, and oxygen desaturation between groups ($p>0.05$).

5. Discussion

In this study, we evaluated the effects of administering systemic ondansetron together with spinal anesthesia using levobupivacaine on various clinical parameters and block characteristics in a cohort of 40 patients. Our results indicated no significant differences between Group L (levobupivacaine alone) and Group OL (levobupivacaine plus ondansetron) regarding demographic characteristics, non-invasive hemodynamic parameters,

or oxygen saturation levels at multiple time points. Additionally, the incidence of nausea, agitation, hypotension, hypertension, arrhythmia, bradycardia, and oxygen desaturation was comparable between the groups. Interestingly, while the onset times for both motor and sensory blocks were similar, the regression and termination times for sensory blocks were significantly shorter in the ondansetron group. These findings suggest that ondansetron may influence sensory block characteristics without affecting overall hemodynamic stability or other side effects commonly associated with spinal anesthesia.

Table 2. Comparative analysis of onset, regression, and termination times for motor and sensory blocks across groups.

Time frames	Group L (Mean ± SD)	Group OL (Mean ± SD)	p value
To reach maximum sensory block (min)	10.05 ± 4.33	8.25 ± 2.9	0.131
For 2-segment regression of sensory block (min)	114.85 ± 17.64	73.45 ± 15.99	<0.001
For complete resolution of sensory block (min)	141.8 ± 20	94.45 ± 16.35	<0.001
To onset of motor block (min)	11.2 ± 3.65	10.65 ± 3.23	0.617
For motor block regression (min)	135.2 ± 21.53	132.6 ± 15.73	0.665
For complete resolution of motor block (min)	152.25 ± 21.58	149.65 ± 16.04	0.668

Studies investigating the effects of intravenous ondansetron on the block characteristics of intrathecal bupivacaine occupy an important place in the literature, often presenting conflicting results [9,10]. While some research suggests that the concomitant use of ondansetron may positively influence block characteristics when administered with intrathecal bupivacaine, other studies report limited or no observed effect. This discrepancy highlights the need for further investigation into the pharmacological effects of ondansetron and its interactions with bupivacaine. Therefore, these conflicting findings should be carefully evaluated in the context of clinical practice and anesthesia management.

Ondansetron may affect the duration of spinal anesthesia through various mechanisms, including its antiemetic effect, modulation of serotonin-related pain pathways, and potential direct neurological influence on spinal cord neurons [10,11]. Additionally, its pharmacokinetic properties might alter the absorption and distribution of bupivacaine, and by reducing anxiety, it can help maintain physiological stability, enhancing the anesthetic's effectiveness [12]. These factors together provide a possible explanation for ondansetron's impact on spinal anesthesia characteristics.

In our study, we observed that although ondansetron did not have a significant impact on the duration of the motor block during spinal anesthesia, it notably shortened the duration of the sensory block. This finding is clinically concerning, as a shortened sensory block is generally considered undesirable in the context of spinal anesthesia. The primary objective of spinal anesthesia is to provide sufficient and sustained sensory anesthesia to ensure that patients remain pain-free and comfortable throughout the entire duration of the surgical procedure. A reduction in sensory block duration could potentially result in the premature return of sensation, leading to inadequate anesthesia and patient discomfort if the surgery is still ongoing [13,14]. This outcome runs counter to the fundamental purpose of spinal anesthesia, which is to maintain an effective and reliable sensory block for the necessary duration of the surgery.

Moreover, shortening the sensory block could introduce complications such as the need for additional anesthetic interventions during surgery or even the conversion to general anesthesia if the spinal block wears off too quickly [15]. This would not only increase the complexity of anesthesia management but could also lead to higher risks for the patient and a less predictable course of anesthesia.

Considering these potential clinical implications, we propose that ondansetron be administered at the end of the surgical procedure rather than before or during spinal anesthesia. This would allow the antiemetic benefits of ondansetron to be utilized without interfering with the desired duration of sensory anesthesia. Until more studies are published that confirm or refute the findings of our study, it may be prudent to exercise caution when using ondansetron in conjunction with spinal anesthesia, particularly in cases where maintaining a prolonged sensory block is critical for surgical success. Our recommendation is based on the current understanding of the interaction between ondansetron and spinal anesthesia, but further research is essential to clarify the long-term clinical significance of this interaction.

One of the primary limitations of our study is the absence of a formal sample size calculation. Our study included a total of 40 patients, with 20 patients in each group; however, without a predetermined sample size calculation, the statistical power of our findings may be limited. This lack of power could potentially affect the generalizability of the results, and future studies with larger, calculated sample sizes are necessary to validate our conclusions. Additionally, our study did not assess patient-reported outcomes such as the Quality of Recovery (QoR) score or similar measures, which would have provided valuable insights into the patients' overall postoperative recovery experience, including factors such as comfort, well-being, and satisfaction. Including such assessments would have enriched our evaluation of the clinical impact of ondansetron on spinal anesthesia. Incorporating these parameters into future research could provide a more comprehensive understanding of

the anesthetic and postoperative effects, which was a missed opportunity in our current study.

6. Conclusions

In conclusion, our study demonstrated that intravenous ondansetron significantly shortened the sensory block duration without affecting the motor block in patients undergoing spinal anesthesia with levobupivacaine. This finding suggests a potential interference with the intended duration of sensory anesthesia, which may be clinically undesirable. Administering ondansetron at the end of surgery could help avoid this effect, though further research is needed to support this approach.

Acknowledgements

None declared.

Funding

The authors received no financial support for the research, authorship, and/or publication of this manuscript.

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 Dr. Lütfi Kırdar Kartal Education and Research Hospital. Written informed consent was obtained from the participants. All methods were performed in accordance with relevant guidelines and regulations.

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