

Comparison of Ondansetron & Dexamethasone Alone and Combination as Prophylaxis in Post Operative Laparoscopic Surgeries

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Abstract

Background: Post-operative nausea and vomiting is very much prevalent and unpleasant complaints with laparoscopic surgeries that leads to numerous emergencies so antiemetic prophylaxis reduced complications associated with nausea and vomiting. **Aim and Objectives:** To compare an efficacy of ondansetron & dexamethasone singly as well as a combination of both dexamethasone & ondansetron in the patients for those who undergoes laparoscopic surgeries and have a requirement of rescue anti-emetics. **Methods:** Sample size of the study was 150 patients (50 patients per group) which was between the age group of 20 years to 50 years of ASA I, II for those who chiefly requires a general anesthesia for laparoscopic surgeries in an arbitrary clinical trial. Therefore, 150 patients was divided into 3 group of 50 each of name Ondansetron group (O), Dexamethasone group (D) and OD group and respective drugs was administered 10 minutes before induction, and post-operative patients were evaluated at time interval of 0 to 6 hours (early vomiting category), 6 to 24 hours (delayed vomiting) to check the degree of nausea, vomiting along with the requirements of antiemetic drug. **Results:** Nausea was the bottom-most in Combination Group OD (considered as 6%) when compared to Ondansetron Group O (considered as 20%) & Dexamethasone Group D (considered as 12%). For vomiting incidence, results were opposite. It was less in OD Group (i.e. 4% only) when compared to O Group (i.e. 12%) & D Group (i.e. 16%). The requirement for antiemetic drug in the above-mentioned groups of O, D and OD was 26, 20 and 6 respectively. Last but not the least, incidence of vomiting & failure in prophylaxis was observed and analyzed in D Group during initial to 6 hours of duration. Also requirement was more for anti-vomiting drug of post-operation within 6 to 24 hours observed in O Group compare to OD Group. **Conclusion:** Combination therapy of ondansetron (Group O) & dexamethasone (Group D) shows adequate control of PONV with delayed PONV which was being better controlled than early PONV (as and when compared to ondansetron & dexamethasone one singly). The need of adjunct antiemetics was emphatic reduced in initial 24 hours of duration.

Keywords: Ondansetron; Dexamethasone; PONV; Laparoscopic Surgery.

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Introduction

Post-operative nausea as well vomiting was very frequent, common and well identified irritating complications along with anesthesia and surgery activities. It guides to several emergencies such as wound dehiscence, bleeding, delayed discharge process of hospitals [1], aspiration of gastric contents, hospitalization unexpectedly, shows less satisfaction among the patients. There were several explanations for post-operative nausea & for vomiting during the process of laparoscopic surgery which includes pharyngeal stimulation due to peritoneal distension, Anesthetic agents, opioids, CO₂ insufflations, pain.

Contributing factor for above mentioned causes are Hypertension, Hypoxia, Psychological factors (Age/ Gender/ Medical history of earlier nausea & vomiting), Vestibular disturbances, Rough handling, Duration of operation, Diaphragmatic irritation, Visceral organ irritation etc.

Now-a-days, use of combination of anti-emetics that measures at different receptors and acquisition of multi-modal approach has been prescribed to handle such problem.

The current study was designed in such a manner to assess an efficacy of dexamethasone & ondansetron single as well combination of both ondansetron and dexamethasone for prevention of post-operative nausea as well as vomiting [2]. Furthermore, fluid & electrolyte loss accompanying vomiting can cause dehydration and life-threatening electrolyte imbalance. Following were at least 3 kinds of vomiting:

- Attributed to anesthetics
- Reflex responses
- Opioids

Our next investigation unfolded spectrum of non-anesthetics factors in the pathogenesis of Post operative nausea and vomiting. It was a general trend to decrease in the incidence & intensity of the problem due to

- Modifications in anesthesia practice from opioid
- Use of less emetic anesthetic agents
- Anesthesia to non-opioid or supplemented opioids to lighter & non ether anesthesia
- Refinement of operative techniques and identification of patient predictive factor
- Improved pre & post-operative medication

Even after several medical advancements still nausea & vomiting continue within acceptable frequency with surgery & anesthesia which also known to be a big little problem [3]. Persistence nausea/ vomiting might have some serious medical consequences as well as financial implication in delayed discharge process of hospitals.

