Comparative Evaluation Of Ondansetron Used Alone And In Combination With Dexamethasone In Prevention Of Post Operative Nausea And Vomiting Following Laparoscopic Cholecystectomy In Females

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Citation

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Abstract

Post operative nausea and vomiting (PONV) continue to be frequent occurrences, even when conventional antiemetics are prophylactically used. In a randomized double blind study, 60 female patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia were divided into 2 groups of 30 patients each and received 4 mgs of Ondansetron (Group I) or a combination of Ondansetron 4 mgs and 4 mgs of dexamethasone (Group II) pre- operatively. Patients were observed for 24 hours post operatively and interpretation of symptoms of nausea and vomiting was done according to Gan and Alexander scale (0-2). 70 % of patients in Group II and 43 % patients in Group I did not experience PONV; the difference was statistically significant ($p<0.01$). 3 patients (10%) in Group II and 10 patients (33%) in Group I required rescue antiemetic medication during the 24 hour study period. The difference was found to be highly significant($p<0.001$) The difference in the incidence of PONV between the two groups after 6 hours to 24 hours was highly significant ($p<0.001$). It was concluded that prophylactic administration of combination of Ondansetron and dexamethasone is effective than Ondansetron when used alone, in reducing in incidence of PONV with prolonged effects.

INTRODUCTION

Post operative nausea and vomiting are considered as very unpleasant side effects of anaesthesia, causing distress and dissatisfaction to patients. Post operative nausea and vomiting (PONV) can occur after general, regional or local anaesthesia. [1] An overall estimate of PONV is approximately 20 – 30 % of all adult surgical patients. [2] Most investigators have reported a significantly higher incidence of nausea and vomiting after surgery in female adults compared to male adults. [2] The incidence of PONV after day care and laparoscopic surgeries varies from 36 – 82 % during immediate post operative recovery and can be as high as 73 % in certain gynecological procedures [3] .

Anesthesia related factors associated with emesis included premedication, inhalational agents, opioids, postoperative pain, patient mobilization, hemodynamic instability and initiation of oral intake. [4] Many different antiemetic drugs are available for treatment of PONV. Balanced antiemesis, using drug combinations with different mechanisms and site of action is a better and worthwhile approach than single drug therapy. [5,6] Extensively studied $5HT_3$ antagonist Ondansetron has been considered with dexamethasone for effective prophylaxis against PONV.

The present study was undertaken to evaluate the efficacy of $5HT_3$ antagonist Ondansetron alone and in combination with Dexamethasone for the prevention of PONV in female undergoing laparoscopic cholecystectomy.

MATERIAL AND METHODS

This prospective randomized double blind study included 60 female patients aged 18 – 55 years, belonging to ASA I or II class, undergoing laparoscopic cholecystectomy under General Anaesthesia. A proper approval from the local ethics committee and informed consent was taken from the patients included in the study. In the preoperative holding area, patients were randomly allocated into two groups of 30 patients each and received study medications prepared by a single person in identical 5 ml sringe and all study medications were diluted upto 4 ml in 0.9 % saline in order to ensure blinding.

Group I patients were given 4 mgs of Ondansetron diluted to 4 ml in 0.9 % (Ondansetron group)

Group II patients received combination of 4 mgs of Ondansetron with 4 mgs of dexamethasone diluted to 4 ml in 0.9 % saline. (Combination group)

