Section: Anaesthesiology

Original Research Article

COMPARATIVE STUDY OF INTRATHECAL FENTANYL AND MIDAZOLAM FOR PREVENTION OF NAUSEA AND VOMITING DURING CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA

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ABSTRACT

Background: Nausea and vomiting are the most unavoidable adverse effects during cesarean delivery under spinal anesthesia. Hence, lipophilic opioids have been used intrathecally to minimize PONV. **Materials and Methods:** Out of 96 patients, 32 patients were grouped in three—group I received intrathecal placebo, group II received IT midazolam 2 mg, and group III received IT fentanyl 12.5 mg. Study agents were co-administered along with 2.0 ml hyperbaric pubivacine (0.5%). **Result:** The emetic episodes were least in group III—nausea 4 (4.1%), retching 2 (2.0%), and vomiting 1 (1.0%)—followed by group II, which had 7 (7.2%) cases of nausea, while the highest incidence was in group I. Adverse reactions like shivering were 0% in group III, 2 (2.2%) in group II, and 3 (3.3%) in group I, but pruritus was 3 (3%) only in group III, and neonatal effects like Apgar scores and NACS scores were quite normal in neonates belonging to all three groups. **Conclusion:** It is proved that midazolam or fentanyl significantly minimizes the incidence of nausea and vomiting during the intraoperative and early postoperative periods during cesarean delivery.

INTRODUCTION

Nausea and vomiting remain a big problem in cesarean delivery under spinal anesthesia. Many pharmacological agents diminish or regulate PONV, but all have significant adverse effects.[1] Recently intrathecal (IT) administration of lipophilic opioids such as fentanyl and benzodiazepines like midazolam has been reported to minimize the incidence of PONV in cesarean delivery under spinal anesthesia.[2] Neither of the two pharmacological agents has been known to possess antiemetic properties. Probably they reduce the incidence of emesis by improving the quality and duration of pain relief with 0.5% bupivacaine.[3] However, the benefits of analgesia have to be balanced against their known adverse effects.[4] Hence, an attempt is made to compare the two lipophilic opioids so the pros and cons of both drugs can be evaluated.

MATERIALS AND METHODS

96 (Ninety-six) full-term pregnant patients admitted at the obstetrics and gynecology department of Government medical college, Nagarkurnool ,Telangana 509360 were studied.

Inclusive Criteria: Full-term parturient of ASA physical status I, scheduled for elective cesarean delivery. The patients who gave their consent in writing for the study were selected.

Exclusive Criteria: The patients having a history of hyperemesis gravidarum and contraindications to regional anesthesia. Patients who had GIT diseases, fetal prematurity (36 weeks), or those who had received antiemetics 24 hours prior to surgery and ASA physical status II and III patients were also excluded from the study.

Methods: The parturient was given a 150 mg ranitidine tablet orally as premedication 90-100 minutes before surgery. The patients were attached to routine monitoring devices, and baseline blood pressure, heart rate, ECG, and pulse oximetry values were recorded. Ringer lactate solution 20 ml/kg was given IV to every patient before spinal anesthesia.

A dural puncture was performed at the L3-L4 interspace with a 25-gauge spinal needle. The blocks were performed with the patient in the lateral decubitus position. The patients were randomly allocated using a random number table to receive intrathecally one of the medications. The study solutions were constituted of 2 ml of hyperbaric bupivacaine (0.5%) plus 0.5 ml of normal saline (Group I), 2 mg of midazolam (Group II), and 12.5

µg of fentanyl (Group III) in total. The volume of study agents was 2.5 ml; the study agents were injected IT by an anesthesiologist.

After injection of the study solution, the patients were turned to a supine position with a 15° wedge under the right hip for left uterine displacement. Oxygen (3 liters) was administered via face mask. The decrease in systolic blood pressure (more than 20% from baseline values and/or less than 90 mmHg) immediately after spinal injection was treated by increasing the rate of intravenous fluid administration, by exaggerating the uterine tilt, and by injecting 5 to 10 mg of IV ephedrine. The level of analgesia was assessed by pinprick before surgical incision. The surgical technique was uniform for all patients and included exteriorization of the uterus. 10 IU of oxytocin was given intravenously after delivery of the baby and clamping of the umbilical cord. An attending pediatrician assessed the neonatal Apgar scores at 1 and 5 minutes after delivery. Postoperatively, patients were observed for 3 hours, and pulse rate, oxygen saturation, and blood pressure were monitored every 10 minutes. A urinary catheter was left in situ according to our institutional protocol and was removed after 24 hours.

