A comparative study of antiemetic effects of intravenous ondansetron, intravenous dexamethasone and their combination during elective cesarean section under spinal anesthesia

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Abstract

Background: Nausea and vomiting are frequently seen in patients undergoing cesarean section under spinal anesthesia. It is a major problem, not only for patient but for the surgeon and the anesthesiologist as well. ***Objective:*** We aimed to compare the antiemetic effect of ondansetron and dexamethasone combination with that of the use of each agent alone to decrease the incidence of post-delivery intraoperative nausea and vomiting during cesarean section under spinal anesthesia. ***Materials and methods:*** A randomized, prospective study was performed on 60 patients undergoing elective cesarean section under spinal anesthesia. Patients received 4mg ondansetron in group A, 5mg dexamethasone in group B and 4mg ondansetron plus 5mg dexamethasone in group C intravenously 1 minute after the umbilical cord was clamped. Frequency of post-delivery intraoperative nausea and vomiting episodes were recorded. ***Results:*** A total of 60 patients were included in this study. There were 20 patients in group A, 20 patients in group B and 20 patients in group C. There were no statistically significant difference between the groups in terms of baseline characteristics and intraoperative managements. Frequency of intraoperative nausea, retching and vomiting experiences were similar between the groups($p>0.05$) ***Conclusion:*** Single dose of 4 mg ondansetron or 5 mg dexamethasone given intravenously are both effective agents for the control of post-delivery intra-operative nausea and vomiting in cesarean section under spinal anesthesia, however, the combined use of these agents is no better than both used alone.

Key words: Ondansetron, dexamethasone, cesarean section, spinal anesthesia, nausea and vomiting

J Cox Med coll 2018;5(2): 12-15

Introduction

Nausea and vomiting during spinal anesthesia for cesarean section still remains a major problem, not only for patient but for the surgeon and anesthesiologist as well. The physiological and anatomical changes during pregnancy like high level of progesterone causing smooth muscle relaxation, increase in gastrin secretion, decrease in gastrointestinal motility and lower esophageal sphincter tone make the pregnant women prone to nausea and vomiting[1]. Cesarean delivery performed under spinal anesthesia is associated with a relatively high incidence (50%-60%) of intraoperative, post-delivery nausea and vomiting, when no prophylactic antiemetic is given[2,3].

Ondansetron is a selective antagonist of the 5-hydroxytryptamine 3 receptors and is a very effective agent in the prevention and treatment of chemotherapy induced[4], intraoperative and postoperative nausea and vomiting[5,6]. Dexamethasone is a corticosteroid with antiemetic and high anti-inflammatory effects. Use of dexamethasone in combination with the other drugs has been reported to increase the antiemetic or analgesic efficacy, and minimal side effects have been reported when it is used as a single agent[7-8]. The mechanism of antiemetic effect of dexamethasone has been incompletely understood but it is thought to be caused by inhibition of prostaglandin synthesis, by showing anti-inflammatory efficacy and by causing a decrease in the release of endogenous opiates[9].As an antiemetic agent, it has been used a dose ranging between 2.5-10 mg per day[9,10].

Since nausea and vomiting can occur by a variety of different mechanisms, combination of different anti-emetics are used to prevent or treat these symptoms[11]. By the help of these combinations, multiple routs that can lead to nausea and vomiting can be blocked[12]. Effect of addition of dexamethasone to ondansetron in the control of post-operative nausea and vomiting (PONV) has been studied before, but in this study we investigated the efficacy of this combination for the

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control of post-delivery intraoperative nausea and vomiting (IONV). In this study, we aimed to compare the antiemetic efficacy of ondansetron and dexamethasone combination with that of the single use of each agent to decrease the incidence of post-delivery IONV during cesarean section under spinal anesthesia.

Materials and Methods

This randomized controlled prospective clinical study was carried out from September 2017 to December 2017 at different private hospital in Dhaka city after obtaining informed consent from the patients. This study was performed on 60 ASA physical status I and II female patients between 20 to 35 years of age undergoing elective cesarean section under spinal anesthesia. Patients with a gastrointestinal disease, drug allergy, infection, diabetes, glaucoma, preeclampsia, eclampsia were excluded from the study. In the operation theatre multichannel patient monitor that included heart rate, non-invasive blood pressure and pulse oximetry were applied to all the patients. An intravenous access was established by 18 G IV cannula and preloading was done then infusion continued at a rate of 1.5 ml per kg per hour. Under all aseptic precautions, with the patient on sitting position L4- L5 inter vertebral space was identified and lumber puncture was performed through midline approach using a disposable sterile 25 G Quincke spinal needle and 2.5 ml of 0.5% heavy bupivacaine was administered to the subarachnoid space after free flow of CSF. Patients were then turned to supine position with a wedge placed under the right hip to avoid aorto-caval compression until the delivery of the baby. Oxygen was delivered to all patients at a rate of 5L/ min via a face mask. Before the surgical incision, the level of sensory blocked was assessed. Surgery was allowed only after sensory level of anesthesia up to T6 reached. A continuous monitoring was done for pulse rate, respiratory rate and oxygen saturation throughout the intraoperative period. Non-invasive blood pressure was monitored at 3 min interval and in case of hypotension BP was measured every minute. Spinal induced hypotension was defined as a fall in systolic blood pressure of 20% from base line or less than 90 mm Hg. Hypotension was treated by bolus infusion if Ringer Lactate and 5 mg of IV ephedrine repeated as necessary until the BP reached to acceptable level. Within 1 minute after the umbilical cord was clamped, the study drug was administered to the mother intravenously. The antiemetic study drugs were prepared and administered to the mother according to the following 3 groups.

Group A (n=20) received 4 mg ondansetron diluted to 5 ml normal saline + 5 ml normal saline.

