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Original Research

EFFICACYOFSUB-HYPNOTICDOSEOFPROPOFOLORDEXAMETHASONE FOR ATTENUATION OF INTRATHECAL MORPHIN - INDUCED POST - OPERATIVE NAUSEA AND VOMITING IN PARTURIENT UNDER CESAREAN SECTION - A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background: *Preventing nausea and vomiting in women undergoing post cesarean section played an important role in improving quality of care, enhanced patient satisfaction in breastfeeding and caring for the newborns.This study aimed to determine the incidence of postoperative nausea and vomiting among parturients receiving sub-hypnotic dose of propofol or dexamethasone as prophylaxis after cesarean section under intrathecal morphine to extend post-operative analgesia and the side effects of these drugs on patients.*

Methods: *The study was conducted on 180 pregnant women with written informed consent.All pregnant women under spinal anesthesia were supplemented with intrathecal morphine for postoperative extended analgesia andeach recruited parturient was assigned to one of 3 groups using random allocation software. 60 parturients in each group were allocated to 0.5 mg/kg of propofol or 8 mg of dexamethasone (for post - operative nausea and vomiting prophylaxis) and NaCl 0.9% for the control group. Postoperative nausea and vomiting (PONV) incidence, heart rate, blood pressure, SpO2, respiratory rate, Richmond Agitation Sedation Scale (RASS) score and side effects of propofol and dexamethasone were recorded.*

Results: *It was noted that the incidence of post-operative nauseasignificantly decreased in the propofol group (18,3%) or the dexamethasone group (20%) compared with the control group (51,7%) (P < 0.05).Similarly, post-operative vomiting was significantly reduced in the propofol group (6,7 %) or the dexamethasone group (8,3 %) compared with the control group (21,7%) (P < 0.05).There were no changes among parturients from the control group, propofol group, and the dexamethasone group regarding heart rate, blood pressure, SpO2, respiratory rate and RASS score. 11(18,3%) from the propofol group experienced pain. There were no side - effects related to dexamethasone.*

Conclusion: *This study's findings suggested that a sub- hypnotic dose of propofol could be as effective as dexamethasone in preventing PONV in parturient undergoing cesarean section under spinal anesthesia with intrathecal morphine to extend post-operative analgesia. There were no effects on vital signs, except for pain on propofol injection.*

Key words: *Post - operative nausea and vomiting, subarachnoid space, morphin, analgesia, post - operative, cesarean section.*

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I. BACKGROUND

Post - operative nausea and vomiting (PONV) caused discomfort for the parturients, particularly in surgical patients under general anesthesia.With no prior prophylaxis, approximately 30% of all patients suffered from nausea and vomiting in the post- anesthetic period, whereby the highest incidence could be found in the first 6 hours following surgery.Compared to the plethora of literature about PONV, little attention has been paid to nausea and vomiting occurring during or after regional anesthesia, including spinal anesthesia [1-3].

Its incidence was estimated up to93 % ofparturients post cesarean sectionunder intrathecal morphine to extend post-operative analgesia.

Post-operative vomiting (POV) not only cause discomfort but also increases pain,and the risk of choking and aspiration, leadingtohydro-electrolyte disorders, delayed awakening from anesthesia and increased healthcarecost for the patients.

Prophylaxis to reduce these adverse effects to occur played an important role in improving the quality of care and treatment post-operatively for the patients [4].

The Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting in 2020 provided recommendations for preventing and treating PONV in high-risk patients, particularly the implementation of a general multimodal PONV prophylaxis of two or more interventions.

Propofol anesthesia, regional anesthesia, adequate fluid replacement, pharmacological interventions (haloperidol, NK-1 receptor antagonist, subsedatory propofol, perphenazine, scopolamine, 5-HT3 antagonist, dexamethasone), and non-pharmacological interventions like acupuncture were among these interventions [5].

The choice of a prophylactic treatment that was both safe and effective for the mother and the fetus was one of the challenges in preventing nausea and vomiting in women under cesarean sections.

The systematic reviews addressed dexamethasone efficacy in reducing nausea and vomiting following surgery underintrathecal morphine. Furthermore, the trials on sedatives and hypnotics such as propofol or midazolam also brought similar outcomes [6-8]. In a number of endoscopic and ENT operations in Vietnam, the use of low-dose dexamethasone and propofol for the prevention and treatment of nausea and vomiting has been examined. However, there were no reports on sub-hypnotic dose of propofol as prophylaxis after cesarean section under intrathecal morphine to extend post-operative analgesia[2,9-12].