Earlier, pharmacological efforts for removal of incidence or reduction in the risk of emesis have included to administered anti-histaminics, anti-cholinergics and dopamine antagonists. Physical maneuvers were also included to impose the following

- Nothing per os regimens
- Application of cricoid pressure
- Ingestion of antacid solutions
- Pre-anesthetic suctioning of gastric contents
- Avoiding inflation of stomach during ventilation by mask

As a result, nothing was entirely successful either a combination or alone in mitigating the distressing occurrence of emesis & its potential sequel. Our study was conducted to analyse efficacy of ondansetron and dexamethasone single as well as combination of both of these and then to compare efficacy for prevention of post-operative nausea & vomiting in laparoscopic surgeries so that we can observe or compare the requirements of rescue antiemetic in the study group mentioned.

Methodology

This comparative study was conducted in 150cases (50 per group) with age groups starting from 20 years to 50 years with physical status as ASA I & II those who adopted for elective laparoscopic surgeries for example laparoscopic cholecystectomy, laparoscopic sterilization etc. Patients were randomized here by computer generated blocks according to below 3 groups:

- Group O (n=50) which was as receiving ondansetron alone
- Group D (n=50) which was as receiving dexamethasone alone
- Group OD (n=50) which was as receiving combination of dexamethasone & ondansetron

The following were excluded exceptionally:

- Patients who denied for the study
- Patients who received opioids, NSAIDS or

- antiemetic agents 24 hours prior to surgery
- Patients with physical status of ASA III/ IV
- Pregnant/ lactating females
- Patients under ASA I/ II with history of motion sickness or migraine
- Patients where laparoscopy was converted to laparotomy

Methods

For the purpose of pre-operative evaluation, visit was conducted on a very previous day of surgery along with detailed history & current complaints noted. Following were done

- General & Systemic examination of cardio vascular, respiratory & central nervous system
- Bleeding & clotting time
- Routine laboratory investigations for hemoglobin (HB) level, total count/ differential count, routine urine, blood urea nitrogen & serum creatinine
- ECG

Pre-operative order: All sufferers for this were advised to remain NIL orally after mid night.

*On the operation day intravenous cannulation with 18G catheter was established.

- Study medication Ondansetron 4 mg to group O, Dexamethasone 8 mg to group D & both Ondansetron + dexamethasone to group OD was administered to patients 10 min before induction of anesthesia.
- Patient were pre-medicated with inj. Glycopyrrolate 0.2 mg + 1 mg midazolam + Fentanyl 2 µg/kg & induced by inj. propofol 2 to 2.5 mg/kg. Tracheal intubation was facilitated by inj. vecuronium 0.1 mg/kg. Baseline NG tube was placed for emptying the gastric contents. Anesthesia was maintained by N₂O + O₂ + Isoflurane / sevoflurane. (0.6 to 0.8%). Intermittent doses of vecuronium were given during anesthesia to maintain adequate muscle relaxation.
- Intra operative monitoring HR, BP, SpO₂, ECG, EtCO₂ & urine output was carried out. During laparoscopic surgery abdomen was insufflated with CO₂ at a pressure of 8 to 12 mm Hg. On the completion of operation the abdomen was deflated by the surgeon. At the end of surgery the patient was extubated by reversing the patient with 0.05 mg/kg Neostigmine & 0.2 mg

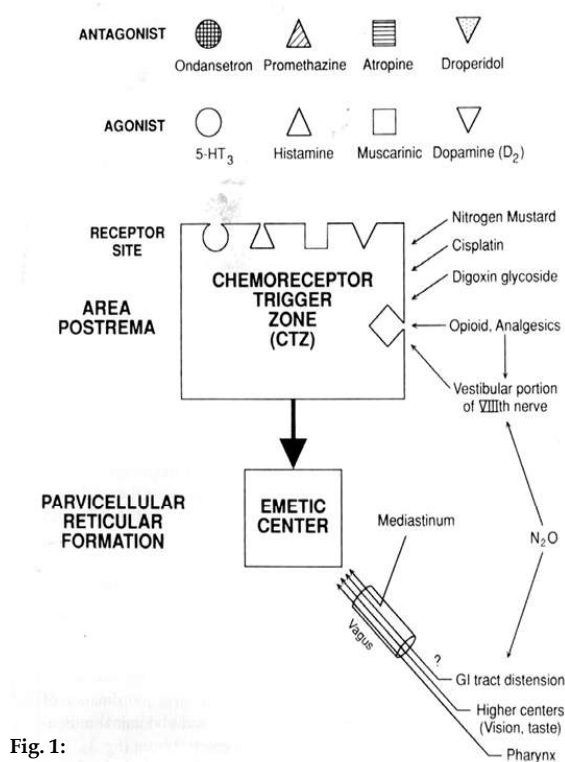


Fig. 1:

Glycopyrrolate. Duration of anesthesia was noted.