Intraoperative, post-delivery emetic episodes were recorded by direct questioning. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as the labored, 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. They were assessed according to the Bellville's score (5) (0=no nausea, 1=retching, 2=retching, and 3=vomiting).

Metoclopromide was long administered as a 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.

The predetermined sample size was chosen by using power analysis based on the assumption that the incidence of no emetic symptoms or signs (which will be considered as the primary end point) in patients receiving placebo will be 40%. An improvement from 40 to 75% will be considered as clinically important with α=0.05 and β=0.2. The analysis showed that 30 patients per group will be sufficient.

The duration of the study was January 2025 to July 2025.

Statistical Analysis: To compare the incidence of emetic symptoms of three groups, the ANOVA test was applied. Episodes of emetic symptoms of emetics, in evidence of adverse intraoperative events, were classified with percentages. The statistical analysis was carried out in SPSS software.

RESULTS

Table-1: Comparison of Mean parameters among three study groups in operative management

a) Induction management (in minutes): 13.2 (±0.2) in groups-I, 12.2 (±0.3) in group-II, 13.5 (±0.4) in group III, F value is 153 and p<0.001.
b) Skin incision delivery interval (in minutes): 7.6 (±0.2) in group-I, 6.5 (±0.1) in group-II, 8.3 (±0.2) in group-III, F value is 878 and p<0.001.
c) Uterine incision – Delivery internal (in minutes): 37.2 (±0.2) in group-I, 35.3 (±0.2) in Group-II, 43.5 (±0.2) in group-III, F value is 10.2 and p<0.001.
d) Duration of surgery (in minutes): 41.6 (±0.6) in group-I, 43.2 (±0.2) in group-II, 45.2 (±0.32) in group-III, F value is 946 and p<0.001.
e) Duration of uterus exteriozed (in minutes): 20.2 (±0.2) in group-I, 21.3 (±0.5) in group-II, 19.2 (±0.2) in group-III F value 320 and p<0.001
f) Total Ephedrine dose (mg): 13.2 (±0.8) in group-I, 8.2 (±1.3) in group-II, 13 (±0.6) in group-III and F value is 285 and p<0.001.

Table-2: Classification of patients as per their Emetic Episodes

- No Nausea: 8 (8.3%) in group-I, 20 (20.8%) in group-II, 25 (26.06%) in group-III,
- Nausea: 11 (11.4%) in group-I, 7 (7.2%) in group-II, 4 (4.1%) in group-III
- Retching: 8 (8.3%) in group-I, 3 (3.12%) in group-II, 2 (2.0%) in group-III
- Vomiting – 5 (5.2%) in group-I, 2 (2.1%) in group-II, 1 (1.01%) in group-III

Table-3: Comparison of adverse intra-operative events

Hypotension: 15 (15.6%) in group-I, 18 (18.7%) in group-II, 17 (17.7%) in group-III.

Shivering: 3 (3.1%) in group-I, 2 (2.02%) in group-II, zero in group-III

Pruritis: only observed in group-III 3 (3.1%)

Rate of respiration: 14 in group-I, 12 in group-II, 12 in group-III

Table-4: Study of Neonatal effects Apgar score:

- At 1st Minute: 9 (8.10) in group-I, 9 (6.10) in group-II, 9 (7.10) in group-III.
- At 5 Minutes: 10 (9.10) in group-I, 10 (7.10) in group-II, 10 (8.10) in group-III.

NACS scores

At 15 Minutes: 37.3 (±1.6) in group-I,

At 2 hours: 30.2 (± 1.2) in group-I, 37.6 (±1.2) in group-II, 37.3 (± 2.2) in group-III

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Table 1: Comparison of mean parameters among study groups in operative management Total No. of patients: 96

Parameters	Mean ±SD				
	Group I (32)	Group II (32)	Group III (32)	F value	P value
Comparison of Induction Management (min)	13.2 (±0.2)	12.22 (±0.3)	13.5 (±0.2)	153	<0.001*
Skin Incision – Delivery Interval (min)	7.6 (±0.2)	6.5 (±0.1)	8.3 (±0.2)	878	<0.001*
Uterine Incision – Delivery Interval (min)	37.2 (±0.2)	35.3 (±0.4)	43.5 (±0.2)	10.2	<0.001*
Duration Surgery (min)	41.6 (±0.5)	43.2 (±0.3)	45.3 (±0.3)	946	<0.001*
Duration of exteriozed (min)	20.2 (±0.2)	21.3 (±0.5)	19.2 (±0.2)	320	<0.001*
Total Ephedrine dose (mg)	13.2 (±0.8)	8.2 (±1.3)	13 (±0.6)	285	<0.001*

