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Effect of Using Midazolam and Propofol in Low Doses for Intraoperative Nausea and Vomiting Prevention in Pregnant Women Underwent Cesarean Section under Regional Anesthesia

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Aim: To investigate if and how severe intraoperative nausea and vomiting occur following elective cesarean sections performed under spinal anesthesia using sub-hypnotic dosages of midazolam and propofol.
Study Design: Clinical trial.
Methodology: The current study was conducted at the Gynecology and Obstetrics Department of a Teaching Hospital in Baghdad, Iraq. The study included 90 full-term pregnant women with single viable fetuses who underwent elective C/S by spinal anesthesia and were randomly assigned to

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one of three groups: group A included 30 women who received propofol, group B included 30 women who received midazolam, and Group C included 30 women who received placebo. The Bellville scoring score was used to assess nausea and vomiting. The Richmond Agitation Sedation Score (RASS) was used to assess sedation intraoperatively.

Results: Patients in group C had the highest prevalence of nausea and vomiting (56.7%), which was significantly different from groups A (16.7%, P=0.001) and B (13.3%, P=0.001); however, there was no statistically significant difference between groups A and B (P= 0.717). The group B patients had the highest prevalence of drowsiness (20%), which was substantially different from group C (3.3%, P=0.044), whereas there were no statistically significant differences between groups A and B (P= 0.278) or A and C (P= 0.3).

Conclusion: Low doses of midazolam or propofol administered after cesarean section (after the umbilical cord has been clamped) can lessen intraoperative nausea and vomiting without significantly lowering blood pressure or heart rate, with midazolam being more effective than propofol in this regard.

Keywords: Spinal anesthesia; propofol; midazolam; IONV; C/S; Iraq.

1. INTRODUCTION

A common problem in cesarean section (C/S) is intraoperative nausea and vomiting (IONV) under regional anesthesia. During and after childbirth, nausea and vomiting can occur and may hurt the mother's and family's health [1]. Although nausea and vomiting are not uncommon in a wide variety of surgical operations, this problem arises even more often in C/S under regional anesthesia [2]. In the world, the incidence of IONV was found in the range of 40% to 80% during C/S under spinal anesthesia [3]. Increased visceral stimulation, hypotension, stretching of the peritoneum (exteriorization of the uterus), increased intragastric pressure, opioid use, and use of uterotonic substances [4]. The mother's health and, more crucially, the consequences on the newborn determine the outcome of the anesthetic, whether spinal or general [5]. Patients' health may be seriously jeopardized; Critical anesthesiological complications like airway obstruction, aspiration pneumonitis, and wound dehiscence are rare and primarily associated with intra- and postoperative nausea and vomiting in patients undergoing general surgery, where 72% of patients are afraid of it and 71% experience significant discomfort [6]. Numerous studies have attempted to develop both drug and non-medication remedies, such as ondansetron, metoclopramide, droperidol, ginger, acupressure, and acupuncture, in light of the high occurrence of IONV [7]. Even though these medications have been shown to lower the frequency of nausea and vomiting, several of them were only hesitantly accepted as routine PONV treatments for pregnant women [8]. Numerous researches on spinal anesthetics have shown that multimodal prophylaxis is superior to stopping vomiting and nausea, especially in C/S [9]. Midazolam, propofol, and ondansetron are just a few of the medications that have been used to reduce nausea and vomiting. The mechanism through which midazolam prevents nausea and vomiting is currently unknown. Dopamine input and adenosine reuptake in the chemoreceptor trigger zone (CRTZ) appear to be constrained by midazolam. At the CRTZ, this results in a reduction of adenosine-mediated dopamine synthesis, release, and postsynaptic action. Adenosine binds to the gamma-aminobutyric acid receptor and suppresses the release of 5-HT3 and dopaminergic neuronal activity [10]. Propofol had unique antiemetic properties. The processes underlying antiemetic actions are not fully understood. Numerous researchers have carried out numerous studies to pinpoint the mechanism [11]. This study aims to evaluate the effect of midazolam and propofol in low doses on the occurrence and severity of IONV during elective C/S under spinal anesthesia.

2. MATERIALS AND METHODS

Study Design, Setting, and Time: This clinical trial investigation was conducted at Gynecology and Obstetrics Department at a Teaching Hospital in Baghdad, Iraq, over the course of one year, from October 2021 to October 2022.

