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Efficacy of ondansetron alone, dexamethasone alone and combination of ondansetron and dexamethasone for PONV for patients undergoing under general anaesthesia

Dr. Pratiksha Chitta
Assistant Professor**,** Department of Anaesthesiology, Gandhi Medical College, Secunderabad, India

Dr. Gouthami Mothe
Assistant Professor, Department of Anaesthesiology, Gandhi Medical College, Secunderabad, India

Dr. Mrunalini Alugolu*
Assistant Professor, Department of Anaesthesiology, Gandhi Medical College, Secunderabad, India
*Corresponding author

Dr. Kaleru Sai Leela
Senior resident, Department of Anaesthesiology, Gandhi Medical College, Secunderabad, India

***Abstract*---**Aim: To compare the efficacy of Ondansetron alone, Dexamethasone alone and combination of Ondansetron and Dexamethasone for postoperative nausea and vomiting for patients undergoing elective surgeries under general anaesthesia. Materials and methods: A prospective randomized comparative study in Ninety patients (of either sex belonging to ASA I and II physical status) posted for elective surgeries (under General Anaesthesia) were selected and were randomly allocated into three groups; Dexamethasone (Group A) alone, Ondansetron (Group B), and Dexamethasone and Ondansetron (Group C). Results: There was no significant difference in the baseline parameters among the groups Intra-operatively and post-operatively, we did not observe any statistically significant differences within or between the groups. The results of our study revealed that patients receiving Ondansetron and Dexamethasone had significantly lesser incidence of PONV when compared with either Dexamethasone alone or Ondansetron alone during the first 24 hours postoperative period. The incidence of PONV was 13.2%, 18.98%, and 36.3% respectively In

our study, the complete response occurred in 86.8% of the cases in Dexamethasone and Ondansetron combination group, 81.02% in Dexamethasone alone group and 63.7% in Ondansetron alone group. With regard to PONV (by severity), episodes of nausea, retching, and vomiting were seen in all the Groups but no patient in either of groups had severe vomiting. We observed that PONV complaints were very common in patients who underwent Cholecystectomy surgery (42.86%). In this study, we have noticed that more is the duration of surgery, more is the chance of complaining of PONV. While only 23.8% patients with the duration of surgery less than 180 minutes had PONV, 76.2% with the duration of surgery more than 180 minutes had PONV complaints. Conclusion: The combination of Ondansetron plus Dexamethasone is better than either Ondansetron or Dexamethasone alone as a prophylactic in preventing PONV following elective surgeries under General Anaesthesia.

***Keywords*---**ondansetron, dexamethasone, postoperative nausea and vomiting (PONV), general anaesthesia.

Introduction

Postoperative nausea and vomiting (PONV) remain common and distressing complications following surgery. PONV can delay discharge and recovery and increase medical costs. The high incidence of PONV has persisted in part because of the tremendous growth in ambulatory surgery and the increased emphasis on earlier mobilization and discharge after both minor and major operations. Pharmacological management of PONV should be tailored to the patients' risk level using the PONV scoring system to minimize the potential for these adverse side effects in the postoperative period. A combination of prophylactic antiemetic drugs should be administered to patients with moderate-to-high risk of developing PONV in order to facilitate the recovery process. Optimal management of perioperative pain using opioid-sparing multimodal analgesic techniques and preventing PONV using prophylactic antiemetics are key elements for achieving an enhanced recovery after surgery. Strategies that include reductions of the baseline risk (e.g., adequate hydration, use of opioid-sparing analgesic techniques) as well as a multimodal antiemetic regimen will improve the likelihood of preventing PONV[1].

(PONV) is the second common complaint with pain being the most common. PONV is one of the commonest and unpleasant side effects following anaesthesia and a surgery. The overall incidence is approximately 30% nowadays. It can lead to wound dehiscence, bleeding, aspiration of gastric contents, delay in recovery and discharge. PONV remains a significant problem in modern anaesthetic practice with the adverse consequences such as delayed recovery, unexpected hospital admission, delayed return to work of ambulatory patients, pulmonary aspiration, wound dehiscence, and dehydration. Considering increasing demand for ambulatory surgery, a holistic approach should be attempted before and during surgery to prevent PONV. The goal of PONV prophylaxis is therefore to

