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A COMPARATIVE STUDY OF ONDANSETRON AND RAMOSETRON FOR PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract

Introduction: Laparoscopic cholecystectomy is now being routinely performed for cholelithiasis. The most common and distressing symptoms following surgery and anesthesia are pain, nausea and vomiting. Pain causes suffering drawing immediate attention and hence has received much more interest in the last few decades than Post Operative Nausea and Vomiting (PONV).

Materials and Methods: After approval from the St Martha's Hospital Ethical Committee and completion of written informed consent, we studied 80 patients undergoing elective laparoscopic cholecystectomy at St Martha's hospital from October 2010 onwards for a period of 2 years. A written informed consent was obtained from all the patients satisfying the inclusion criteria. The selection of patients was carried out randomly into the two groups. Group A: received .1mg/kg Inj Ondansetron, Group B: received .6mcg/kg Inj Ramosetron.

Results: Since p value is >0.05, we infer that there is no statistical difference in the average mean of the age between the two treatment groups. Since p Value is >0.05, we conclude that there is no affiliation between Gender and the treatment groups. Since p Value is >0.05, we conclude that there is no affiliation between Rescue Antiemetic and the treatment groups.

Conclusion: Inj Ondansetron 4 mg and Inj Ramosetron 0.3 mg (intravenous administration) are equally effective in decreasing the incidence of PONV after laparoscopic cholecystectomy under general anesthesia, and that no drug is superior to the other among the two. However, the two advantages we noticed with Inj Ramosetron were Convenience of administration once a day as against thrice with Ondansetron. Cost effectiveness of Ramosetron Rs. 32 per ampoule (per day) as against Ondansetron Rs. 28 X 3=84 per 3 ampoules (per day).

Key Words: Laparoscopic cholecystectomy, cholelithiasis, Ondansetron, Ramosetron.

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INTRODUCTION

Laparoscopic cholecystectomy is now being routinely performed for cholelithiasis. The most common and distressing symptoms following surgery and anesthesia are pain, nausea and vomiting. Pain causes suffering drawing immediate attention and hence has received much more interest in the last few decades than Post Operative Nausea and Vomiting (PONV).[1]

The incidence of PONV following laparoscopic surgeries is relatively high, 40 to 75 %. They can be more distressing especially after ambulatory surgeries, delaying the hospital discharge, prolonging stay, and increasing costs. Therefore prevention and treatment of PONV helps inpost-operative recovery and increases patient satisfaction.[2]

In spite of advances from opioid and deep anesthesia to non opioid or supplemented opioid, to ether and non ether anesthesia, improved pre and post operative medications, refinement of operative techniques and identification of patient predictive factors, nausea and vomiting still occur with unpredictable frequency. Hence it has been described as the "big little problem".[3]

Potential new entries into anti emetic pharmacopeia in 1991 were the 5HT3 receptor antagonists which lack effects on cholinergic, adrenergic, dopaminergic or histamine receptors. These 5HT3 receptors are located both peripherally in the vagal nerve terminals and centrally (CTZ) so that the anti emetic property can be mediated centrally, peripherally or both.[4]

They have little effect on lower esophageal sphincter pressure, gastric emptying time or small bowel transit time. By 5HT3 selectivity, the undesirable side effects such as dysphoria, sedation and extra pyramidal symptoms are avoided.[5]

Currently available5HT3antagonists Ondansetron, granisetron and dolasetron share a comparable anti emetic efficacy and favorable adverse effect profiles. However they have a short duration of action and provide anti "vomiting" effect without providing a comparable anti "nausea" effect".[6]

Ramosetron, a newly developed 5HT3 antagonist has shown more potency and longer duration of action as compared to other drugs in this class. This is because the drug exhibits more potent and sustained antagonistic actions against 5HT3 receptors, than existing 5HT3 receptor antagonist type antagonists. The elimination half time of Ramosetron, 9 hrs is longer than that of Ondansetron which is 3.5 hrs and granisetron 4.9 hrs. A minimum of 0.3 mg Ramosetron is required to effectively prevent PONV during the first 48 hrs of surgery.

MATERIALS AND METHODS

After approval from the St Martha's Hospital Ethical Committee and completion of written informed consent, we studied 80 patients undergoing elective laparoscopic cholecystectomy at St Martha's hospital from October 2010 onwards for a period of 2 years.

Study period: From October 2010 to October 2012.

Source of data: Inpatients of St. Martha's hospital, Bangalore undergoing laparoscopic cholecystectomy under general anaesthesia

Type of study: A comparative and prospective study

Inclusion criteria

- Patients belonging to ASA Physical status I and II
- Patients aged 20-60 years

Exclusion criteria

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- Patients who have received antiemetic within 24 hours before surgery
- Patients with a history of gastro intestinal disease
- Patients with a history of motion sickness
- Patients with a history of post operative emesis
- Patients who are pregnant
- Patients who are menstruating
- Patients with abnormal ECG finding

Materials

- Injection Ondansetron 4 mg / 2ml ampoule (2mg/ ml)
- Injection Ramosetron 0.3 mg / 2ml ampoule (0.15mg/ml)

Methodology: A written informed consent was obtained from all the patients satisfying the inclusion criteria. The selection of patients was carried out randomly into the two groups. **Group A**: received .1mg/kg Inj Ondansetron**, Group B**: received .6mcg/kg Inj Ramosetron,

