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Propofol as an antiemetic for managing post-operative nausea and vomiting in parturient undergoing cesarean section under spinal anesthesia: A randomized control trial with implications for oncology

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ABSTRACT

Many women who undergo caesarean section suffer from nausea and vomiting symptoms during and after surgeries. This study aims to assess the ability of propofol to reduce the severity of nausea and vomiting symptoms after Caesarean Section (CS). Randomized clinical trial was conducted on ninety parturients from January to December 2022 at the obstetric unit (single-center) of AL–Shafaa private Hospital Diyala, Iraq. Two equal groups were compared; the first group received continuous 1% propofol infusion (10 mg/mL) and the second group received placebo (0.9% saline). Results showed statistically significant difference between the control group (saline) and the antiemetic medication (propofol) in post-cesarean nausea (relative risk 0.514; 95% CI 17.3%–39.6%; p=0.003) and vomiting incidence (relative risk 0.695; 95% CI, 4.39%–22.5%; p=0.014), respectively. Moreover, the request for ondansetron was lower in propofol group (four patients) than the placebo group (ten patients) with a relative risk of 0.437; 95% CI, 3.52%–21.57%; p=0.074. Findings of this study support the previous studies about the effectiveness of propofol as antiemetic to lower the incidence of post-operative nausea and vomiting.

Keywords: cancer, clinical, colorectal, expression, pathological, TIGD3

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INTRODUCTION

During SC procedure, many women Experience Intraoperative Nausea and Vomiting (IONV) while undergoing spinal anesthesia. Studies have reported that the incidence of IONV during CS ranges from 35% to 60% [1, 2]. These complications can lead to various issues such as patient discomfort, interference with surgery, increased procedure time, risk of bleeding, inadvertent surgical trauma, and the risk of pulmonary aspiration of gastric contents [3]. Furthermore, IONV can cause dehydration, electrolyte imbalances, and other complications that can significantly prolong the patient's recovery time [3]. To effectively manage IONV during cesarean section, healthcare providers can employ both prophylactic and therapeutic measures. Prophylactic measures may include preoperative fasting, the administration of antiemetics, and proper positioning of the patient. Therapeutic measures may involve the administration of rescue antiemetics as necessary. The choice of prophylactic and therapeutic measures should be personalized and based on various factors, including the patient's medical history, risk factors for IONV, and potential anesthesia response [4].

Numerous studies have examined both medication and non-medication therapies for preventing and treating IONV during cesarean section [4-6]. Antiemetics such as ondansetron, and metoclopramide are commonly used for PONV prevention but have also been studied for their efficacy in preventing and treating IONV during cesarean section. Ginger, acupressure, and acupuncture are non-medication therapies that have also been investigated for their effectiveness in reducing IONV [7]. However, some of these medications were not originally intended for use in pregnant women, and their safety during pregnancy has not been fully established. Additionally, some medications may not be appropriate for all women depending on their medical history and other factors. Hence, there is a need for more research into the safety and efficacy of various

treatments for IONV during cesarean section, as well as the development of more targeted and personalized prophylaxis and treatment options [4, 5, 8]. This could involve the development of new medications specifically for use in pregnant women or the investigation of alternative non-medication therapies. Propofol, an intravenous anesthetic agent with inherent antiemetic properties, is widely used in clinical practice. Several studies have demonstrated that a bolus dose or continuous infusion of propofol can effectively reduce the incidence of both PONV and IONV [9, 10]. In recent years, low-dose propofol infusion (1.0 mg/kg/h) has been investigated as a prophylactic measure for IONV during and after cesarean section, with promising results reported in several clinical trials [11, 12]. However, further research is needed to confirm the safety and efficacy of low-dose propofol infusion for the prevention of IONV, including identification of the optimal dosing regimen and patient selection criteria. Additionally, it is crucial to consider potential side effects and drug interactions when using propofol, as with any medication. Notably, there is few information about the treatment of immediate nausea and vomiting in parturient undergoing CS [13]. Our hypothesis aimed to fill this research gap by suggesting that a safe and effective approach to reduce the incidence of IONV in this population could be achieved through a continuous infusion of propofol, along with bolus doses for immediate control, when compared to a placebo.

