ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Outcome of ondansetron on subarachnoid block-induced hypotension in infraumbilical surgeries

Renganathan S[1], Navin C[2], Ganesh Prabhu SC[3]

[1]Associate Professor, [2]Junior Resident, [3]Professor, Department of Anaesthesia, Velammal Medical College Hospital and Research Institute, Madurai, Tamil Nadu, India

Submission: 19-02-2025 Revision: 03-04-2025 Publication: 01-05-2025

ABSTRACT

Background: Bradycardia and hypotension are common post-subarachnoid block (SAB) complications that can result in adverse outcomes. The 5-HT3 receptor antagonist ondansetron, which is often used as an antiemetic, has recently been studied for its possible effect on preserving hemodynamic stability during SAB. **Aims and Objectives:** This study aimed to assess the effect of prophylactic intravenous (IV) ondansetron administration on the incidence of SAB-induced hypotension and bradycardia in patients undergoing infraumbilical surgery. **Materials and Methods:** This prospective, randomized, controlled study included 100 patients undergoing infraumbilical surgery under spinal anesthesia. Patients were randomly divided into two groups: control (placebo, n = 50) and ondansetron (8 mg IV, n = 50). Systolic blood pressure, mean arterial pressure (MAP), and heart rate were the hemodynamic parameters measured at baseline and 5, 10, 15, 20, and 30 min after SAB. The incidence of hypotension and the need for vasopressors were the primary outcomes. The prevalence of bradycardia and atropine use was secondary outcomes. **Results:** The incidence of SAB-induced hypotension was significantly lower in the ondansetron group (14%) than in the control group (44%) (P = 0.001). Ephedrine use was also significantly lower in the ondansetron group (14% vs. 44%, P = 0.001). MAP remained significantly higher in the ondansetron group at 10-, 15-, 20-, and 30-min post-SAB (P < 0.05). The incidence of bradycardia was not significantly different between the groups (P = 0.559). **Conclusion:** Prophylactic ondansetron administration significantly decreased the incidence of SAB-induced hypotension and the need for vasopressors. Ondansetron may contribute to improved hemodynamic stability during spinal anesthesia, thereby lowering the risk of related complications.

Key words: Spinal anesthesia; Hypotension; Ondansetron; Vasopressor; Hemodynamic stability

Access this article online

Website: https://ajmsjournal.info/index.php/AJMS/index

DOI: 10.71152/ajms.v16i5.4470

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Subarachnoid block (SAB), or spinal anesthesia, is widely used for infraumbilical surgeries due to its advantages over general anesthesia.[1] However, a significant disadvantage is the elevated incidence of hypotension, caused by sympathetic blockade, which diminishes systemic vascular resistance and venous return.[2] This hemodynamic instability can lead to severe perioperative complications, including nausea, dizziness, organ hypoperfusion, and cardiac events.[3]

Management of SAB-induced hypotension often involves intravenous (IV) fluids, vasopressors (such as ephedrine and phenylephrine), and strategic patient posture.[4] Even with these initiatives, some individuals continue to experience hypotension, requiring different preventative approaches. One technique utilizes ondansetron, a selective 5-HT3

Address for Correspondence:
Dr. Renganathan S, Associate Professor, Department of Anaesthesia, Velammal Medical College Hospital and Research Institute, Madurai - 625 009, Tamil Nadu, India. **Mobile:** +91-9500025879. **E-mail:** renganathansockalingam@gmail.com

receptor antagonist mostly used to reduce post-operative nausea and vomiting.[5,6]

Recent evidence indicates that ondansetron can contribute to stabilizing hemodynamics after SAB by blocking the Bezold-Jarisch reflex (BJR). This 5-HT3 receptor-mediated reflex causes an increase in vagal tone, bradycardia, and a worsening of hypotension.[7,8] By blocking these receptors, ondansetron has been postulated to mitigate the reflex-mediated cardiovascular depression associated with SAB.[9] In addition, serotonin receptors in vascular smooth muscle contribute to vasodilation following SAB, and their inhibition by ondansetron helps to maintain vascular tone and systemic blood pressure. Furthermore, ondansetron may have a role in enhancing baroreceptor reflex activity, thereby improving compensatory hemodynamic responses to decreased systemic vascular resistance induced by SAB.[10]