- Pre anesthetic evaluation included general examination, systemic examination of cardiovascular, respiratory and central nervous systems and examination of airway and spine for any disease and deformity
- Other investigations were carried out as applicable before taking up the patient for surgery.
- Premedication with Tab Pantoprazole 40 mg per orally on the night before the scheduled surgery.
- All patients were kept nil orally from 10 pm the night before surgery
- At 7 AM, on the morning of surgery, regular medications with sip of water (anti hypertensives, anti thyroid drugs) were administered
- All patients were monitored intra operatively with a cardiac monitor-Heart rate, ECG lead II, Non Invasive Blood pressure ,Respiratory rate, Pulse oximetry (SpO2) and Capnography (ETCO2)
- Large bore IV access was secured and crystalloid infusion started.
- Premedication with Inj Fentanyl 1.5 mcg/kg, Pre oxygenation for 3 minutes with 100% O2
- Induction with Inj Propofol 2mg/kg
- Muscle relaxation with Inj Vecuronium 0.1mg/kg followed by conventional laryngoscopy and intubation with a snugly fitting cuffed endotracheal tube appropriate to the patient
- Maintenance with O2 + N2O + 1-2% Isoflurane
- Ventilation was controlled mechanically and adjusted to maintain ETCO2 between 30 and 35 mm Hg
- Muscle relaxation was achieved using Inj Vecuronium as required
- Naso gastric tube was passed to promote deflation of stomach and emptying of gastric contents which was suctioned before endotracheal extubation. Removal as per the Surgeon's orders.
- Patients received a single dose of either Inj Ramosteron 0.6mcg/kg or Inj Ondansetron 0.1 mg/kg slowly over 2-5 minutes.
- Inj Ondansetron, fifteen minutes and Inj Ramosetron thirty minutes before the end of surgery were administered. In the pilot study conducted, Inj Ramosetron was also administered at fifteen minutes before the end of surgery. However, it was found to be most effective when given thirty minutes before the end of surgery.

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- Isoflurane inhalation was cut off approximately 10 minutes before the end of surgery. Patients were adequately reversed with Inj. Neostigmine 0.05 mg/kgbw and Inj Glycopyrrolate 0.01 mg/kg and trachea was extubated after fulfilling the extubation criteria.
- Patients were shifted to Post anesthesia care unit (PACU).
- After recovery from anesthesia, PONV experienced by the patients was recorded during the first 3 hours (0-3hrs) and the next 3-24 hrs by observation and direct questioning.
- PONV was recorded by THE SEVERE EMETIC SCALE[56]

SEVERE EMETIC SCALE[56]

PONV	Score
No nausea	1
Mild nausea	2
Severe nausea	3
Vomiting	4

- Inj Metoclopramide was administered IV if two or more episodes of vomiting occur within 24 hours after recovery of anesthesia as a rescue antiemetic
- Inj Diclofenac 75 mg IM was used as the rescue analgesic
- The details of any adverse event throughout the study period 0 – 24 hours after anesthesia was also be recorded by observation and general questioning or by spontaneous report of the patient.
- Drowsiness / sedation was assessed as 0=awake, 1=drowsy / sedated
- Hypotension when
- Systolic blood pressure intra operative <80 mm Hg

Diastolic blood pressure intra operative < 60 mmHg

- Headache, dizziness and constipation were noted as side effects for a period of 24 hrs after recovery from anesthesia.

Method of Statistical Analysis: The following methods of statistical analysis have been used in this study. The results for each parameter (numbers and percentages) for discrete data and averaged (mean $\pm$ standard deviation) for continuous data are presented in Table and Figure. Proportions were compared using Chi-square test of significance, The Student 't' test was used to determine whether there was a statistical difference between study groups in the parameters measured. In all the above test the "p" value of less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using Statistical Package for Social Science (SPSS) package.

RESULTS

Study Groups: Group A: INJ ONDANSETRON 0.1mg/kg bw(4mg)**,** Group B: INJ RAMOSETRON 6 mcg/kg bw (0.3 mg).

TABLE 1: Mean Age in Groups with Group A and Group B

	N	Mean Age	SD	Min.	Max.	't' value	'p' value

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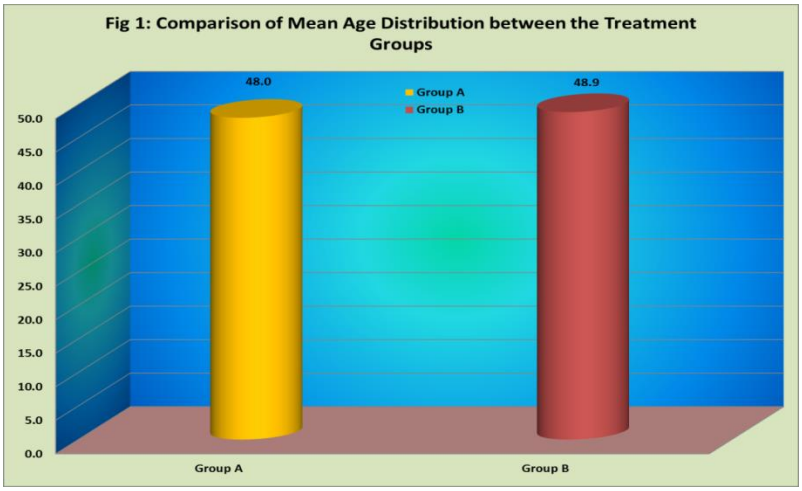
Group A	40	48.00	9.767	28	70	0.209	0.649
Group B	40	48.85	6.565	38	60		



Inference: Since p value is >0.05, we infer that there is no statistical difference in the average mean of the age between the two treatment groups

