Original Article

Preventing Intraoperative Nausea and Vomiting During Cesarean Delivery under Spinal Anesthesia: A Comparison of Effects of Prophylactic Cyclizine, Metoclopramide, and Placebo

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Abstract

Background: Nausea and vomiting are undesirable intraoperative events among women during cesarean delivery under subarachnoid block. Therefore, prophylaxis is recommended. **Aims:** This study was undertaken to compare the effect of intravenous cyclizine with metoclopramide administered before achieving subarachnoid block. **Patients, Materials and Methods:** The study was conducted among women booked for elective cesarean section using the subarachnoid technique. This is a prospective, randomized, double-blinded study that compared the effect of single doses of cyclizine, metoclopramide, and placebo in preventing intraoperative nausea and vomiting among the selected patients. We obtained ethical clearance from the Hospital Research and Ethics Committee as well as written informed consent from each patient involved. The inclusion criteria include women aged 18–45 years with term singleton pregnancy scheduled for elective cesarean section, having the American Society of Anesthesiologists (ASA) physical status grades 1 and 2, with no known contraindications to spinal anesthesia, allergy to study drugs or local anesthetic agents. Patients were excluded if they declined, have a history of allergy to metoclopramide or cyclizine, have pregnancy-induced hypertension, hyperemesis gravidarium, motion sickness, gastrointestinal disease or glucose intolerance. One hundred and twenty parturients with ASA status I-II were recruited and assigned to three groups. All medications were administered intravenously: normal saline in Group I, metoclopramide in Group II, and cyclizine in Group III. Data were collected with study pro forma produced for the study. The Statistical Package for the Social Sciences (SPSS) Version 20.0 was used for analysis of the data collected. **Results:** The incidence of nausea was least in Group III. There were similar findings for retching and vomiting. **Conclusion:** We, therefore, concluded that cyclizine is superior to metoclopramide in preventing nausea in women undergoing cesarean section under spinal anesthesia.

Keywords: Cyclizine, intraoperative vomiting, parturient, spinal anesthesia

Introduction

Spinal anesthesia is currently the preferred anesthetic technique for cesarean section when applicable. The technique, however, has its complications,[1] one of which is intraoperative nausea and vomiting (IONV). This may or may not be accompanied retching. The incidence of IONV during spinal anesthesia has been found to vary between 37% and 75% when no prophylactic antiemetic is given compared to when prophylaxis is given.[1] These symptoms may have an unfavorable impact on the birthing experience. Nausea and vomiting can also complicate intraoperative care as the patient may be predisposed to aspiration of vomitus. Furthermore, the protrusion of abdominal contents would cause disturbance to the surgeon during the procedure.[2]

A number of pharmacological agents have been administered for the treatment and prevention of IONV: 5-hydroxyltryptamine (5-HT_3) antagonist (e.g., ondansetron and granisetron), dopamine receptor antagonist (e.g., metoclopramide), butyrophenones (e.g., droperidol), and anticholinergic agents (e.g., atropine).[3] Certain critical limiting factors are linked with them. These include cost with 5-HT_3 antagonist

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and extra-pyramidal symptoms (tremor, bradykinesia, and dyskinesia) with dopamine receptor antagonist.[3] Antihistamines (H_1 receptor antagonist) such as cyclizine have antiemetic effect but have not been commonly used in our local population as prophylaxis for nausea and vomiting during spinal anesthesia. The purpose of this study is to assess the effect of cyclizine, metoclopramide, and placebo given before subarachnoid block for the prophylaxis of IONV in our hospital.

Aims

The aim of this study was to evaluate the efficacy and safety of intravenous cyclizine, metoclopramide, and placebo, in preventing IONV during cesarean section under spinal anesthesia.

Patients Materials and Methods

Study population

This comprised of women scheduled for elective cesarean section under spinal anesthesia in our hospital.

