A COMPARATIVE STUDY OF METOCLOPRAMIDE AND ONDANSETRON FOR POSTOPERATIVE NAUSEA AND VOMITING IN LOWER SEGMENT CAESAREAN SECTION

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ABSTRACT

BACKGROUND

Postoperative Nausea and Vomiting (PONV) is very common in the postoperative period causing discomfort to the patient and also delays discharge. Antiemetic drugs are beneficial for treatment of PONV. We have selected IV metoclopramide (10 mg) and IV ondansetron (4 mg) to compare their efficacy and safety for prophylactic use in postoperative nausea and vomiting in Lower Segment Caesarean Section (LSCS) under spinal anaesthesia.

MATERIALS AND METHODS

We have conducted the study after obtaining the permission from the institutional ethics committee and after obtaining written informed consent in 100 patients aged above 18 years belonging to ASA grade 1 and 2 scheduled to undergo elective LSCS under spinal anaesthesia.

RESULTS

Incidence of nausea was more in group-M than group-O at 2 hours, incidence of vomiting decreased in group-O than group-M and the incidence of retching was reduced significantly in group-O patients at 2 hours.

CONCLUSION

We conclude from our study that IV ondansetron, a $5HT_3$ antagonist in the dose of 4 mg has proved as a better prophylactic drug when compared to IV metoclopramide 10 mg in prevention of PONV in LSCS under spinal anaesthesia.

KEYWORDS

Spinal Anaesthesia, Caesarean Section, PONV, Metoclopramide, Ondansetron.

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BACKGROUND

Nausea and vomiting are the most common complications of surgery done under regional or general anaesthesia and is frequently seen in the postanaesthesia care unit. Incidence of postoperative nausea and vomiting is as high as 75-80%.[1] PONV remains a continuing problem with an average incidence of 20-30%. It is noted that the incidence is more common in females, especially in LSCS under subarachnoid block. PONV can be such unpleasant experience that patients often rate it worse than postoperative pain.[2] PONV is one of the commonest complaints following anaesthesia, and can result in morbidity like wound dehiscence, bleeding, pulmonary aspiration of gastric contents, fluid and electrolyte disturbances, delayed hospital discharge, unexpected hospital admission and decreased patient satisfaction.[3]

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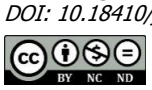

The predictors of PONV are-[4]

- Female gender.
- Non-smoking status.
- Previous history of PONV.
- Motion sickness.
- Use of postoperative opioids.
- Age.
- Hydration status.
- Body habitus.
- Medical condition.
- Type of anaesthesia.
- Duration of anaesthesia.
- Type of surgery.
- Postoperative hypotension.

Low blood pressure may lead to brain stem ischaemia, which is thought to activate the circulatory, respiratory and vomiting centres grouped together. Neuraxial anaesthesia also changes the function of the gastrointestinal tract.[5] Sympathetic blockade by local anaesthetics creates unopposed vagal action resulting in gastrointestinal hyperactivity. The efficacy of vagolytic agents to relieve nausea during spinal anaesthesia has been taken as evidence of the importance of this mechanism.[6] PONV can

result from stimulation of any of these receptors, namely dopamine, serotonin, muscarinic, cholinergic, histamine and opioid receptors.

AIMS

- To compare the efficacy and safety of prophylactic use of intravenous ondansetron (4 mg) and metoclopramide (10 mg) in preventing or reducing the incidence of postoperative nausea and vomiting in women undergoing elective LSCS under subarachnoid block.
- To evaluate any side effects associated with the use of these drugs.

MATERIALS AND METHODS

We carried a prospective randomised single-blinded study performed over a period of 20 months from August 2015 to March 2017 in the Department of Anaesthesiology at Maharajah's Institute of Medical Sciences, Vizianagaram. After obtaining written informed consent, 100 women patients aged above 18 yrs. belonging to ASA 1 and 2 scheduled to undergo elective LSCS under spinal anaesthesia were enrolled in the study and were randomly allocated into 2 groups 50 each.

Group M- The group received IV metoclopramide 10 mg.
Group O- The group received IV ondansetron 4 mg.