Table 2: Statistical Analysis: Age Distribution Between The Two Study Groups

	Age					**Total**	χ^2 value	'p' value
	<=30 yrs	**31-40 yrs**	**41-50 yrs**	**51-60 yrs**	**61-70 yrs**			
Group A	2	8	17	10	3	40	6.940	0.139
	5.0%	20.0%	42.5%	25.0%	7.5%	100.0%		
Group B	0	8	15	17	0	40		
	.0%	20.0%	37.5%	42.5%	.0%	100.0%		
Total	2	16	32	27	3	80		
	2.5%	20.0%	40.0%	33.8%	3.8%	100.0%		

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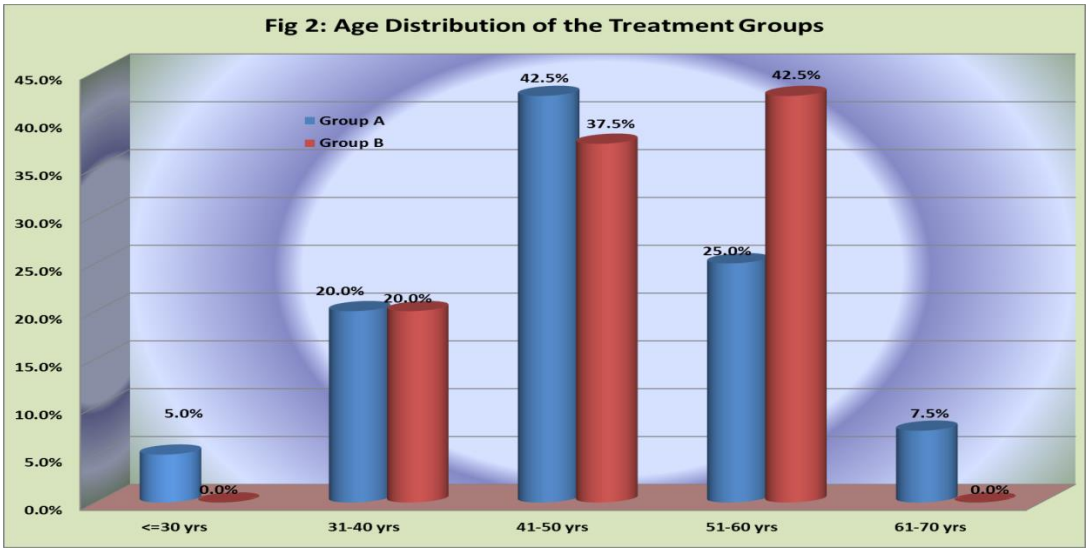


Table 3: Sex Distribution between the Two Study Groups

	Gender		Total	χ^2 value	'p' value
	Male	**Female**			
Group A	18	23	40	2.650	0.104
	45.0%	55.0%	100.0%		
Group B	11	29	40		
	27.5%	72.5%	100.0%		
Total	29	51	80		
	36.3%	63.8%	100.0%		

Inference : Since p Value is >0.05, we conclude that there is no affiliation between Gender and the treatment groups.

Table 4: Statistical Analysis: Requirement Of Rescue Antiemetic Between The Two Study Groups

	Rescue Antiemetics		Total	χ^2 value	'p' value
	Yes	**No**			
Group A	2	38	40	2.061	0.162
	5.0%	95.0%	100.0%		
Group B	0	40	40		
	.0%	100.0%	100.0%		
Total	2	78	80		
	2.5%	97.5%	100.0%		

Inference : Since p Value is >0.05, we conclude that there is no affiliation between RESCUE

ANTIEMETICand the treatment groups.

Table 5: Statistical Analysis: ASA Physical Status Distribution Between The Two Study Groups

	ASA Grade		Total	χ2 value	'p' value
	Grade 1	Grade 2			
Group A	19	21	40	0.460	0.602
	47.5%	52.5%	100.0%		
Group B	23	18	40		
	55.0%	45.0%	100.0%		
Total	41	39	80		
	51.3%	48.8%	100.0%		

Inference : Since p Value is >0.05, we conclude that there is no affiliation between ASA Grade and the treatment groups.

Table 6: Statistical Analysis: Requirement Of Rescue Analgesic Between The Two Study Groups

	Rescue analgesic		Total	χ2 value	'p' value
	Yes	No			
Group A	6	34	40	1.127	0.268
	15.0%	85.0%	100.0%		
Group B	3	37	40		
	7.5%	92.5%	100.0%		
Total	9	71	80		
	11.3%	88.8%	100.0%		

Inference : Since p Value is >0.05, we conclude that there is no affiliation between RESCUE ANALGESICand the treatment groups.

Table 7: Statistical Analysis: Weight Distribution Between The Two Study Groups

	N	Mean Body Weight	SD	Min.	Max.	't' value	'p' value
Group A	40	60.80	7.826	40	78	0.232	0.639
Group B	40	61.58	6.868	45	75		

Inference : Since P-Value is >0.05, we conclude that there is no difference in the mean Body wt of the two treatment groups.

Table 8: Statistical Analysis: Between the Two Study Groups

(a) Duration of Surgery (in min)

	N	Mean	SD	Min.	Max.	't' value	'p' value
Group A	40	88.70	8.471	70	110	0.183	0.870
Group B	40	89.48	7.733	76	109		

Inference : Since P-Value is >0.05, we conclude that there is no difference in the mean Surgery Time of the two treatment groups.

