Original Article

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A Comparative Study of Intrathecal Midazolam and Intravenous Metoclopramide to Prevent Nausea and Vomiting During Elective Cesarean Delivery Under Spinal Anesthesia

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Abstract

Background: The antiemetic efficacy of metoclopramide and midazolam was shown before. The aim of the present study was to compare the efficacy and safety using intravenous metoclopramide and intrathecal midazolam for the prevention of nausea-vomiting in parturient undergoing cesarean section under spinal anesthesia. *Methods:* This prospective and randomized double blind study was conducted in 100 parturient aged between 21 and 30 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 incidence of nausea-vomiting and any other adverse effect were recorded during intraoperative and early postoperative period and compared between two groups by using chi-square test. *Results:* The incidence of nausea-vomiting was 36% with intravenous metoclopramide and 10% with intrathecal midazolam. No clinically adverse events caused by study agents were observed in either group. *Conclusion:* Intrathecal midazolam 2mg significantly reduces the incidence of nausea-vomiting when administered with 0.5% hyperbaric bupivacaine for cesarean section under spinal anesthesia.

Keywords: Nausea; Vomiting; Cesarean Section; Spinal Anesthesia; Metoclopramide; Intrathecal Midazolam.

Introduction

Perioperative nausea-vomiting is a frequent complains during spinal anesthesia for cesarean section and can occur in as many as 66% of cesarean section [1]. This can be distressing to patients and may increase the risk of gastric aspiration [2]. Various agents like droperidol, metoclopramide, ondansetron etc have been used to decrease this complain with variable results. However, their use has been discouraged because of their side effects such as intense sedation, restlessness, dystonic reactions and extrapyramidal symptoms [3-7] in addition to high cost [8].

Metoclopramide is in use as an antiemetic for many years. Intrathecal midazolam has been shown to reduce the incidence of nausea-vomiting in patients undergoing cesarean section [9, 10].

We designed this randomized, double blinded study to assess and compare efficacy of intravenous metoclopramide and intrathecal midazolam for the treatment of nausea-vomiting in parturient presenting for cesarean section under spinal anesthesia.

Methods

After obtaining approval from institutional ethical committee and written informed consent, 100 ASA physical status I, full term parturient aged 21 to 30 years, presenting for cesarean section under spinal anesthesia were included in the study. Pregnant patients with history of motion sickness, hyperemesis gravidarum, contraindication to regional anesthesia or sensitivity to any study drugs were excluded from the study.

Parturient were fasted overnight and received tab ranitidine 150 mg orally with sips of water as premedication 90-100 min before surgery. On arrival to operative room, peripheral intravenous access was secured with 18G cannula and patients were preloaded with ringer lactate solution at 20 ml/kg before spinal anesthesia. Routine monitoring

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devices were attached and baseline blood pressure, heart rate, ECG and pulse oximetry values were recorded. Spinal anesthesia was performed by using 25G whitacre needle at L_2-L_3 or L_3-L_4 interspace in left lateral decubitus position. The patients were randomly allocated into two groups of 50 each to receive one of the medications according to group.

Group I: Intravenous normal saline 2ml and intrathecal 2ml of hyperbaric bupivacaine 0.5% + 0.4 ml of midazolam + 0.1ml of normal saline.

Group II: Intravenous metoclopramide 2ml (10mg) and intrathecal 2ml of hyperbaric bupivacaine 0.5% + 0.5 ml saline.

Study drugs were prepared by an anesthesiologist not involved in this study. Immediately after intrathecal injection, patients were placed supine with left uterine displacement All patients received supplemental oxygen via facemask. NIBP, HR, SpO_2 were performed at 2 min interval for 10 min, then 5 min interval for rest of the procedure. The level of sensory blockade was recorded 10 min after intrathecal injection. Hypotension was treated with intravenous ephedrine (5-15mg). Vomiting or retching by patients in either study group was treated with 4mg of intravenous ondansetron. Intravenous fentanyl 50 µg was used to treat the pain. Intraoperative and postoperative nausea-vomiting were assessed by an observer blinded to treatment group allocated. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as labored, spasmodic, rhythmic contraction of respiratory muscle without the expulsion of gastric content; vomiting was defined as forceful expulsion of gastric content from the mouth [3]. These were assessed according to the Belville´s score [11] (0= no nausea; 1= nausea; 2= retching and 3= vomiting). The neonates were evaluated using APGAR score. Data were reported as mean ± SD or percentage. The statistical analysis was done by Student …t test and Chi-square test. A $p < 0.05$ was considered as significant.

Results

Maternal demographics were not different between groups [Table-1]. The level of anesthesia was considered sufficient for the surgical procedure as an adequate sensory block up to T6 was documented in all patients. There were no significant differences in blood pressure and heart rate between two groups. Hypotension was noted in 9 (18%) patients in group II compared to 7 (14%) patients in group I as shown in Table-2. Hypotension was treated with intravenous fluids and injection ephedrine. No significant difference in ephedrine use amongst the study group was observed.