Patients with history of motion sickness, migraine, PONV during a previous surgery and pregnant and lactating females were excluded from study. In the operating room, after establishing an IV line, the study medication was administered one minute prior to induction of anaesthesia. The anaesthetic sequence was standardized. Anaesthesia was induced with 5.5 mg / kg of 2.5 % thiopentone sodium, morphine 0.1 mg / kg and midazolam 1 mg iv. Tracheal intubation was facilitated with suxamethonium 2 mg / kg b.w. i.v. Anaesthesia was maintained with 66 % N_2O in oxygen and muscle relaxation was achieved with Atracurium 0.5 mgs /kg supplemented with 0.5 – 1% halothane. After tracheal intubation, a nasogastric tube was placed to promote baseline empting of stomach of air and gastric contents, which was removed at the end of surgery before tracheal extubation. During surgery, patients were positioned in the reverse Trendelenberg position with the right side of the table elevated. The abdomen was insufflated with CO_2, to an intraabdominal pressure of 10 – 14 mm Hg. Intra operative monitoring included EGG, pulse oximetry, non invasive blood pressure monitoring, which recorded systolic, diastolic and mean arterial blood pressure every 5 minutes. Duration of anaesthesia, surgery and CO_2 insufflation was also recorded in each patient. At the end of surgery neuromuscular block was reversed with Neostigmine and Atropine

After surgery patients were observed for a period of 24 hours by the same anaesthetist. Diclofenac sodium 75 mg i/m was used as a rescue analgesic if patient complained of pain and requested for analgesia.

The incidence of nausea and vomiting was recorded every 6 hourly for a period of 24 hours. No distinction was made between vomiting and retching (retching event was considered as vomiting event).

Nausea and vomiting was evaluated on a three point scale.

0 = none
1 = nausea
2 = vomiting

Rescue antiemetic medication was given in the form of injection (Ondansetron 0.1 mg / kg b.w., and repeated if the patient experienced severe nausea; if there were more than 3 emetic episodes with in a period of 15 minutes or if patient asked for it.

Pain intensity was assessed using a 10 cm visual analogue (VAS 0 = no pain to 10 =severe pain). Pain intensity was classified into 3 categories for easy statistical analysis. Severe if VAS score >7, moderate if VAS score 3 –7, mild if VAS score < 3. Data thereby collected was statistically evaluated and analyzed.

RESULTS

There was no statistical difference between the groups with regards to age, body mass index, duration of surgery and anaesthesia, duration of CO2 insufflation. The variation of VAS score between the two groups at 1 and 2 hours was statistically insignificant (p=0.245 and 0.269 respectively). The variation in VAS score at 3, 4 & 24 hours was again statistically insignificant. No patient experienced severe pain (score > 7) at any stage of time in both groups.

In group I (Ondansetron group), a complete response (PONV score 0) was observed in 21 patients (70%) during 0 – 6 hours after anaesthesia, whereas during further study intervals, complete response was seen in lesser number of patients, with score 0 in only 13 patients (43.33 %) at 24 hours post operatively. Similarly during 0 – 6 hours of study 7 patients (23.3%) had nausea (PONV score 1) where as 2 patients (6.67%) had vomiting (PONV score 2), showing an overall incidence of emetic episode in 9 patients (30%). The incidence of emetic episode increased further during next study intervals and was 56.67 % at 24 hours post operatively.

In group II (combination group), during 0 – 6 hours after anaesthesia complete antiemetic response (PONV score 0) was observed in 25 patients (83.33%) which during further study intervals remained more or less same, and at 24 hours postoperatively was seen in 24 patients (80%).

The overall incidence of emetic episode during 0 – 6 hours of study was 16.66 % with nausea (PONV score 1) seen in 4 patients (13.33%) and vomiting (PONV score 2) only in 1 patient (3.34%). At 24 hours after the surgery, the incidence of emetic episode was 20 % with only 6 patients experiencing nausea and vomiting.

During 0 – 6 hours after anaesthesia (16.67%) patients in

group II and 9 (30%) patients in group I reported nausea and vomiting with insignificant variation, whereas at 6 – 12 hours after anaesthesia, the variation in the incidence was significant (p=0.047) with 6 (20%) patients in group II reporting nausea and vomiting as compared to 13 (43.37) patients in group I.

Similarly the incidence of nausea and vomiting was found to be highly significant between the groups during 12 – 18 and 18 – 24 hours, with 7 (23.33%) and 6(20%) patients in group II as compared to 17 (56.67%) patients in group I reporting nausea and vomiting during each time intervals.