(b) Awakening Time (in min)

	N	Mean	SD	Min.	Max.	't' value	'p' value
Group A	40	6.813	.6178	5.8	8.0	6.779	0.019
Group B	40	6.507	.5121	5.6	8.0		

Inference : Since p Value is <0.05, there is difference in the mean Awakening Time of the two treatment groups. Awakening time for Group B is shorter than A

(c) Duration of Anaesthesia (min)

	N	Mean	SD	Min.	Max.	't' value	'p' value
Group A	40	104.15	7.678	90	121	1.993	0.182
Group B	40	101.80	7.205	88	120		

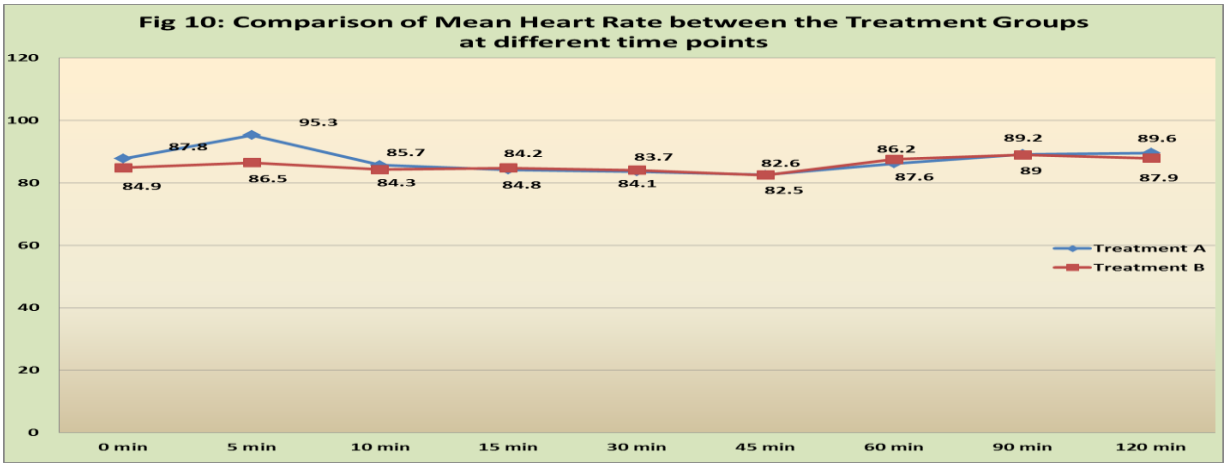
Inference : Since P-Value is <0.05, we conclude that there is no difference in the mean Anesthesia Time of the two treatment groups.

Table 9: Comparison of Intra Operative Heart Rates between the Two Study Groups

Parameter: HR

Time		N	Mean	SD	Min.	Max.	't' value	'p' value
0 min	Group A	40	87.8	10.52	66	110	1.313	0.255
	Group B	40	84.9	12.06	68	110		
5 min	Group A	40	95.3	10.33	72	116	11.956	<0.001
	Group	40	86.5	12.23	65	116		

	B							
10 min	Group A	40	85.7	10.03	65	111	0.315	0.576
	Group B	40	84.3	11.43	67	111		
15 min	Group A	40	84.2	10.92	60	110	0.058	0.810
	Group B	40	84.8	11.31	64	110		
30 min	Group A	40	83.7	11.15	59	112	0.023	0.881
	Group B	40	84.1	11.18	64	112		
45 min	Group A	40	82.6	11.35	60	112	0.002	0.968
	Group B	40	82.5	11.06	62	112		
60 min	Group A	40	86.2	18.74	49	128	0.141	0.708
	Group B	40	87.6	15.01	68	128		
90 min	Group A	40	89.2	16.88	56	127	0.003	0.955
	Group B	40	89.0	14.82	69	127		
120 min	Group A	40	89.6	15.84	58	123	0.255	0.615
	Group B	40	87.9	14.19	70	123		



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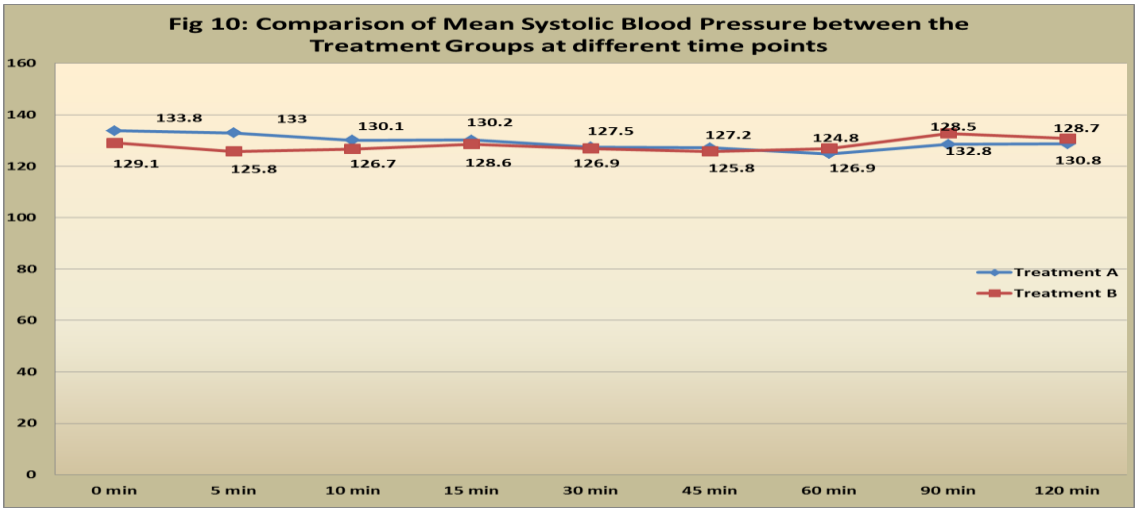
Inference:No difference in mean Heart rate of the two groups except **at 5min.**

