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A Study of Effectiveness of Granisetron in Reducing the Incidence of Post Operative Nausea and Vomiting in Patients Undergoing Lower Segment Cesarean Section

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Abstract

Context: Availability of large number of agents which prevent emesis and continued research for newer drugs to treat emesis indicated the magnitude of the problem and lack of satisfactory regimes. *Aims:* To study the effectiveness of granisetron in reducing the incidence of post operative nausea and vomiting in patients undergoing lower segment cesarean section. *Settings and Design:* Hospital based cross sectional study was conducted at SVS Hospital and Medical College, Mahabubnagar. *Methods and Material:* 75 women of ASA grade-l and 2 aged between 20-35 years weighing between 45-65 kg at term posted for elective cesarean section under spinal anesthesia were enrolled for the study. Patients were randomly allotted into three groups of 25 each. Patients belonging to group A received injection Ondansetron 4 mg, group B received injection Granisetron 2 mg and group C received injections normal saline 2 ml IV. *Statistical Analysis:* Patient data were analyzed by Chi-Square test and p value less than or equal to 0.05 was taken as statistically significant. *Results:* Incidence of post operative nausea and vomiting (PONV) was more in control group i.e. 44% and it was only 16% in the granisetron group. Among the patients with ondansetron group it was 20%. Granisetron was found to be effective in controlling the vomiting compared to placebo and ondansetron. In group A, 4 patients, in group B, 3 patients and 1 patient in group C had headache. *Conclusion:* Granisetron 2 mg was slightly more effective than IV Ondansetron 4 mg in preveting PONV following cesarean delivery under spinal anesthesia.

Kewords: Ondansetron; Granisetron; Prevention; Nausea; Vomiting; Efficacy; ASA Grade.

Introduction

Pain and emetic problems are the usual side effects following anesthesia and surgery [1]. Among patients who undergo cesearean section, nausea and vomiting are much more troublesome. Sometimes it is more uncomfortable than pain after surgery. It was found that the incidence of nausea and vomiting is high amounting to 66% among cesearean delivery done under regional anesthesia unless antiemetic agents are used prophylactically. The occurrence of peripartum emesis the course of surgery under regional anesthesia casues lot of discomfort and distress and disturbs the patients as well as surgeons [2].

Availability of large number of agents which prevent emesis and continued research for newer drugs to treat emesis indicated the magnitude of the problem and lack of satisfactory regimes.

It was observed that glycopyrrolate could successfully minimize the occurrence of nausea and vomiting among those who undergo spinal anesthesia for cesearean section patients without affecting neonatal outcome. Dexamethasone decreases drug induced vomiting when added o antiemetic regimen and also acts as potential useful prophylaxis for post operative nausea and vomiting (PONV).

Droperiodol reduces the occurrence of nausea and emesis among peripartum patients under spinal

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anesthesia. But its use may lead to long duration sedation and depression of the respiration.

Metoclopramide has been considered the most effective single agent of prophylaxis for PONV by Lussos et al [3] in some patient's metoclopramide may cause distressing extra pyramidal symptoms and sedation because of its activity as dopamine antagonist.

These drugs are generally antihistamines, dopamine antagonists with counted adverse effects such as dysphoria, sedation, extra pyramidal effects, tachycardia etc.

Ondansetron later was found to be more effective and with less side effects. Recently granisetron has been reported to be better than ondansetron. Hence present study was carried out to study the effectiveness of granisetron in reducing the incidence of post operative nausea and vomiting in patients undergoing lower segment cesarean section.

Materials and Methods

Present hospital based study was carried out to study the effectiveness of granisetron in reducing the incidence of post operative nausea and vomiting in patients undergoing lower segment cesarean section.

Institutional Ethics Committee approval was obtained. Informed consent was taken from all selected and eligible patients. 75 women of ASA grade-l and 2 aged between 20-35 years weighing between 45-65 kg at term for elective cesarean section under spinal anesthesia were enrolled for the study. Any patient having a history of acid peptic disease or hepatic dysfunction with past history suggestive of PONV or any antiemetic medication, PIH, diabetes, H/O nausea and vomiting 24 hours before initiation of anesthesia were not included in the present study.

