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

Abstract

Background: Intraoperative nausea and vomiting while under regional anesthesia is a common problem in C/S and is caused by a number of different processes. The health of the woman and her family may be harmed by nausea and vomiting that can occur during and after childbirth. Midazolam and propofol displayed distinct antiemetic characteristics, but the mechanisms underlying these effects are still poorly understood.

Aim of this study: To examine whether intraoperative nausea and vomiting occur and how severe they are after elective cesarean sections under spinal anesthetic using sub hypnotic doses of midazolam and propofol.

Methods: The Gynecology and Obstetrics Department of Baghdad Teaching Hospital in Baghdad, Iraq, carried out this clinical trial study during the period of one year from October 2021 till October 2022, included 90 full term pregnant women with single viable fetus undergone elective C/S by spinal anesthesia and randomly allocated to one of three groups: Group A included 30 women received propofol, group B included 30 women received midazolam, and group C included 30 women received placebo. Nausea and vomiting were evaluated by means of Bellville scoring score. Sedation was assessed intraoperatively according to Richmond Agitation Sedation Score (RASS).

Results: Highest prevalence of nausea and vomiting was seen among patients of group C (56.7%) and this was significantly different from group A (16.7%, P=0.001) and group B (13.3%, P= 0.001); while no statistical significant difference between group A and B (P= 0.717). Highest prevalence of drowsy level was seen among patients of group B (20%) and this was significantly different from group C (3.3%,

P=0.044); while no statistical significant differences between group A and B (P= 0.278) and between group 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.

Keyword: Spinal anesthesia, propofol, Midazolam, IONV, C/S, Iraq.

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 have a negative impact on the mother's and family's health [(1)]. Although nausea and vomiting are not uncommon in a wide variety of surgical operations, but this problem arises even more often in C/S under regional anesthesia [(2)]. In the world, the incidence of IONV was found in the rage of 40% to 80% during C/S under spinal anesthesia [(3)]. Increased visceral stimulation, hypotension, stretching of 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 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)]. Despite the fact that 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 anesthetic have shown that multimodal prophylaxis is superior to stop 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. 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)]. Aim of this study is 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.

Patients and methods

Study design, setting, and time: The Gynecology and Obstetrics Department of Baghdad Teaching Hospital in Baghdad, Iraq, carried out this clinical trial study during the period of one year from October 2021 till October 2022.

Study Population and sample size: The study included 90 full term pregnant women with single viable fetus undergone elective C/S by spinal anesthesia and randomly allocated to one of three groups:

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

Randomization was done by a computer-generated list of random numbers. Intraoperative nausea and vomiting after delivery were recorded by an anesthesiologist. Patients unfit for spinal anesthesia, had history of significant PONV or motion sickness or vertigo (inner ear dis.), with known allergy from drugs used in the study, had previous C/S or pelvic surgery, morbidly obese patients, received metoclopramide or any anti emetic drugs, with psychological disorders even taking treatment.

Any case with failure of spinal anesthesia, vomiting before administration of drugs of the study, had significant hypotension, with hypoxia due to high spinal or excessive sedation, and with post-partum hemorrhage will be managed accordingly and dropped from the study. All of the patients gave their informed agreement, and as long as the patients' anonymity and the confidentiality of their medical records are upheld, we may record their information for research reasons.

Demographic data, duration of surgery, and systolic, diastolic, mean arterial pressure (MAP), and heart rate was recorded before anesthesia (basic), after induction of anesthesia, before and after drug administration. Weight in kilograms divided by height in meters squared yields the Body Mass Index (BMI). For all subjects, the same scale is used to measure both height and weight. BMI is calculated as follows: weight (kg) x square of height (m^2). Participants were categorized as follows based on BMI:

Underweight or Normal (≤ 24.99 kg/m²), Overweight (25 - 29.99 kg/m²), and Obese (≥ 30 kg/m²). Ephedrine (5 mg at incremental dosages) was used to treat hypotension, which is defined as a more than 20% decrease from baseline pressure or a systolic blood pressure of less than 90 mmHg. Bellville scoring (0: no symptoms, 1: nausea, 2: retching, 3: vomiting) was used to assess nausea and vomiting [(4)]. The Richmond Agitation Sedation Score (RASS), which ranges from 0 (calm and alert) to 3 (restless, agitated, and very agitated), was used to gauge intraoperative sedation [(12)].

