Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
©Scholars Academic and Scientific Publisher
A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

Anaesthesiology

To Compare the Efficacy of Ondansetron & Dexamethasone Alone and Ondansetron plus Dexamethasone in Combination for Prevention of Post-Operative Nausea and Vomiting In Laparoscopic Surgeries

Dr. Shakti Singhal MD.FIPM[1], Dr. Gunjan Agarwal MD[2*], Dr. Ghanshyam Das Singhal MS MCh[3]
[1]Assistant Professor Department Of Anaesthesiology, G.R. Medical College Gwalior Gwalior, India
[2]Associate Professor Department Of Pathology, GIPMER New Delhi, India
[3]Associate Professor Department Of Neurosurgery,GIPMER New Delhi, India

Original Research Article

***Corresponding author**
Dr. Gunjan Agarwal M.D Pathology
Email: dr.gunjan.25@gmail.com

Article History
Received: 17.12.2018
Accepted: 27.12.2018
Published: 30.12.2018

DOI:
10.36347/sjams.2018.v06i12.049

Abstract: Post-operative nausea and vomiting is one of the commonest & most unpleasant complaint following laparoscopic surgeries. It can lead to several emergencies like wound dehiscence, bleeding, aspiration of gastric contents, delayed hospital discharge, unexpected hospital admission and dissatisfaction among patients. This study is intended to compare the efficacy of ondansetron and dexamethasone alone and combinations of dexamethasone plus ondansetron in patients undergoing laparoscopic surgeries, with respect to nausea, vomiting and requirement of rescue anti-emetics. We studied 150patients between age group of 20yr to 50yr of ASA I & II requiring general anesthesia for laparoscopic surgeries, in a randomized clinical trial. 50 patients received 4mg ondansetron, intravenously and another 50 patients received dexamethasone 8mg intravenously and 50 patients received 4mg ondensetron+8mg dexamethasone 10min before induction, post operatively patients were assessed at time interval of 0-6hours and then at 6-24 hours for degree of nausea, vomiting and requirement of antiemetic drug. Vomiting occurring upto 0-6 hours was considered early vomiting and from 6-24 hour as delayed vomiting. Nausea was lower in the combination group OD (6%) when compared to group O of ondansetron (20%) and group D dexamethasone (12%). Incidence of vomiting was also less in combination group OD (4%) when compared to group O Ondansetron (12%) and group D dexamethasone (16%).The need for the antiemetic drug in groups O, D, and OD was 26, 20, and 6 respectively. The incidence of vomiting and failure in prophylaxis was observed in D-group during the first six hrs. The highest need for the anti-vomiting drug within the 6 to 24 hours of post operation was observed in group O compared to the group OD. We conclude that the combination therapy of ondansetron and dexamethasone provides adequate control of PONV, with delayed PONV being better controlled than early PONV (compare to ondansetron and dexamethasone alone) and the requirement of adjunct anti-emetics is dramatically reduced in first 24 hour.
Keywords: Post-operative, nausea, vomiting, ondansetron, dexamethasone.

INTRODUCTION

Postoperative nausea and vomiting are frequent and well recognized unpleasant complications following anesthesia and surgery. It can lead to several emergencies like wound dehiscence, bleeding, aspiration of gastric contents, delayed hospital discharge [1], unexpected hospital admission and dissatisfaction among patients. There can be several reasons for post-operative nausea and vomiting during laparoscopic surgery. These include pharyngeal stimulation, gastrointestinal distension, peritoneal distension, anesthetic agents, opioids, pain, and carbon dioxide insufflations. Other contributory factors are hypertension, hypoxia, vestibular disturbances, psychological factors, age, gender, history of previous nausea and vomiting, motion sickness, duration of operation, rough handling, diaphragmatic irritation, visceral organ irritation etc. These factors necessitate proper pharmacotherapy to avoid post-operative nausea and vomiting. These days use of combination anti-emetics that act at different receptors and adoption of a multimodal approach has been advocated in tackling this problem. The present study is designed to assess the efficacy of dexamethasone and ondansetron alone and ondansetron plus dexamethasone in combination for prevention of post-operative nausea and vomiting. The

fluid and electrolyte loss accompanying vomiting may lead to dehydration and life threatening electrolyte imbalance.

More than one and half century ago John Snow described phenomenon of nausea and vomiting [2]. His was the first extensive description of the phenomenon which was published in 1948, within 18 months of introduction of anesthesia into Great Britain. He observed that vomiting was more likely to occur in patients who have "eaten recently". In most cases the vomiting lasted only for a few minutes but in some it continued for hours and even days. He suspected that movement shortly after operation may have triggered the vomiting. Post-operative treatment included WINE (which he considered more beneficial than smelling salts!) and Battleys solution of opium. During ether era, reported incidence of PONV was as high as 75-80%. Seventy five years ago,

Flagg [3] suggested the PONV may result from causes other than anesthesia. There are at least three kinds of vomiting, the first of which has been attributed to anesthetics such as ether, the second to reflex responses, and the last to opioids. Subsequent investigation unfolded a spectrum of non-anesthetics factors in the pathogenesis of PONV.