Table 2: Classification of patients according to their emetic episodes Total No. of patients: 96

Emetic Episodes	Group I (32)	Group II (32)	Group III (32)
No Nausea	8 (8.3%)	20 (20.8%)	25 (26.04%)
Nausea	11 (11.4%)	07 (7.2%)	4 (4.1%)
Retching	8 (8.3%)	03 (3.12%)	2 (2.0%)
Vomiting	5 (5.2%)	02 (2.0%)	1 (1.0%)

Table 3: Comparison of adverse into operative events Total No of patients: 96

Adverse events	Group I (32)	Group II (32)	Group III (32)
Hypotension	15 (15.6%)	18 (18.7%)	17 (17.7%)
Shivering	3 (3.12%)	02 (2.0%)	0
Pruritis	0	0	3 (3.1%)
Rate of respiration (min/square)	14	12	12

Table 4: Neonatal effects Total No of patients: 96

Particular	Group I (32)	Group II (32)	Group III (32)
Apgar scores			
a) 1 minutes	10 (8.10)	9 (6.10)	9 (7-10)
b) 5 minutes	10 (9.10)	10 (7-10)	10 (8-10)
NACS Scores			
15 min	37.3 (±1.6)	37.2 ±1.2	37.4 (±1.4)
2 hours	30.2 (±1.1)	37.6±1.2	37.3±2.2

NACS = Neurologic and Adaptive capacity scoring

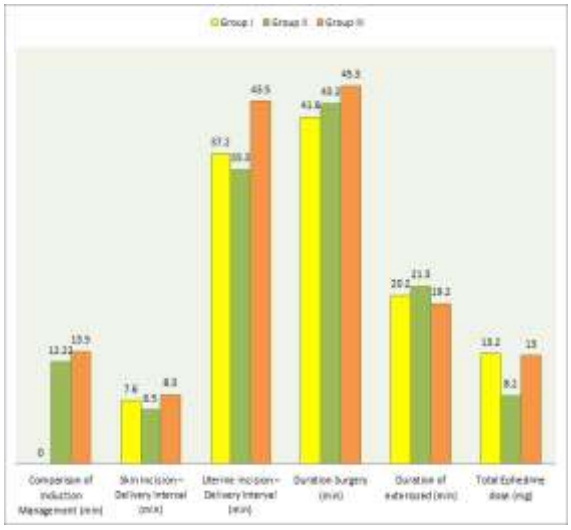

Figure 1: Comparison of mean parameters among study groups in operative management

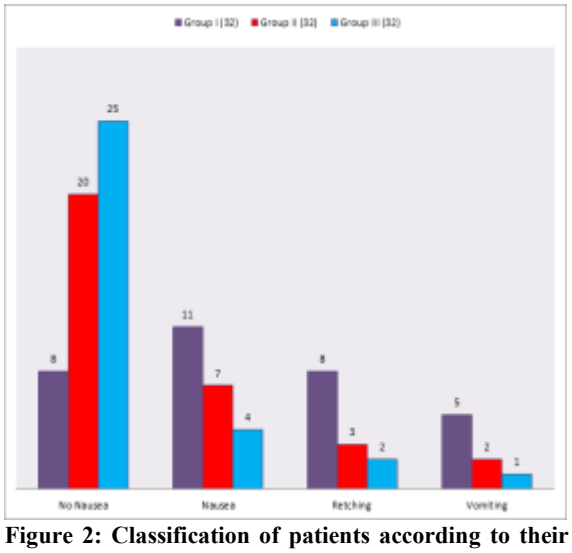

Figure 2: Classification of patients according to their emetic episodes

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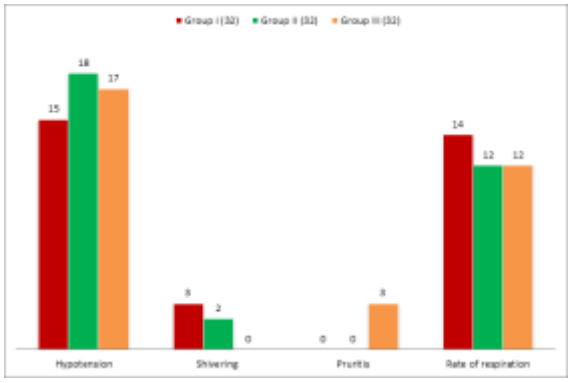