decrease the incidence of PONV and thus patient-related distress and reduce health care costs.[2]
Extensive trials using oral and intravenous ondansetron in various types of patients posted for various surgeries have confirmed the efficacy of the drug with less side effects. However, aetiology of emesis is multifactorial, optimal antiemetic effects are obtained with 5HT3 antagonist in combination with steroids. Dexamethasone has been reported to be effective in reducing PONV in combination with ondansetron. Therefore, various combinations of drugs are on trial to get an optimal result. There are many causes of PONV and so antagonising only one type of receptor is not sufficient in many patients. It is definitely logical to give drugs which have different mechanism of action. The current best available evidence suggests that combination of antiemetics that can act synergistically (even in paediatric cases). However, the evidence (with respect to combination therapy) is fractured and the strength of evidence is very low certainty because not many Randomized Controlled Trials (RCTs) with adequate sample sizes have been conducted with different dosages of combination therapy in all kinds of surgeries performed under General Anaesthesia. So, this study was designed to compare the efficacy of Ondansetron alone and Dexamethasone alone and in combination in preventing PONV in elective surgeries under General Anesthesia to test the strength of evidence of the current best available evidence.

Patients and Methods

A prospective randomized comparative study 90 Patients of both genders of ASA grade I and II of age group 18-60 years posted for elective surgeries under general anaesthesia. Mediciti Institute of Medical sciences, January 2019 – April 2020.

Inclusion Criteria

Patient aged between 18-60 years, Physical status ASA I and II , Surgeries under general anaesthesia and expected duration of surgery longer than 30 minutes

Exclusion Criteria

Patients who received opioids, NSAIDS or antiemetic agents 48 hrs prior to surgery, history of allergic reaction to any drug or food**,** motion sickness or migraine, drug abuse or smoking and previous history of PONV. After obtaining the written informed consent, study population was randomly divided into three groups with 30 patients in each group.

- Group A will receive Dexamethasone 8 mg intravenously just before induction.
- Group B will receive Ondansetron 4 mg intravenously half an hour before extubation.
- Group C will receive both Dexamethasone 8 mg before induction and Ondansetron 4 mg half an hour before extubation intravenously.

Parameters to be monitored are preoperative non-invasive blood pressure, Mean arterial pressure, pulse/Heart rate, oxygen saturation with pulse oximeter, three lead ECG.

Statistical Analysis

Data was entered into Microsoft Excel and statistical analysis was done using IBM SPSS Statistics for Windows version 23.
Level of significance was set at P< 0.05.
A "P" value less than 0.05 was considered as the minimum value for statistical significance.
P value < 0.0001 was considered to be highly significant.

Chi Square Test

For a 2 x 2 contingency table,
Chi square value = Degree of freedom (df)= (r-1) (c-1)

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

O = Observed Frequency
E = Expected Frequency

Demographic data like age and weight were compared using student's t test. Sex distribution was compared using Pearson Chi Square test. Patients' vital parameters like systolic and diastolic blood pressure (SBP & DBP), heart rate (HR), respiratory rate (RR) and oxygen saturation were compared using student's t-test. Bar charts and line charts were used as appropriate throughout the analysis.

Results

As planned and documented in the methodology section of this study, we collected the data, entered the same into excel sheet and conducted statistical analysis by using SPSS software (ver:23). A p < 0.05 was considered statistically significant. The three groups were comparable with regard to age, weight, gender, BMI and ASA grading. The mean age was 37.07 ± 13.29 for the Dexamethasone Group (Group A), 41.03 ± 11.79 for the Ondansetron Group (Group B), and 41.47 ± 13.37 for the Dexamethasone + Ondansetron Group (Group C) (p = 0.1655).