There has been a general trend towards a decrease in the incidence and intensity of the problem because of a change in anesthesia practice from opioid and deep ether anesthesia to non-opioid or supplemented opioids to lighter and non-ether anesthesia, use of less emetic anesthetic agents, improved pre and post-operative medication, refinement of operative techniques and identification of patient predictive factors. However in spite of these advances, nausea and vomiting still occurs with unacceptable frequency in association with surgery and anesthesia. It has been described as "a big little problem [4]." Persistence nausea vomiting can have serious medical consequences to the patient as well as financial implication in delayed discharge from the hospital. Now a number of acceptable surgical procedures has increased in the field of ambulatory anesthesia, the need to find more effective alternatives to the options available, has become more urgent. The potential cost saving by performing these procedures on an ambulatory basis may be neglected by an unanticipated postoperative admission for intractable nausea. In addition, although intractable nausea is distressing possibly dehydrating and not easily manageable at home, the expense of a hospital stays is disproportionate to the actual morbidity of nausea for most healthy outpatients. Thus the therapy of last resort hospitalization is ultimately unsatisfactory for the patient, the anesthesiologist and the surgeon. Even lesser degree of post-operative nausea and vomiting are often perceived as failure of therapy, rather than as unavoidable consequences of the perioperative experience. In most instances the latter is in fact the case because of imperfect treatment options available till date. When queried about previous anesthetic experiences many patients are heard to lament about the distressing nausea after a prior procedure and begged to be spared of that experience again [5]. Previous pharmacological efforts to diminish the incidence or reduce the risk of emesis have included administering antihistaminics, anticholinergics, and dopamine antagonists. Physical maneuvers have included imposing various "Nothing per os[4]". Regimens, pre-anesthetic suctioning of gastric contents, application of cricoid pressure, avoiding inflation of the stomach during ventilation by mask and ingestion of antacid solutions. None of the above, alone or in combination have been entirely successful in mitigating the distressing occurrence of emesis and its potential sequel.

AIMS

- To analyse the efficacy of ondansetron alone
- To analyse the efficacy of dexamethasone alone
- To analyse the efficacy of ondansetron plus dexamethasone in combination.
- To compare the efficacy for prevention of post-operative nausea and vomiting in laparoscopic surgeries.

OBJECTIVES

- To observe the incidence of nausea and vomiting in post-operative period.
- To observe and compare requirement of rescue antiemetic in study groups.

MATERIALS AND METHODS

Source of Data

One hundred fifty of physical status ASA I and ASA II who will be undergoing laparoscopic surgery were included in the study. Patients will be randomized by computer generated blocks. Randomization will be done under three groups as under:

Group O (n=50) – receiving ondansetron alone
Group D (n=50) – receiving dexamethasone alone
Group OD (n=50) – receiving dexamethasone and ondansetron in combination

Method of data collection

- Duration of study: one year.
- Sample size: Minimum of 150 cases 50 in each arm

Inclusion Criteria

- Patients aged between 20 – 50 yrs
- Physical status ASA I and II
- Scheduled for elective laparoscopic surgeries e.g. laparoscopic cholecystectomy, laparoscopic sterilization etc.

Exclusion Criteria

- Patient's refusal for the study.
- Patients with physical status of ASA III and IV
- Patients who received opioids, NSAIDS or antiemetic agents 24 hrs prior to surgery
- Patients under ASA I and II but with history of
  - Motion sickness or migraine
  - Alcohol, drug abuse or smoking
  - Patient in which laparoscopy is converted to laparotomy.
  - Pregnant or lactating female
  - Patient on chronic steroid therapy.

Methods

Preoperative evaluation

Preoperative visit was conducted on the previous day of surgery. Detailed history and present complaints were noted. General and systemic examination of cardio vascular, respiratory and central nervous system were done. Routine laboratory investigations like hemoglobin level, total count and differential count, routine urine, blood urea nitrogen and serum creatinine, bleeding and clotting time, ECG were done.

Preoperative order

Patients were advised to remain nil orally after mid night. On the operation day intravenous cannulation with 18G catheter was established.

Study medication Ondansetron 4mg to group O, Dexamethasone 8mg to group D and both Ondansetron plus dexamethasone to group OD was administered to patients 10 min before induction of anesthesia.