A study on non-obstetric surgeries found that prophylactic IV ondansetron significantly reduced the incidence of SAB-induced hypotension from 50% in the placebo group to 27.8% in the ondansetron group. Furthermore, the group receiving ondansetron needed vasopressor assistance less often (13.9% vs. 27.8%).[10] The incidence of hypotension did not vary significantly across the groups in another randomized controlled trial (RCT) that compared ondansetron alone to combined fluid preloading and vasoconstrictors, indicating that ondansetron could provide a similar substitute for conventional preventative strategies.[11]

Despite these findings, the overall effectiveness of ondansetron in preventing SAB-induced hypotension remains unclear. Some studies have reported a reduction in hypotension rates and vasopressor use, whereas others have found minimal benefits. Further research is needed to clarify its role, especially in different patient populations and surgical settings.[7]

Despite various preventive strategies, hypotension following SAB remains a persistent challenge in infraumbilical surgeries. Conventional management techniques, including IV fluid therapy and vasopressor administration, have limitations, necessitating the exploration of alternative interventions. Ondansetron, through its inhibitory effect on the 5-HT3 receptor, may provide an effective strategy for mitigating SAB-induced hypotension.[12]

Aims and objectives

The purpose of our study was to determine whether ondansetron administered before spinal anesthesia decreases the risk of hypotension during the initial 30 min of surgery and its impact on the occurrence of bradycardia following spinal anesthesia.

MATERIALS AND METHODS

This study was a prospective, RCT was conducted on 2024 June–2024 December in a tertiary care hospital involving 100 patients undergoing infraumbilical surgeries under spinal anesthesia, with 50 patients in each group. The study was approved by the Institutional Ethics Committee (IEC No: VMCIEC/102/2024) before its commencement, and informed consent was taken from all the patients.

Inclusion and exclusion criteria

Patients with American Society of Anesthesiologist I or II and aged ≥18 years were included; those with contraindications for neuraxial anesthesia, hypersensitivity to ondansetron, use of clonidine during spinal anesthesia, anticoagulant therapy, heart failure, kidney or liver disease, or systemic or localized infection at the puncture site were excluded from the study.

Methods

Patients were randomly assigned to two groups: the ondansetron group (n=50), receiving 8 mg IV ondansetron 5 min before SAB, and the control group (n=50), receiving a placebo. Standard monitoring was applied to all patients, and a crystalloid preload of 10 mL/kg^{-1} was administered before spinal anesthesia (Figure 1).

Spinal anesthesia was performed in a sitting position using hyperbaric bupivacaine (15 mg) with opioid adjuvants, followed by immediate supine positioning, and surgery was commenced. Hemodynamic parameters, including systolic blood pressure (SBP) and heart rate (HR), were recorded at baseline and at 5, 10, 15, 20, and 30-min post-SAB. Hypotension, that is, SBP <90 mmHg, was treated with 5 mg ephedrine, and bradycardia, that is, HR <50 bpm, was treated with 0.5 mg of atropine. The main outcome was the occurrence of hypotension within the first 30 min following SAB, and the secondary outcomes were the occurrence of bradycardia, use of vasopressors, and changes in SBP and HR.

Ethical approval was obtained (VMCIEC/102/2024), and data on demographic characteristics, intraoperative hemodynamics, and treatment interventions were recorded meticulously for analysis.

Statistical analysis

Data were presented as mean, standard deviation, frequency, and percentage. Continuous variables were compared using the independent sample t-test and categorical variables using the Chi-square test. Significance was defined by $P<0.05$. Data analysis was performed using IBM-SPSS version 21.0.

