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Metochlorpramide versus Midazolam in Avoiding Perioperative Nausea and Vomiting In Pregnant Women: A Clinical Comparative Study

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Abstract **Original Research Article**

Nausea and vomiting are common side effects in parturients undergoing caesarean delivery performed underspinal anaesthesia can be very unpleasant to the patients. The aim of the present study was to compare the efficacy and safety using intravenous metoclopramide and midazolam for the prevention of nausea vomiting in parturient undergoing cesarean section under spinal anesthesia. This prospective and randomized double blind study was conducted in 100 parturient aged between 21 and 40 years, ASA physical status É, scheduled to undergo elective cesarean section under spinal anesthesia. Parturient presenting for cesarean section with standardized 0.5% hyperbaric bupivacaine 2 ml spinal anesthesia were randomized to intravenous metoclopramide 10 mg (group I) or intrathecal midazolam 2mg (group II). The nausea, retching and vomiting were observed in 12%, 10%&4% patients in midazolam group, 52%, 20%& 2% patients of metoclopromide groups. Hypotension was observed in both groups, but respiratory failure was observed in 38% patients of midazlam group, but not found in metaclopromide group. Both drugs were effective in controlling the peri operative nausea and vomiting in this study.

Keywords: Midazolam, Metoclopramide, Caesarean delivery, Nausea and vomiting.

INTRODUCTION

Intraoperative nausea and vomiting (IONV) or postoperative nausea and vomiting (PONV) affecting women undergoing regional anesthesia for cesarean section is an important clinical problem since these techniques are used widely. The underlying mechanisms of IONV and PONV in the obstetrical setting mainly include hypotension due to sympathicolysis during neuraxial anesthesia, bradycardia owing to an increased vagal tone, the visceral stimulation via the surgical procedure and intravenously administered opioids.

The reported incidence of nausea and vomiting during caesarean performed under regional anaesthesia varies from 50% to 80% when no prophylactic antiemetic is given [1, 2]. Therefore, use of prophylactic antiemetics in parturients undergoing caesarean delivery is recommended by some authors [3, 4].

Many factors affect this complication such as patient mental status, the kind of surgery, stretch of visceral peritoneum, decompensated hypotension, using narcotics, and factors which tighten the uterus [5,6]. In patients, this complication makes perilous problems, by preventing nausea and vomiting, they feel consent and comfort [7]. Although in most cases nausea and vomiting are controlled spontaneously, sometimes it can result in complications such as aspiration, suture dehiscence, esophageal rupture, subcutaneous emphysema, and pneumothorax [8]. Nausea and vomiting resulted in different problems such as delayed discharging from postanesthesia care unit, high length of hospital stay, high risk of aspiration, and serious problems. Ability to recognize which patient is in the high risk for nausea and vomiting and to do preventive acts, can yield in patient consent in postanesthesia care unit because most of them believe that nausea and vomiting are the results of postoperative pain[9].

Compared to the plethora of literature about PONV, little attention has been paid to nausea and vomiting occurring during or after regional anesthesia. Especially in these patients, nausea and vomiting are also present during the surgical procedure causing discomfort for the parturient (and her escort), impair surgical conditions for the gynecologist and can lead to medical side effects such as aspiration of gastric

content, enhanced intra- and postoperative pain and even bleeding or surgical trauma [10].

Midazolam is a short-acting benzodiazepine with a rapid onset of action. In recent years, midazolam has been reported to be effective for prophylaxis of PONV by bolus administration before or after induction of anaesthesia or postoperative continuous infusion.

Metoclopramide has multiple sites of action. It is a prokinetic drug that acts by increasing the tone of the lower oesophageal sphincter. It also has an anti-dopaminergic action on the chemoreceptor trigger zone and at higher doses has an anti-serotonergic activity.

The aim of the present study was to compare the efficacy and safety using intravenous metoclopramide and midazolam for the prevention of nausea and vomiting in parturient undergoing cesarean section under spinal anesthesia.

MATERIALS AND METHODS

Results In this prospective, randomized, double-blind study, conducted at Mamata medical college, Khammam, Telangana state, after obtaining verification and informed consent from hospital Ethic Committee and understudied units, 100 female patients in Class 1 and 2 of American Statistical Association with the age range of 20–40 years who experienced cesarean with spinal anesthesia were selected. Patients with history of gastrointestinal disorders, motion disorders, drug hypersensitivity, glaucoma, preeclampsia, eclampsia, mental illness, and also patients, who took antiemetic medicines 24 h before section, were excluded from the research.

Antiemetic medicines were provided in the form of syringes containing 5 ml of normal saline solution and were injected by a second party who was unaware of what the syringes contain. The study drugs For Group 1 (midazolam 2mg) and Group 2 metoclopramide 10 mg was added to 5 ml diluted normal saline were prepared and injected intravenously 1–2 min after cord clamping.