Anesthesia

Pre-operative monitoring

- Noninvasive blood pressure
- Three lead ECG
- Oxygen saturation with pulse oximeter
- Pulse/ Heart rate

Anesthesia technique for laparoscopic surgery

Patient was premedicated with inj. Glycopyrrolate 0.2mg + 1mg midazolam+Fentanyl 2µg/kg and induced by inj. propofol 2 to 2.5 mg/kg. Tracheal intubation was facilitated by inj. vecuronium 0.1mg/kg. Baseline NG tube was placed for emptying the gastric contents. Anesthesia was maintained by N_2O + O_2 + 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, SpO_2, ECG, EtCO2 and urine output was carried out. During laparoscopic surgery abdomen was insufflated with CO_2 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 and 0.2 mg Glycopyrrolate. Duration of anesthesia was noted. In the post-operative period patients vitals was monitored. All post-operative cases were followed up at 0 to 6 hrs, 6 to 24hrs for post-operative nausea and vomiting.

Assessment

The episodes of vomiting and nausea were recorded in number of patients from 0 to 6 hrs, 6 to 24hrs for post-operative nausea and vomiting.

Requirement of anti-emetic drug in number of patients were recorded from0 to 6 hrs, 6 to 24hrs in postoperative period.

Statistical Analysis

Incidence of nausea, vomiting and number of patients needing rescue antiemetic were compared using 'Chi Square' test.

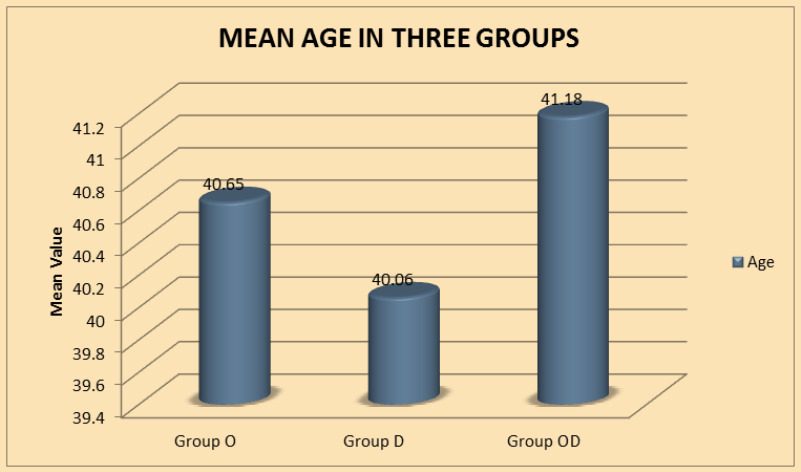
'p-Value' of <0.05 was considered significant.
'p-Value' of >0.05 was considered insignificant.

OBSERVATIONS AND RESULTS

Table-1: Age wise distribution of the patients

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

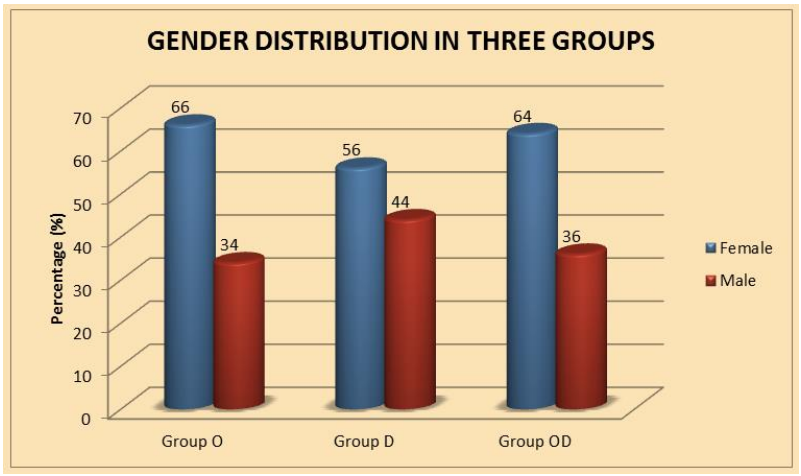
Table no.1 shows mean age in group O 40.65±9.0, group D 40.06±8.2 and group OD 41.18±7.51.



NS: Not significant

Table-2: Distribution of the patients according to their 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	



NS: Not significant

Table no. 2 shows Sex distribution in each group. In group 'O' 33 i.e. 66% were females and 17 i.e. 34% were males. In group 'D', 28 i.e. 56% were female and 22 i.e. 44% were males. In group OD 32 i.e. 64% were female and 18 i.e. 36% were males.

Table-3: Incidence of Nausea in Three Groups in 0-6 hours and 6-24 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

Statistical Analysis Table

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

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)

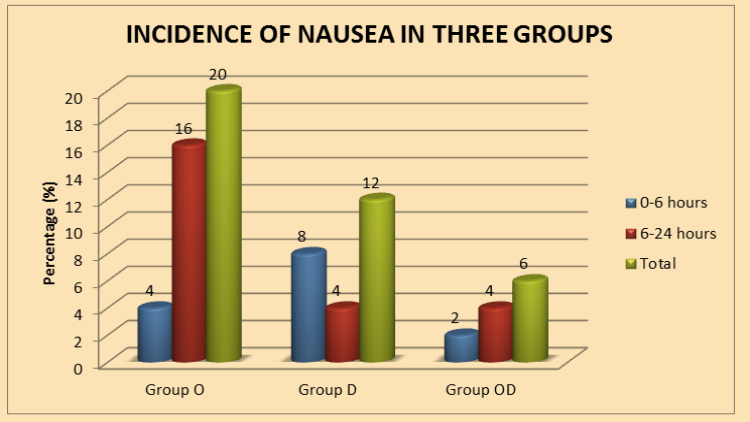


Table 3 shows the incidence of nausea in group O is 2 i.e. 4%, group D is 4 i.e. 8% and OD is 1 i.e. 2% within the first 0-6 hrs.