In post-operative period, monitoring of patient's vitals were done. All post-operative cases were followed up from 0 to 6 hours, then 6 to 24 hours for the purpose of post-operative nausea & vomiting. The requirements of anti-emetic drug in several patients were also recorded and noted from initial to 6 hours and then 6 to 24 hours in post-operative period.

Statistical Analysis

The analysis was performed with the help of SPSS trial version 23 tool for Windows statistical software package (SPSS inc., Chicago, il, USA) and Primer tool for the generation of descriptive and inferential statistics. The categorical data were presented as numbers (or in percent) and the quantitative data were presented as mean and standard deviation values. The difference in proportion was analyzed by using chi square test for which statistical significance was set to $p < 0.05$.

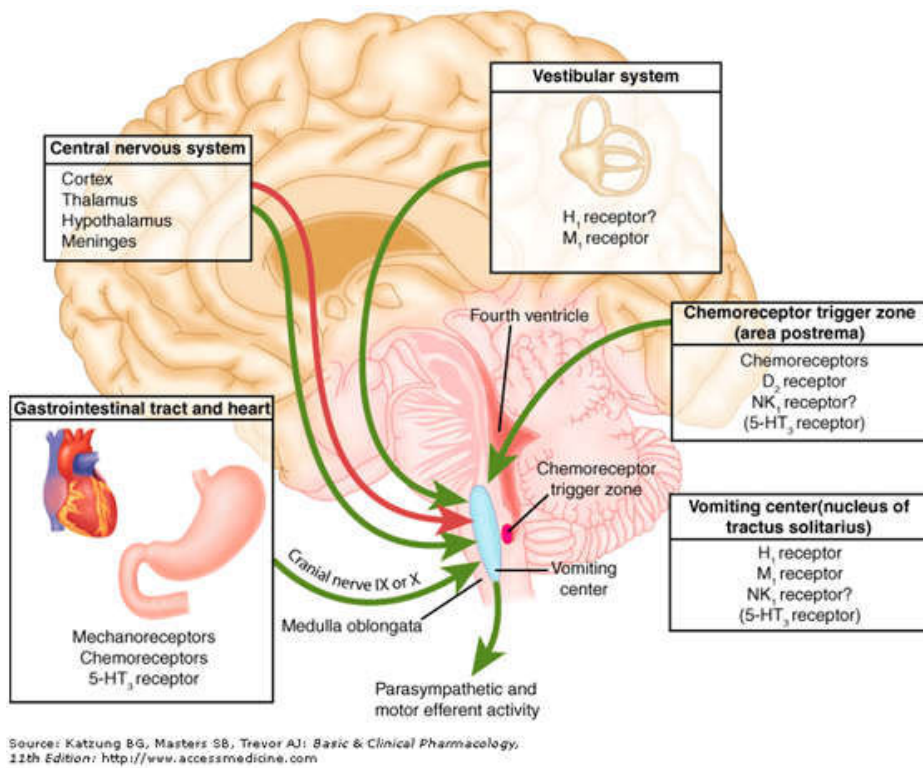


Fig. 2:

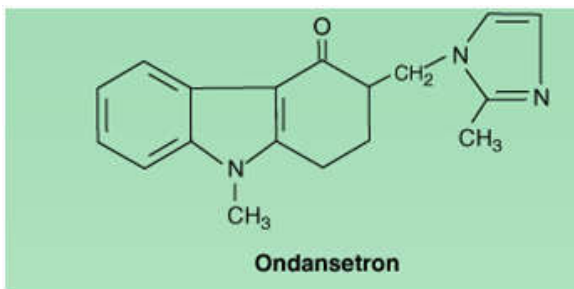
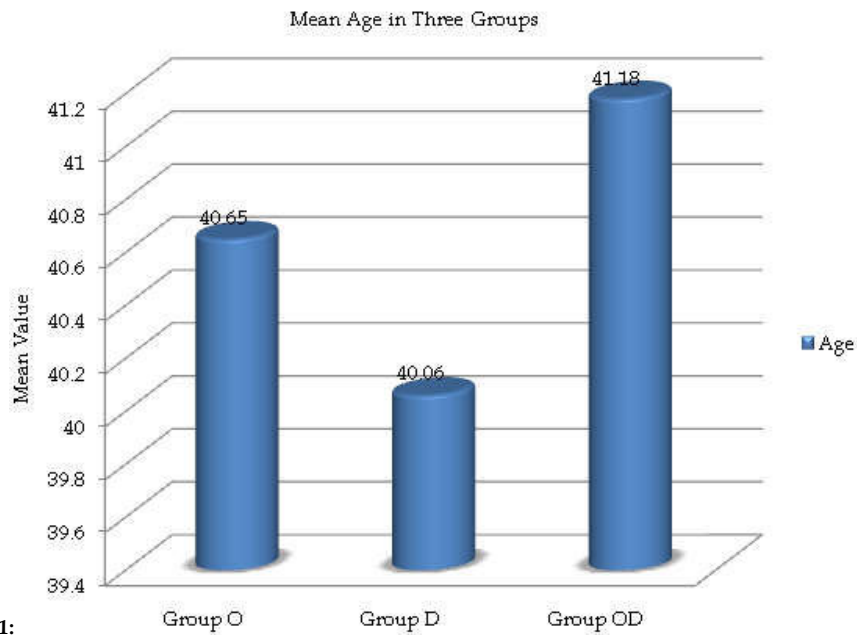


Fig. 3:

Observations and Results

Table 1: Description of characteristics of the cases among the groups (Age)

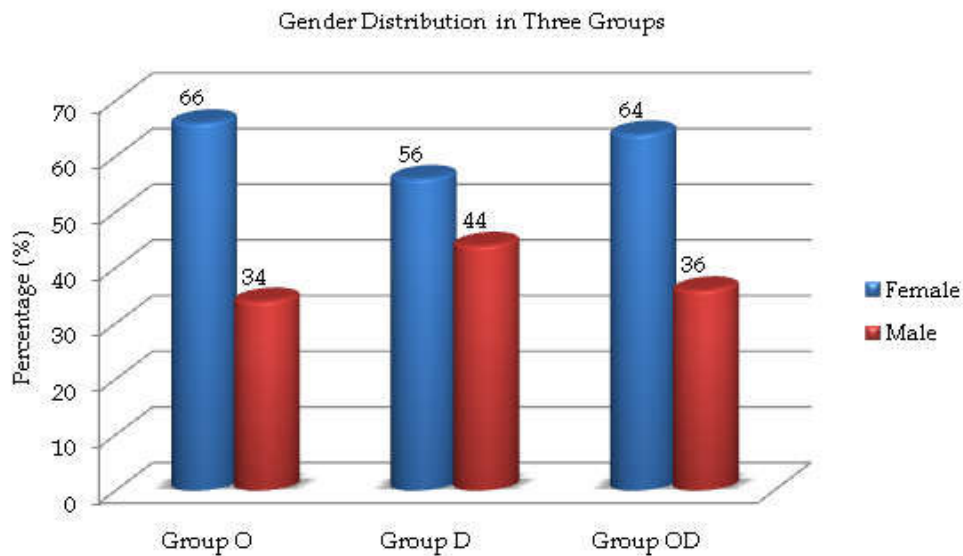
Parameter	Group O (mean ± SD)	Group D (mean ± SD)	Group OD (mean ± SD)	p value
Number of Patients	50	50	50	
Age	40.65 ± 9.0	40.06 ± 8.2	41.18 ± 7.51	0.81, NS



Graph 1:

Table 2: Description of characteristics of the cases among the groups (Gender)

Gender	Group O		Group D		Group OD		P value
	No.	%	No.	%	No.	%	
Female	33	66.00	28	56.00	32	64.00	0.81, NS
Male	17	34.00	22	44.00	18	36.00	
Total	50	100.00	50	100.00	50	100.00	



Graph 2:

Table 3: Incidence of Nausea (3 groups) for initial 6 hours & then 6 to 24 hours

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	2	4.00	4	8.00	1	2.00
6-24 hours	8	16.00	2	4.00	2	4.00
Total	10	20.00	6	12.00	3	6.00

