



ORIGINAL RESEARCH PAPER

Anesthesiology

TO STUDY AND COMPARE THE EFFECT OF TIME OF ADMINISTRATION OF ONDANSETRON IN CONTROLLING POSTOPERATIVE NAUSEA AND VOMITING

KEY WORDS: Post Operative Nausea and Vomiting (PONV), Ondansetron, VAS

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ABSTRACT

Background: Pain and Emesis are the most commonly presenting and distressing symptoms following anaesthesia and surgery in a patient. No single agent is totally effective against Post Operative Nausea and Vomiting (PONV), inspite of plenty of antiemetic drugs available. Female gender has always been the strongest risk factor for PONV with an odds ratio of ~3:1. This study was done to determine the best time of administration of ondansetron and comparing the efficacy in controlling PONV and Pain postoperatively.

Objective: To study the efficacy of ondansetron in controlling PONV when given 20 minutes pre operatively and 20 minutes before the extubation.

Results: The results in both groups were clinically and statistically significant. Ondansetron given before extubation prevents PONV better than given before induction.

Conclusion: We conclude that Ondansetron is effective in controlling PONV when given 20 minutes before extubation.

INTRODUCTION:

Pain and Emesis are the most commonly presenting and distressing symptoms following anaesthesia and surgery in a patient. No single agent is totally effective against Post Operative Nausea and Vomiting (PONV), inspite of plenty of antiemetic drugs available because of the multifocal etiology of PONV. Female gender has always been the strongest risk factor for PONV with an odds ratio of ~3:1. PONV is a common presentation with unpleasant complications following anaesthesia and surgery, such as - wound dehiscence, bleeding, aspiration of gastric contents, delayed hospital discharge.^[1]

This condition is so critical for the patients, that preventing PONV is much more important than controlling the pain following a surgery. Thus, reducing the incidence of PONV by using various antiemetic drugs enhances the satisfaction of patient, reduces the recovery time and hospital stay.^[2]

In laparoscopic cholecystectomy the incidence of PONV ranges from 25% to 42% when there is no antiemetic treatment given prophylactically. Many antiemetic drugs including - Anticholinergic drugs (Scopolamine, Atropine), Steroids (dexamethasone), Dopamine antagonist drugs (promethazine, prochlorperazine and metoclopramide), 5HT₃ receptor antagonists (ondansetron, granisetron, dolasetron) and Antihistaminic drugs (diphenhydramine, hydroxyzine), are available these days.^[3]

Historically, other techniques like olive oil and insulin glucose infusion were reported to be effective. In 1912, Robert Ferguson described the use of olive oil via per oral route immediately after partial restoration of consciousness and postulated that oil in the stomach "absorbed any residual ether that might be there".^[4]

Flagg postulated that PONV may result from various other causes than anesthetics. He also said that - "there are atleast three kinds of vomiting the first of which has been attributed to anesthetics such as ether, the second to reflex responses, the last to opioids". Subsequent studies showed a spectrum of non-anesthetics factors linked in the pathogenesis of PONV.^[5]

Recently, Propofol in sub hypnotic doses has been proven to be an effective anti-emetic in chemotherapy^[6] and PONV.^[6] Newer antiemetics like Neurokinin-1 (Substance-P antagonist) are under development.^[7]

Ondansetron is a highly selective 5-HT₃ receptor antagonist, which inhibits nausea and vomiting caused by cytotoxic agents and radiation. Its action is believed to be mediated via antagonism of 5-hydroxytryptamine receptors located in the chemoreceptor trigger zone in the area postrema of the brain and possibly on vagal afferents in the upper gastrointestinal tract. Ondansetron also causes an increase in the rate of gastric emptying.

MATERIALS & METHODS:

Source of Data: The study was conducted between September 2015 to September 2016. Sixty patients of physical status ASA-I, ASA-II, ASA-III posted for elective surgeries under general anaesthesia, patients of female sex, between the age group 20-60 years were included in the study. Computer-generated blocks will randomize patients. Randomization was done under two groups of 30 patients each, as under:

Group OI - Inj. Ondansetron 8 mg 20 minutes before induction.

Group OE - Inj. Ondansetron 8 mg 20 minutes before extubation.