As a result, this study aimed to determine the incidence of postoperative nausea and vomiting among parturients receiving sub-hypnotic dose of propofol or dexamethasone as prophylaxis after cesarean section under intrathecal morphine to extend post-operative analgesia and the side effects of these drugs on patients.

II. MATERIALS AND METHODS

2.1. Study design

Between May 2020 and May 2021, a prospective comparative descriptive study (Randomised controlled trial) was conducted at the Department of Anesthesia and Resuscitation A, Hue Central Hospital.

2.2. Subjects

Inclusion criteria: All women aged 18 - 45 years, American Society of Anesthesiologists Physical Status (ASA-PS) value of 2-3,were scheduled to undergo elective cesarean section under spinal anesthesia with intrathecal injection of morphine to extend post-operative analgesia. Pfannenstiel transverse suprapubic incision for cesarean section and informed consent for the study.

Exclusion criteria: Cardiovascular disease, respiratory disease, and mental disorders; BMI greater than 35.Contraindications to anesthesiaincludespinal abnormalities, local infection at puncture site, coagulation disorders, and allergic reactions to local anesthetics.It failed spinal anaesthesia. Blood loss ≥ 500 ml during C-section. History of long-term opioid use or allergy to opioids. No interview consent in the post-operative period.

Each recruited parturient was assigned to one of 3 groups using random allocation software.60 parturients in each group were allocated 0.5 mg/kg of propofol (sub - hynoptic dose - group P) or 8 mg of dexamethasone (group D)(for post-operative nausea and vomiting prophylaxis) and NaCl 0.9% for the control group (group C).

2.3. Methods

Pregnant women at 36 weeks gestation were evaluated for standard pre-anesthesia in accordance with the hospital's maternity care protocol.

When C- section was indicated along with spinal anesthesia chosen, women were counseled to participate in the study and were enrolled and randomly assigned to receive either 0.9% NaCl, dexamethasone, or propofol for postoperative nausea and vomiting (PONV) prophylaxis.

According to the standard procedure authorized by Hue Central Hospital's Professional Council, spinal anesthesia would be performed. Inject a mixture of local anestheticChirocaine® 0.5%, 8 - 10 mg (1.6 - 2 mL) and Opiphin® 10 mg/mL 0.1 mg.

If the women werefrom group P, an intravenous injection of 0.5 mg/kg propofol would be given 10 minutes before the end of surgery. If the women werefrom group D, 8 mg of dexamethasone was given. If the women were from group C, 5 mL of 0.9% NaCl would be given intravenously 10 minutes before the end of surgery.We administered Primperan® (metoclopramide) 10 mg intravenously as a "rescue" medication if the women had nausea following surgery. After using propofol, if the women experienced sedating symptoms like somnolence or were not fully awake, the medication would be stopped and the mother's respiratory status would be monitored until the symptoms disappeared. Patient data were collected and analyzed, including nausea, vomiting, pulse, systolic blood pressure, diastolic blood pressure, mean blood pressure, respiratory rate, SpO2, pruritus, urinary retention, sedation level, propofol side effects (hypotension, transient apnea), dexamethasone side effects (edema, hypertension, hyperglycemia, epigastric pain ...)

2.4. Data processing

The medical statistical program SPSS 16.0 was used for data entry and processing (SPSS Inc, Chicago III). The number of cases and percentages were used to express categorical variables, whereas the mean and standard deviation were used to express continuous variables with a normally distributed distribution. With a p-value of 0.05, the algorithms were statistically significant.