In the operating room, patients were monitored primarily by noninvasive blood pressure monitoring, electrocardiogram, and pulse oximetry. All patients received between 15 and 20 ml for each 1 kg (up to 1500 ml) normal saline before any treatment. Spinal anesthesia was injected via a 25-gauge needle, in a sitting position, and through a space between the third and fourth lumbar vertebrae, 0.5% hyperbaric bupivacaine 2 mls was injected in subarachnoid space. Patients were placed in backward sleeping position and they were prevented from hypotension. Patient's bed was rotated to the left between 15° and 20° to prevent from aortocaval compression by the uterus. The patient received 2–3 L oxygen/min through a face mask. Every 1–3 min, patient's pressure was measured and it was used from 5 to 10 mg intravenous ephedrine or increasing the speed of infusion of normal saline to prevent from hypotension, if systolic blood pressure is below 100 mm Hg or more than 20% decrease in initial systolic blood pressure. Maternal bradycardia (defined as heart rate less than 60 beats/min) was treated with IV atropine 0.5 mg. The surgical technique was uniform for all patients. Duration of completion of surgery was recorded.

Nausea and vomiting cases were analyzed and recorded for intra- and post-operation. The patients were evaluated for side effects including sedation, respiratory depression, and nausea and vomiting, by a researcher who was blinded to the details of the study until 3 hours after the end of surgery.

Assessment for PONV was continued every 4 hours until the first 24 h. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit**;** retching was defined as the laboured, spasmodic, rhythmic contractions of the respiratory muscles without the expulsion of gastric contents; vomiting was defined as the forceful expulsion of gastric contents from the mouth.

Metoclopramide 10 mg was administered as rescue antiemetic with the occurrence of two or more emetic episodes. The details of any other adverse events due to the study drug were recorded. The neonate was evaluated using the neurologic and adaptive capacity score (NACS) within 30 minutes after delivery and at 2 hours of age. Data were placed in prepared forms and were analyzed statistically.

The collected data were analyzed by SPSS for Windows, version 20.0 (SPSS, Chicago, IL, USA). In order to analyze the data, Fisher's exact test, Chi-square, and Fisher's exact test were used. In all comparisons, the significant level was considered <0.05.

RESULTS

The present clinical study consists of 100 parturients divided into two groups, Group 1 (midazolam 2mg) and Group 2 (metoclopramide 10 mg). The demographic data was shown in table 1. No significant differences were noted in demographic characteristics.

Table-1: Demographic data

Parameter	Group-1 Midazolam	Group-2 metoclopramide
No	50	50
Primigravida	22	19
Multiparous	28	31
Age (years)	23.38 ± 2.47	22.48 ± 2.20
Height (cms)	160.07 ± 4.95	160.18 ± 4.82
Weight (kgs)	60.48 ± 2.48	60.02 ± 2.02
Gestation age in weeks	39±1	39±1
Duration of surgery	54.52±10.45	53.34±8.97

The level of anaesthesia was considered sufficient for the surgical procedure because no patient had a sensory level below T4–T5. The amount of ephedrine used for the treatment of hypotension was similar between the groups.

Table-2: Side effects comparison in two Groups

	Midazolam	Metoclopramide
Hypotension	10%	8%
Respiratory depression	38%	0%
Nausea	12%	52%
Retching	10%	20%
vomiting	4%	2%
Patient satisfaction	98%	90%

The sedation scores showed that the patients in midazolam group showed a sedation level between 3 and 5, but the patients in metoclopramide group had a sedation score between 1 and 3. The neonatal outcome was assessed by APGAR scoring system at 1min and 5min and NACS at 15 min and 2 hours

Table-3: The comparison of APGAR and NAC scores

APGAR	1 Minutes		5 Minutes	
Group	Group-1	Group-2	Group-1	Group-2
Mean	7.36±1.01	7.7±0-98	9.8±1.2	9.6±0.92
NACS	15 Minutes		2 hours	
Group	Group-1	Group-2	Group-1	Group-2
Mean	37.36±0.97	38.1±1.02	37.85±0.87	37.9±0.95

Unpaired student t test results found to be same for both 1min and 5min. P value and statistical significance. The two-tailed P value equals 0.2547. By conventional criteria, this difference is considered to be not statistically significant. Neonatal Apgar Scores and Neurologic and Adaptive Capacity Score (NACS) did not differ amongst the study groups (table 6). Thus, it seems unlikely that there were any neonatal adverse effects related to the use of intrathecal midazolam or metaclopromide.

DISCUSSION

Nowadays, about 7% of all surgical procedures worldwide are cesarean sections [11] and the majority of them are performed with neuraxial blockades, i.e, epidural anesthesia, spinal anesthesia or a combined spinal–epidural anesthesia.

Current literature indicates a high incidence of IONV during CS under SPA up to 80% [12]. Pregnant women are already likely to suffer from nausea and vomiting because of the pregnancy itself. This is applicable not only to the first 3 months of pregnancy but also to the third and last trimester due to the reduced tone of the esophago-gastric junction and an increased intra-abdominal pressure [13].

