Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 2, April - June 2017 (Part–2)
DOI: http: / / dx.doi.org / 10.21088 / ijaa.2349.8471.4217.6

Comparative Study of Intravenous Ondansetron and Dexamethasone for Amelioration of Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy

Amitesh Pathak*, Samiksha Parashar*, Om Prakash Sanjeev*, Sorabh Garg, Caroline Moriyama**, (Col) Supriyo Ganguly*****

Abstract

Background: Postoperative nausea and vomiting (PONV) is considered most unpleasant experience by the patients in postoperative period. In particular, following laparoscopic procedures the incidence of PONV is very high. The present study is aimed to assess the magnitude of PONV after laparoscopic cholecystectomy and to compare the relative effectiveness of two drug Ondansetron and Dexamethasone. *Subjects and Methods:* Ninety adult patient of either sex in the age group of 20 to 50 years of ASA I or II were randomly divided into one of the two groups of forty-five each. Group A patients received 4 mg of ondansetron intravenously towards end of surgery. Group B patients received 8 mg of Dexamethasone injection at the time of induction of anaesthesia. Postoperatively, the patients were assessed for episodes of nausea, vomiting and need for rescue antiemetic at intervals of 0–1, 1-2, 2-4, 4-8, 8-12, 12-24 hours. *Results:* The incidence of PONV up to 4 hours after surgery was 6 and 9 in Group A and Group B respectively ($p>0.05$). Thereafter during 4 to 12 hours after surgery, the incidence of PONV was 12 and 4 respectively in Group A and Group B ($p<0.05$). About 38% female patients had PONV compared to 20% male patient in-group A. Also 27% female patients had PONV compared to 18% male patient in-group B. *Conclusion:* Prophylactic Ondansetron in a dose of 4 mg given near the end of surgery and prophylactic Dexamethasone in a dose of 8 mg given at the time of induction is highly effective in reducing the incidence of PONV for 4 hours and 8 hours respectively after surgery. Compared to male population female sex seems to be an independent risk factor for PONV.

Keywords: Ondansetron; Dexamethasone; Laparoscopic Cholecystectomy.

Introduction

Post operative nausea and vomiting (PONV) is one of the most common side effect associated with surgical procedures [1,2]. In particular after laparoscopic surgeries, the incidence of PONV is high and ranges between 53-72% [3,4]. While, PONV is rarely fatal, it is considered to be one of the most unpleasant postoperative symptoms[5]. Additionally it may lead to various complications like pulmnary aspiration of vomitus, increased intracranial pressure etc. Persistent nausea and vomiting may result in dehydration, electrolyte imbalance, pulmonary aspiration of gastric content and delayed discharge from the hospital particularly after outpatient surgery [5,6]. As more and more patients undergo day care surgery, the humanitarian and economic implications of PONV are becoming increasingly significant.

The cause of postoperative nausea and vomiting is multifactorial. A number of pharmacological and non-pharmacological methods to reduce PONV have been tried in the past with variable success but still the best is to come [7]. These methods include acupuncture, acupressure, and drugs like droperidol [8], metoclopramide [9,10], atropine[8], hyoscine[9], cyclizine[11], and perphenazine, promethazine [9,12].

Ondansetron is highly selective 5HT3 antagonist [13,14]. It has

Author's Affiliation:
*Senior Resident, Department of Anaesthesiology, Dr. RML Institute of Medical Sciences, Gomti Nagar, Lucknow, Uttar Pradesh 226010. **Attending Consultant ***Senior Consultant, Department of Anaesthesiology, St. Stephens Hospital, New Delhi, Delhi 110054.

Corresponding Author:
Amitesh Pathak, House No. 1/ 167, Viram khand, Gomti Nagar, Lucknow, U P. India.
E-mail: amiteshomatic@gmail.com

Received on 28.03.2017
Accepted on 15.04.2017

been used successfully in chemotherapy induced emesis and is also known to be effective in preventing and treating PONV. The antiemetic effect of dexamethasone is reported to be equal to or better than 5HT3 antagonists [9]. Also adverse effects of dexamethasone are extremely rare[4].