III. RESULTS

During the study period from May 2020 to May 2021, 180 women were included in the study. Our results were as follows:

Table 1: Age, height, weight and BMI

Patient characteristics	**Researched group**			**p**
	Propofol TB ± ĐLC	**Dexamethason** TB ± ĐLC	**Control** TB ± ĐLC	
Age (years)	30,03 ± 5,65	29,90 ± 5,13	29,13 ± 4,62	> 0,05
Height (cm)	154,50 ± 4,99	154,62 ± 4,99	156,17 ± 5,44	> 0,05
Weight (kg)	61,95 ± 6,96	60,97 ± 6,68	62,08 ± 8,10	> 0,05
BMI (kg/m^2)	25,97 ± 2,80	25,53 ± 2,80	25,42 ± 2,81	> 0,05

The average age and height of the women participating in the study were 29.71± 5.12, and 155.09 ± 5.17 cm, respectively. The average mass index (BMI) and weight were 25.64 ± 2.80 kg/m2, and 61.67 ± 7.25 kg, respectively. Pregnant women's height, weight, and BMI were not statistically significantlydifferent between research groups (p > 0.05).

Table 2: Rate of post-operative nausea and vomiting

Symptom	**Researched group**						**p**
	Propofol		**Dexamethason**		**Control**		
	n	**%**	**n**	**%**	**n**	**%**	
No symptom	45	75,0	43	71,7	16	26,6	< 0,05
Nausea	11	18,3	12	20,0	31	51,7	

Vomiting	4	6,7	5	8,3	13	21,7	
Nausea and vomiting	15	25%	17	28,3%	44	73,4%	
Total	60	100	60	100	60	100	
p1 < 0,05		*p2* < 0,05			*p3* > 0,05		

The postoperative nausea rates from group P, D and C were 18.3%, 20%, and 51.7%, respectively. The postoperative vomiting rates from groups P, D and C were 6.7%, 8.3%, and 21.7%, respectively. Compared togroup C, there was a statistically significant difference in PONV rate between the study groups ($p < 0.05$). There was no statistically significant difference ($p > 0.05$) in PONV rate between the groups P and D.

Table 3: Utilization of rescue drugs

Rescue drug	**Researched group**						**p**
	Propofol		**Dexamethason**		**Control**		
	n	**%**	**n**	**%**	**n**	**%**	
Use	4	26,7	5	29,4	12	27,3	> 0,05
Don't use	11	73,3	12	70,6	32	72,7	
Total	15	100	17	100	44	100	
p1 > 0,05		*p2* > 0,05			*p3* > 0,05		

The rate of rescue antiemetics use in the P group, D group and C group were 26.7%, 29.4%, and 27.3%, respectively.In comparison to group C, there was no statistically significant difference in rescue antiemetics use rate between the study groups ($p > 0.05$). There was no statistically significant difference ($p > 0.05$) in rescue antiemetics use rate between the groups P and D.

Table 4: Propofol's adverse affects

Propofol's adverse affects		**Propofol**	
		n	**%**
Pain at the injection site	No	49	81,7
	Yes	11	18,3
Hypoten-sion	No	60	100,0
	Yes	0	0,0
Bradycardia	No	60	100,0
	Yes	0	0,0
Temporary stop breathing	No	60	100,0
	Yes	0	0

In group P, there were 11 cases of pregnant women experiencing pain at the injection site (18.3%) and no more side effects such as hypotension, bradycardia, or temporary apnea.

IV. DISCUSSION

We conducted this study to assess the efficacy of propofol in preventing postoperative nausea and vomiting (PONV). Regarding the findings, in our study, 25% of the pregnant women from group P experienced PONV. When compared to group C whose rate was 73.4%, this rate was considerably lower, similar to the results from the other studies domestically and internationally.

In contrast to what the author Numazaki et al. reported, our study found a reduced incidence of postoperative nauseaand vomiting in group P. 60 women who got propofol (1 mg/kg/hour) and 60 women who received a placebo (Intralipid) immediately upon cord clamping were compared in Numazaki s' study; results showed that in the propofol infusion group, postoperative nausea rate was 33% lower than that in the control group, by a factor of 67%. The use of systemic opioids to control postoperative pain may be the cause of this discrepancy [3]. In contrast, in our study,the rate of

postoperative nausea was higher than those of the authors Kampo, Radra, and Rasooli's investigation of a group of pregnant women who underwent surgery and were given subarachnoid opioids to treat postoperative pain. The effectiveness of propofol at sub-sedation doses in reducing postoperative nausea was tested by Kampo et al. in 345 women undergoing spinal anesthesia along with subarachnoid morphine divided into three groups at random. Propofol was administered to one group (115 women), metoclorapamide was administered to another group, and a control group was also included. According to the findings, only 8.7% of patients in the propofol group experienced post-operative nausea, compared to 7% in the metoclorapamide group and up to 93.9% in the control group.