Table1
Comparision of demographic details in present study

AGE (in years)	GROUP (n=30)	GROUP (n=30)	GROUP (n=30)	T	P	T	p	t	p
				A&B		A&C		B&C	

	Mean	SD	Mean	SD	Mean	SD	1.302	0.986	0.326	0.426	1.173	0.09
	37.07	13.29	41.03	11.79	41.47	13.37						
Weight in kgs	56.53	10.45	56.27	11.85	60.03	9.65	0.635	1.16	1.183	0.651	0.753	0.153
BMI(Kg/m^2)	22.10	1.81	22.17	1.62	22.43	1.72	0.413	1.08	0.261	0.431	0.531	0.153
Duration of surgery in minutes	159.33	41.25	173.67	44.64	181.17	47.23	1.291	0.100	0.632	0.264	1.907	0.03

The mean weight of Group A was 56.53 ± 10.45, Group B was 56.27 ± 11.85, and that of those in the Group C was 60.03 ± 9.65 (p = 0.106), Distribution of gender in the groups was also comparable (p = 0.732). There were 12 males and 18 females in the Group A, 11 males and 19 females in the Group B, and 12 males and 18 females in the Group C. (p = 0.732). The BMI of the subjects in study were comparable. The mean BMI of Group A was 22.10 ± 1.81, Group B was 22.17 ± 1.62, and that of those in the Group C was 22.43 ± 1.72 (p = 0.114). On comparative analysis, Group A and Group B were comparable with no statistically significant difference between the Groups (p = 0.1008), even the Group A and Group C were comparable (p = 0.264), however statistically significant difference (p = 0.03) was noticed between B and C Groups (which may have been because of unusually (unexpectedly) more time taken by a couple of surgeries in the Group C, or the occurrence may be purely by chance). Distribution of subjects, in the three groups, based on ASA grading was comparable too (p = 0.732). There were 21 subjects with ASA Grade 1 and 9 with ASA Grade 2 in Group A, 20 subjects with ASA Grade 1 and 10 with ASA Grade 2 in Group B, and 21 subjects with ASA Grade 1 and 9 with ASA Grade 2 in Group C (p = 0.873) .

Table 2
Pre-operative vital parameters

	A-GROUP (n=30)		B-GROUP (n=30)		C-GROUP (n=30)		T	P	T	P	t	p
	AVG	SD	AVG	SD	AVG	SD	A&B		A&C		B&C	
HR (Per Min)	80.17	4.71	81.67	4.60	78.17	6.44	-0.182	0.428	-0.591	0.278	-0.477	0.317
SBP (mmHg)	123.30	5.91	123.90	6.56	121.53	6.22	-0.116	0.453	-1.125	0.132	-0.97	0.167
DBP (mmHg)	77.73	4.86	79.03	5.18	76.63	4.31	-0.654	0.257	-3.605	0.067	-2.975	0.219
MAP (mmHg)	92.89	4.08	93.99	4.27	91.67	3.40	0.24	0.405	-2.109	0.079	-2.56	0.066
SPO_2 (%)	99.10	0.40	99.30	0.47	99.17	0.38	-0.711	0.239	-1.384	0.085	-0.674	0.251

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All the mean values of hemodynamic parameters are insignificant on comparision.

Table 3
Intra-operative and post-operative hemodynamics

	A-GROUP (n=30)		B-GROUP (n=30)		C-GROUP (n=30)		T	P	T	P	t	p
	AVG	SD	AVG	SD	AVG	SD	A&B		A&C		B&C	
Base line	82.87	12.71	76.73	10.97	77.70	7.16	-0.656	0.257	-1.409	0.082	-0.624	0.267
15 min	84.77	11.72	79.40	10.07	81.00	6.91	-1.609	0.056	-3.334	0.07	-1.642	0.052
30 min	82.00	7.93	79.17	8.85	79.57	6.21	1.634	0.107	-0.216	0.829	-2.203	0.031
60 min	79.00	6.90	78.77	7.64	77.97	6.60	0.813	0.419	-0.972	0.334	-1.926	0.058
Postop 0-6 hrs	77.27	10.80	79.57	8.81	80.23	7.05	0.037	0.97	-1.423	0.16	-1.508	0.136
Post op 6-12 hrs	77.97	6.70	78.23	7.13	79.30	4.75	-0.172	0.758	-0.481	0.368	-0.369	0.287
Post op 12-24 hrs	81.27	6.19	78.93	6.64	79.70	4.88	-0.621	0.336	-1.523	0.243	-0.791	0.065

The HR in the Group A, Group B, and Group C right from the baseline until 24 hours post-operatively was comparable – and there was no statistically significant difference between the groups (A & B; A & C and; and B & C) ($p > 0.05$ in all the instances of measurement at 15 minutes, 30 minutes, 60 minutes intra-operatively and at 0-6 hours, 6-12 hours and 12-24 hours post-operatively).