Although various studies have proved the antiemetic efficacy of dexamethasone or ondansetron when compared with placebo after laparoscopic cholecystectomy [15,16,17,18]. In most of these studies, both the drugs were administered at the time of induction. Drawing any inference from these studies is not justifiable due to different pharmacodynamics of the two drugs. Ondansetron has shorter duration of action and dexamethasone is long acting but onset of peak action is delayed. So the present study is designed to compare the efficacy of i.v. ondansetron given at the end of surgery and i.v. dexamathasone given at induction for amelioration of PONV.

Aim and Objectives

1. To compare the relative effectiveness of the two drugs used prophylactically for amelioration of PONV.
2. Evaluate the influence of variants such as sex of the patient and duration of surgery on incidences of PONV.
3. To observe any undesirable effects such as hypotension, pain, dizziness, headache following therapy.

Subjects and Methods

Study Design

The present study was a randomized and prospective study. Necessary approval of hospital ethical committee was taken. Ninety adult patients of either sex in the age group of 20-50 years of ASA(American Society of Anaesthesiologist) grade I or II admitted to St. Stephen's Hospital, Delhi, scheduled for elective laparoscopic cholecystectomy under general anaesthesia were enrolled for this study.

The exclusion criteria were as follows.

Patients who were categorized under ASA III or more.

Who had history of motion sickness,

Hypersensitivity to study drugs,

History of Post-operative nausea and vomiting

Smoking history,

Migraine attacks in the past

Patients in whom conversion to open cholecystectomy was done.

Those patients who were on steroid therapy.

Patients who had received antiemetic within 48 hrs.

Group Allocation and Interventtion Plan

Randomization was done using computer generated random numbers table. The patients were randomly divided into two groups, Group A (Ondansetron) and Group B (Dexamethasone), of forty-five patients each.

Study medications were prepared by the site anaesthesiologist, who was not involved in any other part of the study. As the timing of study drug administration was different in two groups, there was chance of investigator bias. So along with study drug preparation, an identical saline filled syringe was also prepared. The site anaesthesiologist labeled the syringes as I (for giving during induction) and E (to be given at end of surgery) to guide the timing of drug administration by the investigator. The investigator was kept blind for the group of patient and also for the contents of syringes. Contents of syringe I was administered at induction and contents of syringe E was adminstered at the end of surgery to all participants of the study.

Group A (Ondansetron Group)

Syringe I: Filled with 5ml saline.

Syringe E: Filled 2ml ondansetron with saline to make total volume 5ml.

Group B (Dexamethasone Group)

Syringe I: Filled with 2 ml dexamethasone (8mg) with saline to make total volume 5ml.

Syringe E: Filled with 5ml normal saline.

Pre-Anesthetic Management

A detailed pre anesthetic checkup was done in all the patients, which included a detailed history and thorough physical examination. The necessary routine investigations were carried out in all the patients. An informed consent was taken from the patients. The patients were asked to restrict oral intake at least six hours before surgery. All patients were shown the

visual analogue scale and were appraised about the same during a preoperative visit one day prior to surgery. All the patients received Tab diazepam 10 mg at night and 5 mg in the morning of surgery and also Tab ranitidine 150 mg on the night of the surgery.

Anesthetic Procedure

Baseline Monitoring

On arrival to the operating room, normal saline infusion was started. Total amount of fluid required intraoperatively was calculated on per kg basis in all patients. Pre induction monitors were connected, which included electrocardiography, noninvasive blood pressure monitoring, and oxygen saturation through pulse oxymetry.

Anesthetic Technique

Patients were pre-oxygenated for 3 minutes and premedicated with 0.2mg/kg of midazolam. Induction was accomplished by thiopentone sodium (2.5%) 3-5mg/kg, fentanyl 2 microgram/kg. After the loss of eyelash reflex neuromuscular blockade was achieved with inj. vecuroinum 0.1mg/kg. After 3 minute of assisted ventilation tracheal intubation was done with an appropriate sized endotracheal tube. Anesthesia was maintained with isoflurane with air in oxygen. Ventilation was controlled to maintain end tidal carbon dioxide of 35-40 mm of Hg. A nasogastric tube was inserted for baseline emptying of the stomach. Pulse rate, blood pressure, ECG, SpO2, EtCO2 and intra-abdominal pressure were monitored throughout the operation. Study drug was administered as described above.