* Dexamethasone's effectiveness in preventing postoperative nausea and vomiting (PONV):

Similar to propofol, it was unclear how dexamethasone worked to prevent postoperative nausea. Dexamethasone's antiemetic effect, however, has been attributed by some authors to its ability to stabilize membranes, inhibit inflammatory mediators (such as protein C, tissue necrosis factor, and interleukin), and prevent the formation of metabolites like prostaglandins, histamine, and somatomedin [13,14].

In our study, in group D, 28,3% womenexperienced PONV. Thispercentage was statistically considerably lower than the control group (73.4%) when compared to the control group. This preventative impact was consistent with the findings of the study.

* Comparing the efficacy of propofol and dexamethasone for preventing postoperative nausea, our study found no statistically significantdifferences. Even though the P group experienced fewer cases of nausea and vomiting than the D group (25% versus 28.3%), this difference was not statistically significant. The rescue antiemetic use rate in the P group, the D group, and the C group were 26.7%, 29.4%, and 27.3%, respectively. Kampo et al. noted that the PONV rate of the control group taking "rescue" antiemetics was 9.7 times greater than that of the propofol use group and 2.5 times higher than that of the metoclopramide use group.

* Concerning Propofol's side effects:

Pain on propofol injection (POPI): In our study, 11 cases (18,3%) had pain at the injection site. This was a typical common symptom of drug use mentioned in the Desousa review.POPI was due to irritation of venous adventitia, leading to the release of mediators such as kininogen from the kinin cascade, causingdiscomfort while injecting propofol. Some medications, such as lidocaine, ketamine, and metoclopramide, can be used with propofol injection to avoid POPI [3,15].

Respiratory depression: No respiratory depression was found in pregnant women at sedative dose during the trial, without influencing the mother's ability perceived to interact with and care for her child. The RASS value of 0 in our study demonstrated that the administration of propofol at a dose of 0.5 mg/kg was adequate sedative and safe [16,17].

Hypotension and bradycardia: Pharmacologically, Propofol had effects on hemodynamics during anesthesia induction. If the patient continued spontaneous breathing, the main cardiovascular effectswould be a decrease in arterial blood pressure, with little to no changes in heart rate and no remarkable decrease in cardiac output. If patients receive assisted ventilation or positive pressure ventilation, there would be more intense and frequent cardiac output decrease. A strong opioid (like fentanyl) added as a pre- medication also significantly lowered cardiac output and respiratory muscle effort. At doses below sedation levels, no hypotension and bradycardia were observed when propofol was use for the prophylaxis of postoperative nausea. This outcome may partly be affected by spinal anesthesia- induced hypotension prophylaxis (phenylephrine or ephedrine) [18]. In this study, we did not include a pre-history of postoperative nausea in the exclusion criteria to minimize the possibility of affecting the study results. Moreover, a reliable way of evaluation when subsequent measures were the same and occurred under the same clinical conditions. One-way evaluation scales had the benefit of being straightforward and simple to use. They may be used repeatedly for comparison and to help studythe effectiveness of the antiemetic medication. The Klockgether-Radke scale had the drawback of being an one-way evaluation that ignored the multidimensional aspects of nausea and vomiting. Similarly, measuring maternal satisfaction with the quality of care practices served as an indirect way to assess how well intervention strategies worked.

Pregnant women's satisfaction was measured using a subjective method; therefore, the value was low. To reduce pain at the propofol injection site in our trial, we did not employ any medications (such as lidocaine). The satisfaction of the study's pregnant women may also be impacted by this pain. Blood glucose testing needed to be incorporated into the study so that the side- effects of dexamethasone may be evaluated more objectively.

V. CONCLUSION

18.3% of the group using propofol experienced nausea, compared to 20% of the group using dexamethasone, and 51.7% of the control group using sodium chloride 0.9% experienced postoperative nausea and vomiting. In the study group using propofol, dexamethasone, and the control group, the rates of postoperative vomiting were 6.7%, 8.3%, and 21.7%, respectively.

Pulse, blood pressure, SpO2, and respiratory rate did not change in the study groups. In the propofol group, the rate of pain on the injection site was 18.3%. Dexamethasone had no adverse effects.

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