Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Comparative Study of Dexamethasone Addition to Granisetron and Palonosetron in Preventing Post-operative Nausea and Vomiting in Cesarean Section under Spinal Anaesthesia

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Abstract

Background: Post-operative nausea and vomiting (PONV) are defined as nausea and vomiting that occurs within 24 h after surgery done under general/regional/local anesthesia. Nausea and vomiting in the post-operative period occur in 20–30% of patients and together are the second most common symptom after pain. The present study was designed to compare addition of dexamethasone to granisetron and palonosetron in preventing PONV in cesarean section under spinal anesthesia.

Materials and Methods: This prospective, randomized, and double-blind study was carried on 100 parturients admitted in Government Medical College and associated Guru Nanak Dev Hospital, Amritsar, aged 20–35 years of ASA grade I and II scheduled for elective caesarean under spinal anesthesia. Aims and objective of this study was primarily to compare the effectiveness of dexamethasone to granisetron and palonosetron in preventing PONV in cesarean section under spinal anesthesia. The secondary aim of our study was hemodynamic monitoring and to see any side effects/complications related to the above drugs.

Results: The incidence of postoperative nausea, retching, and vomiting was less in group PD as compared to group GD during 0–24-h period but the difference came out to be statistically non-significant ($P > 0.05$). Hemodynamic parameters during pre-operative, intraoperative, and post-operative period were comparable. Incidence of bradycardia and hypotension in both groups was also comparable.

Conclusion: Although palonosetron is better than granisetron, the cost-effectiveness of granisetron makes it a more commonly used drug in a setting with a limited resources.

Key words: Dexamethasone, Granisetron, Palonosetron, Post-operative nausea vomiting

INTRODUCTION

Post-operative nausea and vomiting (PONV) is defined as nausea and vomiting that occurs within 24 h after surgery done under general/regional/local anesthesia. Nausea and vomiting in the post-operative period occurs in 20–30% of patients and together are the second most common symptom after pain.[1] Nausea is defined as a subjective unpleasant sensation associated with awareness of the urge to vomit, usually felt in the back of the throat and epigastrium and is accompanied by the loss of gastric tone and reflux of the duodenal contents into the stomach. Vomiting is defined as forceful expulsion of gastric contents from mouth and is brought out by the powerful sustained contraction of abdominal muscles, descent of diaphragm, and opening of gastric cardia. There are several factors attributing to nausea and vomiting in patients undergoing cesarean section such as pressure on stomach and gut, neural factors as vagal reflexes elicited by irritation of parasympathetic nerve endings in the abdomen. PONV can lead to delay in recovery time,

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www.ijss-sn.com

Month of Submission : 01-2023
Month of Peer Review : 02-2023
Month of Acceptance : 02-2023
Month of Publishing : 03-2023

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prolonged nursing care, prolonged hospital stay, and increase in total health care costs.[2] Granisetron is a selective 5HT3 receptor antagonist, more potent, and has longer acting properties against cisplatin-induced emesis than ondansetron.[3] Palonosetron, a newer second generation 5HT3 antagonist has been approved by the United States Food and Drug Administration for prevention of PONV in 2008.[3] Dexamethasone (8 mg) decreases chemotherapy induced emesis when added to antiemetic regimen. The present study was conducted to compare to efficacy of dexamethasone addition to granisetron and palonosetron for prevention of PONV in patients undergoing cesarean section under spinal anesthesia.