Patient were allocated randomly in equal numbers (n=25 in each group) into three different groups. Patients belonging to group A received injection Ondansetron 4 mg group B received injection Granisetron 2 mg and group C received injections normal saline 2 ml IV.

In the preoperative assessment patients were enquired for H/O motion sickness, H/O previous exposure to anesthesia and H/O PONV vital signs like respiratory rate, heart rate and blood pressure were recorded in every patient. Investigations urine albumin, urine sugar, Blood Hb%, urea, sugar, creatinine, blood grouping were noted.

For prevention of hypotension, before the administration of spinal anesthesia, every patient was given 20 ml/kg Ringer's Lactate solution. Each patient received injection Ranitidine 50 mg IV for acid prophylaxis. Before entering the operation theater patients were randomized to receive either 2 mg Granisetron or 4 mg Ondansetron or 2 ml normal saline IV. Pulse rate, respiratory rate and Blood pressure of each woman were recorded before spinal anesthesia.

The patients were given left lateral position and a 23 G Quincke spinal needle wall introduced through midline approach at L3–L4 interspace. Patients received 1-1.2 ml xylocaine subarachnoid injection. After giving spinal anesthesia women were put in the supine position with 15 wedges below right hip for left uterine displacement to avoid aortocaval compression. All patients were given oxygen using facemask at a flow rate 3 its/minute. Following confirmation of spinal block by loss of sensation to cold and pinprick to T4 - T5 level, surgery was started. Oxytocin (10 units) was administered though IV infusion at the time of cord clamping.

Every 5 minutes, till delivery, blood pressure was recorded. And then every 10 minutes until the patient was shifted to recovery room. At the recovery room, BP measurement was recorded every 30 minutes up to 4 hours by trained nursing staff. The decrease in systolic BP (>20%) of baseline value and / or <90 mm Hg) after spinal anesthesia was treated by increasing the rate of IV fluid administration and 3 mg increments of ephedrine IV every 3-5 minutes until resolution of hypotension, pulse rate respiratory rate and oxygen saturation were monitored and recorded also during surgery.

Emetic episodes (nausea and / or vomiting) experienced by women were recorded intra operatively and up to 4 hours post operative period in post operative ward. Request for pain relief during post operative period was complied with 75 mg diclofenac sodium given through IM route.

Interpretation of emetic episodes by grading system
Grade 0- No nausea and vomiting
Grade 1- Mild nausea
Grade 2- Mild to moderate nausea or retching
Grade 3-single episode of vomiting
Grade 4-Recurrent Vomiting

Statistical Analysis

Patient data were analyzed by Chi-Square test and p value less than or equal to 0.05 was taken as statistically significant.

Results

There were 75 patients of ASA grade I and II. They were divided into three groups: 25 patients (Group A) received injection. Ondansetron 4 mg, 25 patients (group B) received injection Granisetron 2 mg and 25 patients (Group C) received 2 ml normal saline intravenously 15 minutes before spinal anesthesia.

Table 1 shows demographic profile of study subjects. All the three groups were similar in terms of age, weight, ASA grade I and II, history of motion sickness, history of PONV. Statistical test like t value where mean was used and chi square value where percentage was used, were used. The p value was more than 0.05 for all above parameters studied. Thus we can say that all the three group patients were comparable and ready for further study.

Table 2 shows effect of ondansetron and granisetron on pulse rate, respiratory rate and blood pressure. The effect was studied for pre operative, intra operative; post operative 0-2 hours and post operative 2-4 hours. It was found that the range of pulse rate, respiratory rate and blood pressure in all the three groups during pre operative, intra operative, post operative 0-2 hours and post operative 2-4 hours was similar. Hence there was no statistically significant difference between the action of Ondansetron and Granisetron.