Group B (n=20) received 5 mg dexamethasone diluted to 5 ml normal saline + 5 ml normal saline.

Group C (n=20) received 4 mg ondansetron diluted to 5 ml normal saline + 5 mg dexamethasone diluted to 5 ml normal saline . After delivery of the fetus, 10 units of oxytocin was administered to the patients.

During the intraoperative post-delivery period nausea, retching and vomiting episodes were recorded. Besides questioning the patient in every 3 minutes about these emetic symptoms, the patients were also requested to report the symptoms that occur at the intervals. Drug related complications were recorded during the study period. A standardized surgical technique was used in all cesarean section.

For the statistical analysis, continuous data were presented as mean±standard deviation (SD). One-way ANOVA and t- test were used for parametric data analysis and Chi-squire tests were used to analyze non parametric data. $P< 0.05$ was considered statistically significant.

Results

There were total 60 patients, with 20 patients in each of the three groups. The three groups were similar with regard to demographic characteristics (Table I) and operative management (Table II). All patients had an adequate level of surgical anesthesia (T6-T4) before incision. There were no statistically difference between the three groups in regards to blood pressure, heart rate and other vital parameters. In an intraoperative post delivery period, the episodes of emetic symptoms (nausea, retching and vomiting) was almost similar to patients of all the three groups (Table III). 3 (15%) patients in ondansetron group 3 (15%) patients in dexamethasone group and 2 (10%) patients in ondansetron and dexamethasone combination group experienced nausea $p >0.05$. The incidence of vomiting was seen in 1 (5%) patient in each groupondansetron group, dexamethasone group and combination group $p>0.05$. There was no excessive drowsiness or clinically significant respiratory depression in any of the study patients.

Table-I: Demographic data of patients

	Group A (ondansetron gr.)	Group B (dexamethasone gr.)	Group C (combination gr.)
Age (years)	24.82±6.26	25.15±5.96	25.31±5.26
Weight (Kg)	62.37±5.74	63.12±5.32	62.91±6.17
Height (cm)	153.07±8.22	154.12±7.87	153.82±9.17
Gestational age (weeks)	37.17±2.24	37.33±2.34	37.81±2.08
Multipara (%)	3(15%)	2(10%)	3(15%)

Table-II: Operative management

	Group A (ondansetron gr)	Group B (dexamethasone gr)	Group C (combination gr)
Time of operation (min)	38.72±4.17	41.13±3.27	39.38±3.72
Skin incision to delivery of fetus (min)	3.18±.64	3.78±.42	3.52±.76
Uterine incision to delivery of fetus (sec)	48±3.0	50±1.5	47.5±2.5
No. of patients with hypotension who required ephedrine (%)	3(15%)	2(10%)	2(10%)
Peak sensory block of height T4 (%)	11(55%)	13(65%)	14(70%)

Table-III: Incidence of intra-operative emetic symptoms

	Group A (ondansetron group)	Group B (dexamethasone group)	Group C (combination group)	p value
No symptoms	15(75%)	14(70%)	14(70%)	p>0.05
Incidence of nausea	3(15%)	3(15%)	2(10%)	p>0.05
Incidence of retching	1(5%)	2 (10%)	2 (10%)	p>0.05
Incidence of vomiting	1 (5%)	1 (5%)	1 (5%)	p>0.05

Discussion

The Precise etiology of (intraoperative nausea and vomiting) IONV remains unknown and various factors have been implicated[13]. Hypotension is probably the most important cause of IONV that occurs during cesarean section under spinal anesthesia. Hypotension can induce the emetic symptoms by leading to cerebral hypoperfusion. Prevention of hypotension is therefore important for prevention of IONV. In this study we specially evaluated the incidence of post-delivery IONP. Because the nausea and vomiting before the delivery period is specially related with spinal anesthesia induced hypotension which can be prevented by performing the necessary preventive measures. Because in our study, in contrast to those reported in the previous studies[14], interval from skin incision to delivery of fetus and the interval from uterine incision to delivery of fetus in all groups were very short. So the predelivery period was very short in the present study. So we thought that it would be better to investigate the nausea and vomiting in the post delivery period which is more difficult to control.

In this study 75% patient in group A (ondansetron group) were free of emetic symptoms. Similarly 70% patients in both group B (dexamethasone group) and group C (combination group) were symptoms free (Table III). There was no statistically significant difference between the groups in prevention of IONV (p>.0.05). F Wadood et al[15] while comparing the efficacy of ondansetron and ondansetron plus dexamethasone for prevention of PONV found no statistically significant difference between the two groups of patients. The result was similar to our study. Demirhan A et al[16] also found no significant difference between the antiemetic efficacy of ondansetron, dexamethasone and the combination of both agents. Olaondo et al[17], A Kumar et al[18] and Shahryar Sane et al[19] found that combined use of dexamethasone and ondansetron seems to increase the antiemetic efficacy than the single agent used alone, although they have not given any specific reason for their findings. But in our study there was no statistically significant difference between the groups as the incidence of nausea (Table III)in group A and group B were 15% and group C was 10% (p>0.05) . Incidence of vomiting (Table III) in our study was 5% in all three groups (p>0.05).

The limitation of our study may be, we administered dexamethasone within 1 minute after umbilical cord was clamped. Wang et al[20] have shown that dexamethasone took long to achieve its antiemetic effects. This may explain why there was lack of more antiemetic effect in dexamethasone and combination group in our study.

Conclusion

We can conclude from this study that, single dose of 4 mg ondansetron or 5 mg dexamethasone given intravenously are both effective agents for the control of post-delivery IONV. However, combined

use of these agents does not seem to increase the efficacy over that achieved by the single use of each agent.

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