Study design

This is a prospective, randomized, double-blinded, placebo study. The power of study was 80% with a significance level of 5% while a provision of 10% was made for attrition. A total of 120 parturients were recruited. The participants were divided into 3 groups by envelope randomization. They were 40 in each group: Group I – saline, Group II – metoclopramide, and Group III – cyclizine. Twenty (20) minutes before establishing spinal anesthesia, Group I received 2 ml of 0.9% saline, Group II received 10 mg of metoclopramide in 2 ml, and Group III were given 50 mg of cyclizine diluted with water for injection to 2 ml intravenously. Patients were monitored and records of nausea, vomiting, and retching, and vital signs and side effects of drugs were made. Neonatal APGAR scores were also recorded.

Each patient had been educated on the nausea numerical rating scale for assessing the severity of nausea: 0 (indicating "No nausea or no urge to vomit") to 10 (indicating "unbearable nausea or unbearable urge to vomit"). Following strict asepsis, subarachnoid block was achieved using 25G Quincke spinal needle and hyperbaric bupivacaine 0.5%, 12.5 mg (2.5 ml). Vital signs monitored were noninvasive blood pressure, heart rate, arterial oxygen saturation (SpO_2), electrocardiography, and respiratory rate using DAS 4000 multiparameter monitor (General Electric, Wisconsin USA). The figures obtained were recorded on the anesthetic chart every 2 min for the first 10 min and thereafter every 5 min for the duration of the surgery and in the recovery room.

Nausea was graded: 1–3 = mild nausea, 4–6 = moderate nausea, while 7–10 = severe nausea. For rescue antiemetics, intravenous promethazine 25 mg was administered when patients had moderate-to-severe nausea and vomiting. Patients were monitored for hypotension. Hypotension was defined as decrease in systolic or mean arterial blood pressure of >20% from the baseline value. Hypotension was treated using crystalloid infusion and ephedrine administration at 6 mg intravenous boluses. Total dose of ephedrine administered to each patient was recorded. Sedation was assessed using a 6-point scale (Inova Sedation Assessment Scale): 1 = alert, 2 = occasionally drowsy, 3 = dosing intermittently, 4 = asleep easy to awaken, 5 = difficult to awaken, 6 = unresponsive. APGAR scores for the neonates in the Ist and 5th min were also recorded.

Data collection

Data were collected with study instrument designed for the study.

Study criteria (inclusion and exclusion criteria)

The inclusion criteria include women aged 18–45 years with term singleton pregnancy scheduled for elective cesarean section, having the American Society of Anesthesiologists physical status Grades 1 and 2, with no known contraindications to spinal anesthesia, allergy to study drugs or local anesthetic agents. Patients were excluded if they declined, have a history of allergy to metoclopramide or cyclizine, have pregnancy-induced hypertension or glucose intolerance. Other exclusion criteria were an established history of gastrointestinal disease, motion sickness or hyperemesis gravidarium, intake of antiemetic or emetogenic medications (e.g. opioids) within the previous 24 h or had local anesthetic systemic toxicity.

Ethical consideration

Ethical clearance was obtained from the Hospital Research and Ethics Committee as well as written informed consent from each patient.

Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Version 20.0 (SPSS Inc., Chicago, IL, USA). Continuous and categorical variables across the groups were summarized using frequency, percentages, means, and standard deviations. Continuous variables over time within the groups were compared using analysis of variance. Chi-square test was used to analyze association between categorical variables. Results were presented as tables and charts and $P < 0.05$ were considered statistically significant.

Results

One hundred and twenty (120) patients were enrolled in the study. One patient was converted to general anesthesia due to failed spinal, one required intraoperative analgesic, one had received another antiemetic drug mistakenly administered by the assistant, and another one was sedated due to anxiety. Therefore, a number of 4 patients were excluded from the analysis. The remaining 116 parturients were 39 in Group I, 39 in Group II, and 38 in Group III. They were similar in their demographic characteristics, $P > 0.05$ [Table 1].