MATERIALS AND METHODS

After institutional ethical committee approval and informed written consent from the participant, a prospective, randomized, and double-blind study was carried in Government Medical College and associated Guru Nanak Dev Hospital, Amritsar. Parturient aged 20–35 years of age and ASA Grade I and II scheduled for elective cesarean delivery under spinal anesthesia were included in the study. Patients with the previous history of subacute intestinal obstruction, hiatus hernia, previous gastric surgery, history of motion sickness, severe cardiac, respiratory, neurological diseases, and bleeding disorders were excluded from the study. Patients with medical history of pre-eclampsia, diabetes, placenta previa were also excluded from the study. All patients included in the study were examined in detail during pre-anesthetic checkup after taking fully informed consent in their vernacular language. Systemic Examination was done for respiratory system, cardiovascular system, and nervous system. All routine investigations were done. Patients were randomly divided into two groups of 50 each, that is, Group GD and Group PD. Each group received one of the following two drug regimens. Group GD (n = 50) received Inj. Granisetron 40 μg/kg and Inj. Dexamethasone 8 mg diluted in normal saline to make 5 mL given intravenously. Group PD (n = 50) received Inj. Palonosetron 1 μg/kg and inj. Dexamethasone 8 mg diluted in normal saline to make 5 mL given intravenously. On the day of surgery, all the vitals parameters were recorded preoperatively. After shifting the patient to the operation theatre, multiparameter monitor was attached to the patients and a continuous monitoring of pulse rate, blood pressure, respiratory rate, and SPO_2 was done. After venous cannulation, patient was preloaded with ringer lactate solution (15 mL/kg) before giving spinal anesthesia. Under all aseptic precautions, patient was made to lie in left decubitus position. Patient's back was painted with povidone iodine solution and drapped with sterile sheet, 2.2 mL of inj. bupivacaine 0.5% hyperbaric was injected slowly over 15 s through a 25 G spinal needle inserted in L3-L4 intervertebral space. Patient was shifted to supine position, with the left uterine displacement using a wedge under the right hip or 15° table tilt. If there was any difficulty in giving drug in L3-L4 space then L2- L3 intervertebral space was used but no head down tilt was given. Level of analgesia was assessed by pinprick method and surgery was allowed to start when T10 level was achieved. Oxygen was started at a rate of 5 L/min in all patients through facemask. Maternal bradycardia and hypotention were noted and prevented intraoperatively. Any episode of nausea and vomiting was noted during intraoperative period. The drugs under study were administered intravenously immediately after clamping the umbilical cord as discussed above. Any episode of nausea, retching, or vomiting was noted for 24 h in the post-operative period. Nausea is verbal rating scale where patients describe their symptoms as NAUSEA SCORE (No Nausea: 0; Mild Nausea: 1–3; Moderate Nausea: 4–6; and Severe Nausea: 7–10). Total number of episodes of vomiting were counted and those with two or more episodes of vomiting were given the rescue medication Inj. Metoclopramide 10 mg intravenous. Patients were shifted to recovery room where they were monitored postoperatively.

Statistical Analysis

After taking consultation with statisticians and monitoring parameters of the study, that is, nausea, retching, and vomiting, blood pressure, oxygen saturation, respiratory rate, pulse rate, pain score, adverse effects of the study drugs, etc. and to make the power of the study more than 85%, this study was conducted in 50 each. The data from the present study was systematically collected, compiled, and statistically analyzed to draw relevant conclusion. Sample size was calculated keeping in view at most 5% risk, with minimum 85% power and 5% significance level (significant at 95% confidence interval). Data were recorded in a Microsoft excel spread sheet and analyzed using Statistical Package for the IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp., Chicago. Continuous data were presented as mean with standard deviation. Categorical data were expressed as percentages. Numerical variables were normally distributed and were compared using Chi-square test for non-parametric data and independent "t"-test for parametric data. The P-value was then determined to evaluate the level of significance. The results were analyzed and compared to the previous studies to draw relevant conclusions.

OBSERVATION AND RESULTS

The mean age in groups GD and PD was 26.24 ± 3.32 and 25.50 ± 3.23 years respectively. In Group GD, the mean weight of patients was 62.52 ± 4.67 kg and in Group PD,

the mean weight was 62.12 ± 5.75 kg. In Group GD, 38 (76%) patients were of ASA grade I and 12 (24%) patients were of ASA grade II. In Group PD, 42 (84%) patients were of ASA grade I and 8 (16%) patients were of grade II. In Group GD, there were 10(20%) primipara patients and 40(80%) patients were multiparous. While in Group PD, there were 9 (18%) primipara patients and 41(82%) were multiparous patients. Hence, in relation to demographic profile, there was no significant difference between the two groups ($P > 0.05$) as in Table 1.

Post-operative nausea, retching, and vomiting were observed in 10%, 8%, and 6% of patients, respectively, in Group GD whereas only 6% of patients experienced nausea and 4% of patients were having retching and vomiting in Group PD during 0–6 h period. The same difference was maintained during 7–12 h and 13–24 h. Hence, the incidence of post-operative nausea, retching and vomiting was less in group PD as compared to Group GD during 0–24 h period but the difference came out to be statistically non-significant ($P > 0.05$) as in Table 2.

Out of 50 patients in each group, 6 (12%) patients required rescue antiemetic in group GD. Only 2 (4%) patient required rescue antiemetic in group PD during post-operative period. Requirement of rescue pain relief among the two groups was comparable. Group GD required rescue analgesic in 5 (10%) patients whereas Group PD required rescue analgesic in 3 (6%) patients as in Table 3.