Anaesthesia technique for surgery: Premedication was done with Injection Glycopyrrolate 0.2mg + 1mg Midazolam + Fentanyl 2µg/kg in all the cases followed by induction with Injection Propofol 2 to 2.5 mg/kg. Tracheal intubation was facilitated by Injection Atracurium 0.1mg/kg. All the cases were maintained with N₂O/Air + O₂ + Isoflurane /sevoflurane (0.6% to 0.8 %). Injection Atracurium was given intermittently during anaesthesia to maintain adequate muscle relaxation. At the end of surgery the cases were extubated by reversing with 0.05 mg/kg Neostigmine and 0.2 mg Glycopyrrolate. Each case was monitored diligently pre operatively, intra operatively and post-operatively.

Assessment: The episodes of vomiting and nausea were recorded in every case from 0-6 hours, 12hours and 24 hours for PONV. Time to first rescue antiemetic administration in either of the patient group was noted.

Pain was assessed by VAS score at 0-6 hours, 12 hours and 24 hours interval.

STATISTICAL ANALYSIS:

Incidence of nausea, vomiting and number of patients needing rescue antiemetic were compared using 'Pearson Chi Square' test. The assessment of pain post surgery was done using VAS and were compared with "Student T test for two sample mean".

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

RESULT:

The majority of the patients of ondansetron before induction were in the age group 21-40 years, while majority of the patients in the ondansetron before extubation were in the age group 41-60 years.

In both groups, majority of the patients had undergone open surgery in comparison to lesser proportion who had undergone laparoscopic surgery. Maximum duration of surgery was seen in the ondansetron before extubation group (139.17 ± 56.20 minutes), followed by ondansetron before induction group (120.67 ± 47.17 minutes).

Table no 1 shows that at 1st hour post operatively, PONV grade 0 was seen in 15 and 17 patients of Ondansetron before intubation (OI) and Ondansetron before extubation (OE) groups respectively. PONV grade 1 was seen in 11 and 9 patients of OI and OE groups respectively. PONV grade 2 was seen in 4 patients each of OI and OE groups respectively and was not significant.

Also at 2 hours, 4 hours and 6 hours post operatively, there was lesser incidence in PONV seen in patients of OE group than OI group and were statistically significant. (p value = 0.008, 0.017, 0.001 respectively)

There was no significant co relation seen thereafter at 12 hours and 24 hours postoperatively.

TABLE 1 : Comparison of PONV Grading in Relation to Different Times of Monitoring Post Operatively

Time Period	PONV	Ondansetron Before Intubation	Ondansetron Before Extubation	All	Chi-Square Test	P Value
1 Hr	0	15 50%	17 56.67%	32 53.33%	0.325, Df= 2	0.850 Not Significant
	1	11 36.67%	9 30%	20 33.33%		
	2	4 13.33%	4 13.33%	8 13.33%		
2 Hr	0	9 30%	19 63.33%	28 46.67%	11.964, Df= 3	0.008 Significant
	1	8 26.67%	9 30%	17 28.33%		
	2	10 33.33%	2 6.67%	12 20.00%		
	3	3 10.00%	0 0.00%	3 5.00%		
4 Hr	0	10 33.33%	22 73.33%	32 53.33%	10.221, Df= 3	0.017 Significant
	1	9 30.00%	5 16.67%	14 23.33%		
	2	7 23.33%	2 6.67%	9 15.00%		
	3	4 13.33%	1 3.33%	5 8.33%		
6 Hr	0	7 23.33%	19 63.33%	26 43.33%	15.872, Df= 3	0.001 Significant
	1	12 40.00%	4 13.33%	16 26.67%		
	2	6 20.00%	0 0.00%	6 10.00%		
	3	5 16.67%	7 23.33%	12 20.00%		
12 Hr	0	26 86.67%	27 90.00%	53 88.33%	3.819, Df= 2	0.148 Not Significant
	1	4 13.33%	1 3.33%	5 8.33%		
	3	0 0.00%	2 6.67%	2 3.33%		
24 Hr	0	28 93.33%	28 93.33%	56 93.33%	4.00, Df= 2	0.135 Not Significant
	1	2 6.67%	0 0.00%	2 3.33%		
	3	0 0.00%	2 6.67%	2 3.33%		

TABLE 2 : Comparison of VAS in Relation to Different Time of Monitoring Post Operatively

