

Research Article

Evaluation of Efficacy of Metoclopramide, Dexamethasone and Their Combination for the Prevention of Postoperative Nausea and Vomiting (PONV) in Patients Undergoing Cesarean Section

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Received: 12 April 2019; **Accepted:** 03 May 2019; **Published:** 10 May 2019

Abstract

Background: Nausea and/or vomiting following regional anaesthesia in pregnant females undergoing caesarean section is a major clinical problem. This study was conducted to compare the efficacy of metoclopramide, dexamethasone, and their combination for preventing intra operative & post-operative nausea and vomiting (PONV) following spinal anaesthesia given for caesarean section in patients.

Materials and Methods: A total of 120 full term pregnant females of ASA I & II grade with uncomplicated pregnancies were included in this prospective randomized double blind study. Patients were randomly allocated to three groups. The group D (n= 40) received 8 mg dexamethasone, group M (n=40) received 10 mg of metoclopramide while group D+M (n= 40) received 8 mg dexamethasone along with 10 mg of metoclopramide intravenously immediately before administration of spinal anaesthesia. Intraoperative and post operative emetic episodes (nausea, retching, and vomiting) was noted as well as any other adverse effects.

Results: During intraoperative period all parturients had PONV score 0. Postoperatively at first hour number of full responders in group D, M and D+M were 29/40 (72.5%), 30/40 (75%), 38/40 (95%) and the difference was statistically significant (Group D Vs Group D+ M, P value -0.013 and Group M Vs Group D+ M, P value-0.025). At 3rd hour postoperatively 9 patients in Group D, 8 patients in Group M and 1 in Group D+ M, had PONV score 1 (Group D Vs Group D+ M, P value -0.014 and Group M Vs Group D+ M, P value-0.029). No patient had any vomiting episodes over the time period of 24 hrs.

Conclusion: Combined use of dexamethasone and metoclopramide as a prophylactic antiemetic was significantly better for the prevention of PONV as compared to the use of dexamethasone and metoclopramide alone.

Keywords: Metoclopramide; Dexamethasone; PONV; Caesarean section

1. Introduction

Postoperative nausea and vomiting (PONV) is a very common complication after anaesthesia and surgery [1,2]. This complication is related to age, gender, drugs, hemodynamic changes, anaesthetic techniques [3]. PONV is an obnoxious experience that many patients find worse than pain [4-6], and even most of patients claim that suffering from pain is better than PONV [5]. Caesarean delivery performed under regional anaesthesia is associated with a relatively high incidence (50%-80%) of intraoperative and postoperative nausea and vomiting, when no prophylactic antiemetic is given [7, 8]. In spite of current advances to minimize PONV, the incidence of PONV during the first day varies between 20% and 30% [9]. Efficient prevention and management of PONV is a major concern post operatively [10]. A number of treatments has been planned in order to reduce PONV, such as 5-HT3 antagonists, dopamine receptor antagonists, and antihistamine drugs. Each of these treatments is associated with demerits, like cost with 5-HT3 antagonists, extrapyramidal symptoms associated with dopamine receptor antagonists, excessive sedation and tachycardia associated with antihistamine drugs [11]. Drug combinations are deemed to be more useful for balanced anti-emesis. The purpose of the present study was to test the hypothesis of a likely synergistic effect between dexamethasone (which was found to be better in decreasing nausea, [12] and act by supposedly decreasing 5-HT levels in the brain, [13, 14]) and the prokinetic drug metoclopramide (which act on central dopaminergic D2 receptors, central and peripheral 5-HT3 receptors, peripheral 5 HT4 receptors, [15]) for reducing emetic symptoms (nausea, retching, and associated vomiting) during post operative period following caesarean section after spinal anaesthesia.

2. Materials and Methods

After getting approval from the institutional ethical committee and an informed written consent from pregnant females scheduled for caesarean section, a prospective randomised double blind study was performed in 120 full term parturients of ASA grade I/II, aged between 18 and 35 years, weighing 50-75 kg, height 150-175 cm, and with uncomplicated pregnancies, scheduled for elective caesarean section following spinal anaesthesia. Exclusion criteria were contraindications or allergy for metoclopramide and dexamethasone, use of antiemetic or antidepressive drugs within 24 hrs prior to surgery, regional anaesthesia contraindicated,, patient classified as ASA grade III or IV, established hypertension or glucose intolerance, the presence of a gastrointestinal disease, and a propensity for motion sickness and/or previous PONV, presence of extrapyramidal motor disease, malignant hyperthermia, hepatic insufficiency, pheochromocytoma, mechanical ileus or epilepsy, and current participation in another clinical trial. The study period was between February 2018 and February 2019. Pregnant females were randomly distributed to three groups: The group D (n= 40) received 8 mg of dexamethasone, group M (n=40) received 10 mg of metoclopramide while group D+M (n= 40) received 8 mg dexamethasone along with 10 mg of metoclopramide

intravenously immediately before the administration of spinal anaesthesia. The drug solutions in all groups were administered by an anaesthesiologist who was unaware of the nature of the drug administered. After preloading with Ringer Lactate all pregnant females were given supplemental oxygen via a face mask at a flow rate of three litres per minutes. Routine standard monitoring were applied as per standard guidelines. Spinal anaesthesia was given with 2.5 ml of 0.5% bupivacaine (heavy) via a 26-gauge Whitacre needle at the L3-4 or L4-5 interspace, in the left lateral recumbent position through midline approach. The reduction in systolic BP (>20% from baseline and/or <100 mm Hg) immediately after spinal injection, was treated by increasing the rate of IV fluid administration and by injection of IV Mephentermine in 6 mg increments. In this way, maternal hypotension causing emetic symptoms before and after clamping the umbilical cord, was ruled out.