Study Population and Sample Size: The study involved 90 full-term pregnant women with single viable fetuses who were randomly assigned to one of three groups for elective C/S under spinal anesthesia:

- **Group A:** Included 30 women who received propofol.
- **Group B:** Included 30 women who received midazolam
- **Group C:** Included 30 women who received a placebo.

A computer-generated list of random numbers was used for randomization. An anesthesiologist documented intraoperative nausea and vomiting following delivery. Patients who were deemed unfit for spinal anesthesia had a history of significant PONV or motion sickness or vertigo (inner ear disease), had a known allergy to drugs used in the study, had previous C/S or pelvic surgery, were morbidly obese, received metoclopramide or any anti-emetic drugs, and were suffering from psychological disorders while receiving treatment.

Any case of spinal anesthetic failure, vomiting before administration of study medicines, substantial hypotension, hypoxia owing to high spinal or excessive sedation, and post-partum bleeding will be addressed appropriately and dropped from the study. All of the patients gave their informed consent, and we may record their information for research purposes as long as their identity and the confidentiality of their medical records are maintained.

Demographic information, operation length, and systolic, diastolic, mean arterial pressure (MAP), and heart rate were all recorded before anesthesia (basic), after anesthesia induction, and before and after drug administration. Body Mass Index (BMI) is calculated by dividing weight in kilograms by height in meters squared. The same scale is used to measure both height and weight for all topics. BMI is computed as follows: weight (kg) x height squared (m2). Based on BMI, participants were classified as underweight or normal (24.99 kg/m2), overweight (25 - 29.99 kg/m2), or obese (30 kg/m2).

Ephedrine (5 mg in incremental doses) was used to treat hypotension, which is defined as a drop in blood pressure of more than 20% from baseline or systolic blood pressure of less than 90 mmHg. To assess nausea and vomiting (4), Bellville scoring (0: no symptoms, 1: nausea, 2: retching, 3: vomiting) was utilized. To assess intraoperative sedation, the Richmond Agitation Sedation Score (RASS), which runs from 0 (calm and alert) to 3 (restless, agitated, and very agitated), was utilized [12].

Procedure: Before the induction of spinal anesthesia, all patients received an IV dosage of normal saline preload solution, which was performed by delivering 12.5 mg (2.5 mL) of hyperbaric bupivacaine 0.5%. The anesthetics were then injected into the T4-T5 dermatomes using a 25-gauge spinal needle (Pencil Point) while the patient was seated to achieve the required level of insensibility. Patients were inclined to the left to prevent aortic compression, and a face mask with five L/min of oxygen was employed. Blood pressure was recorded using an automated cuff blood pressure monitor until neonatal birth and subsequently at five-minute intervals.

Patients were randomly placed into three groups: Group A received propofol (20 mg bolus then 1.0 mg/kg/h infusion), Group B received midazolam (1 mg bolus then 1.0 mg/h infusion), and Group C received no medication. When the umbilical cord was clamped, these drugs were administered intravenously in sub-hypnotic doses immediately.

2.1 Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 26 was used to analyze the data. The data were presented as mean, standard deviation, and ranges. For categorical data, given as frequencies and percentages. The chi-square test was used to test qualitative and frequency data and check for any links between the type of drug consumed and specific characteristics. Analysis of variances (ANOVA) (two-tailed) was used to compare continuous variables between study groups. P values less than 0.05 were considered significant.

3. RESULTS AND DISCUSSION

In this study, no statistically significant differences (P 0.05) were found between study groups in terms of age, BMI, duration of operation, MAP, and heart rate before and after anesthesia induction, as well as before and after medication administration (Table 1).

Table 1. Comparison between study groups in general characteristics

Variable	Study Group			P - Value
	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)	
Age (Year)	27.5 ± 4.2	26.8 ± 5.0	27.1 ± 4.1	0.778
BMI (kg/m^2)	33.62 ± 6.7	32.26 ± 5.4	30.1 ± 6.2	0.421
Duration of operation (Mints.)	44.63 ± 6.3	42.86 ± 8.2	41.5 ± 4.7	0.289
MAP (mmHg)				
Before anesthesia	94.5 ± 9.8	96.3 ± 10.1	97.5 ± 11.8	0.784
After induction of anesthesia	81.4 ± 9.2	80.5 ± 9.5	79.8 ± 8.7	0.921
Before drug administration	80.5 ± 9.6	80.7 ± 10.6	77.6 ± 8.4	0.681
After drug administration	73.2 ± 7.7	72.8 ± 10.4	74.6 ± 8.2	0.812
Heart rate (Beats/minute.)				
Before anesthesia	94.1 ± 6.4	90.8 ± 8.7	91.4 ± 9.3	0.412
After induction of anesthesia	90.4 ± 9.8	88.1 ± 11.7	89.7 ± 8.7	0.872
Before drug administration	91.4 ± 14.7	92.5 ± 7.9	87.8 ± 8.9	0.763
After drug administration	89.2 ± 7.5	87.4 ± 8.6	88.3 ± 6.5	0.638