Time Period	Group	N	Mean \pm SD	T Value	P Value
1 Hr	Ondansetron before extubation	30	1.03 \pm 0.85	5.27	0.000 Significant
	Ondansetron before intubation	30	2.10 \pm 0.71		
2 Hr	Ondansetron before extubation	30	0.93 \pm 1.23	4.37	0.000 Significant
	Ondansetron before intubation	30	2.00 \pm 0.52		
4 Hr	Ondansetron before extubation	30	1.10 \pm 1.24	3.55	0.001 Significant
	Ondansetron before intubation	30	2.07 \pm 0.83		
6 Hr	Ondansetron before extubation	30	1.27 \pm 1.20	3.32	0.002 Significant
	Ondansetron before intubation	30	2.13 \pm 0.77		
12 Hr	Ondansetron before extubation	30	2.60 \pm 0.97	0.25	0.800 Non Significant
	Ondansetron before intubation	30	2.67 \pm 1.06		
24 Hr	Ondansetron before extubation	30	2.27 \pm 0.98	0.37	0.711 Non Significant
	Ondansetron before intubation	30	2.37 \pm 1.10		

The above table (Table no 2) shows that the VAS Score was significantly better in OE group as compared to OI group at 1 hour, 2 hours, 4 hours and 6 hours post operatively. (p value = 0.000, 0.000, 0.001, 0.002 respectively)

Thereafter, comparable and statistically insignificant results were seen at 12 and 24 hours post operatively in both the groups.

DISCUSSION:

Demographic Profile:

Numerous factors can affect post-operative vomiting, such as age, gender, menstrual cycle, obesity, motion sickness, history of post-operative vomiting, anxiety, gastric disorders, operative procedure, duration of the operation, anesthetic technique, anesthetic medication, opioids, postoperative headache and dizziness.^[8,9]

In our study only female patients were included. Patients with BMI more than 30 Kg/m², history of motion sickness were excluded. Standard anesthesia technique with sevoflurane or isoflurane as inhalational agent was used. Both these volatile agents demonstrate similar effect on PONV status. The patients were demographically comparable with age, duration of surgery, type of surgery and fentanyl requirement. Age of patients in all groups was between 21-40 years.

Total Incidence:

The incidence of PONV in laparoscopic cholecystectomy ranges from 25% to 42% when antiemetic treatment is not considered prophylactically.^[9] In our study the incidence of PONV after giving the antiemetic drugs intra-operatively was 56.6% and 53% in groups OI, OE.

Efficacy of Ondansetron in controlling PONV and PAIN Post Surgery:

Our study demonstrated a significant difference in prevention of PONV at interval of 1 hour, 2 hours, 4 hours and 6 hours post operatively in OE group as compared to OI group. However, regarding late post operative nausea and vomiting (12 and 24 hours), no significant difference was found in both groups. (TABLE No. – 1)

Cruz et al. (2008)^[10] conducted a prospective, randomized, double-blind study to determine the most effective timing of ondansetron administration to prevent PONV in patients

undergoing ambulatory plastic surgery procedures estimated to last two hours or more. It was noted that a significant difference ($p<0.05$) in late administration of ondansetron (within 30 minutes prior to completing the surgery) is significantly more effective in the prevention of late PONV than when administered prior to the induction of anesthesia. Another study done by **Tang et al.^[11]**, which compared the effect of timing of administration of ondansetron for prevention of PONV showed similar results as our current study and concluded that administration of ondansetron before extubation is better in prevention of PONV as compared to when given before induction.

Pain is considered to be an independent factor affecting PONV. In our study, the pain assessment postoperatively was done by using VAS score. VAS score was significantly better in ondansetron before extubation than ondansetron before intubation groups in first 6 hours post operatively and thereafter non significant. (Table No. - 2)

CONCLUSION:

It seems logical from our study that ondansetron might be more effective when given before extubation, thereby producing a more sustained antiemetic effect in postoperative period. Incidence of PONV was found to be 53%. This was followed by ondansetron before induction (56.6%).

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 administration of ondansetron before extubation yielded better outcome for preventing PONV and pain during the early postoperative period for first 6 hours than ondansetron before induction in patients undergoing open, laparoscopic, endoscopic procedures under general anesthesia.

Declaration of Conflicting Interests

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