As mentioned earlier, in most cases, a cesarean delivery is performed with neuraxial analgesia techniques [14] such as SPA or EDA. In addition, CSE analgesia is frequently used. Established medications used for an SPA or EDA (local anesthetics and opioids) have a regional effect; they do not pass the placenta to a large extent and presumably do not cause major unintended (adverse) effects to the fetus. But there are also disadvantages regarding neuraxial techniques: The injected local anesthetic does not only specifically block the pain fibers but also leads to a vasodilatation by affecting sympathetic efferences. Due to the induced temporary sympathicolysis, blood pressure fluctuation in terms of significant hypotension can occur. On top of that, the increased vagal tone entails bradycardia which is often accompanied with nausea and vomiting [15].

In our study, rapid fluid infusion with addition of administration of infusion of ephedrine 10 mg was performed for the prevention of maternal hypotension. Some authors recommended the prophylactic infusion of ephedrine for prevention of maternal hypotension [15].

In this we evaluated the IONV using two drugs like midazolam and metachlopromide. The nausea, retching and vomiting were observed in 12%, 10%&4% patients in midazolam group, 52%, 20%& 2% patients of metaclopromide groups. Both drugs were effective in controlling the IONV in this study.

IT midazolam 2 mg and metachlopromide reduced the incidence emetic episodes to 40 percent, which are in agreement with the observations other studies [16,17].

Tarhan *et al*. [18]in their study found an incidence of 66% nausea, 10% retching, 10% vomiting in the group of patients undergoing caesarean section under spinal anaesthesia who received the infusion of midazolam, The results of their study show that the incidence of nausea is higher in the beginning of the operation: 53.3% nausea before delivery versus 10% nausea in post operatively.

Rudra P, Rudra A [19]. Incidence of intraoperative and early postoperative nausea-vomiting was 75% with placebo, 40% with midazolam and 25% with fentanyl (P values with placebo < 0.05, while that between midazolam and fentanyl > 0.05). Adverse events caused by the study agents did not differ significantly.

Jabalameli *et al*. [20] analyzed the effect of midazolam alone and ondansetron alone and also in combination with each other on nausea and vomiting of patients who experienced cesarean with spinal anesthesia. They concluded that nausea and vomiting in patients who received intravenous ondansetron + midazolam were more than the other two groups.

Lee *et al*. [21] in their study compared the prophylactic anti-emetic efficacy of midazolam 2mg and ondansetron 4 mg in 90 patients scheduled for minor gynaecological surgery. They did not find a significant difference between the incidence of nausea and vomiting between the two groups.

Habib *et al*. [22] during a research for analyzing the effect of metoclopramide alone, in combination with ondansetron, adding to infusion of phenylephrine and comparing it with using infusion of phenylephrine alone in patients, who experienced elective cesarean with spinal anesthesia considering nausea and vomiting, concluded that using metoclopramide + ondansetron decreases nausea and vomiting compared to the other groups. The effect of ondansetron was also significant and decreases nausea and vomiting compared to patients who received dexamethasone. However, in recovery room there was not any significant difference between the two groups.

In Lusso *et al.* study [16] Patients in the group receiving metoclopramide had a significantly lower incidence of nausea and vomiting both before and after delivery than the control group (14% versus 81% overall).

In a meta-analysis [23], Administration of metoclopramide (10 mg) resulted in a significant reduction in the incidence of ION and IOV when given before block placement [relative risk (RR) (95% confidence interval, 95% CI)¼ 0.27 (0.16, 0.45) and 0.14 (0.03, 0.56), respectively] or after delivery [RR (95% CI)¼0.38 (0.20, 0.75) and 0.34 (0.18, 0.66), respectively]. The incidence of early (0 –3 or 0–4 h) PON and POV [RR (95% CI)¼ 0.47 (0.26, 0.87) and 0.45 (0.21, 0.93), respectively] and overall (0–24 or 3–24 h) PON (RR 0.69; 95% CI 0.52, 0.92) were also reduced with metoclopramide. Extra-pyramidal side-effects were not reported in any patient. In conclusion, this review suggests that metoclopramide is effective and safe for IONV and PONV prophylaxis in this patient population.

The frequency of intraoperative nausea and vomiting was lower in the midazolam group compared with metoclopramide (15% versus 52.5%). Sedation scores within 3 hour postoperatively were significantly lower in the metoclopramide group. The frequency of respiratory depression was higher in midazolam group. There were some episodes of respiratory depression (respiratory rate of less than 10 bpm) in 17 patients in the midazolam group at the time of surgery treated by verbal stimulation, but no respiratory depression was seen in metoclopramide group. Neonatal outcome was similar in the two groups and all the neonates had Apgar scores > 8 at one and five minutes [24].

CONCLUSION

Intrathecal midazolam 2mg and metoclopramide 10mg both significantly reduces the incidence of nausea vomiting when administered with 0.5% hyperbaric bupivacaine for cesarean section under spinal anesthesia. The nausea, retching and vomiting were observed in 12%, 10%&4% patients in midazolam group, 52%, 20%& 2% patients of metaclopromide groups. Hypotension was observed in both groups, but respiratory failure was observed in 38% patients of midazlam group, but not found in metaclopromide group.

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