The incidence of nausea in group O is 8 i.e. 16%, group D is 2 i.e. 4% and group OD is 2i.e 4% within 6-24hrs.The incidence of nausea in group O is significant higher then group OD ($p<0.05$) within 6-24hrs but no such difference is present between D and OD group($p>0.05$).

Table-4: Incidence of Vomiting in Three Groups in 0-6 hours and 6-24 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

Statistical Analysis Table

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

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)

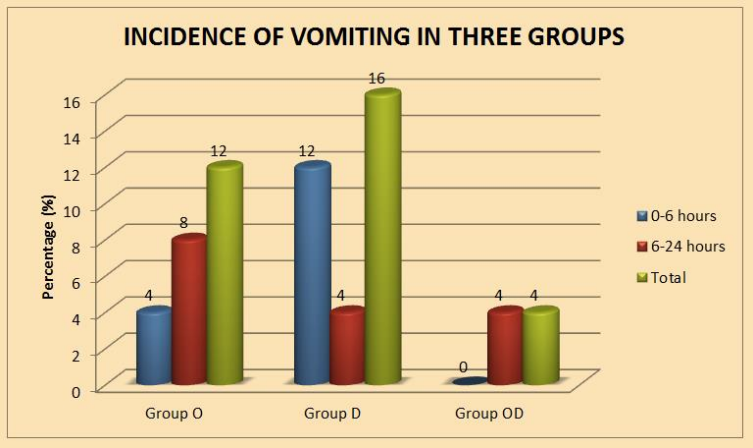


Table 4 shows the incidence of vomiting in group O is 2 i.e. 4%, group D is 6 i.e. 12% and OD is 0 i.e. 0% within the first 0-6 hrs.

The incidence of vomiting in group O is 4 i.e. 8%, group D is 2 i.e. 4% and group OD is 2 i.e. 4% within 6-24hrs.

The incidence of vomiting in group D is significant higher then group OD ($p<0.05$) within 0-6hrs but no such difference is present between O and OD group ($p>0.05$)

Table-5: Incidence of PONV in Three Groups in 0-6 hours and 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

Statistical Analysis Table

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

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)

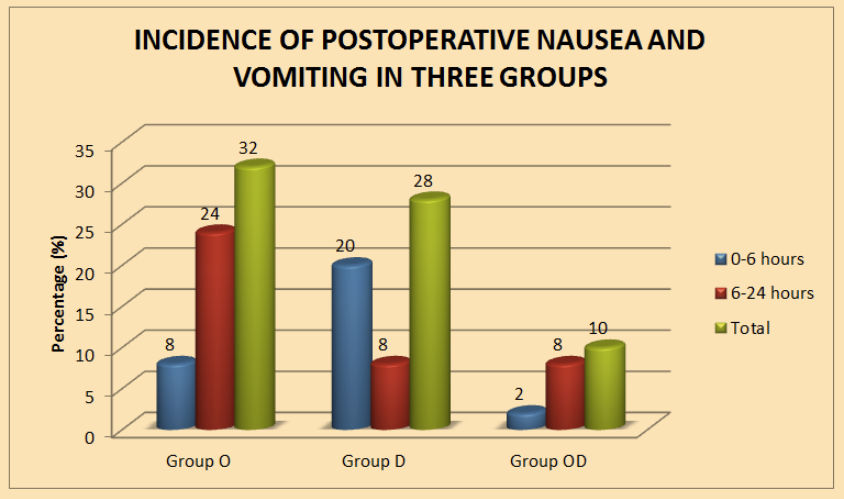


Table 5 shows the incidence of PONV in group O is 4 i.e. 8%, group D is 10 i.e. 20% and OD is 1 i.e. 2% within the first 0-6 hrs.

The incidence of PONV in group O is 12 i.e. 24%, group D is 4 i.e. 8% and group OD is 4 i.e. 8% within 6-24hrs. The incidence of PONV in group D is significant higher then group OD ($p<0.05$) within 0-6hrs and the incidence of PONV is significant higher in O then group OD within 6-24hrs ($p<0.05$).

