Prophylaxis Against Intraoperative Nausea And Vomiting During Spinal Anesthesia For Cesarean Section: A Comparative Study Of Ondansetron Versus Metoclopramide

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Citation

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Abstract

We intended to compare the preventive and therapeutic effects of ondansetron and metoclopramide, on the incidence of intraoperative nausea and vomiting (IONV) during cesarean section (C-section) under spinal anaesthesia. We performed a double-blind placebo-controlled study, including 150 ASA I-II women submitted to spinal anaesthesia for scheduled C-section. Four mg ondansetron (n=49), 10 mg metoclopramide (n=48) or saline (n=50), were administered i.v., depending on their treatment group. Whenever IONV appeared after we treated them with droperidol, if they had not subsided completely after five minutes. Nausea and vomiting occurred in 11.6% of the total cases. They were absent in 91.8% of the ondansetron group, 91.6% of the metoclopramide group and 60% of the placebo group (P<0.001 for both the ondansetron and the metoclopramide groups versus the placebo group, no significant difference between actively treated groups). Emetic symptoms were more frequent after clamping the umbilical cord (25,9%) than prior to it (16,3%) (P<0,05).

Conclusion: This study showed a significantly lower incidence of IONV in the ondansetron and metoclopramide groups than in the placebo group, in women requiring a C-section under spinal anaesthesia. The ondansetron group was not statistically different from the metoclopramide group.

INTRODUCTION

Spinal anaesthesia has been shown to be an easy, rapid and safe technique for C-section 1. Nevertheless, it has some minor side effects, including intraoperative nausea and vomiting (IONV) in more than 66% of the cases 2 3. The abrupt diaphragmatic contractions, present in emesis, are uncomfortable to the patient and may cause protrusion of the abdominal viscera, rendering surgery more difficult and increasing the risk of visceral injuries. If the patient's stomach is full, aspiration is an additional hazard 4. Therefore, it seems advisable to prevent it during spinal anaesthesia for C-section.

Ondansetron has been demonstrated to be an effective and well-tolerated drug for the prevention and treatment of postoperative nausea and vomiting5. Its use in surgical procedures accompanied by frequent postoperative nausea and vomiting seems reasonable6. Metoclopramide and droperidol are also often employed. Droperidol has been demonstrated to be effective in low doses, but its haemodynamic and sedative effects limit its use.7

The purpose of our study was to compare the intravenous administration of 4 mg ondansetron to that of 10 mg of metoclopramide or placebo, given after clamping the umbilical cord, as a preventive measure against IONV during spinal anaesthesia for C-section.

MATERIAL AND METHODS

The local ethical committee approved the study. One hundred and fifty ASA I-II parturient women scheduled to undergo nonemergent C-section and no contraindication for local anaesthesia were included in the study. Patients with preeclampsia, arterial hypertension, postoperative emesis, or fasting for less than 6 hours were excluded.

Each patient received 500 ml of hydroxyethyl cellulose before the dural puncture. Anesthesia consisted of 0.5% hyperbaric bupivacaine (12,5 mg) plus 10 µg of fentanyl, to

achieve a bilateral upper T4-T5 dermatomal level of insensibility. Oxygen 3 ml/min via nasal catheter was given to all patients. 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 bolus intravenous (IV) lactated Ringer's solution and ephedrine in 10-mg increments. Aortocaval compression was avoided by keeping the patient in a left tilt position.

Immediately after clamping on the umbilical cord, each patient received one of the three study drugs IV over 2 min. Randomisation was established by means of a random number table, in a double-blind fashion. Patients in group I received 4 mg of ondansetron; those in group II, 10 mg of metoclopramide, and those in group III, normal saline (placebo) as antiemetic drugs. All drug solutions were diluted to a 10-mL volume with normal saline. Intravenous Droperidol, 0.625 mg, was allowed if IONV had not subsided completely 5 after giving the study drugs.

Demographic, obstetric, and surgical variables were recorded. Statistical methods included analysis of variance for quantitative variables, Chi2 for qualitative variables, and Student's t test for paired data. The level of significance was established at P< 0.05.

RESULTS

There were a total of 147 patients, 49 in the ondansetron group, 48 in the metoclopramide group, and 50 in the placebo (sakline) group. Three patients required general anaesthesia because of inadequate spinal block and were excluded. All the remaining patients (n = 144) had an adequate level of surgical anaesthesia (T5 to T3 sensory level). The three study groups were similar with regard to maternal and obstetric variables (Table 1), and operative management. (Table 2)

Figure 1

TABLE 1: Maternal and obstetrics characteristics. Data are expressed as mean ± SD, except for Apgar score, which is expressed as median an range. There were no statistical differences among the three groups.