Table 10: Comparison of Intra Operative Systolic Blood Pressure between the Two Study Groups

Parameter: SBP

Time		N	Mean	SD	Min.	Max.	't' value	'p' value
0 min	Group A	40	133.8	17.50	96	170	1.575	0.213
	Group B	40	129.1	16.14	96	160		
5 min	Group A	40	133.0	16.41	94	167	4.279	0.042
	Group B	40	125.8	14.79	94	157		
10 min	Group A	40	130.1	16.42	98	160	0.944	0.334
	Group B	40	126.7	15.33	98	160		
15 min	Group A	40	130.2	16.72	96	166	0.211	0.648
	Group B	40	128.6	14.89	100	158		
30 min	Group A	40	127.5	16.60	98	160	0.026	0.871
	Group B	40	126.9	14.97	104	161		
45 min	Group A	40	127.2	17.07	92	164	0.138	0.711
	Group B	40	125.8	15.35	101	162		
60 min	Group A	40	124.8	18.51	92	160	0.284	0.596
	Group B	40	126.9	16.26	104	163		
90 min	Group A	40	128.5	19.86	98	164	1.032	0.313
	Group B	40	132.8	17.47	104	171		
120 min	Group A	40	128.7	20.42	94	166	0.230	0.640
	Group B	40	130.8	19.11	100	173		



Inference : no difference in the mean of Intra Operative Systolic Blood Pressure of the two groups except for**at 5 min.**

Table 11: Comparison of Intra Operative Diastolic Blood Pressure between the Two Study Groups

Parameter: DBP

Time		N	Mean	SD	Min.	Max.	't' value	'p' value
0	Group	40	79.7	12.30	58	105	.000	1.000

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min	A							
	Group B	40	79.7	11.86	56	101		
5 min	Group A	40	82.4	11.00	62	118	8.871	0.004
	Group B	40	75.3	10.23	54	96		
10 min	Group A	40	81.1	10.96	62	115	4.811	0.031
	Group B	40	76.1	9.36	61	98		
15 min	Group A	40	78.9	10.49	60	103	.929	0.338
	Group B	40	76.7	9.91	57	98		
30 min	Group A	40	78.2	10.75	60	108	.677	0.413
	Group B	40	76.3	9.03	60	94		
45 min	Group A	40	77.3	11.34	58	110	.714	0.401
	Group B	40	75.3	9.48	60	96		
60 min	Group A	40	76.7	11.45	60	106	.240	0.625
	Group B	40	75.5	10.41	58	96		
90 min	Group A	40	81.3	11.45	57	103	1.016	0.317
	Group B	40	78.7	12.05	62	103		
120 min	Group A	40	81.2	11.74	57	103	1.291	0.259
	Group B	40	78.1	12.64	60	103		

Inference :no difference in the mean Intra Operative Diastolic Blood Pressure of the two groups except for the **at 5 min & 10 min.**

Table 12: Comparison of Intra Operative Mean Arterial Pressure Between The Two Study Groups

Parameter: MAP

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Time		N	Mean	SD	Min.	Max.	't' value	'p' value
0 min	Group A	40	97.8	11.988	71	123	0.351	0.555
	Group B	40	96.2	12.535	71	117		
5 min	Group A	40	99.3	12.207	73	131	7.304	0.008
	Group B	40	92.2	11.186	70	113		
10 min	Group A	40	97.5	12.306	77	129	3.004	0.087
	Group B	40	93.0	10.733	75	114		
15 min	Group A	40	96.0	12.094	76	118	0.616	0.435
	Group B	40	94.0	10.646	71	116		
30 min	Group A	40	94.6	12.093	77	120	0.319	0.574
	Group B	40	93.2	10.427	75	112		
45 min	Group A	40	93.9	12.451	74	120	0.479	0.491
	Group B	40	92.1	10.739	75	113		
60 min	Group A	40	92.7	12.871	75	118	0.001	0.978
	Group B	40	92.6	11.799	74	115		
90 min	Group A	40	97.1	13.602	71	123	0.014	0.907
	Group B	40	96.7	13.027	78	123		
120 min	Group A	40	97.1	13.995	71	123	0.236	0.636
	Group B	40	95.6	14.211	73	121		

Inference:no difference in the MAP between the two groups except at 5 min.