Table-6: Use of Antiemetic in Three Groups in 0-6 hours and 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

Statistical Analysis Table

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

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)

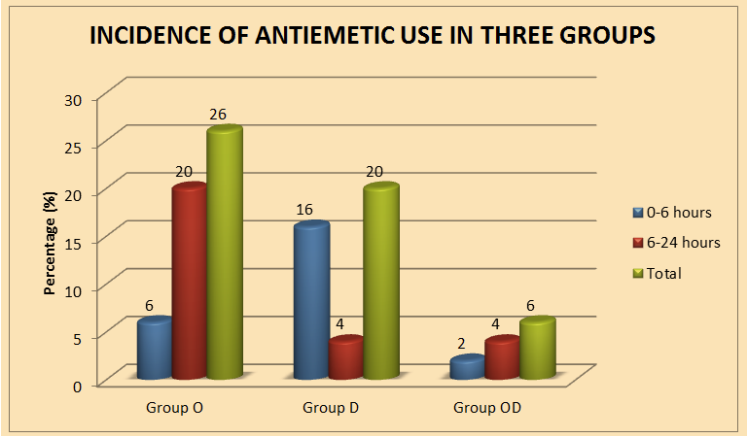


Table no.6 shows the incidence of antiemetic use in group O is 3 i.e. 6%, group D is 8 i.e. 16% and group OD is 1 i.e. 2% within 0-6hrs. The incidence of antiemetic use in group O is 10 i.e. 20%, group D is 2 i.e. 4% and group OD is 2 i.e. 4% within 6-24hrs.

The incidence of antiemetic use in group O is significant higher then group D and group OD ($p<0.05$) but no such difference is present between group O and OD ($p>0.05$) within 0-6hrs.The incidence of antiemetic use in group O is significant higher then group OD ($p<0.05$) but no such difference is present between group O and group D and between group D and group OD ($p>0.05$) within 6-24hrs.

Table-7: 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

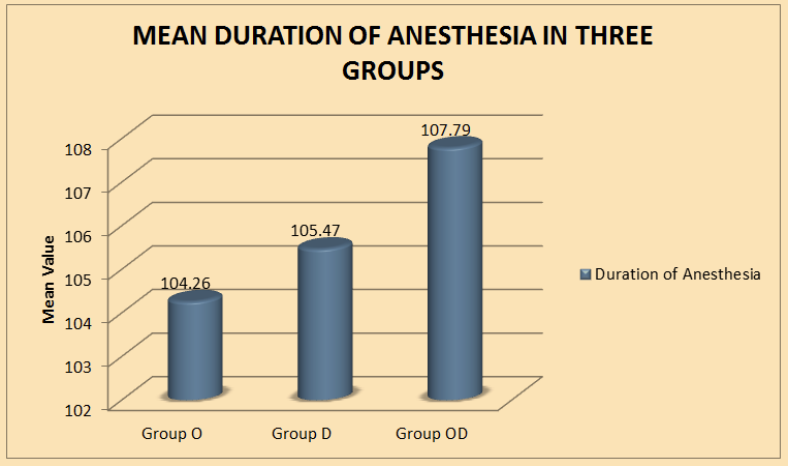


Table 7 shows mean duration of anesthesia in group O 104.26±7.97min, group D 105.47±9.83 min and group OD is 107.79±9.58 min.

DISCUSSION

Post-operative nausea vomiting are the most common complaints after anesthesia and surgery. There is a high incidence of PONV in patients undergoing general anesthesia for laparoscopic surgeries which is due to various reasons including prolonged CO_2 insufflations, residual pneumoperitoneum, gallbladder surgery, isoflurane and glycopyrrolate application, hypotension during the operation, history of movement disorders and PONV [41].

In the current study, the incidence of PONV in patients undergoing laparoscopic surgery who received antiemetic as treatments was compared.

Considering the fact that PONV is inevitable during the laparoscopic surgeries, no placebo drug was applied due to the ethical reasons. The dosage applied in the research was based on the prescription used in other studies[42]. Corticosteroid exerts its effects on specific reception protein and regulates the expression

of corticosteroid-responsive genes. A time sequence for the occurrence of this change in gene expression and protein synthesis is necessary. For this reason, the majorities of the corticosteroids effects do not appear immediately but instead they occur several hours later. As dexamethasone has potent anti-inflammatory [28] effect, it may be beneficial for post-operative pain. This condition can explain the latency of antiemetic effects of dexamethasone. In addition, the prolonged anti emetic effect of dexamethasone can be attributed to the prolonged half-life of this drug (36 to 72 hr) [43]. Dexamethasone is a glucocorticosteroid that has severe antiemetic effects for PONV. The recommended dose for adult patients is 5-10 mg. The antiemetic effect of this drug may be attributed to prostaglandin antagonism, peripheral or central control of serotonin, increase in releasing endorphin and change in penetrability of CSF blood barrier in relation to serum proteins [44].

Ondansetron is selective 5-HT_3 antagonist that is used for its effect in nausea and vomiting due to chemotherapy and radio therapy in addition to surgery [45]. This medicine has minor side effects such as headache, flushing, vertigo and constipation.