METHODS

Study design

Randomized control trial was conducted from January to December 2022 at the obstetric unit (single-center) of AL–Shafaa private Hospital Diyala, Iraq. The ethical committee of the hospital granted approval for the protocol (ID No: SHPH19/12/DEC/2021). The clinical trial adheres to the CONSORT guidelines. Before participating in the study, each parturient received detailed explanation about the study's objectives and provided written informed consent.

Inclusion and exclusion criteria

Pregnant women with gestational age (≥ 36 weeks), aged 19 to 41 years old, scheduled for elective CS under spinal anesthesia and classified as ASA-PS score 1-2 and were willing to participate were included. While women who did not sign the consent, those with a history of nausea and vomiting before pregnancy, drug allergies, co-morbidities, motion sickness, abdominal surgery, or significant blood loss during surgery were excluded.

Sample size

Sample Size=(Z ‾ score) 2 × Standard Deviation × (1-Standard Deviation)/ (margin of error) 2. Considering the 80% confidence interval (Z-score =1.96), Standard Deviation is 0.5 and margin of error = ± 6 or 7%. The final sample size was adjusted between 84 and 114 participants.

Randomization

In this study, the participants were randomly assigned to one of two groups: the propofol group or the control group. The randomization process used a “computer-generated random number table” to ensure that each participant had an equal chance of being assigned to either group. The allocation was “concealed in sealed opaque envelopes” to prevent any potential bias or influence on the assignment of participants. The propofol group received infusion of 1% propofol (10 mg/mL), while the control group received intravenous saline (0.9%). Equal volumes were drawn in a 20-mL syringe and have been administered about 10 minutes-15 minutes before the end of surgery or just after delivery of baby.

Procedures to induce anesthesia and drug application

Prior to surgery, emphasizing that nausea or vomiting did not occur in the last 72 hours. Participants were advised to keep fasting six to eight hours that preceded the surgery. Basic intraoperative monitoring was applied and the baseline vital signs were checked and recorded. The spinal anesthesia procedure for the cesarean section surgery was performed by an independent anesthesiologist who specialized in obstetric anesthesia. The anesthesiologist administered the spinal anesthesia to the patient while in a sitting position. Prior to the procedure, the anesthesiologist injected 2 ml of preservative-free 2% lidocaine into the skin and interspinous ligaments using a 21G hypodermic needle. A lumbar puncture was then performed using a 26G pencil point spinal needle inserted midline at the lumbar region, specifically at the L2-L3 or L3-L4 interspace. The anesthesiologist continued to monitor the patient until the patient's discharge from the hospital.

During the cesarean section surgery, the anesthesiologist monitored the parturient's vital signs every 5 minutes for the first 30 minutes, and then every fifteen minutes. The patient was given supplemental oxygen through nasal prongs, and any hypotension during the surgery was treated with 5 mg-20 mg of intravenous ephedrine. After the baby was delivered, the patient was given intravenous oxytocin to help with uterine contraction. To determine the effect of the anesthesia, an independent anesthesiologist, who was unaware of which drug was administered, was asked to administer either saline (0.9%) or 1% propofol (10 mg/mL) infusion 10 minutes-15 minutes before the surgery ended.

Measurement

PONV was identified either through “spontaneous complaints by patients or scheduled assessments”. The incidence of PONV

was then reported hourly for the first six hours and then twice hourly for the next twenty-four hours using a 3-point Verbal Rating Score (VRS) giving "zero" for none complaint, "1" for nausea, and "2" for vomiting". Patients experiencing significant nausea, vomiting, or those who requested rescue treatment were given 20 mg of intravenous propofol. After 5 minutes, their symptoms were assessed using the VRS scale, and if there was a decrease of at least 50%, it was considered that the symptoms had subsided. If nausea and vomiting persisted, another 20 mg of propofol was given, and a reevaluation was carried out 5 minutes later. If two doses of propofol, 20 mg each, did not alleviate the nausea and vomiting, the patient was given 4 mg of intravenous ondansetron.