Table 13: Comparison of Post Operative Nausea and Vomiting Between the Two Study Groups

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Time		Nausea/vomiting Score				Total	$\chi 2$ value	'p' value
		1	2	3	4			
0 hr	Group A	35	5			40	0.556	0.456
		87.5%	12.5%			100.0%		
	Group B	37	3			40		
		92.5%	7.5%			100.0%		
	Total	72	8			80		
		90.0%	10.0%			100.0%		
1 hr	Group A	35	5			40	0.556	0.456
		87.5%	12.5%			100.0%		
	Group B	37	3			40		
		92.5%	7.5%			100.0%		
	Total	72	8			80		
		90.0%	10.0%			100.0%		
2 hr	Group A	35	4	1		40	1.014	0.602
		87.5%	10.0%	2.5%		100.0%		
	Group B	36	4	0		40		
		90.0%	10.0%	.0%		100.0%		
	Total	71	8	1		80		
		88.8%	10.0%	1.3%		100.0%		
3 hr	Group A	33	6	1		40	2.239	0.328
		82.5%	15.0%	2.5%		100.0%		
	Group B	37	3	0		40		
		92.5%	7.5%	.0%		100.0%		
	Total	70	9	1		80		
		87.5%	11.3%	1.3%		100.0%		
4 hr	Group A	29	11			40	0.621	0.431
		72.5%	27.5%			100.0%		
	Group B	32	8			40		
		80.0%	20.0%			100.0%		
	Total	61	19			80		
		76.3%	23.8%			100.0%		
24 hr	Group A	34	4		2	40	2.270	0.321
		85.0%	10.0%		5.0%	100.0%		
	Group	37	3		0	40		

	B	92.5%	7.5%		.0%	100.0%		
	Total	71	7		2	80		
		88.8%	8.8%		2.5%	100.0%		

Inference : From Above Table we conclude that there is no affiliation between treatment groups & Vomiting Score at any time

Table 14: Comparison of Intra Operative Heart Rates between the Two Study Groups

Parameter: HR

Treatment	Time	N	Mean	SD	Min.	Max.	'f' value	'p' value
Group A	0 min	40	87.80	10.523	66	110	3.464	0.001
	5 min	40	95.28	10.328	72	116		
	10 min	40	85.65	10.027	65	111		
	15 min	40	84.20	10.924	60	110		
	30 min	40	83.70	11.152	59	112		
	45 min	40	82.55	11.348	60	112		
	60 min	40	86.15	18.745	49	128		
	90 min	40	89.18	16.876	56	127		
	120 min	40	89.58	15.844	58	123		
Group B	0 min	40	84.90	12.064	68	110	1.127	0.344
	5 min	40	86.53	12.236	65	116		
	10 min	40	84.30	11.434	67	111		
	15 min	40	84.80	11.314	64	110		
	30 min	40	84.08	11.180	64	112		
	45 min	40	82.45	11.059	62	112		
	60	4	87.5	15.01	68	128		

	min	0	8	4				
	90 min	40	88.98	14.819	69	127		
	120 min	40	87.88	14.193	70	123		

Inference: From the above table we conclude that there is difference in Variancefor Group A of the Heart rate measured at various time interval.However the there is no difference in the variance for the Group B.

Table 15: Comparison of Intra Operative Systolic Blood Pressure between the Two Study Groups

Parameter: SBP

Treatment	Time	N	Mean	SD	Min.	Max.	'f' value	'p' value
Group A	0 min	40	133.80	17.502	96	170	1.025	0.417
	5 min	40	133.00	16.405	94	167		
	10 min	40	130.10	16.416	98	160		
	15 min	40	130.23	16.725	96	166		
	30 min	40	127.48	16.602	98	160		
	45 min	40	127.15	17.074	92	164		
	60 min	40	124.78	18.512	92	160		
	90 min	40	128.53	19.865	98	164		
	120 min	40	128.70	20.415	94	166		
Group B	0 min	40	129.07	16.144	96	160	0.888	0.526
	5 min	40	125.78	14.793	94	157		
	10 min	40	126.65	15.331	98	160		
	15 min	40	128.60	14.887	100	158		
	30 min	40	126.90	14.971	104	161		
	45 min	40	125.80	15.354	101	162		
	60 min	40	126.85	16.257	104	163		

	90 min	40	132.78	17.469	104	171		
	120 min	40	130.78	19.106	100	173		

Inference: From the above table we conclude that there is no difference in Variance for Group A as well as B of the Systolic Blood Pressure measured at various time interval.

Table 16: Comparison of Intra Operative Diastolic Blood Pressure between the Two Study Groups

Parameter: DBP

Treatment	Time	N	Mean	SD	Min.	Max.	'f' value	'p' value
Group A	0 min	40	79.72	12.300	58	105	1.268	0.259
	5 min	40	82.40	11.001	62	118		
	10 min	40	81.10	10.963	62	115		
	15 min	40	78.88	10.489	60	103		
	30 min	40	78.15	10.745	60	108		
	45 min	40	77.25	11.343	58	110		
	60 min	40	76.65	11.448	60	106		
	90 min	40	81.30	11.454	57	103		
	120 min	40	81.18	11.741	57	103		
Group B	0 min	40	79.72	11.865	56	101	0.914	0.505
	5 min	40	75.33	10.232	54	96		
	10 min	40	76.10	9.364	61	98		
	15 min	40	76.68	9.913	57	98		
	30 min	40	76.33	9.025	60	94		
	45 min	40	75.28	9.479	60	96		
	60 min	40	75.45	10.414	58	96		
	90	40	78.65	12.050	62	103		

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	min							
	120 min	40	78.08	12.644	60	103		

Inference: From the above table we conclude that there is no difference in Variance for Group A as well as B of the Diastolic Blood Pressure measured at various time interval.