Patients were advised to remain nil orally after 10 p.m., the day before surgery. When patient is brought to the operation theatre, her pulse rate and BP were recorded. An IV access with 18G cannula was secured. 50 patients received Inj. Metoclopramide 10 mg IV and 50 patients received Inj. Ondansetron 4 mg IV 3-5 minutes before subarachnoid block. Pulse, BP and any side effects were noted. A preloading infusion of dextrose saline 500 mL was given. Subarachnoid block was performed in a left lateral position using 25G Quincke's spinal needle at L3-L4 interspace with Inj. 0.5% heavy bupivacaine of 1.5-2 mL depending on patients was given. Following injection, patient was immediately brought to supine position and time of onset of action to T6 level was noted using pinprick method. Desired operative position was given after 5 minutes. Intraoperative pulse, BP and SpO2 were monitored and maintained. Duration of surgery was noted. The patients were observed for 24 hours postoperatively. Nausea, retching and emesis were recorded at 1st hour (0-1 hr.), 2nd hour (1-2 hrs.), 6th hour (2-6 hrs.) and 24th hours (6-24 hrs.), respectively.

The number of episodes of emesis and type were recorded. Repeated vomiting within 1-2 minutes period was recorded as single emesis. The data was taken as follows-
No emesis - Complete control.
1-2 emesis - Nearly complete control.
3-5 emesis - Partial control.
>5 episodes - Failure.

Similarly, the number of episodes of retching (dry heaves) also were recorded. Nausea was graded as 0, 1, 2 and 3.

0 - None.
1 - Mild.
2 - Moderate.
3 - Severe.

Any side effects appreciated were recorded. The results were tabulated at 1st hr., 2nd hr., 6th hr. and 24th hours, postoperatively. Severe nausea and vomiting were labelled as failure and rescue therapy was initiated with IV ondansetron or metoclopramide and with IV fluids.

Statistical Analysis

Study results were analysed by 'Z' test and Student's 't' test. The level of significance was taken as-

P >0.05 - Not significant.
P <0.05 -Significant.
P <0.01 - Very significant.
P <0.001 - Highly significant.

RESULTS

Age in Years	Group M Number of Patients	Percentage	Group O Number of Patients	Percentage
18-22	22	44	19	38
23-26	18	36	23	46
27-30	8	16	5	10
31-35	2	4	3	6

Table 1. Distribution of Patients According to Age

Group M - Mean ± SD - 23.86 ± 3.50.
Group O - Mean ± SD - 24.18 ± 3.60.
T value - 0.45.
P value - 0.653 (>0.05) not significant.

Body weight Distribution	Group M	Group O
Weight range in kgs	45-65	45-70
	55.54 ± 5.47	54.06 ± 4.42

Table 2. Body Weight Distribution

T value - 1.48.
P value - 0.139 (>0.05) not significant.

Duration of Surgery	Group M	Group O
Duration range in mins.	60-140	60-145
Mean ± SD	91.5 ± 20.16	96.1 ± 20.51

Table 3. Duration of Surgery

T value - 1.13.
P value - 0.26 (>0.05).

Emesis (Episodes)		
	Group M	Group O
1 hr.	14	7
2 hrs.	4	3
6 hrs.	1	0
24 hrs.	0	0

Table 4. Comparison of Emesis (Episodes)

Number of Episodes of Emesis at 1 hr., 2 hrs. 6 hrs. and 24 hrs. were recorded and are shown as-

Comparison of Emesis (Mean Episodes)							
	Group M		Group O		Z value	P value	Remarks
	Mean	SD	Mean	SD			
1 hr.	0.28	0.57	0.14	0.40	1.72	0.08	Not significant
2 hrs.	0.08	0.27	0.06	0.24	0.39	0.69	Not significant
6 hrs.	0.02	0.14	0	0	1.00	0.31	Not significant
24 hrs.	0.0	0.0	0	0			

Table 5. Comparison of Emesis (Mean Episodes)

Though group O has shown less number of emetic episodes in 1 hr. and 2 hrs. than group M, it was not statistically significant.

Nausea (Grades)		
	Group M	Group O
1 hr.	32	16
2 hrs.	13	3
6 hrs.	1	0
24 hrs.	0	0

Table 6. Comparison of Nausea (Grades)

Comparison of Nausea (Mean Grades)							
	Group M		Group O		Z value	P value	Remarks
	Mean	SD	Mean	SD			
1 hr.	0.64	0.83	0.32	0.55	3.20	0.001	Significant
2 hrs.	0.26	0.53	0.06	0.24	2.73	0.006	Significant
6 hrs.	0.02	0.14	0	0	1.005	0.31	Not significant
24 hrs.	0	0	0	0			

Table 7 Comparison of Nausea (Mean Grades)

Incidence of nausea was more in 1st hour in both groups. The nausea grading was significantly low in the group-O compared to group-M at 1 hr. and 2 hrs.

