Comparison of Efficacy of Sub Hypnotic Dose of Propofol and Ondansetron in Attenuating Intrathecal Morphine Induced Nausea and Vomiting in Parturients Under Going Elective Caesarean Section: A Prospective Randomised Double Blinded Study

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ABSTRACT:

Introduction: Intrathecal morphine is widely used for postoperative analgesia in caesarean sections but is frequently associated with postoperative nausea and vomiting (PONV). While ondansetron is a routine prophylaxis, sub-hypnotic doses of propofol have also demonstrated antiemetic properties. This study compared the efficacy of sub-hypnotic dose propofol with ondansetron in preventing intrathecal morphine-induced PONV.

Methods: This prospective, randomized, double-blind study involved 180 ASA Class II parturients aged 18–45 years undergoing elective caesarean section under spinal anaesthesia. Patients were randomly allocated into two groups (Group P and Group O) (n=90) where the Group P received 0.5 mg/kg IV propofol and Group O received 0.1 mg/kg IV ondansetron, administered 15 minutes before the end of surgery. All patients received 10 mg of 0.5% hyperbaric bupivacaine with 0.1 mg intrathecal morphine. The statistical analysis used SPSS version 26.0, with a p-value <0.05 considered statistically significant.

Results: The incidence and severity of PONV were significantly lower in the propofol group compared to the ondansetron group ($p < 0.05$). Specifically, 85.6% of patients in Group P remained symptom-free compared to 65.6% in Group O. Hemodynamic parameters, including the incidence of hypotension (20.0% vs. 22.2%) and bradycardia (7.8% vs. 10.0%), remained comparable between groups ($p > 0.05$). Pruritus incidence and severity were also similar between the two groups.

Conclusion: Sub hypnotic-dose propofol is more effective than ondansetron in reducing the incidence and severity of PONV in parturients receiving intrathecal morphine without compromising hemodynamic stability.

Keywords: caesarean section, Intrathecal morphine, Propofol, Ondansetron, Postoperative nausea and vomiting, pruritus, Spinal anaesthesia

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INTRODUCTION

Postoperative nausea and vomiting (PONV) remain a highly distressing complication in perioperative practice, particularly for patients undergoing caesarean section under neuraxial anaesthesia [1]. Despite clinical advancements, the incidence in obstetric populations ranges from 30% to 80% [2]. The parturients are highly predisposed due to pregnancy-specific physiological changes, including elevated progesterone levels, delayed gastric emptying, and increased intra-abdominal pressure [3].

While spinal anaesthesia with intrathecal morphine represents the gold standard for postoperative analgesia, it frequently triggers side effects like nausea, vomiting, and pruritus via μ-opioid receptor stimulation in the chemoreceptor trigger zone [4]. propofol at sub hypnotic doses offers the advantage

of minimal cognitive impairment. The mitigation of complications is essential to maintain high standards of perioperative care and prevent disruptions to early maternal-infant bonding and successful breastfeeding initiation [5].

Propofol, an intravenous anaesthetic agent widely used for induction and maintenance of anaesthesia, has also been recognized for its significant antiemetic properties, even at sub hypnotic doses. The dual effect of propofol in preventing both nausea and pruritus highlights its potential as an effective agent in managing intrathecal morphine-induced side effects [6]. The use of readily available drugs such as propofol and ondansetron offers a practical and economical approach in high-volume tertiary care centres. In resource-limited settings, such strategies are particularly valuable in ensuring optimal patient care [7,8]. However, despite these promising findings, the role of propofol in comparison to established agents such as ondansetron has not been fully established and warrants further investigation [9].

Identifying highly effective regimens is essential to optimize maternal comfort and enhance clinical recovery pathways in high-volume obstetric settings. This study was done to compare the efficacy of sub hypnotic dose of propofol and Ondansetron in prevention of post operative nausea and vomiting in parturient undergoing elective caesarean section with intrathecal morphine as adjuvant in spinal anaesthesia and to determine the benefit of use of propofol and ondansetron in prevention of pruritus caused by intrathecal morphine.

MATERIALS AND METHODS

This was a prospective, randomised, double-blinded study was conducted at JSS Hospital, Mysuru within the study setting of operation theatre under Department of Obstetrics and Gynaecology from March 2024 to February 2026. The study population consisted of 180 parturients aged 18–45 years, with a gestational age of 37–42 weeks, belonging to ASA physical class II, and scheduled for elective caesarean section. Any patient with known allergies to propofol, eggs, or metoclopramide, as well as those with comorbidities like gestational diabetes or pregnancy-induced hypertension, were excluded.