	ONDANSETRON GROUP I (n=49)	METOCLOPRAMIDE GROUP II (n=48)	PLACEBO GROUP III (n=50)
Age (yr)	30± 5	29± 4	27± 8
Weight (kg)	66± 9	66± 8	67.2± 8
Height (cm)	159± 9	160± 7	161± 7
Gestational age (wi	39.1± 1	38.8± 1	39± 2
Newborn weight (g	3280± 54	3373± 47	3310± 50
Newborn pH venou cord	7.3± 0.1	7.26± 0.1	7.29± 0.2
Apgar score			
1st min	9 (7-10)	9 (7-10)	9 (8-10)
5th min	10 (9-10)	10 (9-10)	10 (9-10)

Figure 2

TABLE 2: Operative management. Data are expressed as mean ± SD, except for incision and tubal ligation which are numbers. There were no statistical differences among the three groups.

	ONDANSETRON GROUP I (n=49)	METOCLOPRAMIDE GROUP II (n=48)	PLACEBO GROUP III (n=50)
Surgical time (min)	58± 22	58± 19	56.5± 18
Blood loss (mL)	408± 118	420± 105	425± 130
Crystalloid (mL)	1223± 297	1275± 201	1260± 189
Incision (n)			
Midline laparotomy	28	31	30
Pfannestiel	21	17	20
Tubal ligation performed (n)	8	12	10

As shown in Table 3, a total of 17 patients (11.6%) suffered from IONV. Ondansetron-treated and metoclopramide-treated patients experienced significantly fewer IONV episodes than placebo-treated (saline) patients. One patient in the ondansetron group, another one in the metoclopramide group (2% of the total), and 15 patients in the placebo group (30%) experienced vomiting (P<0.001 ondansetron or metoclopramide group versus placebo group). IONV were more frequent in the period between clamping the umbilical cord at the end to the surgery (58.8%) to prior than this (41.2%) (P<0.05).

Figure 3

TABLE 3: Distribution of the intraoperative nausea and vomiting (IONV) episodes. Data are number and percentage. There were no significant difference between the ondansetron and the metoclopramide group. * P<0.05 versus control placebo group. * * P<0.001 versus control placebo group.

	ONDANSETRON GROUP I (n=49)	METOCLOPRAMIDE GROUP II (n=48)	PLACEBO GROUP III (n=50)
Pre-clamping cord			
No symptoms (%)	46 (93.9)**	44 (91.7)**	33 (66)
Only nausea (%)	2 (4.1)*	4 (8.3)	11 (22)
IONV (%)	1 (2)	0 (0)	6 (12)
Post-clamping cord			
No symptoms (%)	45 (91.8)**	44 (91.7)**	20 (40)
Only nausea (%)	4 (8.2)**	3 (6.3)**	21 (42)
IONV (%)	0 (0)**	1 (2)**	9 (18)
Rescue droperidol (%	1 (2)	1 (2)	4 (8)

Forty out of the 147 patients (27.2%) had hypotension during surgery and 11 of them (27.5%) experienced IONV, compared with 6 cases (5.7%) in the normotensive group (P<0.001). (Table 4)

Figure 4

TABLE 4: Incidents and variables related with spinal anesthesia for cesarean section. Data are expressed as number and percentaje, except for ephedrine dose which are mean ± SD. * P

	ONDANSETRON GROUP I (n=49)	METOCLOPRAMIDE GROUP II (n=48)	PLACEBO GROUP III (n=50)
Hypotension (%)	12 (24.5)	15 (31.3)	13 (26)
Emetic symptoms			
No symptoms (%)	8 (16.4)	11 (22.9)	2 (4)
Only nausea (%)	3 (6.1)	3 (6.3)	2 (4)
IONV (%)	1 (2)*	1 (2.1)*	9 (18)
Ephedrine Dose (mg	12± 13	11± 13	14± 9

Six of the 17 patients with IONV (35.3%) required droperidol as a rescue antiemetic. The mean amount of ephedrine used was similar among the three groups.

No side effects of ondansentron or metoclopramide were observed in any of the study patients.