Figure 3: Comparison of adverse into operative events

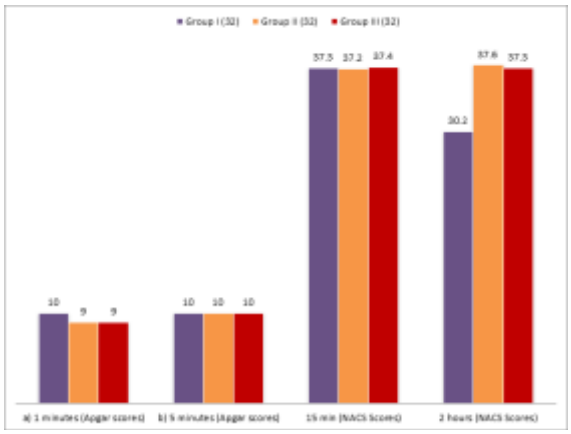

Figure 4: Neonatal effects

DISCUSSION

Present comparative study of intrathecal fentanyl and midazolam for prevention of nausea and vomiting during the cesarean delivery under spinal anesthesia in the Telangana population. In the comparison of mean parameters among three groups in operative management. Delivery interval mean value was 8.3 (±0.2) uterine incisions. The delivery interval (in minutes) mean value was 43.5 (±0.2); the duration of surgery, 45.2 (±0.3), was quite higher in group III, and the p-value was highly significant (Table 1). In the classification of emetic episodes, retching was 2 (2.01%), vomiting was 1 (1.0%), and nausea was 4 (4.4%) in group III, followed by group II (Table 2). Adverse reactions were also lesser in group III, followed by group II (Table 3). Apgar scores and NACS scores were also highly significant (Table 4). These findings are more or less in agreement with previous studies.[5,6,7]

Nausea and vomiting commonly occur during cesarean section (CS) performed with spinal anesthesia (SA). It is frequently related to intraoperative hypotension, peritoneal traction, and exteriorization of the uterus. These problems may be accompanied by visceral pain that stimulates vagal afferents, which occur despite apparently adequate dermatomal sensory blockade (8). It is reported that intra- and postoperative analgesia is necessary to decrease nausea and vomiting. Hence, intrathecal local anesthetics, including opioids like morphine, fentanyl, and benzodiazepines (for example, midazolam), to improve the postoperative analgesia and reduce PONV.[9]

Fentanyl, a phenyl piperidine derivative, is a synthetic μ opioid receptor agonist. Intrathecal fentanyl elevates the quality of spinal anesthesia (SA), increasing both the duration and intensity of SA and decreasing intraoperative nausea and vomiting.[10]

The antiemetic effect of benzodiazepine could be an action at the chemoreceptor trigger zone (CTZ), reducing synthesis and releasing the postsynaptic effect of dopamine. Midazolam decreases dopamine input at CTZ and decreases adenosine uptake, leading to adenosine-mediated reduction in dopamine synthesis.[11] Midazolam also produces postoperative pain relief for women undergoing CS in addition to antiemetic effects.

As hyperbaric bupivacaine is added to fentanyl, it reduces the severe hypotension, nausea, and vomiting.[12]

Nausea and vomiting were reported as high incidence in the placebo group (group I 75%). 40% in group II (40%) (in midazolam) and 25% in group III (in fentanyl); hence, midazolam or fentanyl significantly minimizes the nausea and vomiting episodes in cesarean delivery, but shivering was higher in the midazolam group as compared to the fentanyl group but higher in the placebo group. Intrathecal midazolam or fentanyl has prolonged duration analgesia and prolonged motor and sensory block without any significant hemodynamic compromise.

CONCLUSION

In the present study of all three groups, co-administration of fentanyl 12.5 mg or intrathecal midazolam 2 mg with 0.5% hyperbaric bupivacaine in the subarachnoid injectable to avoid intraoperative discomfort during peritoneal fraction and exteriorization of the uterus and thereby reduce intraoperative and early post-delivery nausea and vomiting. There was not any significant change in hemodynamic status and side effects in any group, including placebo. Such a study has to be conducted on a large number of patients to confirm present significant results.

Limitation of study: Owing to remote location of research centre, small number of patients and lack of the latest techniques, we have limited findings and results.

- This research paper was approved by Ethical committee sciences GMC Nagarkurnool, Telangana -509360.
- No Conflict of Interest
- Self Funding

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