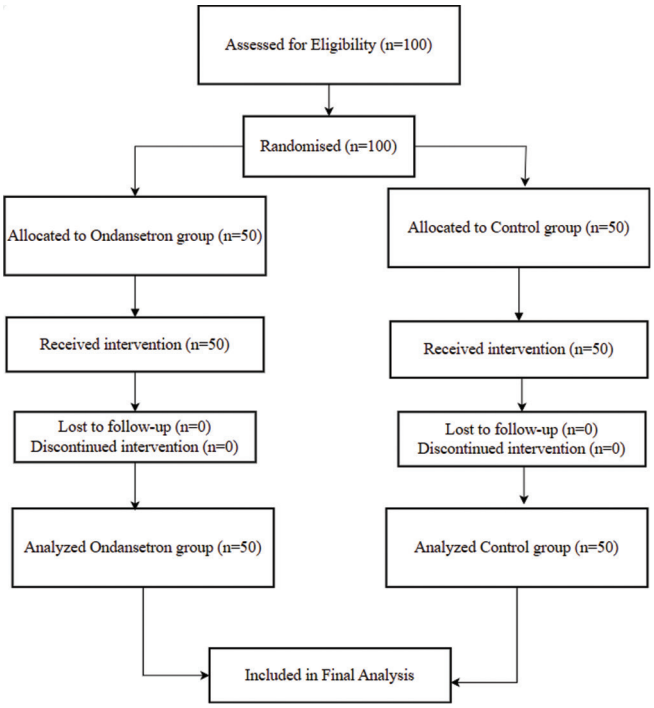

Figure 1: CONSORT flow diagram

RESULTS

The ondansetron group patients had a mean age of 49.23±8.14 years, and the control group had a mean age of 47.81±7.75 years. The mean weight for the ondansetron group was 69.14±7.65 kg, and the control group was 68.29±6.99 kg. The gender ratio in the ondansetron group consisted of 29 males (58%) and 21 females (42%), while the control group consisted of 30 males (60%) and 20 females (40%) (Table 1).

For HR, the baseline values were similar between the ondansetron group (85.14±8.62 bpm) and control group (84.36±9.15 bpm) (P=0.662). At 0 min, HR was 80.06±7.48 bpm in the ondansetron group and 78.93±7.35 bpm in the control group (P=0.447). HR remained comparable between the groups at 5 min (P=0.167), 10 min (P=0.284), and 20 min (P=0.566). However, at 15 min, the HR in the Ondansetron group was significantly higher (81.01±8.86 bpm) than that in the control group (77.45±7.79 bpm) (P=0.035). A significant difference was also observed at 30 min, where HR was 81.83±7.68 bpm in the ondansetron group versus 77.18±7.55 bpm in the control group (P=0.002).

For mean arterial pressure (MAP), the baseline values were comparable between the ondansetron (97.12±7.38 mmHg) and control groups (96.39±8.19 mmHg) (P=0.64). At 0 min, the MAP in the ondansetron group was 95.44±8.75 mmHg, while that in the control group was 93.35±8.92 mmHg (P=0.239). The ondansetron group consistently exhibited higher MAP values than the control group, with significant differences observed at 10 min (P=0.026), 15 min (P=0.035), 20 min (P=0.006), and 30 min (P=0.004). At 30 min, MAP in the ondansetron group was 92.32±7.07 mmHg, whereas in the control group, it was 87.9±8.05 mmHg (Table 2).

The incidence of spinal hypotension was significantly lower in the ondansetron group (7 patients, 14%) than in the control group (22 patients, 44%) (P=0.001). Similarly, the use of ephedrine was required in seven patients (14%) in the ondansetron group versus 22 patients (44%) in the control group (P=0.001), indicating a significantly lower need for vasopressor support in the ondansetron group.

The incidence of bradycardia was low in both groups, occurring in 1 (2%) and 2 (4%) patients in the ondansetron

Table 1: Demographic characteristics

Characteristics	Ondansetron n (%)	Control/n (%)
Age (Mean±SD)	49.23±8.14	47.81±7.75
Weight (Mean±SD)	69.14±7.65	68.29±6.99
Gender		
Male	29 (58)	30 (60)
Female	21 (42)	20 (40)

Table 2: Mean HR and MAP at different time intervals

Parameters	Ondansetron	Control	P-value
HR			
Baseline	85.14±8.62	84.36±9.15	0.662
0 min	80.06±7.48	78.93±7.35	0.447
5 min	80.43±7.47	78.45±6.75	0.167
10 min	81.71±8.77	79.92±7.83	0.284
15 min	81.01±8.86	77.45±7.79	0.035
20 min	80.81±8.99	79.78±8.92	0.566
30 min	81.83±7.68	77.18±7.55	0.002
MAP			
Baseline	97.12±7.38	96.39±8.19	0.64
0 min	95.44±8.75	93.35±8.92	0.239
5 min	95.14±8.5	92.04±8.56	0.0723
10 min	94.01±8.4	90.22±8.37	0.026
15 min	94.85±8.29	91.32±8.22	0.035
20 min	92.71±8.12	88.17±8.13	0.006
30 min	92.32±7.07	87.9±8.05	0.004