After 24 hours post operation. The incidence of PONV and the need to antiemetic drug in patients who used combination of dexamethasone and ondansetron was significantly less than the patients who use done of these drugs. The use of either one of these drugs had similar antiemetic effect. In a study conducted by McKenzie and associates[24], similar results were found.

In addition, Lopez-Olando *et al*.[10] reported that 84 percent of the patients who used combination of dexamethasone and ondansetron had complete response.

In the current study during the first six hours post operation, The incidence of vomiting and 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 and ondansetron with no significant difference in the premature incidence of PONV. This result indicates that the use of dexamethasone is not sufficient to prevent the premature vomiting in patients who undergo surgery [15].

Thomas and Jones [15] demonstrated that 28.3 percent of the patients who use dexamethasone faced failure in prophylaxis within the first 3 hours after the operation. This rate for ondansetron alone or combination of ondansetron – dexamethasone was 22 and 8.6percent, respectively.

Rajeeva *et al.* [22] 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 compare to dexamethasone is an indication of late prophylaxis failure for ondansetron. The half-life of ondansetron is between 4 to 9 hours [46].

Subramaniam and Madan[47] showed that the incidence of premature PONV (in the first 6 hour after the operation) in children who receive dexamethasone is 24.4 percent. For the children who receive ondansetron, this rate was 17.8 percent. These authors also demonstrated that the incidence of late PONV (within 6 to 12 hours) was significantly less in the dexamethasone group compared to the ondansetron group (6.67% *vs.* 24.4% respectively) Similar results were reported in patients undergoing ambulatory surgery[48]. In addition, it was shown that dexamethasone had stronger effect than ondansetron in preventing delayed nausea and vomiting following chemical therapy [49]. In summary, despite all the advances in medical sciences and anesthesiology, the so called simple subject like PONV remains a challenge. Some patients have a history of severe PONV and some surgery operations are associated with the high risk of PONV. Many researches are underway to examine the preferred treatment in this regard.

This is despite the fact that some of these procedures do not look very promising. The limitations of this study included not counting the frequency, severity, length and duration of nausea and vomiting in addition to follow-up recording of the variables of interest after 24 hours past the operation. Also, the length of hospitalization and possible side effects were not examined. However, the results of this study clearly demonstrated that the patients who face PONV and are treated by combined drug prophylactic approach need less antiemetic drug than the patients who receive one drug.

More researches with less limitation are needed to identify the most effective and economic treatment for the surgery operations. According to the findings of the current study, the treatment of PONV is more effective by the combination of ondansetron and dexamethasone than the use of either one of these two in laparoscopic surgeries. More specifically, dexamethasone alone is not very effective to prevent the premature PONV. In addition, using ondansetron alone is less effective in preventing late PONV comparing to

the combination use of ondansetron and dexamethasone.

SUMMARY AND CONCLUSION

Our study was a prospective, randomized and double blind study. A clinical study was undertaken in our institute to compare the efficacy of ondansetron, dexamethasone separately and ondansetron plus dexamethasone in combination for prevention of post-operative nausea and vomiting in laparoscopic surgeries.

After institutional ethical committee approval and written informed consent 150 patients between age group of 20-50 years of ASA I & II, coming for elective laparoscopic procedures under general anesthesia were selected. We studied 150 patients requiring general anesthesia for laparoscopic surgeries, in a randomized clinical trial. 50 patients received 4mg ondansetron intravenously and another 50 patients received dexamethasone 8mg intravenously and 50 patients received 4mg ondensetron+8mg dexamethasone 10min before induction. Post operatively patients were assessed for degree of nausea, vomiting and requirement of antiemetic drug at time interval of 0-6 hours and then at 6-24 hours. Vomiting occurring up to 0-6 hours was considered early vomiting and from 6-24 hour as delayed vomiting. Statistical comparison was done for all variables.

CONCLUSIONS

Nausea was lower in the combination group OD (6%) when compared to group O of ondansetron (20%) and group D dexamethasone (12%). Incidence of vomiting was also less in combination group OD (4%) when compared to group O Ondansetron (12%) and group D dexamethasone (16%).The need for the antiemetic drug in groups O, D, and OD was 26, 20, and 6 respectively. The incidence of vomiting and failure in prophylaxis was observed in D-group during the first six hrs. The highest need for the anti-emetic drug within the 6 to 24 hours of post operation was observed in group O compared to the group OD.

In our study we understood that dexamethasone alone is less effective in control of early PONV as compare to ondansetron alone is less effective in control of late PONV. Therefore, we conclude that the combination therapy of ondansetron and dexamethasone provides adequate control of PONV, with delayed PONV being better controlled than early PONV in patients undergoing elective laparoscopic surgeries under general anesthesia.