Nausea occurred in 14 (36.9%) of patients in Group I, 6 (16.4%) in Group II, and 1 (2.6%) of patients in Group III. The severity of nausea is also shown in Table 2. Retching occurred in 7 (17.9%) and 2 (5.1%) of patients in Groups I and II, respectively. Retching was not documented in Group III. Vomiting occurred in 5 (12.8%), 2 (5.1%), and none of patients in Groups I to III, respectively. However, vomiting was not statistically significant (χ^2 = 5.664, *P* = 0.059) [Table 2].

In Group I, 9 (60%) of patients experienced hypotension with IONV while the figures for Groups II and III were 4 (26.7%) and 1 (5.3%), respectively [Table 3].

For Group I, 15 (38.5%) had a drop in blood pressure but 12 (30.8%) required administration of ephedrine. In Group II, 15 (38.5%) became hypotensive but 11 (28.2%) required ephedrine. While in Group III, 19 (50%) were hypotensive, however, 13 (34.2%) required ephedrine administration [Table 4].

The study also revealed that rescue antiemetic was used more among patients in the placebo group in Group I [Table 4].

Sedation was most common in Group III (χ^2 = 43.614, *P* = 0.001). SpO_2 ranged from 95% to 100% in room air. All neonatal APGAR scores in the 1st min were between 7–9 and 9–10 in the 5th min [Table 5].

Table 1: Demographic characteristics

	Mean±SD			*F*	*P*
	Group I	Group II	Group III		
Age	28.71±7.72	29.12±7.26	31.71±7.79	1.768	0.175
Weight	86.53±12.94	83.45±14.89	86.03±13.94	0.545	0.581

SD: Standard deviation

Table 2: Intraoperative nausea retching vomiting among the groups

	Drug study group			χ^2	*P*
	Group I, *n* (%)	Group II, *n* (%)	Group III, *n* (%)		
IONV (summary)					
Yes	14 (35.9)	6 (15.4)	1 (2.6)	14.659	0.001
No	25 (64.1)	33 (84.6)	37 (97.4)		
Retching					
Yes	7 (17.9)	2 (5.1)	0	9.232	0.010
No	32 (82.1)	37 (94.9)	38 (100.0)		
Vomiting					
Yes	5 (12.8)	2 (5.1)	0	5.664	0.059
No	34 (87.2)	37 (94.9)	38 (100.0)		
Nausea					
No nausea	25 (64.1)	33 (84.6)	37 (97.4)	15.437	0.017
Mild	1 (2.6)	1 (2.6)	0		
Moderate	9 (23.1)	2 (5.1)	1 (2.6)		
Severe	4 (10.3)	3 (7.7)	0 (0.0)		

IONV: Intraoperative nausea and vomiting

Table 3: Hypotension and intraoperative nausea and vomiting

IONV	Hypotension		χ^2	*P*
	Yes, *n* (%)	No, n (%)		
Group I				
Yes	9 (60.0)	5 (20.8)	6.154	0.013
No	6 (40.0)	19 (79.2)		
Group II				
Yes	4 (26.7)	2 (8.3)	2.383	0.180
No	11 (73.3)	22 (91.7)		
Group III				
Yes	1 (5.3)	0	1.027	1.000
No	18 (94.7)	19 (100.0)		

IONV: Intraoperative nausea and vomiting

Discussion

This prospective study demonstrated that administration of 50 mg of cyclizine intravenously before induction of anesthesia is more effective than metoclopramide for the prevention of nausea during the procedure. Malak *et al*., in their study, found that cyclizine was effective when compared with ondansetron and prochlorperazine.[4] Furthermore, Khurshid *et al*. in their study found cyclizine effective as in our study.[5] Nortcliffe *et al*. compared cyclizine and dexamethasone for the prevention of IONV after spinal anesthesia for cesarean section. Their study showed that cyclizine reduced the incidence of nausea from 67% to 33% while dexamethasone reduced the incidence from 67% to 60%.[6] In another study by Grimsehl *et al*. comparing cyclizine and ondansetron use during laparoscopic day-case gynecological surgery, there was no difference between the two.[7]