HR: Heart rate, MAP: Mean arterial pressure

Table 3: Incidence of spinal hypotension, bradycardia, and use of vasopressors and atropine

Category	Ondansetron n (%)	Control n (%)	P-value
Spinal hypotension	7 (14)	22 (44)	0.001
Inj ephedrine	7 (14)	22 (44)	0.001
Bradycardia	1 (2)	2 (4)	0.559
Inj Atropine	1 (2)	2 (4)	0.559

and control groups, respectively (P=0.559). Similarly, the use of atropine for bradycardia was required in 1 patient (2%) in the ondansetron group and 2 patients (4%) in the control group (P=0.559), which was also not significant (Table 3).

DISCUSSION

Our results show that prophylactic ondansetron decreased significantly the frequency of spinal hypotension and the requirement for vasopressor support, while its impact on bradycardia continued to be non-significant. The main outcome was the frequency of hypotension in the first 30 min following SAB. The findings showed that the frequency of spinal hypotension was 14% among patients who received ondansetron compared to 44% among control patients (P=0.001). In addition, the requirement for vasopressor (ephedrine) use was also notably less in the ondansetron group (14% vs. 44%, P=0.001). These findings align with the study by Mendonça et al., (2021), which demonstrated a reduction in spinal hypotension from 50% to 27.8% following ondansetron administration before spinal anesthesia.[11] Similarly, a meta-analysis by Gao et al., (2015) reported that ondansetron administration significantly reduced the risk of SAB-induced hypotension in non-obstetric surgeries (risk ratio [RR]: 0.16, 95% confidence interval [CI]: 0.05–0.51).[7]

The secondary results of our study were the occurrence of bradycardia and atropine requirement. Bradycardia was observed in 2% of ondansetron patients compared with 4% of controls (P=0.559), and atropine infusion was administered to 2% and 4% of patients (P=0.559), respectively. These results suggest that while ondansetron may have a stabilizing effect on HR, the difference in bradycardia rates was not significant. A systematic review by Tubog et al., (2017) identified that administration of ondansetron decreased the risk of bradycardia caused by spinal anesthesia (RR: 0.31, 95% CI: 0.19–0.50),[13] which is contrary to our result where the decrease in incidence of bradycardia was not significant.

Our results further indicated that MAP values remained significantly higher in the ondansetron group than those in the control group at 10 min (P=0.026), 15 min (P=0.035), 20 min (P=0.006), and 30 min (P=0.004) post-SAB. These observations concur with Raghu et al., (2018), who reported that ondansetron administration had a significantly lower rate of hypotension induced by spinal anaesthesia. In their randomized, double-blind trial on 110 elderly patients (aged 50–70 years), hypotension occurred in 39.3% of the ondansetron group (22 patients) compared to 60.7% in the control group (34 patients) (P=0.0359). In addition, ephedrine requirements were lower in the ondansetron group (mean 3.45±1.09 mg) compared to the control group (4.61±1.80 mg, P=0.0107), further corroborating our study's findings that ondansetron reduces the need for vasopressors.[14]

Similarly, a double-blind, randomized, placebo-controlled trial by Nath et al., (2022) on 50 patients found that MAP values were significantly higher in the ondansetron group at 5-, 10-, 15-, and 30-min post-SAB (P<0.05) than those in the placebo group, and the incidence of shivering was lower (4% vs. 28%, P=0.04).[10] These findings align with our study, reinforcing the role of ondansetron in mitigating post-spinal hypotension and reducing vasopressor requirements.