Table 4
Changes in systolic blood pressure

	A-GROUP (n=30)		B-GROUP (n=30)		C-GROUP (n=30)		T	P	T	p	t	p
	AVG	SD	AVG	SD	AVG	SD	A&B		A&C		B&C	
Base line	126.43	13.84	124.43	7.32	122.67	6.02	-0.240	0.81	-0.24	0.405	-0.847	0.400
15 min	127.03	10.00	124.80	7.17	126.47	6.16	-1.122	0.266	-1.122	0.133	-3.00	0.063
30 min	121.90	9.05	121.07	7.33	123.07	5.87	0.480	0.623	0.48	0.316	-3.105	0.003
60 min	119.47	8.14	120.10	7.42	122.67	7.63	1.348	0.182	1.348	0.182	-3.061	0.83
Postop 0-6 hrs	122.97	7.98	122.80	7.27	123.97	6.90	1.351	0.181	0.951	0.345	-0.43	0.665
Post op 6-12 hrs	119.67	7.51	120.63	7.06	120.83	6.10	0.32	0.748	0.268	0.789	-0.051	0.959
Post op 12-24 hrs	119.37	6.71	120.27	6.79	120.30	5.20	0.042	0.966	1.114	0.269	1.183	0.241

DBP												
Base line	80.13	8.95	78.73	6.46	78.53	5.09	-0.066	0.946	0.081	0.935	0.164	0.87
15 min	80.67	8.18	80.77	7.82	81.33	5.13	-1.143	0.257	4.416	0.299	-2.51	0.014
30 min	79.23	7.48	79.10	8.35	80.30	5.60	0.653	0.516	-2.135	0.036	-2.39	0.019
60 min	77.80	6.88	76.97	7.71	79.57	5.54	0.718	0.475	-0.813	0.419	-1.409	0.164
Postop 0-6 hrs	78.63	8.42	80.27	8.14	80.10	6.23	-1.114	0.269	-1.114	0.269	-2.167	0.341
Post op 6-12 hrs	78.27	7.16	79.27	7.93	78.40	5.56	1.457	0.15	0.379	0.705	-1.163	0.249
Post op 12-24 hrs	77.67	7.13	78.03	7.70	77.77	4.75	0.236	0.813	-0.338	0.736	-0.591	0.556

As tabulated in the aforementioned, the SBP was comparable within the groups at different instances of measurements (Baseline, 15 mins, 30 mins, 60 mins into surgery, and postoperatively). There was no evidence of fluctuations in SBP throughout the study period. On intergroup analysis too, SBP was comparable between the Groups at different points of measurement throughout the study period. ($p > 0.05$). With regard to Diastolic Blood Pressure (DBP), the baseline DBP in the Group A was 80.13 ± 8.95 mm Hg, in the Group B was 78.73 ± 6.46, and in the Group C it was 78.53 ± 5.09. There was no instance of decreased on increased DBP throughout the study period. In the intergroup analysis, no statistical and/or clinical significance was evident between the Groups (A & B; A & C and; B & C).

The basal Mean Arterial Pressure (MAP) in the Group A was 95.57 ± 10.17 mm Hg, in the Group B it was 93.97 ± 6.36 and, in the Group C it was 93.24 ± 4.50. We noticed no statistically significant difference within the Groups intra-operatively and post-operatively. When we conducted an intergroup analysis, we found no statistically and/or clinically significant difference between Groups. ($p > 0.05$). The oxygen saturation remained 100% throughout and after surgical procedure in all the Groups (A, B and C) ($p=1$). There was no instance of Respiratory Rate that is lower (Bradypnea) or higher (Tachypnoea) than normal for age throughout the study in any of the subject of any Group.

