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Original Research Article

A STUDY ON COMPARISION OF PALONOSETRON WITH ONDANSETRON FOR PREVENTION OF NAUSEA AND VOMITING DURING POSTOPERATIVE PERIOD IN PATIENTS UNDERGOING ENT SURGERIES

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ABSTRACT

Background: Incidence of postoperative nausea and vomiting (PONV) in susceptible patients can be unacceptably high (70-80% reported incidence). This study was designed to evaluate the effect of palonosetron and ondansetron in preventing PONV in high-risk patients undergoing ENT surgeries conducted under general anaesthesia. **Aim:** The objective of the present studyis to compare the intravenous Palonosetron with intravenous Ondansetron for prevention of nausea and vomiting during postoperative period in patients undergoing ENT Surgeries underGeneral Anaesthesia.

Material and Methods: This was a randomized double blindclinical study conducted on 60 ASA Grade I&II patients scheduled for ENT Surgeries under General Anaesthesia and were randomlydivided into two groups, Group I and Group II, each consisting of30 patients. Group I received 4 mg of Ondansetron I.V and GroupII received 1.5 mcg/kg of Palonosetron I.V, 30 minutes before theinduction of anaesthesia. The incidences of PONV were recorded within the first 72 hours after surgery at intervals of: 0-12 hours,12-24 hours and 24-72 hours. Episodes of PONV were identifiedby spontaneous complaints by the patients, by direct questioningand by Nausea Scale (Visual Analogue Scale) 0 - 10.

Results: There were no differences in the demographic databetween the two study groups. The incidence of PONV was significantly less in the palonosetrongroup (5.55%) as compared to the ondansetron group (43.33%), with a lesser need for rescue antiemetic in the palonosetron group (10% vs. 53%). Both the study groups did not have significantadverse effects reflecting that both the drugs were well-tolerated.

Conclusion: In conclusion, we have found that Palonosetron at adose of 1.5mcg/Kg IV is safe and well-tolerated and proved more effective than Ondansetron 4 mg IV in the prevention of PONV.

Keywords: PONV, Palonosetron, Ondansetron, ENT Surgery.

INTRODUCTION

Nausea and vomiting have been associated for many yearswith the use of general anesthetics and subarachnoid block for surgical procedures. With the change in the emphasis froman inpatient to outpatient, hospital and office-based medical/surgical enhancement, there has been increased interest in the‘big little problem1of PONV.

One of the first extensive descriptions of the phenomenonwas by John Snow, published in 1848, within 18 months ofthe introduction of anaesthesia into Britain. He observed thatvomiting was more likely to occur if the patient had eatenrecently.[2]

There has been a general trend towards a decrease in theincidence and intensity of the problem because of the following

1. Use of anaesthetic agents with less emetic effects.

2. Improved pre-and post anaesthetic medication (e.g. analgesics)
3. Refinement of operative as well as anaesthetic techniques and
4. Identification of patient predictive factors. (Risk factors ofPONV)

However, inspite of these advances, nausea and vomiting stilloccur with unacceptable frequency in association with surgeryand anaesthesia and the description of it as "the big littleproblem" encapsulates much of the general perception.[2]

The various detrimental effects of PONV are

1. **Physical:** Retching and vomiting are fairly violentacts and may place considerable stress upon certainstructures leading to oesophageal tears, resulting in haemorrhage (Mallory – Weiss syndrome) and ruptureof the oesophagous (Boerhaave syndrome), rib fracture, gastric herniation, muscular strain and fatigue. Vomitingmay cause wound dehiscence, intraocular bleeding andbleeding from skin flaps in the upper body after plasticsurgery. The major problem associated with vomiting in thepostoperative period is aspiration of vomitus, respiratoryobstruction and aspiration pneumonia.
2. **Metabolic:** The metabolic effects include anorexia, dehydration and alkalosis with hypokalemia.
3. **Psychological:** Nausea is a very aversive stimulus and if induced by operative experience, may cause life-longaversion to surgery.[2]

Over the years, numerous approaches have been used in themanagement of PONV. Various techniques including olive oiland insulin-glucose infusions were reported to be effective.

Robert Ferguson described the use of olive oil in 1912; hepostulated that oil in the stomach "absorbed any ether thatmay be present there". The effect of atropine was appreciatedby Brown – Sequard as early as 1883 when he wrote "in thevery great majority of cases, the addition of a certain amountof atropine to morphine prevents the nausea and vomiting occurring with morphine alone." Phenothiazines were synthesized originally in the late 19thcentury. In the late1930s, Promethazine was found to haveantiemetic property. Charpentier synthesized chlorpromazine in but sedation and hypotension were limiting side-effects.3The traditional antiemetics include anticholinergics (scopolamine); dopamine receptor antagonists which include the phenothiazines (promethazine), benzamides (metoclopramide) and butyrophenones (droperidol) and benzodiazepines (midazolam and lorazepam). The non–traditional antiemetics include ephedrine, propofol and corticosteroids. The newestclass of antiemetics used for prevention and treatment of PONVare serotonin (5-HT3) receptor antagonists–ondansetron, granisetron, tropisetronpalonosetron and dolasetron. Theseantiemetics do not have adverse effects of older traditional antiemetics.4The annual cost of treatment of PONV in the United States is thought to approach a billion dollars. Available antiemetics like5-HT3 antagonists are effective in very low doses.4Thus, costs can be lowered and drug side-effects prevented whengiven as prophylaxis, lowering the economic burden imposeddue to complications and increased medical care resulting fromPONV.