Retching (Episodes)		
	Group M	Group O
1 hr.	6	4
2 hrs.	6	0
6 hrs.	0	0
24 hrs.	0	0

Table 8. Comparison of Retching (Episodes)

Comparison of Retching (Mean Episodes)							
	Group M		Group O		Z value	P value	Remarks
	Mean	SD	Mean	SD			
1 hr.	0.12	0.33	0.08	0.27	0.6667	0.50286	Not significant
2 hrs.	0.12	0.33	0	0	2.5265	0.0114	Significant
6 hrs.	0	0	0	0			
24 hrs.	0	0	0	0			

Table 9. Comparison of Retching (Mean Episodes)

	Group M	Group O	P value
Nausea			
1 hr.	21 (42%)	14 (28%)	0.14 (not significant)
2 hrs.	11 (22%)	3 (6%)	0.02 (significant)
6 hrs.	1 (2%)	0 (0%)	0.31 (not significant)
24 hrs.	0 (0%)	0 (0%)	
Total 24 hours	21 (42%)	14 (28%)	0.14 (not significant)
Vomiting			
1 hr.	11 (22%)	6 (12%)	0.18 (not significant)
2 hrs.	4 (8%)	3 (6%)	0.69 (not significant)
6 hrs.	1 (2%)	0 (0%)	0.31 (not significant)
24 hrs.	0 (0%)	0 (0%)	
Total 24 hours	12 (24%)	7 (14%)	0.20 (not significant)

Retching			
1 hr.	6 (12%)	4 (8%)	0.50 (not significant)
2 hrs.	6 (12%)	0 (0%)	0.01 (significant)
6 hrs.	0 (0%)	0 (0%)	
24 hrs.	0 (0%)	0 (0%)	
Total 24 hours	7 (14%)	4 (8%)	0.34 (not significant)

Table 10. Frequency of PONV and Retching

DISCUSSION

Postoperative Nausea and Vomiting (PONV) is described as "The Big Little Problem" and from the patients perspective PONV is among the most distressing complication of anaesthesia and surgery.[7] Early studies reported incidence of Postoperative Nausea and Vomiting (PONV) as high as 75-80%.[8] The aetiology of Postoperative Nausea and Vomiting (PONV) is complicated and multifactorial.[9] The occurrence of nausea and vomiting during caesarean section under regional anaesthesia is relatively high without prophylactic antiemetic.[10] Female gender has been associated with higher incidence of postoperative nausea and vomiting compared to male patients.[11,12] On an average, female patients suffer three times more often from postoperative nausea and vomiting than men.[13,14] The incidence of emetic symptoms is high during pregnancy because of increased concentration of progesterone in the body. The increased progesterone level during pregnancy decreases gastrointestinal motility and reduces lower oesophageal pressure.[15] These physiological and anatomical changes may predispose the pregnant patients to develop emetic sequelae. Furthermore, the incidence of nausea and vomiting during regional anaesthesia for caesarean delivery is relatively high. Factors attributed are younger age, surgical skill, peritoneal traction, exteriorisation of the uterus, fundal pressure during difficult delivery, anaesthetic management and prevention of hypotension in women undergoing caesarean delivery with spinal anaesthesia.[16] In 1912, Robert Ferguson described the use of olive oil.[17] Before any specific antiemetic agents became available, various techniques including olive oil and insulin glucose infusions were reported to be effective in reducing the incidence of postoperative nausea and vomiting.

Metoclopramide hydrochloride is a dopamine receptor antagonist and a potent prokinetic drug, which stimulates motility of the upper gastrointestinal tract leading to rapid gastric emptying and is used in the management of some form of nausea and vomiting and in gastroesophageal reflux and gastric stasis.[11]

According to Raphael, optimal dose of ondansetron for preventing postoperative nausea vomiting is 4 mg and half-life is 3 hours.

Datta el al and Kang et al observed that the incidence of emetic complications during caesarean section correlated with the presence of arterial hypotension. Hence, we preloaded the patient with 20 mL/kg of lactated Ringer's solution to prevent hypotension and placed a folded towel under the right buttock to prevent aortocaval compression.[16]

Paxton et al have observed in their study that nausea occurred in 25% of patients who received ondansetron as compared to 59% of patients with metoclopramide.