Table 5
PONV incidence

INCIDENCE	A-GROUP (N=30)	B-GROUP (N=30)	C-GROUP (N=30)	X^2 A&B	P	X^2 A&C	P	X^2 B&C	P
YES	6(18.98%)	11(36.3%)	4(13.2%)	2.052	0.152	0.48	0.488	4.355	0.036
NO	24(81.02%)	19(63.7%)	26(86.8%)						

We observed that 6 subjects in Group A, 11 subjects in Group B and, 4 subjects in Group C had complaints of PONV in some or the other severity. Although Group C was better than Group A and B, and Group A was better than Group B with respect to the incidence of PONV, there was no statistically significant difference between groups ($p=0.115$), however, on intergroup analysis, while there was no statistically significant difference between A & B ($p=0.152$) and A & C ($p=0.48$) Groups, we noticed a statistically significant difference between B & C

groups (p=0.036). On the analysis of PONV based on the severity, we found that in Group A – of the 6 patients who had PONV complaints, 3 patients had just nausea, 2 had retching, and 1 had vomiting. In the Group B – of the 11 patients who had PONV complaints, 7 had a simple nausea, 2 had retching, and 2 had vomiting. In the Group C – of the 4 patients who had complained of PONV symptoms, 3 had nausea and 1 had vomiting. No patient in either of groups had severe vomiting.On intergroup analysis, there was no statistically significant difference between Group A & B (p=0.221) and Group A & C (p=0.1347), however we observed a statistically significant difference between B & C Groups (p=0.0347).

Table 6
PONV incidence by severity

PONV SCORE	A-GROUP (n=30)	B-GROUP (n=30)	C-GROUP (n=30)	X^2 A&B	P	X^2 A&C	p	X^2 B&C	p
1(Nausea)	3	7	3	-0.0771	0.221	1.114	0.1347	1.8502	0.0347
2(Retching)	2	2	0						
3(Vomiting)	1	2	1						
Total	6	11	4						

When all the Groups were combined, of the 21 patients who had PONV complaints – 14 (66.7%) were females and 7 (33.3%) were males. In Group A – of the 6 patients who had complained of PONV symptoms, 4 were females and 2 were males. In the same way, of 11 symptomatic patients in Group B – 7 were females and 4 were males. Similarly, in the Group C – of the 4 patients, 3 were females and 1 was male. Across the Groups, a greater number of females had symptoms than males. However, the difference wasn't statistically significant.

Table 7
PONV *versus* Demographic parameters

Gender	A-Group (N=30)	B-Group (N=30)	C-Group (N=30)	Total	X^2	p
Female	4	7	3	14	0.1705	0.9183
Male	2	4	1	7		
Total	6	11	4	21		
Age (in yeats)						
< 35 Years	1	3	3	7	4.05	0.131
>35 Years	5	8	1	14		
Total	6	11	4	21		
Weight (in Kgs)						
< 55 Years	4	5	1	10	1.713	0.424
>55 Years	2	6	3	11		
Total	6	11	4	21		
ASA grading						

ASA 1	5	9	3	16	0.119	0.942
ASA 2	1	2	1	4		
Total	6	11	4	21		
Surgery Duration (in Minutes)						
≤ 180 Minutes	2	3	0	5	1.713	0.424
≥ 180 Minutes	4	8	4	16		
Total	6	11	4	21		

Demographic parameters are insignificant in comparison in groups. In this study, we have noticed that more is the duration of surgery, more is the chance of complaining of PONV. While only 23.8% patients with the duration of surgery less than 180 minutes had PONV, 76.2% with the duration of surgery more than 180 minutes had PONV complaints.

Table 8
PONV versus diagnosis

Diagnosis	A-GROUP	B-GROUP	C-GROUP	TOTAL
Cholecystectomy	3	3	3	9
ENT related	1	3	0	4
Thyroid	1	4	1	6
Others (Laminectomy, MRM)	1	1	0	2
Total	6	11	4	21

PONV complaints were very common in patients who underwent Cholecystectomy surgery 9 (42.86%), followed by Thyroid related surgeries 6 (28.57%) then were ENT related surgeries 4 (19.04%). Two patients underwent other surgeries. In Group A, 3 (50%) who complained were who underwent Cholecystectomy. It was 3 (29.7%) in the Group B, and 3 (75%) in Group C too.

Discussion

Surgical interventions conducted under general anaesthesia tend to have higher rate of Post-Operative Nausea and Vomiting (PONV) – which is responsible for increased length of stay (LOS). We compared the efficacy of Ondansetron alone, Dexamethasone alone and Ondansetron plus Dexamethasone as an antiemetic prophylaxis for preventing PONV in patients after elective surgeries under General Anaesthesia. In our study, all the three groups – Group A (Dexamethasone Group), Group B (Ondansetron Group), and Group C (Dexamethasone + Ondansetron) – were comparable with regard to Age (p=0.986; 0.426; 0.09 between A&B, A&C, and B&C respectively), Weight (p=1.16; 0.651; 0.153 between A&B, A&C, and B&C respectively), Gender (p=0.732 between the three groups), and BMI index (p=1.08; 0.431; 0.153 between A&B, A&C, and B&C respectively.