During perioperative period the incidence of emetic episodes was significantly lower in group I, where 5 (10%) parturient develop emesis compared to 18 (36%) parturient in group II who had emesis [Table- 3].

Neonatal outcome were similar in both groups [Table- 4].

Table 1: Maternal demographics

Parameters	Group I (n = 50)	Group II (n = 50)
Age (years)	24.18 ± 3.08	23.66 ± 3.13
Weight (kg)	60.41 ± 6.93	62.10 ± 7.63
Gestational age (week)	38 ± 0.60	38.± 1.77
Multiparous (n)	8	7
Baseline blood pressure (mm Hg)	125 ± 7.21	115 ± 11.18
Systole		
Diastole	80 ± 6.01	80 ± 8.16
Pulse rate / min.	85.5 ± 8.73	88.8 ± 12.03

Values are mean ± SD or number of patients.

Table 2: Operative management

Parameters	Group I (n = 50)	Group II (n = 50)
Duration of surgery (min)	54 ± 17.21	57.5 ± 15.10
Duration of exteriorization of uterus (min)	18.75 ± 5	17.5 ± 4.86
Hypotension	9 (18%)	7 (14%)
Apgar score	8 ± 0.64	8 ± 0.64
At 1 min		
At 5min	10	10

Values are mean ± SD or number of patients

Table 3: Incidence of emetic episodes

Emetic episodes	Group I (n = 50) n (%)	Group II (n = 50) n (%)
No Nausea	45 (90%)	32 (64%)
Nausea	3 (6%)	8 (16%)
Retching	1 (2%)	6 (12%)
Vomiting	1 (2%)	4 (8%)

n = number of patients

Discussion

Perioperative nausea-vomiting commonly occur during cesarean section under spinal anesthesia [1]. The etiology of perioperative nausea-vomiting is multifactorial and includes progesterone induced reduction in lower esophageal sphincter tone, increased intragastric pressure, hypotension, exteriorization of uterus and visceral stimulation. These problem may accompanied by visceral pain, that stimulate vagal afferents which occur despite apparently adequate dermatological sensory blockade [2]. Various drugs have been used to prevent perioperative nausea-vomiting, however, either undesirable effects or cost of agents limited their routine use. Metoclopramide is in use as an antiemetic for many years. Antiemetic effect of metoclopramide is well established to decrease intraoperative nausea-vomiting during cesarian section performed with spinal anesthesia; however it may produce extrapyramidal symptoms [7].

Metoclopramide has multiple site of action. It is a prokinetic drug that act by increasing the tone of lower esophageal sphincter. It also has an antidopaminergic action on chemoreceptor trigger zone and at higher dose has an antiserotonergic activity [12, 13].

The mechanism of antiemetic effect of midazolam has not been completely understood. It seems that reduction in anxiety and decrease in dopaminergic input to chemoreceptor trigger zone (CTZ) may be mechanism by which it act [14]. Midazolam may reduce the reuptake of adenosine, which lead to adenosine mediated reduction in the synthesis, release and postsynaptic action of dopamine at the CTZ. Also adenosine reduces dopaminergic neuronal activity and 5-HT_3 release by binding to the gama-amiobutyric acid (GABA) receptor [15].

Intrathecal midazolam have been reported to provide improved intra and postoperative analgesia and thereby decrease discomfort from intraoperative peritoneal manipulation which may initiate emetic episode [16].

In present study, we had compared the efficacy of intravenous metoclopramide and intrathecal midazolam to minimize the incidence of nausea-vomiting in cesarean section. The result of our study revealed that intrathecal midazolam 2mg significantly reduced the incidence of nausea-vomiting compared to intravenous metoclopramide in cesarean section under spinal anesthesia. The lesser incidence of nausea-vomiting in intrathecal midazolam group may be due to improved intraoperative analgesia produced by intrathecal midazolam and thus avoiding the initiation of nausea-vomiting by peritoneal traction, exteriorization of uterus and visceral pain [17].

Our results are in collaboration with Rudra P and Rudra A [18] who concluded that intrathecal midazolam significantly minimizing the incidence of nausea-vomiting during intraoperative and postoperative period in cesarean delivery.

In our study few patients had hypotension in both groups which was treated with intravenous ephedrine. There was no significant difference in ephedrine requirement amongst both groups. Neonatal outcome was similar in both groups. Therefore in this study, intrathecal midazolam had no adverse impact on neonatal condition.

Our results allow us to conclude that the co-administration of intrathecal midazolam 2mg with 0.5% hyperbaric bupivacaine in the spinal anesthesia significantly reduces the incidence of nausea-vomiting and superior to intravenous metoclopramide for the prevention of perioperative nausea-vomiting during cesarean section under spinal anesthesia. Moreover, as midazolam is cost effective, making it an attractive choice for routine use.

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