Malins et al have observed 59% nausea in the ondansetron group and 63% in metoclopramide group.

Naguile et al has observed prophylactic antiemetic treatment with ondansetron resulted in a lower incidence of PONV than metoclopramide ($P<0.02$).

Polati et al concluded that early antiemetic efficacy (abolition of vomiting within 10 mins. and of nausea within 30 mins. from the administration of the study drugs with no further vomiting or nausea episodes during the first hour was reported as 93.1% in the ondansetron group, 66.7% in the metoclopramide group, 35% in the placebo group, suggesting ondansetron 4 mg is more effective than metoclopramide 10 mg and placebo in the treatment of established PONVs.[17]

Age Incidence

In a study by Burtles R et al,[18] they found a correlation between increase in age and decrease in emesis. Average age in present study was 23.86 years in group M and 24.18 years in group O. In this study, the incidence of PONV was more in younger patients in both groups.

Weight Incidence

Obesity is usually seen to be associated with increased incidence of PONV. In a study by McKenzie R et al,[19] they found a higher percentage of patients with emetic episodes in heavier group, average weight in their study was 64.2 kgs.

In this present study, mean weight was 54.57 kgs. The incidence of vomiting was more in patients with weight more than 54.57 kgs. This does not correlate with their study.

Side Effects

Drugs commonly used like metoclopramide, droperidol, domperidone are associated with sedation, hypotension and extrapyramidal symptoms.

In a study by Dupeyron JP et al,[20] they observed low incidence of side effects with ondansetron.

In a randomised double-blind study by Rabey PG, Smith G[21] to compare the prophylactic antiemetic efficacy of ondansetron with droperidol and metoclopramide in 66 patients undergoing general anaesthesia for dilatation and curettage, 10 minutes before induction of anaesthesia, 22 patients received a single intravenous dose of 8 mg ondansetron, 22 others received 1.25 mg of droperidol and the remaining 22 received 10 mg metoclopramide. The incidence of vomiting as 13% with ondansetron, 45% with droperidol and 54% with metoclopramide ($P<0.05$) concluded that preoperative prophylactic administration of ondansetron is superior to droperidol and metoclopramide in the prevention of emetic sequelae after general anaesthesia.

In the study by Pan PH et al[22] of prevention of PONV after LSCS under epidural anaesthesia proved that ondansetron 4 mg IV is more often effective in preventing nausea than metoclopramide 10 mg and achieving complete and major responses during the intraoperative period and the overall 24 hours study period. However, there was no difference between the both groups in reducing frequency of vomiting. For the overall 24 hours study period, the frequency of complete response was significantly higher in group O (74%) than group M (49%). The need for use of emesis basins in the overall 24-hour period was significantly less for group O (15%) compared to group M (33%). Patients in group O rated the overall patient satisfaction as excellent compared with group M (53%).

Metoclopramide hydrochloride is a dopamine receptor antagonist that is structurally similar to procainamide and a potent prokinetic drug, which stimulates motility of the upper gastrointestinal tract leading to rapid gastric emptying and is used in the management of nausea and vomiting. The common side effects of metoclopramide are extrapyramidal syndrome, Parkinsonism, dizziness, headache and tardive dyskinesia. Other side effects are depression, neuroleptic malignant syndrome, supraventricular tachycardia and hypertension.

Ondansetron is the prototype drug of the group, serotonin $5HT_3$ antagonist, which is primarily used for the treatment of chemotherapy and radiotherapy induced nausea and vomiting. The common side effects of ondansetron are headache, tachycardia, prolongation of QT interval, mild sedation, constipation, diarrhoea, dry mouth and hypersensitivity reactions.

The side effects in this study were very low with one patient having extrapyramidal syndrome in metoclopramide group, which was treated with IV diazepam and one patient complained of headache in ondansetron group, which relieved without any treatment. Thus, ondansetron was much more effective in decreasing PONV in LSCS under spinal anaesthesia with low side effect profile.

CONCLUSION

From this study, it was observed that IV ondansetron, a 5HT3 antagonist in the dose of 4 mg was better prophylactic drug than IV metoclopramide in the dose of 10 mg in controlling PONV in LSCS under spinal anaesthesia.

The side effects with these drugs were minimal. In group-M, one patient had an extrapyramidal syndrome, which was treated with IV diazepam and in the group-O one patient complained of headache.

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