Table 1: Demographic profile of study subjects

	Group – A	Group – B	Group – C	Statistical test
Age	24±4	25±3	23±4	t = 1.000, p = 0.3223
Weight	55±7	52±7	54=±	t = 1.5152, p = 0.1363
ASA I/II	23/2	20/5	22/3	t = 1.7150, p = 0.0928
Duration of surgery (Minutes	45±5	48±8	49±7	t = 1.5900, p = 0.1184
H/O Motion Sickness	4 (16%)	3 (12%)	3 (12%)	X^2 = 0.1628, p=0.343
H/O PONV	0	0	0	Not applicable

Table 2: Comparison of pulse rate, respiratory rate and blood pressure among the three groups

Group – A	Preoperative	Intra operative	Post operative: 0-2 hours	Post operative: 2-4 hours
Respiratory rate (per minute)	16-20	16-18	14-16	14-16
Pulse rate (per minute)	78-108	60-100	70-110	70-100
Mean Arterial Blood Pressure (MABP) mmHg	76-96	69-85	79-101	73-95
		Group – B		
Respiratory rate (per minute)	15-18	16-20	16-19	14-16
Pulse rate (per minute)	72-86	68-98	80-110	70-90
Mean Arterial Blood Pressure (MABP) mmHg	74-94	68-88	74-98	78-100
		Group – C		
Respiratory rate (per minute)	14-18	16-20	14-18	13-15
Pulse rate (per minute)	74-104	66-96	82-102	72-92
Mean Arterial Blood Pressure (MABP) mmHg	70-96	66-88	72-92	80-100

Table 3: Emetic episodes among the study subjects

Grading	Group-A	Group-B	Group-C
Grade – 0	20	21	14
Grade – 1	2	2	4
Grade – 2	2	1	3
Grade – 3	1	1	2
Grade – 4	-	-	2
Total emetic episodes	5 (20%)	4 (16%)	11 (44%)

X^2 = 0.1328, p = 0.3578 (between group A and B), X^2 = 4.573, p = 0.01624 (between group B & C)
X^2 = 3.243, p = 0.03588 (between group A & C)

Table 4: Adverse effects among various groups

Adverse Effect	Group – A	Group – B	Group – C
Head ache	4 (16%)	3 (12%)	1 (45)
Drowsiness	2 (8%)	2 (8%)	-
Allergic reactions	-	-	-

Table 3 shows emetic episodes among the study subjects. Incidence of PONV was found to be 44% in placebo group, whereas 16% in Granisetron group, and 20% in Ondansetron group. The difference in the occurrence of PONV was statistically not significant between ondansetron group and the granisetron group ($p > 0.05$). But the difference between the placebo group and either of granisetron group or ondansetron group was significant statistically. It was significantly more in placebo group ($p < 0.05$).

Table 4 shows adverse effects among various groups. In group A, 4 (16%) patients, in group B, 3 (12%) patients and 1 (4%) patient in group C had headache. In group A, 2 (8%) patients and in group B, 2 (8%) patients had drowsiness No patients and developed allergic reactions in any of the three groups.

Discussion

In the present study, there is one similarity regarding methodology, with the study of Lussos et al [3]. Attempts were made to control the occurrence of intra operative nausea and vomiting. Patients had a sensory level block of at least T4-T5 and received supplemental oxygen via face mask. Intravenous crystalloids were liberally administered to prevent hypotension.

Nausea has been considered to be premonitory sign of hypotension and is the subjective feeling of human subjects which precedes vomiting. Brainstem hypoxemia may develop due to hypotension after the initiation of spinal anesthesia and that could directly exaggerate the emesis center and cause emetic symptoms. In our study supplemental oxygen in addition to prehydration and left uterine displacement reduced the occurrence of emesis and nausea.

Histaminic, dopaminergic, muscarinic, 5HT3 and cholinergic are the important neurotransmitter systems involved in emetic response.

Optimal dose of Ondansetron to prevent PONV following caesarean delivery is 4 mg and that of granisetron is 2 mg. Gigillo et al [4], concluded that Ondansetron and Granisetron were having almost similar effect in preventing vomiting, but differs in terms of dose. Dose of granisetron is half to that of ondansetron. They also noted that granisetron IV 2 mg was equivalent to 8-16 mg IV of ondansetron. Moreover, Ondansetron had short half life of 3-5 hours, whereas, Granisetron had half life of 8-9 hours. Thus dose wise granisetron was found to be more effective.