Table 17: Comparison of Intra Operative Mean Arterial Pressure between the Two Study Groups

Parameter: MAP

Treatment	Time	N	Mean	SD	Min.	Max.	'f' value	'p' value
Group A	0 min	40	97.8	11.988	71	123	1.097	0.365
	5 min	40	99.3	12.207	73	131		
	10 min	40	97.5	12.306	77	129		
	15 min	40	96.0	12.094	76	118		
	30 min	40	94.6	12.093	77	120		
	45 min	40	93.9	12.451	74	120		
	60 min	40	92.7	12.871	75	118		
	90 min	40	97.1	13.602	71	123		
	120 min	40	97.1	13.995	71	123		
Group B	0 min	40	96.2	12.535	71	117	0.904	0.513
	5 min	40	92.2	11.186	70	113		
	10 min	40	93.0	10.733	75	114		
	15 min	40	94.0	10.646	71	116		
	30 min	40	93.2	10.427	75	112		
	45 min	40	92.1	10.739	75	113		
	60 min	40	92.6	11.799	74	115		
	90 min	40	96.7	13.027	78	123		

	120 min	40	95.6	14.211	73	121		

Inference: From the above table we conclude that there is no difference in Variance for Group A as well as B of the mean arterial pressure measured at various time interval.

Table 18: Comparison of Post Operative Nausea and Vomiting Between the Two Study Groups

Treatment	Time	Vomiting/Nausea Score				Total	χ^2 value	'p' value
		1	2	3	4			
Group A	0 hr	35	5	0	0	40	20.792	0.144
		87.5%	12.5%	.0%	.0%	100.0%		
	1 hr	35	5	0	0	40		
		87.5%	12.5%	.0%	.0%	100.0%		
	2 hr	35	4	1	0	40		
		87.5%	10.0%	2.5%	.0%	100.0%		
	3 hr	33	6	1	0	40		
		82.5%	15.0%	2.5%	.0%	100.0%		
	4 hr	29	11	0	0	40		
		72.5%	27.5%	.0%	.0%	100.0%		
	24 hr	34	4	0	2	40		
		85.0%	10.0%	.0%	5.0%	100.0%		
	Total	201	35	2	2	240		
		83.8%	14.6%	.8%	.8%	100.0%		
Group B	0 hr	37	3			40	5.556	0.352
		92.5%	7.5%			100.0%		
	1 hr	37	3			40		
		92.5%	7.5%			100.0%		
	2 hr	36	4			40		
		90.0%	10.0%			100.0%		
	3 hr	37	3			40		
		92.5	7.5%			100.0		

		%				%		
	4 hr	32	8			40		
		80.0 %	20.0 %			100.0 %		
	24 hr	37	3			40		
		92.5 %	7.5%			100.0 %		
	Total	216	24			240		
		90.0 %	10.0 %			100.0 %		

Inference: From the above table we conclude that there is no affiliation between Time interval and Vomiting sensation.

STATISTICAL ANALYSIS:

a) **Patient characteristics**:

- **Age**:
  - Mean age of GROUP A: 48 yrs
  - Mean age of GROUP B: 48.85 yrs
- **Sex**:
  - Male : female GROUP A: 18:23
  - Male : female GROUP B: 11:29
- **ASA Physical status**:
  - GROUP A: ASA I: 19 and ASA II: 21
  - GROUP B: ASA I: 23 and ASA II: 18
- **Weight**:
  - GROUP A: Average: 60.8
  - GROUP B: Average: 61.58
- **Average duration of surgery**:
  - GROUP A: 88.7 min
  - GROUP B: 89.48 min
- **Average duration of anesthesia**:
  - GROUP A: 104.15 min
  - GROUP B: 101.8 min
- **Awakening time**:
  - GROUP A: 6.813 min
  - GROUP B: 6.507min

These data showed no significant difference between the two study groups. On statistical analysis, no significant difference was found between the two groups with respect to the recordings of heart rate and blood pressure intra operatively except for the readings at the 5^{th} minute which could not be attributed to the action of either of the drug, as they were administered just prior to extubation. Significant difference was observed in awakening time between the groups. But this could not be explained with

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regard to the action of the two drugs.

b) **Incidence of PONV**

Among 40 patients treated with InjOndansetron(GROUP A),

- 35 patients (87.5%) had no episodes of nausea at the end of 2 hrs, and 34 patients(84%) had no nausea at 24 hrs post operatively.
- Mild nausea was present in 4 patients(10%) in the first two hrs and 4 patients(10%) at 24 hrs post operatively
- 1 patient(2.5%) had severe nausea at 2^{nd} and 3^{rd} hour post operatively.
- 2 patients(5%) reported vomiting at 24 hrs post operatively

Among 40 patients treated with InjRamosetron(GROUP B),

- 36 patients (90%) had no episodes of nausea at the end of two hrs and 37 patients (92.5%) had no nausea 24 hrs post operatively.
- Mild nausea was present in 4 patients(10%) in the first two hrs and 3 patients(7.5%) at 24 hrs post operatively
- No patient complained of severe nausea with GROUP B
- No patient had vomited at the end of 24 hrs post operatively

However, the overall incidence of nausea and vomiting did not have a statistically significant difference among both the groups.

c) **Rescue antiemetic requirement**

Post operatively2 patients (5%) required rescue anti emetic drug for the treatment of vomiting in the group treated with InjOndansetron, whereas in the other group with InjRamosetron, no patient required any rescue anti emetic. But there was no statistical difference among the groups as the p value was 0.162.

d) **Rescue analgesic requirement**

In patients with Inj Ondansetron, 6 patients (15%) received rescue analgesic as compared to 3 patients (7.5%) in the group treated with Inj Ramosetron. When compared statistically, p value=0.268, hence there was no significant difference among the groups in the requirement of rescue analgesia post operatively.

e) **Incidence of sedation, hypotension, headache and constipation**

None of the patients in either the group treated with Inj Ondansetron or the group treated with Inj Ramosetron, had sedation or were drowsy. No patient in either groups reported any head ache or constipation. None of the patients in both groups recorded any episodes of hypotension.