The sample size for this study was estimated to ensure sufficient statistical power to compare the efficacy of sub hypnotic-dose propofol and ondansetron. The baseline variance parameters were extracted from the study reported by Kampo et al. (2019). The sample size determination was prospectively calculated using the standard formula for hypothesis testing of two independent means assuming equal variances [10]. The detailed estimation is as follows:

$$\mathbf{n} = \frac{2\times \mathrm{Sp}^2\times (Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2}{\mu^2 d}$$ where

- Sp^2 **(Pooled Variance):** $\frac{{S_1}^2 + {S_2}^2}{2}$
- S_1 **(Standard deviation in group I):** 5.12
- S_2 **(Standard deviation in group II):** 5.28
- μd **(Mean difference between samples):** 2.17
- α **(Significance level / Alpha error):** 5% (two-sided), $1-\beta$ **(Power):** 80%
- d (**Effect size):** 0.4173

The sample size estimated by using formula=90.06. But the final required sample size was determined to be **90 participants per group (n)**, resulting in a total study population of **180 parturients (N).**

The study was commenced only after obtaining the institutional ethical clearance. The written informed consent was taken either in English and Kannada version for each participant with participant information sheet. The participants were randomly assigned into two groups of 90 each—Group P (Propofol) and Group O (Ondansetron)—using Sequentially Numbered Opaque Sealed Envelopes **(SNOSE)**. Before performing the surgery, a comprehensive pre-anaesthetic evaluation was performed, and baseline hemodynamic parameters were recorded.

In the operating theatre, spinal anaesthesia was administered in the sitting position at the L2–L3 or L3–L4 intervertebral space using a 25G or 27G Quincke needle. All patients received a subarachnoid injection of 0.5% hyperbaric bupivacaine (7.5–10 mg) combined with 0.1 mg of intrathecal morphine. Following the injection, patients were placed in a supine position with a 10 cm wedge under the right buttock to prevent aortocaval compression.

The primary intervention occurred 15 minutes before the end of surgery: Group P received 0.5 mg/kg IV propofol and Group O received 0.1 mg/kg IV ondansetron, both administered slowly.

The intraoperative monitoring included heart rate (HR), systolic and diastolic blood pressure, mean arterial pressure (MAP), and oxygen saturation, recorded every minute for the first five minutes and every five minutes thereafter. Intraoperative adverse events were managed using standardized clinical protocols. The episodes of hypotension (SBP decline >20% baseline) required standard rescue therapy with IV mephentermine. Similarly, instances of bradycardia (HR <60 bpm) were resolved using IV atropine.

All postoperative patients were monitored for 24 hours. The postoperative nausea and vomiting (PONV) were identified by direct scheduled assessments or by a spontaneous complaint by the patients after the surgery. The patient was assessed hourly for the first 4 hours and then every 4 hours using a 3-point ordinal scale (0=none, 1=nausea, 2=vomiting), pruritus was evaluated every 4 hours using a 4-point scale (0=none to 3=severe). The rescue treatment for PONV was 10 mg IV

metoclopramide, and for pruritus, 10 mg oral cetirizine.

The statistical analysis was performed using SPSS version 26.0. The baseline demographic and anthropometric data, ASA physical status, PONV severity score and severity of pruritic were descriptively presented in tables and the continuous variables were analysed using independent sample t-tests and repeated measures ANOVA, while ordinal variables like PONV and pruritus scores were analyzed using the Mann–Whitney U test. A p-value of <0.05 was considered statistically significant.

RESULTS

The baseline measurements of participant characteristics in the study were comparable between the Group P (Propofol) and Group O (Ondansetron). The mean age was 27.84±3.72 years in the Propofol group and 28.11±3.96 years in the Ondansetron group (p=0.637). Similarly, no significant differences were observed in mean weight (68.42±7.81 kg vs. 69.07±8.24 kg; p=0.586), mean height (158.74±5.29 cm vs. 159.12±5.63 cm; p=0.642), mean BMI (27.13±2.96 kg/m² vs. 27.29±3.11 kg/m²; p=0.719), and mean gestational age (38.61±0.82 weeks vs. 38.55±0.87 weeks; p=0.631) [Table 1]. The distribution of ASA physical status was identical in both study groups. All 90 parturients (100%) in the Group P and all 90 parturients (100%) in the Group O were classified as ASA Grade II.