Gralla et al [5] in their study have studied the efficacy of antiemetic. They used the single dose of Granisetron 2 mg. In addition they used IV Ondansetron 32 mg and were given before the chemotherapy with cisplatin. They found that there was no difference between the two therapies.

Bhattacharya D et al [6] in their study, found that incidence of vomiting in ondansetron group was (Group A) 20%, in Granisetron group (Group B) 7%, and in placebo group (Group C) 50%. In our study occurrence of emesis and nausea was 44% in control group (Group C), 20% in Ondansetron group (Group A), and 16% in Granisetron group (Group B). Our results were near to similar to the study of Bhattacharya D et al [6]. They concluded that granisetron was more effective than ondansetron to prevent PONV following day care gynecological laparoscopy.

In this study, we have observed that IV administration of 4 mg Ondansetron and IV administration of 2 mg Granisetron prior to induction of spinal anesthesia or cesarean delivery significantly decreased the incidence of emetic symptoms in comparison to placebo group without any maternal or neonatal defects.

So, to conclude that IV Granisetron 2 mg is slightly more effective than IV Ondansetron 4 mg to prevent PONV following caesarean delivery under spinal anesthesia.

Naguib M et al [7] compared antiemetic efficacy of ondansetron 3 mg, Tropisetron 5 mg, and granisetron 4 mg and compared it with placebo and Metoclopramide 10 mg among patients who were posted for laparoscopic cholecystectomy. They found that Ondansetron was most effective compared to all other groups.

In the study conducted by Roy S et al [8] 60 patients of ASA group I and 2 undergoing middle ear surgery

aged between 12 and 25 years were divided into three groups. Patient belonging to placebo group received normal saline 10 ml Ondansetron group received injection Ondansetron 0.15 mg/kg and Metoclopramide group received Metoclopramide 0.2 mg/kg. The incidences of overall emesis were from 70% to 15% in Ondansetron group. Both Ondansetron and Metoclopramide could prevent nausea significantly as compared to a placebo group. There was statistically no significant difference among Ondansetron and Metoclopramide as regards to their efficacy in preventing nausea.

The prophylactic antiemetic efficacy and safety of Ondansetron was evaluated by Rudra et al [9] in a randomized comparison with Metoclopramide in 40 women undergoing anesthesia, with IV ketamine 2 mg/kg for dilatation and curettage operation. 10 minutes before induction of anesthesia 20 patients received ondansetron 4 mg and 20 patient's metoclopramide 10 mg intravenously. Post operatively control of vomiting was achieved in 80% with Ondansetron and 40% with Metoclopramide.

Prophylactic antiemetic efficacy of single dose IV Granisetron was evaluated by Wilson et al [10] in a randomized double blind, placebo controlled dose ranging study.

Ascaso FJ et al [11] in their comparative study, efficacy of Ondansetron were compared with Metoclopramide for prevention of PONV in patients undergoing cataract surgery. The occurrence of PONV was less in ondansetron group.

Diemunsch P et al [12] have studied 746 male and females undergoing general anesthesia for any type surgical procedure. After experiencing at least one nausea and /or one emetic episode in the 6 hours after recovery from anesthesia, patients received either Ondansetron 4 mg or Metoclopramide 10 mg IV. Patients were observed for PONV for 24 hours after drug administration. Ondansetron was better tolerated than metoclopramide.

Conclusion

Our study suggested that IV Granisetron 2 mg is slightly more effective than IV Ondansetron 4 mg to prevent PONV following cesarean delivery under spinal anesthesia. This dosage also appears safe for the mother and the newborn. We recommend the preoperative use of 4 mg IV Ondansetron or 2 mg Granisetron IV in pregnant patients presenting for caesarean delivery receiving spinal anesthesia. Only drawback with these 5 HT3 antagonists is occasional headache (which is not severe), the cause of which is yet to be explained.

Key Messages

We recommend the preoperative use of 4 mg IV Ondansetron or 2 mg Granisetron IV in pregnant patients presenting for caesarean delivery receiving spinal anesthesia.

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