Procedure: All patients received an IV dose of normal saline preload solution prior to the induction of spinal anesthesia, which was accomplished by administering 12.5 mg (2.5 mL) of hyperbaric bupivacaine 0.5%. The anesthetics were then injected using a 25-gauge spinal needle (Pencil Point) while the patient was seated to obtain the desired amount of insensibility at the T4-T5 dermatomes. In order to prevent aortic compression, patients were tilted to the left, and a face mask was used to provide five L/min of oxygen. Until neonatal birth and then at five-minute intervals, blood pressure was measured using an automated cuff blood pressure monitor. Patients were placed into three groups at random: 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 subhypnotic doses immediately.

Statistical analysis: Version 26 of the Statistical Package for Social Sciences (SPSS) was used to analyze the data. The data were provided as mean, SD, and ranges. expressed as frequencies and percentages for categorical data. To test qualitative and frequency data and look for any connections between the type of drug used and certain factors, the chi square test was performed. The continuous variables were compared between study groups in accordance using analysis of variances (ANOVA) (two tailed). P values less than 0.05 were regarded as significant levels.

Results

In this study, no statistical significant differences detected (P ≥ 0.05) between study groups regarding age, BMI, duration of operation, MAP and heart rate before and after induction of anesthesia, and before and after drug 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/mint.)				
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**

In comparison between study groups regarding nausea and vomiting, highest prevalence of nausea and vomiting was seen among patients of group C (56.7%) and this was significantly different from group A (16.7%, P=0.001) and group B (13.3%, P= 0.001); while no statistical significant difference between group A and B (P= 0.717) (Table 2)

Table 2: Comparison between study groups by nausea and vomiting

Study group	Nausea and vomiting		Total (%) n= 60	P- value
	Yes (%)	No (%)		
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)	

In comparison between study groups regarding sedation level, highest prevalence of drowsy level was seen among patients of group B (20%) and this was significantly different from group C (3.3%, P=0.044); while no statistical significant differences between group A and B (P= 0.278) and between group A and C (P= 0.3) (Table 3).

Table 3: Comparison between study groups by sedation level

Study group	Sedation level		Total (%) n= 60	P- value
	Drowsy (%)	Alert & calm (%)		
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)	

Discussion

Up to 66% of patients who have spinal anesthesia for elective C/S experience nausea and vomiting as a common side effect [13]. Midazolam was equally as efficacious as propofol at preventing PONV in pregnant patients undergoing C/S while under spinal anesthesia [14]. In the current study, patients

who received placebo (group C) had the highest proportion of patients presented with nausea and vomiting (56.7%), and the difference with group A and B was statistically significant (P<0.05). These results were in agreement with results in studies conducted by Tarhan O et al study in 2007 [13], Zabetian H et al in 2016 [15], Khezri MB et al in 2009 [16], and Rasooli S et al in 2014 [4]. Different outcomes were shown in a research by Shahriari A et al in 2010, where they found no evidence of a significant difference in the incidence of nausea and vomiting when subhypnotic dosages of propofol or midazolam were employed [17]. In the current study, 90% of group A patients were alert and calm versus 80% of group B patients. Similar results observed in Rasooli S et al study in 2014 [4].

Recent studies have demonstrated that propofol can reduce intra-operative nausea and vomiting during spinal anesthesia for C/S more effectively than droperidol and metoclopramide. By lowering dopaminergic input to the chemoreceptor trigger zone and so lowering anxiety, it has been suggested that some benefits of benzodiazepines for treating nausea and vomiting exist [18]. In an animal research, propofol reduced synaptic transmission in the olfactory brain, which may be connected to its antiemetic effects by reducing the release of excitatory amino acids like glutamate and aspartate [11]. Midazolam was equally as effective as propofol at preventing post-operative nausea and vomiting in pregnant patients having C/S under spinal anesthesia [14].

In 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.

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