After cesarean section surgery, the intensity of pain was measured using a 100 mm visual analog scale, where 0 mm indicated no pain and 100 mm indicated intolerable pain. If pain relief was needed, the patient received suppository diclofenac 100 mg or injection tramadol 100 mg, or both. Pruritus (itching) was recorded every two hours for 36 hours after surgery on a scale of 0-3 (0 being no pruritus, 3 being severe pruritus). If pruritus occurred or was requested, Cetirizine 10 mg was given. Overall satisfaction with the perioperative experience was assessed on the day of discharge using a scale of 1-4 (1 being poor and 4 being excellent).

Statistical analysis

The data was analyzed using the statistical software SPSS. One-way ANOVA and multiple comparisons by Tukey's test were used to analyze sociodemographic, clinical and other intra and post-operative variables. The student's t-test was used to compare two groups. The mean values were used to represent the data, and results were considered significant if $p<0.05$.

RESULTS

Out of 103 eligible parturient in this study, 13 were excluded from the analysis. The reasons for exclusion were: 7 parturient had a change in delivery method to normal vaginal delivery, 3 parturient had an urgent CS, and 3 parturient had an Estimated Intraoperative Blood Loss (EIBL) more than half Liter. As a result, data from 90 parturient were included in the analysis, with 45 in both the control and propofol groups (Figure 1).

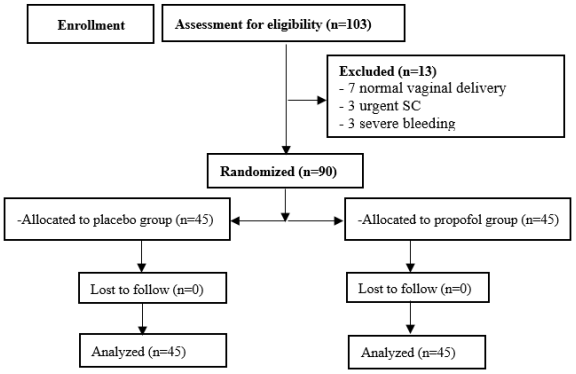

Fig. 1. Flow diagram according to CONSORT statement

The analysis revealed no significant differences among the parturient from the control group, and propofol group with regards to sociodemographic, clinical and intraoperative characteristics (Table 1).

Tab. 1. Sociodemographic and clinical maternal characteristics

Measurement	Placebo group (n=45)	Propofol group (n=45)	p-value
Age (years)	29.02 ± 4.16	30.13 ± 3.75	0.075
Weight (kg)	65.15 ± 8.30	65.22 ± 7.83	0.242
Body mass index (BMI)	28.25 ± 3.45	29.01 ± 4.31	0.321
Gestational age (weeks)	38.5 ± 0.933	38.4 ± 0.756	0.677
Baseline heart rate	88.7 ± 11.3	89.6 ± 10.5	0.456
Baseline systolic blood pressure	124 ± 7.81	125 ± 7.72	0.063
Baseline diastolic blood pressure	80.6 ± 6.44	81.53 ± 6.32	0.082
Duration of surgery (min)	44.3 ± 6.72	45 ± 7.61	0.236
Pre-operation hypotension	29 (64.4)	30 (66.6)	0.523
Post- operative hypotension	13 (28.9)	15(33.3)	0.167
Exteriorization of Uterus	25(55.6)	17(37.8)	0.084
Abdominal irrigation	44(97.8)	43(95.6)	0.936
Total phenylephrine used (mg)	0.787 + 2.12	773 + 1.04	0.786

Data are presented as mean (standard deviation) or n (%)

Table 2, shows that there was a significant distinction between the placebo group and the propofol group with respect to post-delivery nausea (relative risk 0.514; 95% CI 17.3%–39.6%; p=0.003) and vomiting incidence (relative risk 0.695; 95% CI, 4.39%–22.5%; p=0.014). The propofol group had only four patients who required ondansetron compared to the

placebo group which had ten (relative risk 0.437; 95% CI, 3.52%–21.57%; p=0.074) (Table 2). The administration of ondansetron treatment was similar between the two groups during each period after delivery (p>0.05). None of the patients have made a request for supplementary analgesic for pain. Patients and obstetricians in the propofol group reported higher satisfaction levels (Patients: 95% CI−2.07 to −0.3124; p=0.007; obstetricians: 95% CI−1.04 to−2.16; p<0.003).