Dandona *et al*. compared metoclopramide with ondansetron in women who had cesarean delivery under spinal anesthesia. They found that the effect of metoclopramide when administered alone is inferior to that of ondansetron.[8] Isazadehfar *et al*. also found that ondansetron was more effective than metoclopramide.[9] Voigt *et al*. also in their study also found that a combination of metoclopramide with tropisetron was more effective than administration of only metoclopramide.[10] However, according to Gebremedhum *et al*., when compared to a placebo, metoclopramide was more effective.[11]

Magni *et al*. in 2016 reported an incidence of 32% and 7% of nausea and vomiting, respectively, among placebo group.[12] Their finding, though lower than the result in this work (35.9% and 12.8%), could be attributed to the use of lower dose of hyperbaric bupivacaine 10 mg (2 ml). Van de Velde also found that this dose has been noted to cause low incidence of hypotension, nausea, and vomiting.[13]

Hypotension can lead to reduce blood flow to the brain. Furthermore, brain stem ischemia may activate the circulatory, respiratory, and vomiting centers in the medulla.[14] Furthermore, it leads to gut ischemia and release of emetogenic substances such as serotonin.[14] Therefore, hypotension should be actively

Table 4: Hypotension versus ephedrine and antiemetic use among the groups

	Group I, *n* (%)	Group II, *n* (%)	Group III, *n* (%)	χ^2	*P*
Hypotension					
Yes	15 (38.5)	15 (38.5)	19 (50.0)	1.276	0.528
No	24 (61.5)	23 (61.5)	19 (50.0)		
Ephedrine use					
Yes	12 (30.8)	11 (28.2)	13 (34.2)	0.326	0.849
No	27 (69.2)	28 (71.8)	25 (65.8)		
Antiemetic drug use					
Yes	13 (33.3)	5 (12.8)	1 (2.6)	10.354	0.006
No	26 (66.7)	34 (87.2)	37 (97.4)		

Table 5: Side effects associated with the use of study drugs

	Drug study group			χ^2	*P*
	Group I, *n* (%)	Group II, *n* (%)	Group III, *n* (%)		
Sedation					
Sedation grade 1	23 (59.0)	27 (69.2)	4 (10.5)	43.614	0.001
Sedation grade 2	15 (38.5)	12 (30.8)	20 (52.6)		
Sedation grade 3	1 (2.6)	0	14 (36.9)		
SpO_2					
Normal (≥95%)	39 (100.0)	39 (100.0)	38 (100.0)	NA	NA
Low (<95%)	0	0	0		
APGAR					
Normal (7-10)	39 (100.0)	39 (100.0)	38 (100.0)	NA	NA
Abnormal (0-6)	0	0	0		

NA: Not applicable, SpO_2: Arterial oxygen saturation

treated. In our study, the incidence of hypotension was similar across the groups. Furthermore, the dose of ephedrine was not different across the groups ($P > 0.05$).

Butwick *et al*. showed that when hypotension occurred, the incidence of IONV was more.[15] However, our study could not demonstrate that further study is needed to show whether this association between hypotension and IONV is true.

Cyclizine is known to have antiemetic effect with histaminic and anticholinergic properties which may cause sedation.[4] The sedative effect of cyclizine was observed in this study. Grimsehl *et al*. demonstrated that cyclizine for patients undergoing laparoscopic day-case gynecological surgery caused sedation among patients.[7] Sedation may be beneficial to anxious patients.

The APGAR scores of babies whose mothers received any of the study drugs were similar compared to the placebo group. Cyclizine is well tolerated even in pregnancy and has no neonatal and maternal respiratory depression.

Limitations

The authors could not determine the plasma levels of the study drugs in cord blood because of lack of facilities.

Conclusion

Intravenous cyclizine 50 mg administered before induction of spinal anesthesia significantly decreased the incidence of IONV in women undergoing cesarean section under spinal anesthesia.

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Conflicts of interest

There are no conflicts of interest.

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