A major strength of our study is its RCT design, which minimizes selection bias and improves the reliability of our findings. The sample size of 100 patients (50/group) was adequately powered to detect differences in the primary outcomes. In addition, the use of standardized spinal anesthesia protocols and objective hemodynamic measurements enhanced the validity of the study. Nevertheless, our study had some limitations, such as the fact that it was performed in a single-center setting, which might restrict the generalisability of our findings to other populations. Although the reduction in hypotension was significant, the impact on bradycardia was not, likely due to the low occurrence of bradycardia events, which require a larger sample size to identify significant differences. We did not evaluate the long-term outcomes of ondansetron administration beyond the immediate post-operative period.

Our study's overall conclusions are consistent with earlier meta-analyses and clinical trials indicating that ondansetron significantly decreases the occurrence of hypotension from spinal anesthesia as well as vasopressor requirements.[7,11] In addition, our findings suggest that the benefits of ondansetron extend beyond its primary antiemetic properties to hemodynamic stabilization, likely through the inhibition of the BJR, as supported by previous studies.[14]

Despite the growing body of evidence supporting ondansetron's role in preventing SAB-induced hypotension, some studies, particularly those conducted in obstetric populations, have reported no significant effect on blood pressure stabilisation.[5] These discrepancies can be explained by variations in study design, patient groups, and dosages of ondansetron used. In addition, a comparative study between ondansetron and ramosetron found that ramosetron had a more profound effect on stabilizing blood pressure than ondansetron.[15,16]

Future research should focus on multicenter trials with larger sample sizes to confirm the hemodynamic

benefits of ondansetron. Further studies are needed to compare different serotonin receptor antagonists, such as ramosetron and granisetron, in preventing SAB-induced hypotension. Additionally, the dose-response relationship of ondansetron in different patient populations (e.g., elderly, hypertensive, and diabetic) should be investigated.

Limitations of the study

The follow-up period was only 30 minutes post-SAB, preventing long-term assessment. A fixed ondansetron dose was used without evaluating dose-response relationships. Potential confounders, including fluid management and autonomic variations, may have influenced results, requiring further multicenter trials for validation.

CONCLUSION

Our study showed that the prophylactic use of ondansetron markedly decreased the occurrence of hypotension caused by the SAB. Moreover, it highlights that ondansetron not only lowers the need for ephedrine during infraumbilical surgical procedures but may also help mitigate the side effects associated with spinal anesthesia. These findings support the use of ondansetron as a hemodynamic stabilizer in SABs. Further research should focus on optimizing dosing strategies and evaluating long-term benefits in various surgical populations.

ACKNOWLEDGMENT

None.