Table 4: Statistical Analysis

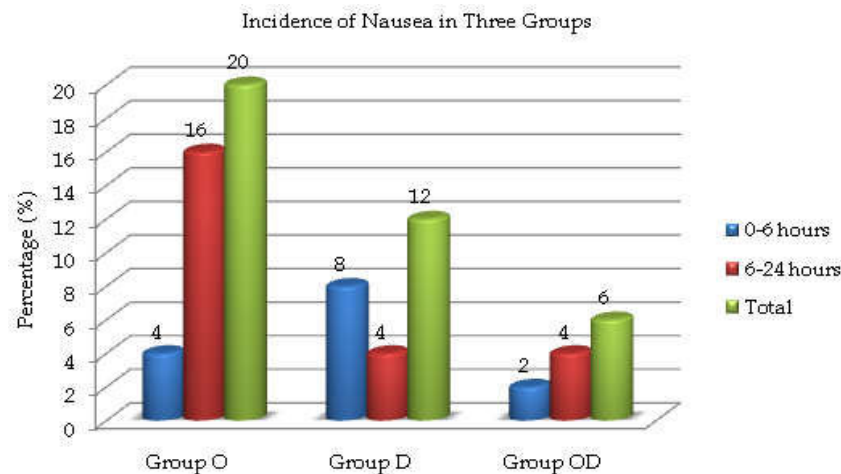
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.42	Not significant
Group O Vs. Group OD	0.60	Not significant
Group D Vs. Group OD	0.18	Not significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.09	Not significant
Group O Vs. Group OD	0.046*	Significant
Group D Vs. Group OD	1.00	Not significant

* Significant (p value < 0.05)

**Graph 3:****Table 5:** Incidence of Vomiting (Groups at 0 to 6 hours & 6 to 24 hours)

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	2	4.00	6	12.00	0	0.00
6-24 hours	4	8.00	2	4.00	2	4.00
Total	6	12.00	8	16.00	2	4.00

Table 6: Statistical Analysis

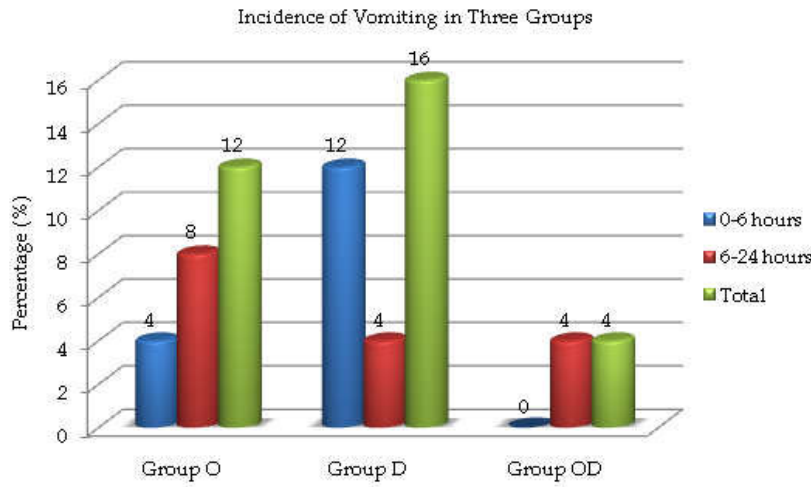
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.26	Not significant
Group O Vs. Group OD	0.23	Not significant
Group D Vs. Group OD	0.01*	Significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.60	Not significant
Group O Vs. Group OD	0.40	Not significant
Group D Vs. Group OD	1.00	Not Significant

* Significant (p value < 0.05)



Graph 4

Table 7: Comparative analysis of Incidence of PONV in 3 Groups (Duration 0-6 & 6-24 hours)

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	4	8.00	10	20.00	1	2.00
6-24 hours	12	24.00	4	8.00	4	8.00
Total	16	32.00	14	28.00	5	10.00