The researchers, authors, clinicians, and anesthesiologists of other studies[3,4,5] also reported comparability in their demographics. Based on ASA grading, there was no statistically significant difference between the groups (p=0.873) in this study. All patients in this study were anaesthetized and operated by same team of surgeon and anaesthesiologists. In our study, the average duration of surgery for Groups A, B, and C found to be 159.17±41.25 minutes, 173.67±44.64 minutes, and 181.17±47.23 minutes respectively. We found no statistically significant difference between A & B Groups (p=0.1008) and A & C Groups (p=0.264). However, statistically significant difference was noticed between B & C Groups (p=0.03) – which was probably because of unusually more time taken by a couple of surgeries in the Group C. This occurrence may be purely by chance too.

Similar to our study, there was no statistically significant difference between the Groups in several studies[5,6] which studied the effectiveness of Dexamethasone alone, Ondansetron alone, and/or Dexamethasone + Ondansetron combination as antiemetic prophylaxis for preventing PONV in patients after elective surgeries under General Anaesthesia. Some studies[5,6] did not report this parameter. PONV after General Anaesthesia is complex and multi-factorial in terms of etiology. Stretch of intra-abdominal organs, peritoneal irritation and phrenic nerve excitation by residual CO_2 in peritoneal cavity which are very important risk factors of incidence of nausea vomiting after laparoscopic surgeries under General Anaesthesia.[7,8] The factors that influence the incidence of PONV are gender (women are more likely to experience PONV), history of motion sickness, smoking, age, delayed gastric emptying, anaesthetic techniques, pain, care in post-operative period, and patient demographics. However, in our study, patients with a history of motion sickness and previous history of PONV were excluded because they had a high incidence of emetic symptoms. If such patient related factors weren't controlled, the number of patients without PONV, in our study, would have changed.

In addition, patients in 3 groups also consumed similar amount of analgesic in post-operative period. Therefore, the difference in incidence of PONV among the groups can be attributed to the study drugs. All the pre-operative vital parameters were comparable in the study groups (A, B, and C). The mean heart rate in the Group A, Group B, and Group C was 80.17±4.71, 81.67±4.60 and 78.17±6.44 respectively (A & B, p=0.428; A & C, p=0.278; B & C, p=0.317). The mean systolic blood pressure (SBP) in the Group A, Group B, and Group C was 123.20±5.91, 123.90±6.56, and 121.53±6.22 respectively (A & B, p=0.453; A & C, p=0.132; B & C, p=0.167). Similarly, the mean diastolic blood pressure (DBP) was also comparable. It was 77.73±4.86, 79.03±5.18, and 76.73±4.37 in the Group A, Group B, and Group C respectively (A & B, p=0.257; A & C, p=0.067; B & C, p=0.219). The comparability was also observed in the mean arterial pressure (MAP). It was 92.89±4.08, 93.99±4.27, 91.67±3.40 in the Group A, Group B, and Group C respectively (A & B, p=0.405; A & C, p=0.079; B & C, p=0.066).

Oxygen saturation levels were 99.10±0.40 in Group A, it was 99.30±0.47 in the Group B and 99.17±0.38 in the Group C too (A & B, p=0.239; A & C, p=0.085; B & C, p=0.251) – with no statistically significant difference between the groups. Hemodynamic comparability was noticed, pre-operatively, in the study groups of almost all the studies[9,10] that were performed to study the effectiveness of

Dexamethasone, and/or Ondansetron and/or Dexamethasone + Ondansetron in the prophylactic treatment of PONV. In our study, the hemodynamic response (HR, SBP, DBP, MAP, SPO_2, and RR) was stable in all the three groups throughout the study. The HR in the Group A, Group B, and Group C right from the baseline until 24 hours post-operatively was comparable – and there was no statistically significant difference ($p>0.05$) between the groups (A & B; A & C and; B & C). There was no evidence of fluctuations in SBP throughout the study period. It was comparable between the Groups at different points of measurement throughout the study period ($p>0.05$). There was no statistically significant ($p>0.05$) decrease or increase in DBP throughout the study period – both within the groups and between the groups. There was no statistically and/or clinically significant difference between the Groups intra-operatively and post-operatively with regard to MAP ($p>0.05$). The oxygen saturation remained 100% throughout and after surgical procedure in all the Groups ($p=1$). There was, no instance of Bradypnea or Tachypnoea throughout the study in any of the patients of all the 3 Groups.