Patient satisfaction score was generated with respect to satisfaction with the study drugs in both the groups. Patients having satisfaction score of 4 and 5 were taken as satisfied. Patients having satisfaction score of 1, 2, and 3 were taken as not satisfied. In Group GD, 40 (80%) patients were satisfied and in Group PD, 45 (90%) patients were satisfied. The difference among the two groups with regard to satisfaction of the patients was statistically non-significant ($P = 0.161$) as in Table 4.

Pulse rate, systolic and diastolic blood pressure, respiratory rate, and SPO2 were comparable at different time intervals during intraoperative (0–60 min) period. During post-operative period, the mean of hemodynamic parameters was taken at 0–6-h, 7–12-h, and 13–24-h period. Both the groups were found to be comparable. Variations were statistically insignificant ($P > 0.05$).

Table 1: Demographic profile

Parameter	Group GD (*n*=50)	Group PD (*n*=50)	*P*-value (NS)
Mean age (in years)	26.24±3.32	25.50±3.23	0.331
Weight	62.52±4.67	62.12±5.75	0.70
ASA status			0.317
I	38	42	
II	12	8	
Parity			
Primipara	10	9	0.414
Multipara	40	41	

DISCUSSION

PONV is one of the most common post-operative problem in anesthesia and remains a challenge especially in obstetric population. The factors responsible for the increase in the incidence of PONV during cesarean section under

Table 2: Comparison of nausea, vomiting, and retching between two groups

Time (in hours)	GD		PD		χ^2 (df=1)	"*P*"-value	Remarks
	No.	%	No.	%			
0–6 h							
Nausea	5	10.00	3	6.00	0.543	0.461	NS
Mild	2	4.00	1	2.00			
Moderate	2	4.00	2	4.00			
Severe	1	2.00	0	0.00			
Retching	4	8.00	2	4.00	0.709	0.399	NS
Vomiting	3	6.00	2	4.00	0.211	0.645	NS
7–12 h							
Nausea	4	8.00	2	4.00	0.709	0.399	NS
Mild	2	4.00	1	2.00			
Moderate	2	4.00	1	2.00			
Severe	0	0.00	0	0.00			
Retching	3	6.00	2	4.00	0.211	0.654	NS
Vomiting	2	4.00	1	2.00	0.344	0.557	NS
13–24 h							
Nausea	1	2.00	0	0.00	0.010	0.314	NS
Mild	0	0.00	0	0.00			
Moderate	1	2.00	0	0.00			
Severe	0	0.00	0	0.00			
Retching	1	2.00	0	0.00	0.010	0.314	NS
Vomiting	1	2.00	0	0.00	0.010	0.314	NS

Table 3: Need for rescue antiemetic in both groups

Rescue antiemetic	Group GD		Group PD		χ^2	"*P*"- value
	No.	%	No.	%		
Given	6	12.00	2	4.00	2.174	0.140
Not given	44	88.00	48	96.00		
Total	50	100.00	50	100.00		

Table 4: Patient satisfication score

Patient satisfaction score	GD		PD		χ^2	"*P*"- value	Remarks
	No.	%	No.	%			
Satisfied (score 4,5)	40	80.00	45	90.00	1.961	0.161	NS
Not satisfied (score 1,2,3)	10	20.00	5	10.00			
Total	50	100.00	50	100.00			

spinal anesthesia are maternal demographics, operative procedures, anesthetic technique, post-operative pain, use of perioperative opioids, anxiety, hypotension, and hypoperfusion of the CNS, abrupt visceral movements, exteriorization of the uterus, traction of the peritoneun, increased intraabdominal pressure, hormonal changes, and use of uterotonic agents. PONV has several undesirable consequences such as delayed mother and baby bonding, delayed breast feeding, pulmonary aspiration of gastric contents, metabolic alkalosis, risk of bleeding and increased intraabdominal pressure causing suture line dehiscence, and incisional hernia. It can cause apprehension and anxiety in subsequent pregnancy. Hence, prevention of PONV is very important.

As pathophysiology of PONV is multifactorial so no single antiemetic drug can provide better prophylaxis. An ideal antiemetic should have quick onset, long duration of action, and minimal side effects. Hence, drugs with different mechanisms of action can be used in combination for better prophylaxis and less side effects of each drug.

In our study, the difference between the two groups was statistically insignificant when demographic parameters were compared, that is, age, weight, ASA grading, and parity.