DISCUSSION

In our study, the treatment groups were similar with regard to patient demographics, surgical procedure, anesthetic administration and analgesics used post operatively. Duration of surgery and Duration of anesthesia were also similar in both the groups. Hence the difference in incidence of PONV among the groups can be attributed to the difference in the agents administered.[7]

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Roila F et al studied the clinical pharmacokinetics of Ondansetron and concluded that 0.1 mg/kg body weight was required for effective antiemesis. Kazemi-Kjellberg F et al studied the relative efficacy of different antiemetics in established PONV where in 7 trials (1265 patients) 11 different antiemetics were tested without placebos and it was shown that Ondansetron 1 to 8 mg prevented further vomiting. Hence in our study we decided to choose a dose of 0.1 mg/kg bw of Inj Ondansetron as optimal effective dose for the prevention of PONV after laparoscopic cholecystectomy.[8]

In a study by Yoshitaka Fujiiet al on prevention of PONV in women undergoing gynecological surgery, 4 groups of 30 members each received either placebo or 0.15, 0.3 or 0.6 mg Ramosetron each. A complete response was seen (defined as no PONV and no need for rescue antiemetic) during 0 to 3 hours after anaesthesia occurred in 40%, 47%, 87%, 90% and up to 24 hours in 43%, 50%, 87% and 90% respectively. In conclusion it was proved that 0.3 mg would be the minimal effective dose to prevent PONV. A double dose of 0.6 mg does not add any significant therapeutic advantage compared to Ramosetron 0.3 mg.[9]

A placebo group was not included in this study for ethical reasons so that all the patients were relieved of distressing PONV experience. In addition, the prophylactic effect of Ondansetron and Ramosetron on PONV had already been established in a number of previous studies.[10]

Effect of timing of Ramosetron administration on the incidence of PONV in patients undergoing laparoscopic surgeries was studied by Sun Yeul Lee et al and it was concluded that the effect of Ramosetron administered immediately after induction or at the completion of surgery was similar to each other on its efficacy as a prophylactic antiemetic in patients undergoing such surgeries. We in our study administered Ramosetron half hour before the end of surgery and Ondansetron fifteen minutes before the procedure ended.[11]

Kim SI et al compared Ramosetron and Ondansetron, and found that Ramosetron 0.3 mg IV was as effective as Ondansetron 8 mg IV. Similarly in a study by Ryu J comparing the same two drugs in 120 patients undergoing laparoscopic cholecystectomy divided into 3 groups (n=40) ratio of complete response was higher (80%) in groups Ondansetron 8 mg and Ramosetron 0.3 mg than Ondansetron 4 mg (58%). Hence it was concluded that Ramosetron 0.3 mg and Ondansetron 8 mg were more effective than Ondansetron 4 mg. Ramosetron 0.3 mg is as effective as Ondansetron 8 mg for prophylactics of PONC after LC.[12]

In the study conducted by Kim S I et al the proportion of patients requiring rescue antiemetics was significantly lower with Ramosetron 15% when compared with the placebo group 41% during 24 hours after surgery. But there were no significant differences in the incidence of nausea and vomiting, severity of nausea and required rescue antiemetic between Ramosetron and Ondansetron groups. Our study too showed similar results, in that, though 2 patients (5%) vomited and required rescue antiemetic in Ondansetron group and no patient had vomited in Ramosetron group, statistical significance was not found.[13]

Ryu J described “Complete Response” as no PONV and no requirement of rescue antiemetic medication during the first 24 hours post operation & showed that it was 75%, 90%, 90% in Ondansetron 8 mg, 4 mg, Ramosetron 0.3 mg. In our study “Complete Response” was 84% and 92.5% in Ondansetron and Ramosetron groups respectively. Again no statistically significant difference was seen. (p=0.352)

Choi YS et al reported no adverse effects with the use of Ramosetron or Ondansetron in their study on the comparison of the above two drugs after spine surgery. Similarly in our study we found no adverse effects after the administration of both the drugs. Hence we concluded that the risk of undesirable side effects did not increase with the above drugs.[14]

In the study by Lee et al did not find a significant difference between the two drugs in the first 24 hours. However, during the 48 hr post-operative period Ramosetron was more effective than Ondansetron. In our study, we gathered information only for the first 24 hours post-anaesthesia period and found no statistically significant data to prove the superiority of one drug over the other.

Studies have proved that though Ondansetron was first 5HT3 receptor antagonist to become clinically available for treatment and prevention of PONV, it is less selective for the 5HT3 receptor compared to other 5HT3 antagonists. It binds to 5HT1B, 5HT1C, α-adrenergic and opioid receptors with low affinity. Systematic review revealed that Ondansetron's prophylactic effect on vomiting is good. But the effect on preventing nausea is less pronounced.[15]

CONCLUSION

From our study on 80 patients undergoing elective laparoscopic cholecystectomy under general anesthesia, we conclude that Inj Ondansetron 4 mg and Inj Ramosetron 0.3 mg (intravenous administration) are equally effective in decreasing the incidence of PONV after laparoscopic cholecystectomy under general anesthesia, and that no drug is superior to the other among the two. However, the two advantages we noticed with Inj Ramosetron were Convenience of administration once a day as against thrice with Ondansetron. Cost effectiveness of Ramosetron Rs. 32 per ampoule (per day) as against Ondansetron Rs. 28 X 3=84 per 3 ampoules (per day).

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