There was no evidence of fluctuation in hemodynamic response either intra-operatively or post-operatively, in the several relevant studies[11,12] (which studied the effectiveness of Dexamethasone, and/or Ondansetron and/or Dexamethasone + Ondansetron in the prophylactic treatment of PONV) we have reviewed. Ionescu D et al[3] (2007) conducted a randomized double-blind study to evaluate the efficacy of ondansetron and dexamethasone in reducing the incidence of postoperative nausea and vomiting and concluded that dexamethasone is more effective in preventing postoperative nausea and vomiting after laparoscopic cholecystectomy than ondansetron. This is mainly determined by a significant reduction in the incidence of postoperative nausea. D'Souza N et al[4] (2011) compared intravenous dexamethasone and ondansetron for the prophylaxis of postoperative nausea and vomiting (PONV) for the patients undergoing laparoscopic gynaecologic surgery and concluded that – Dexamethasone was found to be an efficacious and cost-effective drug for the prophylaxis of PONV. Combination of antiemetic drugs could be an effective method to control severe PONV as there is no single stimulus/cause for PONV.

The results of the study, revealed that patients receiving Ondansetron and Dexamethasone had significantly lesser incidence of PONV when compared with either Dexamethasone or Ondansetron alone during the first 24 hours postoperative period. The incidence of PONV was 13.2%, 18.98%, and 36.3% respectively. The incidence was observed to be 15.4%, 37.3%, and 40% in the Dexa+Ondan group, Dexa group, and Ondan group respectively in another study. In our study, the complete response occurred in 86.8 % of the cases in Dexa+Ondan group, 81.02% in Dexamethasone group and 63.7% in Ondansetron group. Chattopadhyay S et al[9] noticed similar observations in their study (84.6% in Ondansetron plus Dexamethasone group, 64.7% in Dexamethasone group, 62% of the cases in Ondansetron group). This is also comparable to the studies conducted by Ahsan K et al[13], Gautam B et al[14] and Eidey M et al[15]. Ahmed A et al[16] observed no nausea and vomiting in 85% patients.

The results of our study are comparable with several studies with respect to Ondansetron plus Dexamethasone combination. In our study, Dexamethasone 8

mg intravenously in Group A, Ondansetron 4 mg intravenously in Group B, and Dexamethasone 8 mg and Ondansetron 4 mg intravenously in the Group C. In agreement with the aforementioned studies, Kumar A et al[11] (2013) concluded that combination of ondansetron and dexamethasone is safe and effective combination than each drug alone for prevention of PONV and suggested that further studies on prophylactic combination of drugs should be done to make PONV a rare occurrence. Chattopadhyay S et al[9] (2016) too concluded that combination of Ondansetron plus Dexamethasone is better than each drug alone as an antiemetic prophylaxis against PONV following laparoscopic cholecystectomy.

Som A et al[17] (2016) conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) and concluded that combination of a 5-HT3 receptor antagonist and dexamethasone is significantly more effective than 5-HT3 antagonist alone in preventing PONV after laparoscopic surgeries, with possible improvement in postoperative analgesia. P.Flubacher and his anaesthetist colleagues[18] (2017) concluded that ondansetron, when given with a moderate dose of dexamethasone, is more effective than saline in preventing nausea or vomiting after paediatric tonsillectomy. Thongrong C et al[6] (2018) conducted a prospective, double-blinded, randomized control trial to evaluate the effects of dexamethasone and ondansetron for preventing PONV in patients who underwent microvascular decompression (MVD) surgery and authors concluded that dexamethasone and ondansetron 4 mg seemed to decrease the incidence of PONV in the first 24 hours but not significantly, therefore, further studies are to be carried out by escalating either dexamethasone dose or the dose of ondansetron or both.

