COMBINED USE OF METOCLOPRAMIDEAND DEXAMETHASONE AS A PROPHYLACTIC ANTIEMETIC IN ELECTIVE CESAREAN SECTION UNDER SPINAL ANESTHESIA*

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Abstract

Background: Nausea and vomiting during regional anesthesia for cesarean section still remain a major problem. We compared the efficacy of dexamethasone plus metoclopramide with dexamethasone alone for preventing nausea and vomiting during and after spinal anesthesia for cesarean section in parturients.

Methods: The study was performed in 72 full term parturient women of ASA I & II (American Society of Anesthesiology Grade I & II), aged between 19 and 37 years with uncomplicated pregnancies. The group I (n = 36) received 8 mg of dexamethasone intravenously immediately when the surgery started, while group II (n = 36) received 8 mg of dexamethasone plus 10 mg of metoclopramide. The type and number of episodes of nausea and emesis were recorded, as well as any other adverse effects.

Results: During the intraoperative period, a complete response (no emesis, no rescue) was noticed in 83% of patients in Group I and in 86% of patients in Group II. The incidence of nausea during both intra and postoperative periods was not different between the two groups. Metoclopramide was associated with impaired taste and smell and hot flushes.

Conclusions: 10 mg of metoclopramide did not improve the incidence of emetic symptoms in patients undergoing cesarean section when combined with 8 mg of dexamethasone.

Introduction

Cesarean delivery under regional anesthesia has become increasingly popular over the past decade as a result of increased patient acceptability, improved fetal condition at birth and greater maternal safety[1,2].

Nausea and vomiting during regional anesthesia for cesarean section still remain a significant problem not only for the patient, but also for the surgeon and the anesthesiologist as well. The etiology of intraoperative nausea and vomiting is complex; it may be attributed to surgical stimulation, hypotension, vagal stimulation and uterotonic drugs. Patient demographic data and anesthetic technique also can play a role[3].

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A number of treatments has been introduced in order to reduce post operative nausea and vomiting (PONV), such as 5-HT3 antagonists (ondansetron and granisetron), dopamine receptor antagonists, and antihistamine drugs. However, each of these treatments is associated with critical limiting factors, namely cost with 5-HT3 antagonists, extrapyramidal symptoms with dopamine receptor antagonists, excessive sedation and tachycardia with antihistamine drugs[4].

Almost all previous researches on PONV prevention were using single prophylactic antiemetic drug. We hypothesized that a metoclopramide-dexamethasone combination is more effective than dexamethasone alone in reducing the incidence of emetic symptoms. To test this hypothesis, we compared the efficacy of dexamethasone plus metoclopramide with dexamethasone alone for preventing nausea and vomiting during and after spinal anesthesia for cesarean section in parturients.

Parturients and Methods

After local ethics committee approval and informed consent from the participants, the study was performed in 72 full term parturient women of ASA I & II (American Society of Anesthesiology Grade I & II), aged between 19 and 37 years with uncomplicated pregnancies, who were scheduled for elective cesarean delivery under spinal anesthesia. Exclusion criteria were contraindications for metoclopramide, use of antiemetic or antidepressive drugs, patient classified as American Society of Anesthesiologists grade III or IV, presence of extrapyramidal motoric disease such as malignant hyperthermia, hepatic insufficiency, pheochromocytoma, mechanical ileus or epilepsy, intended or probable postoperative administration of propofol, stomach tube, and current participation in another clinical trial.

The study period was between August 2010 and April 2011. Parturients were randomly assigned to the following study groups using a sealed envelope technique: Group I (n = 36) received 8 mg of dexamethasone intravenously immediately when the surgery started, while group II (n = 36) received 8 mg of dexamethasone plus 10 mg of metoclopramide intravenously at the beginning of the surgery. The drug solutions in all groups were prepared by one anesthesiologist and they looked identical. Another anesthesiologist, who was blinded to the study, gave the drugs.

All parturients received 1000 ml of lactated Ringer's solution IV over 30 min before spinal injection. All patients received oxygen via a face mask at a flow rate of three liters per minutes starting from the induction of spinal anesthesia. Patients were positioned in the left lateral decubitus or sitting position and a 25 gauge spinal needle was introduced through mid-line approach at the L3-L4 inter-space. Patients received a subarachnoid injection including 2 ml of 5% isobaric bupivacaine with 10 µg fentanyl. Surgery started when a sensory block up to T5 dermatome was obtained. Hypotension was defined as a reduction of more than 20% from baseline pressure or if systolic blood pressure was less than 90 mmHg and managed with intravenous lactated Ringer's solution and ephedrine bolus in 3 mg increments.

Each patient was observed by an anesthesiologist blinded to which antiemetic the patients had received and asked for the intra-operative and postoperative occurrence of nausea and vomiting.

The number of episodes of emesis and type were recorded. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit; Vomiting was defined as the forceful expulsion of gastric contents from the mouth[5].