Table 8: Statistical Analysis

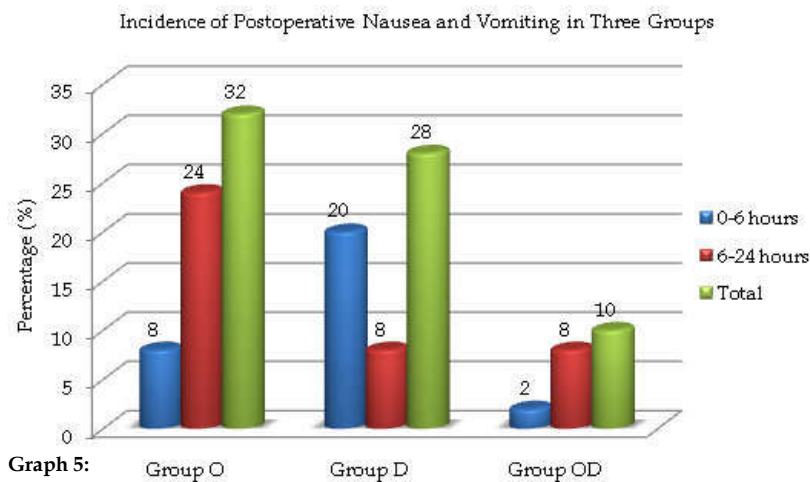
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.08	Not significant
Group O Vs. Group OD	0.19	Not significant
Group D Vs. Group OD	0.003*	Significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.09	Not significant
Group O Vs. Group OD	0.025*	Significant
Group D Vs. Group OD	0.7	Not significant

* Significant (p value < 0.05)



Graph 5:

Table 9: Comparative analysis of use of Antiemetic in 3 Groups (0-6 & 6-24 hours)

Time Interval	Group O (N=50)		Group D (N=50)		Group OD (N=50)	
	No.	%	No.	%	No.	%
0-6 hours	3	6.00	8	16.00	1	2.00
6-24 hours	10	20.00	2	4.00	2	4.00
Total	13	26.00	10	20.00	3	6.00

Table 10: Statistical Analysis

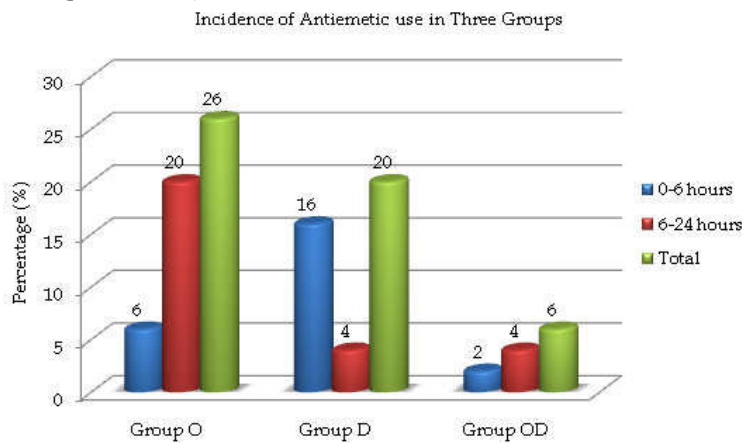
a. In 0-6 hours

Group	P value	Significance
Group O Vs. Group D	0.047*	Significant
Group O Vs. Group OD	0.60	Not significant
Group D Vs. Group OD	0.01*	Significant

b. In 6-24 hours

Group	P value	Significance
Group O Vs. Group D	0.056	Not significant
Group O Vs. Group OD	0.012*	Significant
Group D Vs. Group OD	1.00	Not significant

* Significant (p value < 0.05)

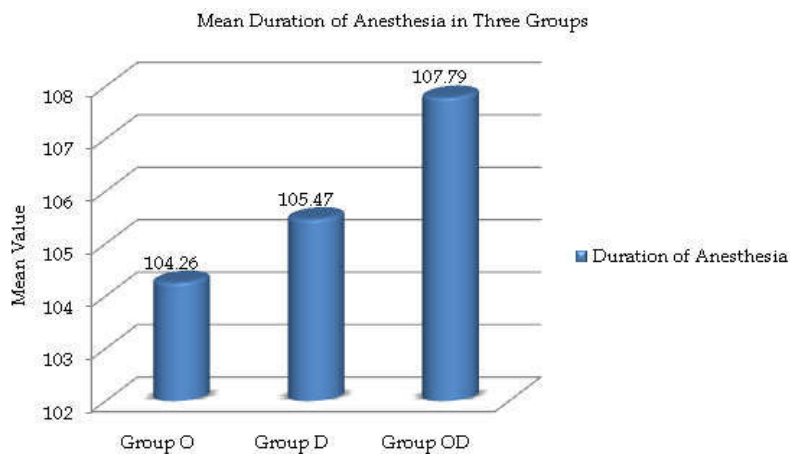


Graph 6:

Table 11: Duration of Anesthesia in these patients

Duration of Anesthesia	Group O (mean ± SD)	Group D (mean ± SD)	Group OD (mean ± SD)	P value
Duration	104.26 ± 7.97	105.47 ± 9.83	107.79 ± 9.58	0.169, NS

NS: Not significant



Graph 7:

Table 11 shows mean duration of anesthesia in group O 104.26 ± 7.97 min, group D 105.47 ± 9.83 min and group OD is 107.79 ± 9.58 min.