At the end of surgery, residual neuromuscular blockage was reversed with neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg). After extubation half hourly monitoring of pulse rate, blood pressure and oxygen saturation was extended to recovery period up to 2 hours. Any other side effect such as mental confusion, dizziness, abnormal movements and pain requiring analgesics during recovery period were noted.

Study Variables

The post-operative duration of 24 hours was divided into six intervals of 0-1, 1-2, 2-4, 4-8, 8-12 and 12-24 hours. Episodes of post-operative nausea and vomiting and injection metoclopramide requirement as a rescue anti-emetic and VAS scoring were recorded. Metoclopramide 10mg intravenous was used as the rescue antiemetic if the patients vomited more than once or when patient demanded.

Postoperative nausea and vomiting was assessed using 3-point scale (0-none, 1- nausea, and 2-vomiting; Table 1). Patient who had no incidence of PONV within 24 hours were categorized as having complete response and patients in whom either nausea or vomiting occurred during 24 hours postoperatively were considered as incident cases.

Statistical Analysis

Comparison of observation among different groups was done and statistically analyzed using Chi-square test, Student t test, Mann-Whitney-U test and N-par test. Assuming alpha=0.05, Number of cases =45 in each group and taking total PONV at 24 hours as significant parameter the power of the study comes out to be 80%.

Observations and Results

Demographic variables were comparable between the groups (Table 1). Incidence of PONV in both the groups during 24 hour postoperatively was divided into 6 fixed intervals (Table 2). The incidence of PONV up to 4 hours after surgery was 6 and 9 in Group A and Group B respectively($p>0.05$). Thereafter during 4 to 12 hours after surgery, the incidence of PONV was 12 and 4 respectively in Group A and Group B ($p<0.05$).

About 38% female patients had PONV compared to 20% male patient in-group A. Also 27% female patients had PONV compared to 18% male patient in-group B. Compared to male population female sex seems to be an independent risk factor for PONV. On further statistical analysis incidence of PONV was found to be significantly higher in females as compared to males in both the groups (Table 3).

As shown in Table 4, the incidence of PONV was about 50% (47% in group A and 40% in group B) in patients who underwent surgery for 60-90 minutes. The finding is consistent in both the groups, whereas in patients in whom duration of surgery was between 30-60 minutes has only 22% incidence of PONV($p<0.05$). Mean Metoclopramide consumption (in mg) was 3.55 in Group A and 3.43 in Group B and were comparable (Table 5). The VAS score was comparable between the groups at different time intervals (Table 6).

Table 1: Age and weight distribution in both groups

	Group A	Group B	P value
AGE (Mean±S.D)	40.06±9.609	37.66 ±8.287	0.18
Weight (Mean±S.D)	63.90±10.40	61.27±7.38	0.08
Sex(M / F)	10 / 35	11 / 34	0.12

Table 2: Incidence of PONV in Group A and B at different time duration

Time in hours	Incidence of PONV in GROUP A N (%)	Incidence of PONV in GROUP B N (%)	P value
0-1	1(2.22)	4(8.88)	0.085
1-2	2(4.44)	3(6.66)	0.065
2-4	3(6.66)	2(4.44)	0.058
4-8	5(11.10)	1(2.22)	0.005
8-12	4(8.88)	1(2.22)	0.005
12-24	0	0	
In 24 hours	15 / 45(33.33)	11 / 45(24.44)	0.086

Table 3: Effect of sex on the incidence of PONV.

Group	Sex	No. of Patient	Incidence of PONV	P value
Group A	Male	10	2	0.001
	Female	35	13	
Group B	Male	11	2	0.001
	Female	34	9	

Table 4: Effect of duration of surgery on PONV in both groups

Groups	30-60 mins			60-90 mins			P value
	No. of pts	Inc. PONV	%	No. of pts	Inc. of PONV	%	
Group A	26	6	23	19	9	47	0.024
Group B	35	7	20	10	4	40	0.016

Table 5: Statistical analysis of metoclopramide consumption in 24 hours in both groups.

	Group A	Group B	P value
Mean	3.552	3.43	0.085
S.D.	6.088	6.39	

Table 6: Comparison of Mean VAS scores at between different time intervals between the groups.