Tab. 2. Nausea and vomiting among patients in placebo and propofol groups

Measurement	Placebo group (n=45)	Propofol group (n=45)	p-value
Intraoperative nausea*	23 (51.1)	11 (24.4)	0.003
Intraoperative vomiting*	12 (26.7)	5 (11.1)	0.014
Initial treatment for IONV*	16 (35.6)	8 (17.8)	0.025
Relief after initial treatment	13 (28.9)	7 (15.6)	0.063
Additional treatment for IONV	3 (6.67)	2(4.45)	0.323
Ondansetron treatment for IONV	10 (22.2)	4(8.89)	0.074

*Statistically significant

DISCUSSION

Most of cesarean section surgeries, can result in PONV when no antiemetic is given. Multiple of surgical and none-surgical related factors can cause PONV, including stimulation of various body parts during surgery, surgical pain, bleeding, medications, and anesthesia-related causes like hypotension and opioids. Peak block height ≥ T5, use of procaine, baseline heart rate ≥ 60 beats/min are some specific anesthesia-related causes of PONV [1-3].

Previous studies [11–13], have shown that continuous infusion of propofol can effectively prevent nausea and vomiting during CS. Consistent with the findings of Niu et al. [14] and colleagues, our study also demonstrated a significant reduction in the incidence of nausea in the propofol group compared to the placebo group. In addition, our study showed a significant improvement in the desire to vomit in the propofol group, which was not reported in Niu 's study. These results suggest that the use of propofol infusion, in addition to immediate bolus doses, may be a safe and effective prophylactic measure for reducing the incidence of IONV during cesarean section.

In contrast, recent evidence suggests that sub-hypnotic doses of propofol can significantly reduce the occurrence of nausea and vomiting in patients undergoing cesarean delivery with spinal anesthesia [15]. Studies by Kampo et al. [16], and Chatterjee et al. have shown that propofol resulted in a lower incidence of PONV compared to control [17].

Some reasons might enhance the most likely to use the infusion of propofol on sub-hypnotic doses, such as the hesitancy in the use of intrathecal opioids due to the fears of its possible addictive properties and side effects including the pruritus, nausea, and vomiting, as reported by Koju et al. [18, 19].

In addition, some patients experienced injection pain caused by propofol even with using lidocaine. Moreover, lidocaine was found to be ineffective in reducing pain in a significant proportion of patients [20]. In this study, certain variables were kept constant for both study groups such as the type of surgery, anesthesia technique, anesthetic drugs, and the level of the spinal block. Additionally, the duration of anesthesia and surgery were similar, and there was no significant difference in age, weight, and BMI of patients between the two groups. The results indicate that the observed difference in the incidence and severity of Postoperative Nausea and Vomiting (PONV) between the two groups is completely related to the tested drugs. This study has limitations that should be noted. Firstly, we did not assess the occurrence of nausea and vomiting before delivery, although we prevented it by avoiding hypotension. Secondly, we used the same propofol dose for all patients and did not compare different doses.

CONCLUSION

The study revealed that administering a continuous infusion of propofol targeted to a plasma concentration of 1000 ng/mL resulted in a reduced need for a propofol 20 mg bolus and effectively prevented post-delivery nausea and vomiting. The study suggests that combining a continuous infusion of propofol with a 20 mg bolus or with additional antiemetic drugs may be an effective strategy to decrease the incidence of intraoperative nausea and vomiting. However, further research is needed to confirm these findings and identify the optimal dosing regimen and patient selection criteria for propofol use in this setting.

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