Discussion

Our comparative study observed that the post-operative nausea as well as vomiting were the most common complaints after laparoscopic surgery. There is also a high incidence of PONV in patients undergoing general anesthesia for laparoscopic surgeries which is due to many reasons as listed including prolonged CO₂ insufflations, gallbladder surgery, residual pneumoperitoneum, isoflurane & glycopyrrolate, history of movement disorders, hypotension during the operation and PONV [4] (Dexamethasone acts as an antiemetic [5])

- Reducing level of 5-hydroxytryptophan in neural tissue by depleting its precursor tryptophan.
- Dexamethasone potentiates main effect of ondansetron as an antiemetic by sensitizing its receptor.
- Anti-inflammatory properties of dexamethasone prevent release of serotonin in the gut.
- Prolonged antiemetic effect of dexamethasone can be attributed to the prolonged half-life of this drug (36 to 72 hr)[6].
- After 24 hours post operation we observed that the incidence of PONV & the need to antiemetic drug in patients who used combination of dexamethasone & ondansetron was significantly less than the patients who use alone of these drugs. The use of either one of these drugs had similar antiemetic effect. In a study conducted by McKenzie & associates [8], similar results were found.
- Ondansetron is selective 5-HT₃ antagonist that is used for its effect in nausea & vomiting due to chemotherapy & radiotherapy in addition to surgery [7]. This medicine has minor side effects such as headache, flushing, vertigo & constipation.
- In the current study during the first six hours post operation, the incidence of vomiting & the need for antiemetic drug in the group that received dexamethasone was significantly higher than the group that received either ondansetron or a combination of dexamethasone & ondansetron with no significant difference was observed in incidence of PONV. This result indicates that the use of dexamethasone is not sufficient to prevent the premature vomiting in patients

who undergo surgery. Rajeeva *et al.* [9] showed that the combination of ondansetron - dexamethasone controls the late PONV more effectively than the premature PONV.

- In this study, within the 6 to 24 hours post operation, the patients who used ondansetron after the operation needed more antiemetic drug than the patients who received the combination dose ($p = 0.012$), however, no significant difference was found between the group that received dexamethasone compared to the patients who received ondansetron ($p^2 = 0.05$). The shorter duration of effectiveness for ondansetron compared to dexamethasone is an indication of late prophylaxis failure for ondansetron. The half-life of ondansetron is between 4 to 9 hours [46].

Last but not the least, forget about the advancements in medical sciences & anesthesiology, still PONV remains a challenge.

Conclusion

The following were the conclusion that we have observed:

- Nausea level was lower in combination Group OD (i.e. 6%) as compared to Group O of ondansetron (i.e. 20%) & Group D dexamethasone (i.e. 12%). Incidence of vomiting was too less in Group OD (i.e. 4%) as compared to Group O (i.e. 12%) & Group D (i.e. 16%).
- The need for the antiemetic drug in groups O, D, & OD was 26, 20 & 6% respectively. The incidence of vomiting & failure in prophylaxis was observed in D-group during the first 6 hrs. The requirement of anti-emetic drug within 6 hours to 24 hours of post-operation observed higher in Group O in comparison to Group OD.
- In our study we have concluded that ondansetron & dexamethasone used single was less effective in control of early PONV compared to combination of all two. Hence we concluded that combination therapy of ondansetron & dexamethasone gives adequate control of PONV along with delayed PONV being better controlled as compared to early PONV in patients who undergoes elective laparoscopic surgeries under general anesthesia.

Limitations: The following were the key limitation of our study:

- Avoided counting frequency, length, severity and time duration of nausea or vomiting to follow-up recording of variables of interest (i.e. after 24 hours of operation)
- Length of hospitalization & expected side effects were not examined
- Result of our study shows that patients faced PONV were treated by combined drug prophylactic approach which required less antiemetic drug as compared to patients who receive 1 drug only

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