REFERENCES

1. Ali MA, Hala S, El-Ghaffar AB, Ibrahim NM, Attia AM and Atallah PS. Safety and analgesic efficacy of spinal versus caudal block in pediatric infra-umbilical surgery. Med J Cairo Univ. 2019;87:2277-2283.
   https://doi.org/10.21608/mjcu.2019.54393
2. Critchley LA. Hypotension, subarachnoid block and the elderly patient. Anaesthesia. 1996;51(12):1139-1143.
   https://doi.org/10.1111/j.1365-2044.1996.tb15051.x
3. Ibrahim AS, Hussien RM and Ahmed HM. Intravenous ondansetron for attenuation of post spinal anesthesia hypotension. QJM. 2021;114 Supp 1:i15-6.
   https://doi.org/10.1093/qjmed/hcab086.035
4. Bhardwaj N, Jain K, Arora S and Bharti N. A comparison of three vasopressors for tight control of maternal blood pressure during Cesarean section under spinal anesthesia: Effect on maternal and fetal outcome. J Anaesthesiol Clin Pharmacol. 2013;29(1):26-31.
   https://doi.org/10.4103/0970-9185.105789
5. Mohamed S, Befkadu A, Mohammed A, Neme D, Ahmed S, Yimer Y, et al. Effectiveness of prophylactic ondansetron in preventing spinal anesthesia-induced hypotension and bradycardia in pregnant mother undergoing elective cesarean delivery: A double blinded randomized control trial, 2021. Int J Surg Open. 2021;35:100401.
   https://doi.org/10.1016/j.ijso.2021.100401
6. Šklebar I, Bujas T and Habek D. Spinal anaesthesia-induced hypotension in obstetrics: Prevention and therapy. Acta Clin Croat. 2019;58(Suppl 1):90-95.
   https://doi.org/10.20471/acc.2019.58.s1.13
7. Gao L, Zheng G, Han J, Wang Y and Zheng J. Effects of prophylactic ondansetron on spinal anesthesia-induced hypotension: A meta-analysis. Int J Obstet Anesth. 2015;24(4):335-343.
   https://doi.org/10.1016/j.ijoa.2015.08.012
8. Yun Sin LL. Management for Spinal-Induced Hypotension in Elective Cesarean Section; 2017. Available from: https://core.ac.uk/download/pdf/235084093.pdf [Last accessed on 2025 Jan 24].
9. Golparvar M, Saghaei M, Saadati MA and Farsaei S. Effect of ondansetron on prevention of post-induction hypotension in elderly patients undergoing general anesthesia: A randomized, double-blind placebo-controlled clinical trial. Saudi J Anaesth. 2015;9(4):365-369.
   https://doi.org/10.4103/1658-354X.159455
10. Nath S, Aggarwal N, Saha A and Srivatsava A. Prophylactic efficacy of intravenous ondansetron in prevention of spinal anaesthesia induced hypotension. Int J Health Sci. 2022;6(S8):3142-3153.
    https://doi.org/10.53730/ijhs.v6ns8.12807
11. Mendonça FT, Junior LC, Gersanti RC and Araújo KC. Effect of ondansetron on spinal anesthesia-induced hypotension in non-obstetric surgeries: A randomized, double-blind and placebo-controlled trial. Braz J Anestesiol. 2021;71(3):233-240.
    https://doi.org/10.1016/j.bjane.2020.12.028
12. Mohamed SA, Hussam AM, Abdallah SA, Sarhan KA and Shaban AM. Ondansetron is an effective alternative to decrease the incidence of postspinal hypotension in healthy subjects undergoing infra-umbilical surgeries compared to combined volume loading and vasoconstrictors: Randomized controlled trial. Open Access Maced J Med Sci. 2018;6(12):2363-2368.
    https://doi.org/10.3889/oamjms.2018.491
13. Tubog TD, Kane TD and Pugh MA. Effects of ondansetron on attenuating spinal anesthesia-induced hypotension and bradycardia in obstetric and nonobstetric subjects: A systematic review and meta-analysis. AANA J. 2017;85(2):113-122.
14. Raghu RK, Kumar S, Rajaram G, Nikhil N and Damodar P. Effect of ondansetron in the prevention of spinal anesthesia-induced hypotension. J Sci Soc. 2018;45(3):125.
    https://doi.org/10.4103/jss.JSS-45-18
15. Shin HJ, Choi ES, Lee GW and Do SH. Effects of preoperative serotonin-receptor-antagonist administration in spinal anesthesia-induced hypotension: A randomized, double-blind comparison study of ramosetron and ondansetron. Reg Anesth Pain Med. 2015;40(5):583-588.
    https://doi.org/10.1097/01.AOA.0000489464.84285.72
16. Gao C, Li B, Xu L, Lv F, Cao G, Wang H, et al. Efficacy and safety of ramosetron versus ondansetron for postoperative nausea and vomiting after general anesthesia: A meta-analysis of randomized clinical trials. Drug Des Devel Ther. 2015;9:2343-2350.
    https://doi.org/10.2147/DDDT.S80407

Authors' Contributions:
RS- Has conceptualized the study and played primary role in compiling, analysis, and interpretation of data. All the drafts were prepared, reviewed, and final draft was approved by; **NC-** Has contributed in data collection, data entry, data analysis and literature review; **GPSC-** Has contributed in fine tuning, reviewed the results and reviewed the manuscript; All the authors have read and approved the final version of the manuscript. All the authors take complete responsibility for the content of the manuscript.

Work attributed to:
Department of Anaesthesia, Velammal Medical College Hospital and Research Institute, Madurai, Tamil Nadu, India.

Orcid ID:
Dr. Renganathan S- https://orcid.org/0000-0002-2578-8645
Dr. Navin C- https://orcid.org/0009-0005-2603-801X
Dr. Ganesh Prabhu SC- https://orcid.org/0009-0001-1222-9713

Source of Support: Nil, **Conflicts of Interest:** None declared.