Table 2. Comparison between study groups by nausea and vomiting

Study group	Nausea and vomiting		Total (%)	P- value
	Yes (%)	No (%)	n= 60	
A	5 (16.7)	25 (83.3)	30 (50.0)	**0.717**
B	4 (13.3)	26 (86.7)	30 (50.0)	
A	5 (16.7)	25 (83.3)	30 (50.0)	**0.001**
C	17 (56.7)	13 (43.3)	30 (50.0)	
B	4 (13.3)	26 (86.7)	30 (50.0)	**0.001**
C	17 (56.7)	13 (43.3)	30 (50.0)	

Table 3. Comparison between study groups by sedation level

Study group	Sedation level		Total (%)	P- value
	Drowsy (%)	Alert & calm (%)	n= 60	
A	3 (10.0)	27 (90.0)	30 (50.0)	**0.278**
B	6 (20.0)	24 (80.0)	30 (50.0)	
A	3 (10.0)	27 (90.0)	30 (50.0)	**0.3**
C	1 (3.3)	29 (96.7)	30 (50.0)	
B	6 (20.0)	24 (80.0)	30 (50.0)	**0.044**
C	1 (3.3)	29 (96.7)	30 (50.0)	

In terms of nausea and vomiting, patients in group C had the highest prevalence (56.7%), which was significantly different from group A (16.7%, P=0.001) and group B (13.3%, P=0.001); however, there was no statistically significant difference between groups A and B (P= 0.717). (Table 2)

In terms of sedation level, patients in group B had the highest prevalence (20%), which was significantly different from group C (3.3%, P=0.044), while there were no statistically significant differences between groups A and B (P= 0.278) or A and C (P=0.3) (Table 3).

As a typical side effect of spinal anesthesia for elective C/S, nausea, and vomiting affect up to 66% of patients [13]. In pregnant patients undergoing C/S while under spinal anesthesia, midazolam was just as effective as propofol in avoiding PONV [14]. Patients who received a placebo (group C) experienced the highest proportion of nausea and vomiting (56.7%) in the current trial, and the difference between groups

A and B was statistically significant (P0.05). These findings agreed with those of Tarhan et al. in [13], Zabetian et al. in [15], Khezri et al. in [16], and Rasooli et al. in [4]. In a 2010 study, Shahriari et al. discovered no evidence of a substantial difference in the incidence of nausea and vomiting when sub-hypnotic dosages of propofol or midazolam were used [17]. In the current study, 90% of patients in group A were alert and relaxed, compared to 80% of patients in group B. Similar findings were seen in Rasooli S et al. [4] investigation. Recent studies have demonstrated that propofol can reduce intra-operative nausea and vomiting during spinal anesthesia.

Droperidol and metoclopramide are more effective for C/S. It has been proposed that benzodiazepines have some benefits for treating nausea and vomiting by diminishing dopaminergic input to the chemoreceptor trigger zone and therefore lowering anxiety [18]. Propofol lowered synaptic transmission in the olfactory brain in animal studies, which may be related to its antiemetic effects by lowering the release of excitatory amino acids such as glutamate and aspartate [11].

In pregnant women undergoing C/S under spinal anesthesia, midazolam was similarly efficacious as propofol in reducing postoperative nausea and vomiting [14]. Finally, low doses of midazolam or propofol given after a cesarean section (after the umbilical cord has been clamped) can reduce intraoperative nausea and vomiting without significantly lowering blood pressure or heart rate, with midazolam being more effective than propofol in this regard. The limitation of the current study is that it was carried out in one center only in Baghdad city.

4. CONCLUSION

Low dosages of midazolam or propofol given after a cesarean section (after the umbilical cord has been clamped) can reduce intraoperative nausea and vomiting without reducing blood pressure or heart rate much, with midazolam being more effective than propofol in this regard.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethical committee approval has been collected and preserved by the author.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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