Repeated vomiting within 1 to 2 minutes period was recorded as single emesis. The data were taken as follows:

- No vomiting: complete control
- 1 to 2 vomiting episodes: Nearly complete control
- 3 to 5 vomiting episodes: Partial control
- >5 vomiting episodes: Failure
- No nausea: 0
- Mild nausea: 1
- Moderate nausea: 2
- Severe nausea: 3

The details of any other adverse effects were noted throughout the study after general questioning

of the patients by the anesthesiologists or spontaneous mention by the patients. Severe nausea and vomiting was labelled as failure and rescue therapy was initiated with IV ondansetron and IV fluids.

Postoperative analgesia was provided with IV paracetamol and nefopam, the routine analgesic treatment in our institution.

Twenty four hours after surgery, the patients evaluated the general satisfaction. The evaluation was performed with a linear numerical scale ranging from 0 (complete dissatisfaction) to 10 (complete satisfaction).

Data are presented as mean ± standard deviation (SD). Parametric data were analyzed using unpaired tests. Non parametric data were analyzed using chi-square. A value of $p < 0.05$ was considered significant.

Sample size was predetermined by power analysis based on the expectation that the reduction of the incidence of PONV in the Group I would be 40%, with a 30% additional reduction in the Group II. The α error was set at 0.05, and β error at 0.2. According to power analysis, a sample size of 33 patients per group was considered adequate. We decided to enroll 36 patients per group.

Results

None of the 72 enrolled parturients was withdrawn for any reason.

The treatment groups were comparable with regard to maternal demographics (Table I) and operative management (Table II). The level of anesthesia was sufficient for the surgical procedure, and no patient had a sensory level below T3-5 (midclavicular line) as tested by pinprick. The amount of ephedrine administered for the treatment of hypotension was similar between the 2 groups. Apgar scores were superior to 8 in all neonates at 1 and 5 minutes.

Table I

Maternal Demographics

	Group I (n = 36)	Group II (n = 36)
Age (year)	26 ± 4	26 ± 5
BMI (kg/m²)	24 ± 2	24 ± 2
Multipara	12	13
Gestational age (week)	39 ± 1	39 ± 1

Values are mean ± sd or n. BMI: body mass index.

Table II

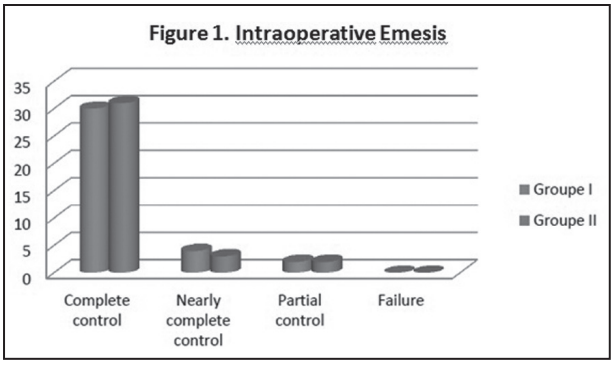
Operative Management

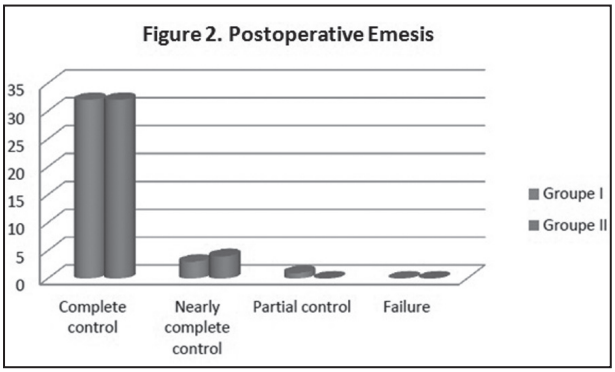
	Group I (n = 36)	Group II (n = 36)
Duration of surgery (min)	46 ± 14	44 ± 13
Previous cesarean section	7	8
Uterus exteriorized	2	2
Tubal ligation performed	6	5
Total ephedrine (mg)	5.5 (0-12)	6.5 (0-12)

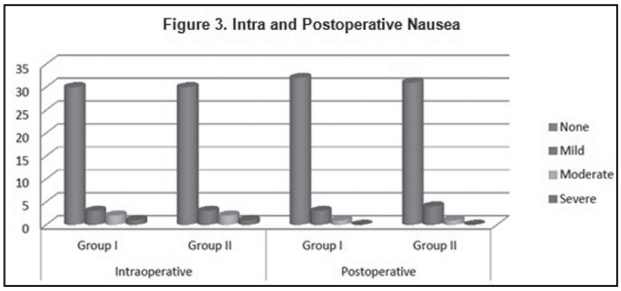
Values are mean ± sd, median (range), or n.

During the intraoperative period, a complete response (no emesis, no rescue) was noticed in 83% of patients in Group I and in 86% of those in Group II (Fig. 1). The corresponding rates during the first 24 h after surgery were 88% in both groups (Fig. 2). Thus, complete response during and after surgery was similar in Groups I and II.