VAS Score		Group A	Group B	p value
VAS 0-1 hr	Mean	4.42	3.88	0.058
	S.D.	1.469	1.170	
VAS 1-2 hr	Mean	3.75	3.40	0.147
	S.D.	1.069	0.96	
VAS 2-4 hr	Mean	3.37	3.088	1.000
	S.D.	.960	0.848	
VAS 4-8 hr	Mean	3.13	3.53	0.061
	S.D.	0.99	0.967	
VAS 8-12 hr	Mean	3.32	3.35	0.616
	S.D.	1.423	1.090	
VAS 12-24 hr	Mean	3.20	3.64	0.026
	S.D.	0.894	1.28	

Discussion

Results of our study revealed that the incidence of PONV was similar in both the groups. But the timing of onset of PONV in post operative period was different in the groups. There was also increased incidences of PONV in female patients in both the groups. Duration of surgery was also found to affecting the incidences of PONV and longer duration of surgery was associated with increased incidences of PONV.

The test drugs were administered at different times

during the operation as for ondansetron it was administered at the end of surgery because it has a relatively short elimination half-life of 3.5-4 hours [3] in adults and giving the drug at the end of surgery would have a more sustained effect in the postoperative period.

Dexamethasone was given one minute before the induction of anesthesia because onset time of dexamethasone injection is approximately after two hours, which is the expected duration of laparoscopic cholecystectomy, so the antiemetic effect is best appreciated when it is given at the time of induction of anesthesia. It has a long half-life of 36-48 h after a single dose of 8 mg i.v. given before induction of anesthesia [19].

The selection of drug dosages was based on the previous work that demonstrated that these doses were effective. For antieme tic prophylaxis, ondansetron has been used in a dose range of 4-8 mg [3]. The recommended dose on body weight basis is 0.1 mg/kg [11]. The choice of a 4-mg ondansetron dose was based on studies that suggested this was the optimal dose for the prophylaxis of PONV [13]. The minimum effective antiemetic dose of dexamethasone is 2.5 mg and the most commonly used dose in adults is 8 mg [4]. Liu and his colleagues have suggested a dose of 0.15mg/kg of dexamethasone, up to a maximum dose of 10 mg for prevention of post-operative nausea and vomiting.

We found that total incidence of PONV in 24 hours was 33% in the Ondansetron group and 24% in dexamethasone group. Our results were consistent with the studies conducted by Wang[17] et al and Yamacerhan[4] et al in patients undergoing laparoscopic cholecystectomy, the slight difference in the incidence of PONV in dexamethasone group may be due to use of Propofolin their study.

In the first hour of postoperative period, the incidence of PONV in Ondansetron group was 2.22% compared to 8.88% in Dexamethasone group. Although there was no significant difference (P value=0.06). This difference was consistent with the observations by Wang et al [12], probable reason could be comparatively quicker onset of anti-emetic action of ondansetron compared to dexamethasone.

From 4 to 8 hours postoperatively, the incidence of PONV was 11.10% in Ondansetron group and 2.2% in Dexamethasone group. We found that Ondansetron did not give much protection at 8 hours, while it is very effective at first 4 hours. From 8 to 12 hours postoperatively, the incidence of PONV was 8.88%in Ondansetron group and 2.22%in Dexamethasone group. The difference was also statistically significant with a P value<.05. From 12 to 24 hours postoperatively, there was no incidence of PONV in both the group.

Metoclopramide 10mg intravenous was used as the rescue antiemetic if the patients vomited more than once or when patient demanded. The difference in Metoclopramide requirement was not statistically significant between ondansetron group and dexamethasone group.

About 38% female patients had PONV compared to 20% male patients in Group A. Also 26% female patients had PONV compared to 18%male patients in group B. Compared to male population female sex seems to be an independent risk factor for PONV.

The incidence of PONV was about 50%(47% in group A and 40% in group B) in patients who underwent surgery for 60-90 minutes. The finding is consistent in both the groups. Whereas in patients in whom duration of surgery was between 30-60 minutes only 20-25% of patients had PONV. The results were similar to previous stating that increased duration of surgery has positive correlation with the incidence of PONV.