Table 1: Baseline measurements of patient characteristics (N= 180)

Baseline patient characteristics (Mean ± SD)	**Group P (n=90)**	**Group O (n=90)**	**P-value ***
Age (years)	27.84 ± 3.72	28.11 ± 3.96	0.637
Weight (kg)	68.42 ± 7.81	69.07 ± 8.24	0.586
Height (cm)	158.74 ± 5.29	159.12 ± 5.63	0.642
BMI (kg/m²)	27.13 ± 2.96	27.29 ± 3.11	0.719
Gestational Age (weeks)	38.61 ± 0.82	38.55 ± 0.87	0.631

**Independent sample t-test*

The severity of postoperative nausea and vomiting (PONV) differed significantly between Group P (Propofol) and Group O (Ondansetron). A substantially higher proportion of patients in the Group P experienced no PONV symptoms, with 77 patients (85.6%) reporting a score of 0 compared to 59 patients (65.6%) in Group O. Nausea alone was observed in 8.9% of patients receiving propofol and 15.6% receiving ondansetron, while vomiting occurred in 5.6% and 18.9% of patients, respectively. The difference in PONV severity distribution was statistically significant (p=0.003), indicating that subhypnotic-dose propofol was more effective than ondansetron in reducing the incidence and severity of intrathecal morphine-induced postoperative nausea and vomiting [Table 2].

Table 2: Post operative nausea and vomiting (PONV) scores between Propofol and Ondansetron groups (N=180)

PONV Score	**Group P (n=90)**	**Group O (n=90)**	**P-value ***
0 (None)	77 (85.6)	59 (65.6)	0.003
1 (Nausea)	8 (8.9)	14 (15.6)	
2 (Vomiting)	5 (5.6)	17 (18.9)	

The severity of pruritus was comparable between Group P (Propofol) and Group O (Ondansetron), with no statistically significant difference observed (p=0.962). Most participants in both groups did not experience pruritus, accounting for 73.3% of patients in Group P and 71.1% in Group O. Mild pruritus was reported in 15.6% and 16.7% of patients, while moderate pruritus occurred in 8.9% and 10.0% of patients in the respective groups. Severe pruritus was uncommon and occurred in only 2.2% of patients in each group [Table 3].

Table 3: Severity of pruritis between Propofol and Ondansetron groups (N=180)

Severity of pruritis	**Group P (n=90)**	**Group O (n=90)**	**P-value ***
None	66 (73.3)	64 (71.1)	0.962
Mild	14 (15.6)	15 (16.7)	
Moderate	8 (8.9)	9 (10.0)	
Severe	2 (2.2)	2 (2.2)	

The time-wise analysis of postoperative nausea and vomiting (PONV) during the first 24 hours demonstrated a lower incidence in Group P (Propofol) compared to Group O (Ondansetron) across all observation periods. During the first 0–4 hours, PONV occurred in 8.9% of patients receiving propofol compared with 20.0% receiving ondansetron, showing a statistically significant difference (p=0.034). Although lower incidences were also observed in the Group P during 4–8 hours (4.4% vs. 11.1%), 8–12 hours (1.1% vs. 5.6%), and 12–24 hours (0.0% vs. 3.3%), these differences did not reach statistical significance (p>0.05) [Table 4].

Table 4: Time-wise incidence of PONV in patients during initial 24 hours (N=180)

Time Interval	**Group P (n=90)**	**Group O (n=90)**	**P-value ***
0–4 hrs	8 (8.9)	18 (20.0)	0.034
4–8 hrs	4 (4.4)	10 (11.1)	0.095
8–12 hrs	1 (1.1)	5 (5.6)	0.099
12–24 hrs	0 (0.0)	3 (3.3)	0.080

The incidence of pruritus during the first 24 postoperative hours was similar in both Group P (Propofol) and Group O (Ondansetron) at all assessed time intervals. During the 0–4 hours period, pruritus occurred in 8.9% of patients in the Propofol group and 10.0% in Group O (p=0.798). Comparable findings were observed during 4–8 hours (11.1% vs. 12.2%; p=0.818), 8–12 hours (4.4% vs. 4.4%; p=1.000), and 12–24 hours (2.2% vs. 2.2%; p=1.000). No statistically significant differences were noted at any time point [Table 5].