All patients received oxytocin 10 units as slow i.v infusion after delivery of the baby. For postoperative analgesia 100 ml (1 gm) of paracetamol infusion was given intravenously towards the end of surgery. Intraoperative and post delivery emetic episodes (nausea, retching, and associated vomiting) were analysed at the 1st, 3rd, 6th, 12th and 24th hrs postoperatively. The drug administrator and the patients were blinded to the study drug used. The severity of PONV was measured on a four-point (0-3) scoring system. PONV score 0=no nausea and no retching; 1=complaining of sickness and retching; 2=vomiting one or two times in 30 min; 3=vomiting more than two times in 30 min [16]. Nausea was termed 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 termed as the forceful expulsion of gastric contents from the mouth. The number of complete or total responders was recorded. Complete or total response was defined as no nausea, vomiting and/or retching and when there was no need of rescue anti-emetic medicines within 24 h. If vomiting occurred or PONV score was 2 or more, IV ondansetron 4 mg was given. Any need for additional drug and side-effects like headache, dizziness and drowsiness were recorded.

3. Statistical Analysis

Data was analyzed using IBM SPSS 21 software using ANOVA and chi-square test. Results were expressed in mean±SD. A P value<0.05 was considered as statistically significant.

4. Results

None of the 120 enrolled parturients were excluded from the study. All the three groups were comparable in respect of age, weight, height, BMI and duration of surgery (Table 1).

	Group D (40)	Group M (40)	Group D+ M (40)	P Value
Age (yrs)	26.10 ± 2.34	25.67 ± 2.24	25.52 ± 1.92	0.474
Weight (Kg)	60.00 ± 2.51	60.70 ± 2.35	61.05 ± 2.51	0.265
Height (cm)	154.10 ± 2.75	155.62 ± 3.50	155.27 ± 3.61	0.103
BMI (Kg/met ²)	25.29 ± 1.14	25.11 ± 1.24	25.37 ± 1.31	0.636
Duration of Sx (Mint)	53.57 ± 6.05	54.37 ± 6.11	55.75 ± 5.83	0.265

Table 1: Demographic profile and duration of surgery.

The number of total responders (no vomiting, no rescue anti-emetics) in all four groups over the time period of 24 hrs and four-point nausea score (0-3) recorded intraoperatively and postoperatively at 1st, 3rd, 6th, 12th, 24th hrs were given in Table 2. Postoperatively at first hour, number of total responders in group D, M and D+M were 29/40 (72.5%), 30/40 (75%), 38/40 (95%) and the difference was statistically significant (Group D Vs Group D+ M, P value- 0.013 and Group M Vs Group D+ M, P value- 0.025).

At 3rd hour postoperatively, 9 patients in Group D, 8 patients in Group M and 1 in Group D+ M, had PONV score 1 (Group D Vs Group D+ M, P value - 0.014 and Group M Vs Group D+ M, P value- 0.029). None of the patients had any vomiting episodes over the time period of 24 hrs (Table 2). Comparison of mean PONV score at various time intervals between four groups was given in Table 3.

The hemodynamic parameters, oxygen saturation, ECG changes were recorded and analysed intra-operatively and no significant difference between the groups was recorded. No incidence of hypotension was noted in any of patients in the postoperative 24 hr period. The patients were observed for side-effects during the 24 hr postoperative period. None of the patients had any clinically serious side-effects.

	PONV Score	Group D (40)	Group D+M (40)	P value	Group M (40)	Group D+M (40)	P value
Intraoperatively	0	40	40	-	40	40	-
	1	0	0		0	0	
	2	0	0		0	0	
	3	0	0		0	0	
1st hour	0	29	38	0.013*	30	38	0.025*
	1	11	2		10	2	
	2	0	0		0	0	
	3	0	0		0	0	
3rd hour	0	31	39	0.014*	32	39	0.029*
	1	9	1		8	1	
	2	0	0		0	0	
	3	0	0		0	0	
6th hour	0	40	40	-	40	40	-
	1	0	0		0	0	
	2	0	0		0	0	
	3	0	0		0	0	
12th hour	0	40	40	-	40	40	-
	1	0	0		0	0	
	2	0	0		0	0	

	3	0	0		0	0	
24 th hour	0	40	40	-	40	40	-
	1	0	0		0	0	
	2	0	0		0	0	
	3	0	0		0	0	

Table 2: Complete responders and nausea score over the time periods.* - Fisher's Exact Test.