Conclusion

Prophylactic Ondansetron in a dose of 4 mg i.v given near the end of surgery is highly effective in reducing the incidence of PONV for 4 hours after surgery. Prophylactic dexamethasone in a dose of 8 mg i.v given at the time of induction is highly effective in reducing the incidence of PONV for 8 hours after surgery. Female sex and longer duration is associated with increased incidence of P ONV.

Key Messages

Both Antiemetic significantly reduced the incidence of PONV. Ondansetron provides better prophylaxis against PONV in early better postoperative period. Text.

References

1. Gordon Yuill, Carl Gwinnutt, Department of Anaesthetics, Hope Hospital, Eccles Old Road, Salford, Manchester, UK. M6 8HD. Postoperative nausea and vomiting. World Federation of Societies of Anesthesiologists. 2003; Issue 17:Article 2.
2. Tong J. Gan, Tricia Meyer, Christian C. Apfel, Frances Chung, FRCPC, Peter J. Davis, Steve Eubanks,

Anthony Kovac, Beverly K. Philip, Daniel I. Sessler, James Temo, Martin R. Trame'r and Mehernoor Watcha, . Consensus Guidelines for Managing Postoperative Nausea and Vomiting. AnesthAnalg 2003; 97:62–71.

3. Lerman.J. Surgical and patient factors involved in post operative nausea and vomiting. Br.J. Anesth 1992; 69(suppl):24s-32s.
4. Cameron .H.A, Reyntjens.A.J, Lake-Bakaar.G. Cardiac arrest after treatment with intravenous Domperidon. Br.Med.J 1985; 290:160.
5. Tong J. Gan, MB. Evidence-based management of postoperative nausea and vomiting. Canadian Journal of Anesthesia *2003;* 50:R5.
6. WatchaM.F, White P.F. Post operative nausea and vomiting .its etiology, treatment and prevention. Anesthesiology.1992; 77:162-184.
7. Fisher M.D. The "big little problem" of postoperative nausea and vomiting; do we know the problem yet. Anesthesiology 1997; 87:1271-1273.
8. MatsonA, PalazzoM. Postoperative nausea and vomiting. Recent advances in anesthesia, Churchill Livingstone .1995; vol 19:107-127.
9. Burtles.R, Peckett.B.W. Postoperative Vomiting: some factors affecting its incidence. Br.J.Anesth .1957; 29:114-123.
10. Thune A, Appelgren.L, Haglind.E. Prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Eur j surgery 1995; 161:265-268.
11. Rowbotham.D.J. Current management of postoperative nausea and vomiting. Br.J.Anesth. 1992; 69(suppl.1):46s-59s.
12. Thune A, Appelgren.L, Haglind.E. Prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Eur j surgery 1995; 161:265-268.
13. Joslyn. A.F. Ondansetron. Clinical development for postoperative nausea and vomiting: current studies and future directions. Anesthesia, 1994; 49(suppl): 34-37.
14. J.G. Hardman, A.G. Gilman, L.E. Limbird. Goodman and Gilman's –The pharmacological basis of therapeutics, 9th edition 1996; McGraw Hill: 929.
15. Markman. M, Sheidler. V.R.N, Ettinger.D.S. Antiemetic efficacy of Dexamethasone. N England J Med 1984; 311:549-552.
16. Liu.KHsu.C.C, Chia.Y.Y. Effect of Dexamethasone on postoperative emesis and pain. Br.J.Anesth 1998; 80:85-86.
17. Jhi-Joung Wang, Shung-Tai Ho, Jann-Inn Tzeng, and Chao-Shun Tang. The Effect of Timing of Dexamethasone Administration on its efficacy as a prophylactic antiemetic for Postoperative Nausea and Vomiting. AnesthAnalg 2000; 91:136–9.
18. Jenkins, L.C. and Lahay, D. Central mechanisms of vomiting related to catecholamine response: Anaesthetic implication. Canad. Anaesth. Soc. J.1971; 18: 434-441.
19. Koivuranta M.K, Laara .E, Ryhanen P.T. Antiemetic efficacy of prophylactic Ondanesetron in laparoscopic cholecystectomy. Anesthesia 1996; 51:52-55.