The incidence of nausea in both intra and postoperative periods was not different between the two groups (Fig. 3). The occurrence of mild nausea was more common in postoperative period (19%) than







in intraoperative period (16%), while the incidence of moderate nausea was slightly lower in postoperative period (5%) than in intraoperative period (11%) in all patients. No severe nausea was noted in postoperative period in both groups.

Hypotension incidence and sedation score were similar in the two groups. Metoclopramide was associated with impaired taste and smell (3 parturients), and hot flushes (3 parturients). The results were significant (Table III).

Table III
Adverse events

	Group I	Group II	P value
Events after Metoclopramide was given			
Hypotension	29	31	0.28
Tachycardia	24	26	0.36
Skin reaction	0	0	1
Postoperative events			
Headache	3	2	0.73
Dizziness	1	1	1
Sedation	0	0	1
Dry mouth	2	3	0.73
Alteration of taste or smell (or both)	0	3	0.04
Itching	0	0	1
Skin reaction	0	0	1
Allergy	0	0	1
Delirium on awakening	0	0	1
Central anticholinergic syndrome	0	0	1
Dyskinesia or extrapyramidal symptoms	0	0	1
Hot flushes	0	3	0.04

Discussion

The incidence of emetic symptoms is high during the pregnancy because of increased concentration of progesterone in the system, which causes smooth muscle relaxation, decreases lower esophageal sphincter tone, decreases gastrointestinal motility and increases gastric secretion[6]. Additionally, there is a higher predisposition to intra operative nausea vomiting among patients at the end of their pregnancies, as a consequence of increased intra-abdominal pressure. Moreover, when these pregnant women undergo spinal anesthesia for cesarean section; an additional risk of intraoperative post delivery emetic symptoms is added; this can be attributed to post induction hypotension, which may lead to brainstem hypoxia and stimulation of vomiting center[7,8].

To avoid the influence of hypotension on the results, rapid fluid infusion, left uterine displacement, or administration of ephedrine were performed, so that the occurrence of hypotension, during and after cesarean section under spinal anesthesia, can be attributed to the drug combination.

Dexamethasone has been found to be effective in reducing the occurrence of PONV in adult patients undergoing major surgeries[9,10]. Dexamethasone modulates neurotransmitter or glucocorticoid receptor density in the nucleus of the solitary tract, the raphe nucleus and the area postrema. The onset of action after a single dose of four to height mg is about two hours and the duration is about 12 to 24 hours. It has also been used to reduce pain after caesarean delivery[11]. A quantitative systematic review of dexamethasone has recommended a dose of height mg for PONV prevention[9].

Metoclopramide, which is a dopamine and serotonin receptor antagonist, was discovered almost 40 years ago and has been used as an antiemetic since the 1960s[12,13].

Metoclopramide 10 mg IV is suggested to be the optimal dose for PONV following general anesthesia[13,14]. A quantitative systemic review recently showed that metoclopramide did not have significant anti-nausea effects or late anti-vomiting effects[13]. The anti-vomiting effect of metoclopramide was present only within 6 hours following its administration[13].

None of the currently available antiemetics is entirely effective, perhaps because most of them act through the blockade of one type of receptor[15]. Therefore, it is possible that a combination of antiemetics with different sites of activity would be more effective than one drug alone.

The use of 5-HT3 antagonists in prevention of PONV is more common nowadays. We were able to use ondansetron only as a rescue therapy due to lack of the product and its high cost.

We chose to evaluate the use of a metoclopramide-dexamethasone combination in comparison with dexamethasone alone for reducing nausea and vomiting in patients during and after spinal anesthesia for cesarean section.

Our results showed that 10 mg of metoclopramide did not improve the incidence of emetic symptoms in patients undergoing cesarean section when combined with height mg of dexamethasone. These results are in agreement with a multicenter study which recommended a combination of 8 mg of dexamethasone and highly dose of metoclopramide (25 or 50 mg)[16]. Unfortunately, this multicenter study did not evaluate the efficacy of combinating these two antiemetic therapies for reducing emetic episodes during cesarean delivery performed under regional anesthesia.

Patients receiving metoclopramide showed a significant increased incidence of impaired taste and smell, and hot flushes, but otherwise, no extrapyramidal symptoms or other unpleasant side effects were experienced. These events may cause a discomfort for parturients.

Our study has some limitations that might have influenced the findings. First, our sample size was small. The second deficiency in this study design is the failure to include a third group receiving metoclopramide alone.

Conclusion

Combined use of dexamethasone and metoclopramide as a prophylactic antiemetic did not show any significant results compared to the use of dexamethasone alone. In addition to that, the increase of the incidence of hot flushes and impaired taste and smell suggest reconsidering the utility of metoclopramide as a prophylactic antiemetic. A bigger sample or a third group receiving metoclopramide alone could lead to break new grounds.

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