Group	Intra-operatively	1 st hrs	3 rd hrs	6 th hrs	12 th hrs	24 th hrs	P value
Group D	0.000± 0.00	0.275 ± 0.45	0.150 ± 0.36	0.000 ± 0.00	0.000± 0.00	0.000± 0.00	0.000
Group M	0.000± 0.00	0.250 ± 0.43	0.200 ± 0.40	0.000 ± 0.00	0.000± 0.00	0.000± 0.00	0.000
Group D+M	0.000± 0.00	0.050 ± 0.22	0.025 ± 0.15	0.000 ± 0.00	0.000± 0.00	0.000± 0.00	0.250

Table 3: Comparison of mean PONV score at various time intervals between three groups.

5. 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 oesophageal sphincter tone, decreases gastrointestinal motility and increases gastric secretion [17]. The etiology of intraoperative nausea and associated vomiting is complicated; it may be attributed to many factors like surgical stimulation, hypotension, vagal stimulation and uterotonic drugs. Patient demographic data and anaesthetic technique also can play a role [18]. Caesarean delivery performed under regional anaesthesia has become very popular over the past few years as a result of increased patient acceptability, improved fetal condition at birth and greater mother safety [19, 20].

Moreover, when these parturients women undergo spinal anaesthesia for caesarean section; there is a risk of intraoperative and post delivery emetic symptoms, this can be related to post induction hypotension, which may cause brainstem hypoxia and stimulation of vomiting center [21, 22]. Dexamethasone, a corticosteroid, is an effective antiemetic drug, with minimal side effects [23-29]. It was first reported as an excellent antiemetic in patients receiving cancer chemotherapy [26]. Since then, it has been widely given in the prevention of nausea and vomiting after chemotherapy [27-29]. Several studies have shown that dexamethasone reduces the incidence of PONV in patients of laparoscopic cholecystectomy, laparoscopic and gynecological surgery, thyroidectomy and caesarean delivery [20, 22, 25, 30-34]. The commonly used dose is 8 to 10 mg [23, 24], but the minimal dose required is 5 mg for PONV in patients undergoing thyroidectomy [25]. Dexamethasone is also effective treatment for PONV after LC [22]. The onset of action after a single dose of four to eight mg is about two hours and the duration is about 12 to 24 hours.

It has also been given to reduce pain after caesarean delivery [35]. A study on dexamethasone has recommended a dose of eight mg for PONV prevention [23]. However, its antiemetic action, at least in part, may be via the blockage of the corticoreceptors in the nucleus tractus solitarius of the brain [35]. It may also exert its antiemetic action through some peripheral mechanism [23-25]. Metoclopramide is a benzamide derivative and mediates its effect by antagonism of dopamine and serotonin 5-HT₃ receptors [36]. Metoclopramide 10 mg is a conventional antiemetic drug, largely and safely used at this dose in adults for PONV [37].

Although its antiemetic efficacy is under debate, some controlled trials performed during gynecological and obstetric procedures [38-41] showed that metoclopramide 10 mg is effective and safe. The anti-vomiting effect of metoclopramide was present only within 6 hours following its administration [15]. The use of 5-HT₃ antagonists in prevention and treatment of PONV is more common nowadays. We were able to use ondansetron only as a rescue therapy due to its high cost. We chose to evaluate the use of a metoclopramide and dexamethasone combination in comparison with single drug alone for reducing nausea and associated vomiting in parturients during and after spinal anaesthesia for caesarean section. Our results showed that combination of dexamethasone and metoclopramide was more effective for preventing PONV as compared to single drug alone.

Our study confirms the observation of Henzi et al. [15] regarding the poor anti-emetic effect of metoclopramide in the dose of 10 mg IV, and Levitt et al. [42] that who concluded that combination of dexamethasone and metoclopramide in controlling nausea and vomiting equalled or exceeded that of ondansetron in patients on chemotherapy for breast cancer. Like our study Rasool Kavyannejad et al. [43] Compared dexamethasone and metoclopramide for preventing nausea and vomiting and pain after hernia inguinal surgery by clinical trial on group (M) who received the intravenous 10mg Metoclopramide and the other group (D) received 8 mg Dexamethasone 10 min before extubation and 6 hours after the end of the surgery and concluded that there was no statistically significant difference between two groups in the rate of PONV ($P > 0.05$). But our results are not similar with Frikha M et al. [44] study who concluded that 10 mg of metoclopramide did not improve the incidence of emetic symptoms in parturients undergoing caesarean section under spinal anaesthesia when combined with 8 mg of dexamethasone. The limitation in this study design is the failure to include a fourth group as a placebo alone could lead to break new grounds.

6. Conclusion

Combined use of dexamethasone and metoclopramide as a prophylactic antiemetic showed significant results compared to the use of dexamethasone and metoclopramide.

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Citation: Mohd Asim Rasheed, Arindam Sarkar, Vishal Arora. Evaluation of Efficacy of Metoclopramide, Dexamethasone and Their Combination for the Prevention of Post-Operative Nausea and Vomiting (PONV) in Patients Undergoing Cesarean Section. Anesthesia and Critical Care 1 (2019): 1-9.



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