In group I 10 patients (33.33%) asked for rescue anti-emetic where as in group II only 3 patients (10%) respectively required rescue anti-emetic. Requirement for rescue antiemetic medication in the two groups showed a statistically highly significant difference (p<0.001)

DISCUSSION

Post operative nausea and vomiting (PONV) remains an unpleasant and persistent clinical problem in the surgical patients after anaesthesia. The main patient related factors are age, gender, history of motion sickness, previous post operative nausea and vomiting and pregnancy. The incidence on females has been reported to be very high. [7] Women are more sensitive to emetic stimuli. The mechanism of post operative nausea and vomiting in them is complicated b prevailing hormone status. [8] The management of post operative nausea and vomiting is based primarily on treatment rather than prevention.

The quest for effective antiemetic drug without the potential for sedation, or extra pyramidal symptoms and other side effects lead to development of 5 HT_3 receptor antagonist i.e. Ondansetron. Among steroids, Dexamethasone has been found to have effective antiemetic effect. The mechanism of dexamethasone induced antiemetic activity may involve central inhibiting of prostaglandin synthesis.

Recently drug combination with different mechanism and site of action have been used to achieve enhanced anti-emesis against PONV.

In our study, a complete response (no nausea and vomiting) was observed in 70 % patients in Ondansetron plus dexamethasone group as compared to 43 % in Ondansetron group, the difference was statistically highly significant. A statistically highly significant reduction (p<0.001) in the incidence of PONV was observed in Group II when compared with Group I after the 6 hours of surgery. Only 10 % of patients in Group II required rescue antiemetic medication as compared to 33 % in Group I which was statistically highly significant. Our results are in agreement with the study of Ray Mackenzie et al (1994) [9] who noted a complete response in 38 % of patients in Ondansetron group as compared to 52 % of patients in the combination group. The combination group did not need any rescue antiemetic during the 24 hour post operative period. Rajeeva V et al (1998) [10] also observed that over all incidence of vomiting alone was greater in Ondansetron group (35%) as compared to combination group(8%)[p<0.05]. Our results were also comparable with the study of Lopez Olaondo et al (1996). [11]

In conclusion prophylactic administration of combination of Ondansetron and dexamethasone is more effective than Ondansetron when used alone in reducing the incidence of PONV with prolonged effects.

Figure 1

Table 1: Comparison of demographic data and other characteristic in two groups

Characteristics	Group I	Group II	p value	Remarks
Age (years) mean ± SD	33.37 ± 8.53	32.47 ± 10.18	0.950	NS
Weight in kgs mean ± SD	52.90 ± 7.27	52.70 ± 7.47	0.996	NS
Duration of Anaesthesia in minutes mean ± SD	65.27 ± 18.72	66.67 ± 21.84	0.987	NS
Duration of Surgery in minutes mean ± SD	49.40 ± 16.75	51.93 ± 20.47	0.934	NS
Duration of CO2 insufflation in minutes mean ± SD	46.43 ± 18.62	46.60 ± 20.65	0.619	NS

NS = non significant

Figure 2

Table 2: PONV scores at different time intervals in Group I

PONV score	Time interval			
	0 – 6 hours No. (%)	6 – 12 hours No. (%)	12 – 18 hours No. (%)	18 – 24 hours No. (%)
0 (No nausea / vomiting)	21 (70.00)	17(56.67)	13(43.33)	13(43.33)
1 (Nausea)	7(23.33)	9(30.00)	12(40.00)	12(40.00)
2 (Vomiting)	2(6.67)	4(13.33)	5(16.67)	5(16.67)
Emetic episode	9(30.00)	13(43.33)	7(56.67)	17(56.67)