In our study, when we compared the incidence of nausea between two groups at different time interval from 0 to 24-h period, we found that incidence of nausea was less in PD group as compared to GD group but the difference was statistically insignificant ($P > 0.05$). Our study results are in accordance with the study conducted by Chilana *et al.* in which they observed that incidence of nausea was 5% during 0–6 h period, 5% during 6–12 h period and 0% during 12–24 h period with granisetron + dexamethasone combination.[4] Similarly, a study conducted by Nagappa *et al.* reported 8.6% incidence of nausea during 0–4 h and 11.4% during 4–24 h in granisetron + dexamethasone group.[5] Another study was done by Khuo *et al.* where they found the incidence of nausea with palonosetron + dexamethasone combination was 5% during 0–6 h, 1.7% during 6–12 h, and 3.3% during 12–24 h period.[6]

In the present study, group GD, 3 (6%) patients had retching during 0–6 h period and 3(6%) patients during 7–12 h period had retching. During 13–24 h period, only 1(2%) patient had retching. In Group PD, 2 (4%) patients had retching during 0–6 h period and 2(4%) patients had retching during 7–12 h period. No patient had any episode of retching during 13–24 h period. Hence, we observed that the incidence of retching was less in Group PD as compared to Group GD but the difference was statistically non-significant ($P > 0.05$). Our results of retching were comparable with the study done by Bhattacharjee *et al.* as they also found less incidence of retching in palonosetron (3.3% in 0–3 h, 3.3% in 3–24 h) and granisetron (3.3% in 0–3 h and 3.3% in 3–24 h) groups.[7]

In our study, we found that incidence of vomiting was lower in PD group as compared to GD group but the difference was statistically non-significant ($P > 0.05$). In a study conducted by Khuo *et al.* where they found that the incidence of vomiting in palonosetron +dexamethasone group was 3.4% during 0–6 h period, 0% from 6 to 24 h period. The results of our study were in concordance with the above study.[6] Another study done by Chilana *et al.* where they found the incidence of vomting was 2.5% during 0–6 h period, 2.5% during 6–12 h period, and 0% during 7–12 h in granisetron +dexamethasone which were comparable with our study.[4]

In Group GD, 6 (12%) patients received rescue anti-emetic during post-operative period. In Group PD, only 2 (4%) patients were given rescue anti-emetic in the post-operative period. Although the number of patients requiring rescue anti-emetic in Group PD was less than group GD but the difference was statistically insignificant($P > 0.05$) which is in accordance with the study conducted by Kovac *et al.* in which they found that patients at high risk of PONV who received combination therapy required less rescue antiemetic. Hence, adding dexamethasone to granisetron and palonosetron decreases the requirement of rescue antiemetic medication.[8]

During post-operative period, the mean of hemodynamic parameters was taken at 0–6-h, 7–12-h, and 13–24-h period. Both the groups were found to be comparable and statistically insignificant ($P > 0.05$).Our results were in concordance with the study done by Tahir *et al.* as they also observed that hemodynamic parameters were comparable both during intraoperative and post-operative period at different time intervals.[9]

In Group GD, 40(80%) patients were satisfied and in Group PD 45(90%) patients were satisfied. The difference among the two groups with regard to satisfaction of the patients was statistically non-significant ($P = 0.161$).Our results were comparable to the study done by Srivastava *et al.* where they compared palonosetron + dexamethasone and ondansetron + dexamethasone for prevention of PONV in middle ear surgeries and found that the satisfaction score for the palonosetron + dexamethasone group was 90.31 ± 8.61% which was similar to our study results.[10]

Limitations

We did not include a placebo group because pregnancy is a known risk factor for PONV and we cannot afford to

omit any antiemetic to the patients. As we enrolled patients of ASA class I and II in our study, the results may not be generalized to the patients with higher ASA physical status. We did not evaluate PONV after 24 h.

CONCLUSION

Although palonosetron plus dexamethasone is better than granisetron plus dexamethasone in terms of PONV, requirement of rescue antiemetic and patient satisfication score but the cost effectiveness of granisetron makes it a more commonly used drug in a setting with a limited resources. Further studies are recommended to evaluate the effectiveness of this combination therapy in caesarean section under spinal anesthesia to apply the results to the general population.

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How to cite this article: Sharma A, Taneja A, Mohan B, Mahajan L, Singh A, Kaur H. Comparative Study of Dexamethasone Addition to Granisetron and Palonosetron in Preventing Post-operative Nausea and Vomiting in Cesarean Section under Spinal Anesthesia. Int J Sci Stud 2023;10(12):98-102.

Source of Support: Nil, **Conflicts of Interest:** None declared.