DISCUSSION

Spinal blockade is considered the procedure of choice for elective or urgent C-section in countries such as the United States, where it is used in up to 41% of the cases in some hospitals.8 The effects of spinal anaesthesia on women on their labour period are different from those observed in non-obstetric patients. The distribution of the anaesthetic drug in cerebrospinal fluid (CSF) is less predictable ion the former group, not only because of increased spinal canal pressure9, but also as a consequence of the changes in CSF acid-base balance10 and protein content11. Moreover, side effects, including hypotension, nausea and vomiting, and hypersensitivity to intrathecal opiates, are more common12.

Intraoperative emetic symptoms during abdominal surgery under regional anaesthesia have a multifactorial origin. and factors such as psychological changes (anxiety), arterial hypotension, hypoperfusion of the central nervous system, abrupt visceral movements, and concomitant opiate administration.13 may have an influence on them. Additionally, there is a higher predisposition to IONV among patients at the end of their pregnancies, as a consequence of increased intra-abdominal pressure and hormonal changes. Lussos et al. believe that IONV after delivery are rather related to the surgical manipulation of the uterus, abdominal viscera, and peritoneum, even in the presence of adequate sensorimotor blockade5. Therefore, antiemetic treatment may be effectively administered to a group of surgical patients submitted to a certain procedure, but not for another group having different surgical procedure or anaesthetic techniques14.

Abdominal surgery and the physical disruption and manipulation of abdominal viscera that it induces may cause the release of humoral substances including 5-HT, which may stimulate 5-HT3 receptors on the afferent vagus nerves, triggering the emetic reflex especially in awake patients.2. We chose 4 mg ondansetron as our study dose because it has been shown that it is as effective as higher doses in preventing and treating postoperative nausea and vomiting and it does not induce any side effects15. Pearman et al.16 have suggested that 8 mg of ondansetron may be more effective than 4 mg in women at higher risk of manifesting emetic symptoms. However, we found that 4 mg of ondansetron was well-tolerated and produced no side effects.

In our study, ondansetron and metoclopramide reduce the emetic symptoms in C-section patients from 40% in placebo group to 8% in both treated groups. Similar results have been previously reported.4

Pan et al.2 recently reported that ondansetron is as effective

as droperidol in preventing intraoperative nausea and vomiting during C-section under epidural anaesthesia. Acupressure, a non-invasive variant of acupuncture, is an alternative without side effects 17.. It has been found to be as effective as metoclopramide in this context. Borgeat et al.18 reported the direct therapeutic antiemetic effect of subhypnotic doses of propofol after minor gynaecological, digestive, and orthopaedic surgical procedures. Nevertheless, later studies have shown that this drug does not prevent the emetic complications in elective C-section under spinal anesthesia.19 20

Datta et al.21 and Kang et al..3 in 1982, observed that the incidence of emetic complications during spinal anaesthesia for C-section correlated with the presence of arterial hypotension. Others, such as Carpenter et al.22 reported that hypotension leads to a two-fold increase in the relative risk of IONV. In our study, both conditions coexisted in 11 of patients, 1 out of 12 patients of the ondansetron group (8.3%), 1 out of 15 patients of the metoclopramide group (6.7%), and 9 out of 13 of patients of the placebo group (69.2%). ($P<0.001$)

We administered the antiemetic drug after clamping of the umbilical cord because the effects of ondansetron and metoclopramide on foetuses and new-borns are unknown. Both, ondansetron and metoclopramide have been used for hyperemesis gravidarum and no adverse foetal effects were observed23. Ondansetron is well tolerated without significant side effects. Mild headache and constipation with larger doses of ondansetron are the most commonly reported2 problems. In our study, no side effects of ondansetron and metoclopramide were observed, probably because we used a smaller dose compared to previous reports in which there were some associated side effects.2 4 24

The etiologic factors involved in intraoperative nausea and vomiting during spinal anaesthesia for C-section are so numerous, that larger prospective studies seem to be needed in order to establish the most important risk factors, the best prevention guidelines, and the effectiveness and safety of new antiemetic agents.

To our knowledge, the two drugs studied have not been compared in this context before. We have shown that the IV administration of a bolus of either 4 mg of ondansetron or of 10 mg of metoclopramide, immediately after clamping of the umbilical cord were equally effective in preventing intraoperative emetic symptoms in parturients undergoing C-section under spinal anaesthesia. Metoclopramide, being older and cheaper than ondansetron, should perhaps be considered the first choice in this context.

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