REFERENCES

1. Saeeda Islam PN. Jain, Post-operative nausea and vomiting (PONV): A review article. Indian J. Anaesth. 2004, 48(4): 253-58.
2. P.L.R. Andrews, Physiology of nausea and vomiting. Br. J. Anaesth. 1992; 69(S):2-19.
3. Lerman J. Surgical and patient factors involved in post-operative nausea and vomiting. Br. J. Anaesth. 1992; 69(S): 24-32.
4. Patricia A. Kapur, Editorial: The big “little problem”. Anesth Analg. 1991, 73: 243-245.
5. Hirsch J. Impact of post-operative nausea and vomiting in the surgical setting. *Anaesthsia*. 1994, 49(S): 30-33.
6. Lopez L. –oaondo. Advances in antiemetic pharmacology – ESRA refresher course. 2000 : 1-11
7. Henzi I, Walder B, Martin R, Tamer. Dexamethasone for the prevention of PONV- A quantitative systematic review. A quatitative systemic review. *Anaesth Analog*. 2000;90(1):186-194.
8. Elhakim M, nafie M, Mahmoud k.dexamethasone 8mg in combination with ondansetron 4mg appears to be the optimal dose for the prevention of nausea and vomiting after laparoscopic cholecystectomy. *Can J Anesth*. 2002; 49:922-926.
9. Aouad MT, Siddik SS, Rizk LB, Zayton GM, Baraka AS. The effect of dexamethasone on postoperative vomiting after tonsillectomy. Anesth Analg. 2001 Mar; 92(3):636-40.
10. Lopez-Olaondo L, Carrascosa F, Pueyo FJ, Monedero P, Busto N, Saez A. Combination of ondansetron and dexamethasone in the prophylaxis of postoperative nausea and vomiting. Br J Anaesth. 1996 jun; 76(6):835-40.
11. Rowbotham DJ Current management of postoperative nausea and vomiting. Br J Anaesth. 1992;69(S1):46S-59S.
12. Bodner M, White PF. Antiemetic efficacy of ondansetron after outpatient laparoscopy. Anaesth Analg. 1991;73:250-254
13. Alen E, Himmelseher S. ondansetron in the treatment of postoperative vomiting-a randomized double blind comparison with droperidol and metoclopramide. Anaesth Analg. 1992; 75:561-565.
14. Thomas R, Jones N. Prospective randomized, double-blind comparative study of dexamethasone, ondansetron, and ondansetron plus dexamethasone as prophylactic antiemetic therapy in patients undergoing day-case gynaecological surgery. British journal of anaesthesia. 2001 Oct 1;87(4):588-92.
15. Ronald D. Miller, Miller’s Anaesthesia, sixth edition. 2708-2709.
16. Litman RS, Christopher LW, frank AC. Ondansetron decreases emesis after tonsillectomy in children. Anaesth. 1994; 78:478-481.
17. Roy S, Rudra A. Ondansetron- a new antiemetic to reduce postoperative nausea and vomiting after mastoidectomy. Indian J Anaesth. 1996; 44: 117-117.
18. Diemunsch P, Counseiller C, Clyti M, Mamet JP, the French ondansetron study group. Ondansetron compared with metoclorpramide in the treatment of