Deviating from the effectiveness of the standard combination of Ondansetron and Dexamethasone, Kizilcik N et al[19] (2017) concluded that dexamethasone-dimenhydrinate combination was more effective than dexamethasone-ondansetron in prevention of nausea and vomiting after rhinoplasty operations. Nanjundaswamy et al[10] (2018) found that there is no difference in effectiveness of two combinations, and concluded that – “Granisetron 1mg and Ondansetron 4mg in combination with dexamethasone 8mg are equally effective and safe in decreasing the incidence of PONV in laparoscopic cholecystectomies under general anaesthesia. Similar to the above-mentioned study[3] Kumar A et al[11] (2018) concluded that Palonosetron with Dexamethasone is more effective than Ondansetron with Dexamethasone for prevention of PONV in post-chemotherapy ovarian cancer surgeries receiving opioid-based patient-controlled analgesia.

In congruency with the aforementioned study, Rajnikanth K et al[12] (2019) compared prophylactic Palonosetron and Dexamethasone with Ondansetron and Dexamethasone in patients undergoing Laparoscopic Cholecystectomy – and reported that during 48 h follow-up, the incidence of nausea, vomiting, and PONV was higher in Group II (ondansetron and dexamethasone), but the difference was not statistically significant. Sridharan K and his colleague Sivaramakrishnan G[20] (2019) conducted a network meta-analysis of RCTs with the PONV reducing drugs and concluded that – Dexamethasone and Ondansetron have the best evidence as stand-alone options and the combination is preferred in high-risk category – and suggested to cautious while interpreting the evidence as the estimates might change with head-to-head clinical trial data.

With regard to PONV (by severity), episodes of nausea, retching, and vomiting were seen in all the Groups but, no patient in either of groups had severe vomiting. There was no statistically significant difference between Group A & B (p=0.221) and Group A & C (p=0.1347), however, a statistically significant difference between B & C Groups (p=0.0347). Therefore, the combination Group (Dexa+Ondan) was more effective than the Dexa and Ondan alone. The authors of other studies24,26-29,31-36,42-44 too noticed similar observations.

Across the 3 Groups, greater number of females had symptoms than males. However, the difference wasn't statistically significant. This was based on the types of surgeries and the number of subjects recruited in each gender. In most of the studies, the more affected gender was directly proportional to the greater number of subjects recruited in that particular gender. On combined Group analysis, 33.3% were of age below 35 years and 66.7% of patients were above 35 years of age. There was no statistically significant difference between the Groups (p=0.131). Our study's findings are in agreement with some of the other studies. In the patients who complained about PONV, 47.6% were below the weight of 55 kgs, and 52.4% patients were above the 55 kgs of weight. There was no statistically significant difference between the Groups (p=0.424) and no evidence of any correlation between weight and PONV symptoms in the previously conducted studies.

81% patients who complained of PONV were of ASA 1, only 19% patients were from ASA 2. This difference was probably because 67% patients recruited for study were ASA Grade 1, and 33% were of ASA Grade 2. There was no statistical difference between the Groups (p=0.942). None of the studies reported any kind of correlation between ASA Grading and the incidence of PONV. PONV complaints were very common in patients who underwent Cholecystectomy surgery (42.86%), followed by Thyroid related surgeries (28.57%) then were ENT related surgeries (19.04%). 9.5% patients underwent other surgeries (Laminectomy & MRM). In Group A, 50% who complained were who underwent Cholecystectomy. It was 29.7% in the Group B, and 75% in Group C. However, there was no statistically significant difference between the Groups. The similar result was observed in other studies. In this study, only 23.8% patients with the duration of surgery less than 180 minutes had PONV, 76.2% with the duration of surgery more than 180 minutes had PONV complaints. In Group A, 33.33% patients were in the category of duration of surgery ≤180 minutes and 66.67% patients were in the category of > 180 minutes. In Group B, it was 29.7% and 71.3% patients respectively. In Group C, 100% patients who complained of PONV were in the category of duration of surgery > 180 minutes.

Conclusions

Our study concludes that the combination of Ondansetron plus Dexamethasone is better than either Ondansetron or Dexamethasone alone as a prophylactic in preventing PONV following elective surgeries under General Anaesthesia. We did not find any correlation between PONV and ASA Grading, Weight of patients and/or, Age of the patients. We did not observe any complications related to use of Dexamethasone and Ondansetron.

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