Table 5: Time-wise incidence of pruritis in patients during initial 24 hours (N=180)

Time Interval	Group P (n=90)	Group O (n=90)	P-value *
0–4 hrs	8 (8.9)	9 (10.0)	0.798
4–8 hrs	10 (11.1)	11 (12.2)	0.818
8–12 hrs	4 (4.4)	4 (4.4)	1.000
12–24 hrs	2 (2.2)	2 (2.2)	1.000

DISCUSSION

The present study demonstrates that a sub-hypnotic dose of propofol (0.5 mg/kg) is significantly more effective than ondansetron (0.1 mg/kg) in reducing the incidence and severity of intrathecal morphine-induced postoperative nausea and vomiting (PONV) among parturients [1]. Specifically, 85.6% of Group P remained entirely symptom-free compared to only 65.6% in Group O (p=0.003), with superior efficacy peaking during the first four postoperative hours [2,3]. This clinical advantage likely stems from propofol's multifactorial mechanism involving GABA-A modulation and serotonin reduction in the area postrema, contrasting with the selective 5-HT3 receptor blockade of ondansetron [1, 11].

Importantly, these antiemetic benefits were achieved without compromising hemodynamic stability, as heart rate and mean arterial pressure trends remained comparable between the groups [6, 12]. Conversely, both interventions demonstrated identical, limited efficacy against central μ-opioid receptor-mediated pruritus (p=0.962) [4,5]. This lack of antipruritic efficacy aligns with and Hajian et al. (2016)[13] and Suppapitnarm et al. (2017)[14], who both reported that ondansetron fails to mitigate opioid-induced itch [15, 16] .

Furthermore, the study's findings regarding propofol's high success rate mirror Kampo et al. (2019)[10], who observed a remarkably low PONV incidence of 8.7%, and Mowafy et al. (2020)[17], who noted propofol's numerical superiority over ondansetron. In contrast, the high failure rates of single-agent ondansetron are corroborated by Yin et al. (2017) [15], reporting a 73.3% nausea rate, and Levin et al. (2019) [16], observing a 23.3% nausea rate. These external benchmarks closely match the 20% symptomatic rate observed in this study's ondansetron group [9,18,19]. Additionally, Campos et al. (2019)[20] reported an overall 52.9% PONV rate for ondansetron, highlighting the limitations of selective 5-HT3 antagonists [21,22]. Finally, Wendling et al. (2025) [23] demonstrated that adding promethazine to ondansetron provides no additional benefit, reinforcing the conclusion that standard prophylactic regimens often leave a substantial proportion of obstetric patients symptomatic and vulnerable to inadequate emetic control [24,25].

CONCLUSION

The sub hypnotic-dose of propofol is significantly more effective than ondansetron in attenuating the incidence and severity of postoperative nausea and vomiting in parturients undergoing caesarean sections. The study reveals that propofol group remained entirely symptom-free than the ondansetron group, with superior efficacy peaking during the immediate critical postoperative hours. Both agents provide comparable protection against pruritus induced by intrathecal morphine, with no significant difference observed in their preventive efficacy. Additionally, propofol demonstrates excellent hemodynamic safety by maintaining stable maternal heart rate and blood pressure levels throughout the perioperative period. Consequently, low-dose propofol serves as a safe and superior alternative for enhancing maternal comfort and overall recovery

Limitations: The study was limited to a single centre and healthy (ASA II) term parturients, hence the findings might not be directly applicable to high-risk pregnancies or emergency caesarean deliveries. The delayed adverse effects occurring beyond 24 hours were not evaluated. There were certain qualitative factors not assessed such as maternal satisfaction, breastfeeding success, or neonatal effects, which are essential for a complete understanding of the clinical impact of the interventions.

Recommendations: The clinicians should incorporate sub hypnotic-dose propofol into perioperative antiemetic protocols for high-risk patients. The future researchers should evaluate diverse dosing regimens, combination therapies, and long-term qualitative outcomes, including breastfeeding success and maternal satisfaction, to optimize patient-centered recovery following caesarean sections under spinal anaesthesia. The hospitals and anaesthesia departments may develop standardized protocols that integrate effective antiemetic prophylaxis with multimodal postoperative care pathways.

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CONFLICT OF INTEREST: Nil