established postoperative nausea and vomiting. *Br J Anaesth*. 1997;79:322 326
19. Shende D, Mandal NG. Efficacy of ondansetron and metoclopramide for preventing postoperative emesis following strabismus surgery in children. *Anaesthesia*. 1997;52(5):496-500
20. Fujii Y, toyooka H, Tanaaka H. Prophylactic antiemetic therapy with a combination of granisetron and dexamethasone in patient undergoing middle ear surgery. Br J Anaesth. 1998; 81(5):754-756.
21. Rajeeva V, Bharadwaj N Bharta YK, Dhaliwal LK. Comparision of ondansetron and dexamethasone in prevention of PONV in diagnostic laparoscopy. Can J Anaesth.1999; 46(1):40-44.
22. Hill RP, Labarsky DA, Fortney JT, Phillips-Bute B, Creed MR, Class PSA. Cost effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol or placebo. Anaesthesiology. 2000; 92:958-967.
23. Wang JJ, Ho ST, Liu S, Ho CM. prophylactic antiemetic of dexamethasone in women undergoing ambulatory laparoscopic surgery. Br J anaesth. 2000; 84(4):459-462.
24. Evertt LL. Can the risk of postoperative nausea and vomiting be identified and lowered during the preoperative assessment. Int Anaesthesiology Clic 2002;40:47-60.
25. Watcha MF. PONV. Anaesthesiology Clin N Am 2002; 20:471-484.
26. Sanchez-Ledesma MR, Lopez-Olaondo L, Pueyo FJ, Carrascosa F,Ortega A. A Comparison of three antiemetic combinations for the prevention of PONV. Anaesth Anag. 2002; 95:1590-1595.
27. Lee Y, Hsien-Young L, Pei-Chin L, Shen-Her H, You-Sheng L. dexamethasone prevents PONV most effectively in women with motion sickness. Can J Anaesth. 2003;50(3):232-237.
28. Gan JT, Meyer T, Apfel CC, Chung F, Davis JP, Eubanks S. Consensus guidelines for management of postoperative nausea and vomiting. Anaesth Analg. 2003; 97: 62-71.
29. Rusch D, Eberhart L, Biedler A, Dethling J, Apfel CC. Prospective application of a simplified risk score to prevent PONV. Can J Anaesth. 2005; 52: 478-484.
30. Ching-Liang Ho, Wu-Chou Su, Ruey-Kuen Hsieh, Zhong-Zhe Lin, Tsu-Yi Chao. A randomized double blind parallel, comparative study to evaluate the efficacy and safety of remosetron plus dexamethasone inj. For prevention of acute chemotherapy-induced nausea and vomiting. Japanese journal of clinical Oncology 2010 Apr;40(4):294-301
31. Jae-Woo Lee, Hye Jin Park, Juyoun Choi, So0 Jin Park, Hyoseok Kang, and Eu-Gene Kim, Comparison of ramosetron's and ondensetron's preventive anti-emetic effects in highly susceptible patients undergoing abdominal hysterectomy, Korean J Anaesthsiol. Dec 2011;61(6):488-492.
32. Abbas Ali Ajani, Amol Prakash Singam, Ashok Chaudhari, Aruna Vijay Chandak, Comparison of Ondansetron with Ondansetron and Dexamethasone in prevention of nausea vomiting in abdominal surgery, International Journal of Biochemical and Advance Research. 2013; 4(1).
33. Rose JB, Watcha MF. Postoperative nausea and vomiting. In Benumof JL, Saidman LJ edt. Anaesthesia and complication. 2nd edn. Mosby; 1999:p425-440.
34. Thomas EJ. Healy, A practice of Anaesthesia- Wylie and Churchill- Davidson – Seventh edition. 1030-1032.
35. Beattie WS, Lindblad T, Buckley DN, Forrest JB. The incidence of postoperative nausea and vomiting in women undergoing laparoscopy is influenced by the day of menstrual cycle. Canadian journal of anaesthesia. 1991 Apr 1;38(3):298.
36. Rudra A, Roy Ak. Postoperative nausea and vomiting- review article. Indian J Anaesth. 1996;44:226-240.
37. Colin Dollery, 1999, Therapeutic Drug Vol. I, 2nd edition, Churchill Livingstone1999; O21-O24.
38. Christine R. Culy, Nila Bhana, Greg L. Plosker, Ondansetron; A review of its use as an antiemetic in children. Paediatric drugs. 2001; 3(6): 441-479.
39. Colin Dollery, Therapeutic Drugs Vol. I, 2nd Edition, Churchill Livingstone.1999; D47-D50.
40. Goodman and Gilman's. The pharmacological basis of therapeutics, 9th edition; 249-262, 1459-1486.
41. Koivuranta MK, Laara E, Ryhanen PT. Antiemetic efficacy of prophylactic ondansetron in laparoscopic cholecystectomy. A randomised, double-blind, placebo-controlled trial. *Anaesthesia*. 1996; 51 (1): 52-5.
42. Tramer MR. A rational approach to the control of postoperative nausea and vomiting: evidence from systematic reviews. Part I. Efficacy and harm of antiemetic interventions, and methodological issues. *Acta Anaesthesiol Scand*. 2001;45(1):4-13.
43. Thune A, Appelgren L, Haglind E. Prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. A prospective randomized study of metoclopramide and transdermal hyoscine. *Eur J Surg*. 1995;161(4):265-8.
44. Pearman MH. Single dose intravenous ondansetron in the prevention of postoperative nausea and vomiting. *Anaesthesia*. 1994; 49(Suppl):11-5.
45. Gautam B, Shrestha BR, Lama P, Rai S. Antiemetic prophylaxis against postoperative nausea and vomiting with ondansetron-dexamethasone combination compared to ondansetron or dexamethasone alone for patients undergoing laparoscopic cholecystectomy. *Kathmandu Univ Med J (KUMJ)*. 2008; 6(23): 319-28.
46. McKenzie R, Kovac A, O'Connor T, Duncalf D, Angel J, Gratz I. Comparison of ondansetron

versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynecologic surgery. *Anesthesiology*. 1993; 78(1):21-8.

47. Subramaniam B, Madan R, Sadhasivam S, Sennaraj B, Tamilselvan P, Rajeshwari S. Dexamethasone is a cost-effective alternative to ondansetron in preventing PONV after paediatric strabismus repair. *Br J Anaesth*. 2001;86(1):84-9.
48. Lee A, Done ML. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis. *Anesth Analg 1999; 88(6)*1362-9.
49. Splinter WM, Roberts DJ. Dexamethasone decreases vomiting by children after tonsillectomy. *Anesth Analg*. 1996; 83(5):913-6.