Figure 3

Table 3: PONV scores at different time intervals in Group II

	Time interval			
	0 – 6 hours No. (%)	6 – 12 hours No. (%)	12 – 18 hours No. (%)	18 – 24 hours No. (%)
0 (No nausea / vomiting)	25(83.33)	24(80.00)	23(76.67)	24(80.00)
1 (Nausea)	4(13.33)	4(13.33)	5(16.67)	5(16.67)
2 (Vomiting)	1(3.34)	2(6.67)	2(6.67)	1(3.34)
Emetic episode	5(16.67)	6(20.00)	7(23.33)	6(20.00)

Figure 4

Table 4: Comparison of incidence of PONV during 0 -24 hours between the 2 groups

Group	PONV		p value	Remarks
	Yes No. (%)	No No. (%)		
I	17 (56.66)	13 (43.33)	0.001	Significant
II	9 (30.00)	21 (70.00)		

Figure 5

Figure 1: Comparison of incidence of PONV during 0 -24 hours between the 2 groups

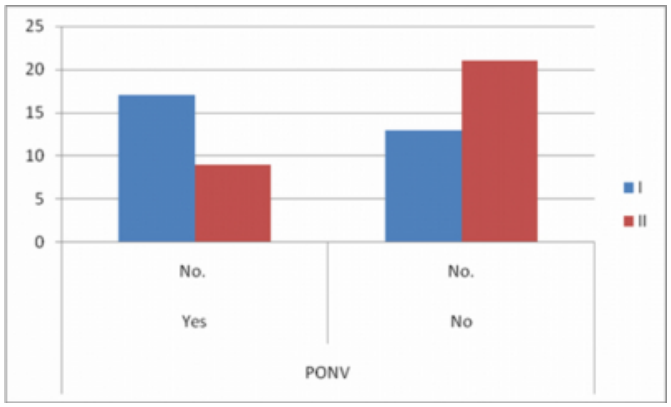


Figure 6

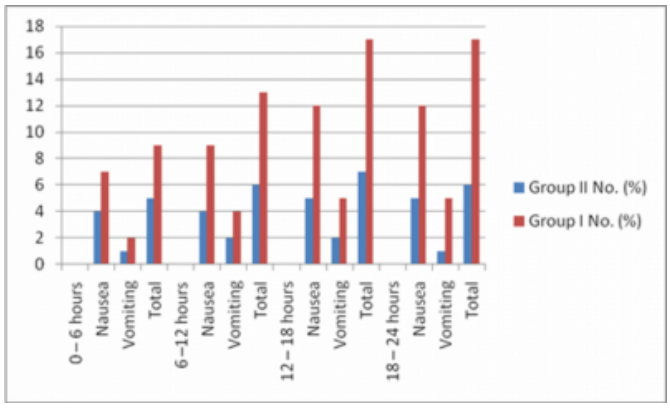
Table 5: Comparison of incidence of nausea and vomiting between 2 groups at various time intervals during 24 hour study period.

Time interval	Group II No. (%)	Group I No. (%)	p value	Remarks
0 – 6 hours				
Nausea	4 (13.33)	7(23.33)	0.253	NS
Vomiting	1 (3.33)	2(6.67)	0.500	NS
Total	5(16.67)	9(30.33)	0.222	NS
6 –12 hours				
Nausea	4 (13.33)	9(30.33)	0.105	NS
Vomiting	2(6.67)	4 (13.33)	0.335	NS
Total	6 (20.00)	13 (43.37)	0.047	S
12 – 18 hours				
Nausea	5(16.67)	12 (40.00)	0.045	S
Vomiting	2(6.67)	5(16.67)	0.212	HS
Total	7(23.33)	17 (56.67)	0.008	HS
18 – 24 hours				
Nausea	5(16.67)	12 (40.00)	0.045	S
Vomiting	1 (3.33)	5(16.67)	0.097	NS
Total	6 (20.00)	17 (56.67)	0.003	HS

NS – Non Significant, S – Significant, HS – Highly Significant

Figure 7

Figure 2: Comparison of incidence of nausea and vomiting between 2 groups at various time intervals during 24 hour study period.



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