The objective of the present study was to compare the intravenous Palonosetron with intravenous Ondansetron for prevention ofnausea and vomiting during postoperative period in patients undergoing ENT Surgeries under General Anaesthesia.

MATERIAL AND METHODS

After obtaining approval from institutes ethical committee and informed consent, a randomized double blind clinical study was conducted on 60 ASA Grade I&II patients scheduled for Surgeries under General Anaesthesia. They were randomly divided into two groups, Group I and Group II, each consisting of 30 patients. Group I received 4mg of Ondansetron I.V and Group II received 1.5 mcg/kg of Palonosetron I.V, 30 minutes before the induction of anaesthesia.

Selection of patients

Inclusion Criteria: Patients of ASA Grades I, and II and Patients between the age group of 20 to 55 years who are to undergo ENT surgeries were included.

Exclusion Criteria: Patients belonging to ASA Grade IV and V, Patients below the age of 20 years, above the age of 55years, History of gastro-esophageal reflux, Patient scheduled to undergo emergency surgery, Patient scheduled to receive propofol during the maintenance phase of anaesthesia, Patientwith vomiting from any organic cause, any drug with a potentialanti-emetic effect within 24 hours prior to the administration of anaesthesia were excluded.

Methods

Preoperative visit was conducted on the previous day of surgeryand a detailed history and present complaints were noted. General and systemic examinations of cardiovascular, respiratory and central nervous system were done. Routine laboratory investigations like complete haemogram, routine urine, blood urea, serum creatinine, and blood sugar, ECG, serum electrolytes, bleeding time and clotting time were done.

All patients received Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg on the previous night and 6 AM on the morning of surgery. Patients were instructed to remain nil orally after 10PM on the previous night of surgery. General anaesthesia with controlled ventilation was used in all patients.

Preoperative pulse rate, blood pressure and peripheral oxygen saturation were recorded in the operation theatre after connecting the following monitors:

1. Continuous electrocardiogram
2. NIBP
3. Pulse oximeter
4. Capnography

Peripheral venous access was established and intravenous fluid was started with 5%dextrose normal saline. Pre-medication with Inj. Midazolam 1 mg IV and Glycopyrrolate0.2 mg IV were given. The study medications were administered intravenously justbefore induction as patients were preoxygenated for 5 minutes before induction of anaesthesia with Inj. Thiopentone sodium4-5 mg/kg IV. Inj. Succinylcholine 1.5 –2.0mg/kg IV was given and endotracheal intubation with appropriate size cuffed tube was done.

Inj. Fentanyl 1-2 µg/kg IV was used for analgesia and Inj. Atracurium 0.5 mg lkg IV or Inj. Vecuronium 0.08 mg/kgIV were used to provide muscle relaxation during surgery depending on the type and duration of the procedure. Maintenance of anaesthesia was with nitrous oxide (50%) and oxygen (50%) with sevoflurane (0.2-0.8%) using controlled ventilation with Bain's circuit. Patients were monitored duringanaesthesia using continuous ECG, heart rate, blood pressure, pulse oximetry and capnography. On completion of surgery, the residual paralysis was reversed with Inj. Neostigmine 0.05 mg/kg IV and glycopyrrolate 0.008mg/kg IV Patients were transported to the recovery room and later to the ward after confirming an adequate level of consciousness and intact reflexes.

The incidences of PONV were recorded with in the first 72hours after surgery at intervals of:

1. 0-12 hours.
2. 12-24 hours and
3. 24-72 hours.

Episodes of PONV were identified by spontaneous complaints by the patients, by direct questioning and by Nausea Scale (Visual Analogue Scale) 0 -10." Complete response" was defined as the absence of nausea, retching or vomiting and no need for rescue antiemetic during the 24-hour observation period. Rescue antiemetic was provided with Inj. Ondansetron 4mg I.V in the event of 1 or more episodes of vomiting depending on the observer's discretion. Observation and results were evaluated and compared between the two groups.

RESULTS

The following were the observations and results of the variables among the Ondansetron group in comparison with the Palonosetron group:

Mean age of patients Ondansetron – 36.6±11.57, Mean age of patients Palonosetron – 35.28±11.68, Sex distribution Ondansetron – 60.13±6.23, Mean weight of patients Palonosetron – 58.97±7.46.

It is observed that the variations found in the Age Group, Sex Distribution and Weight of the patients among the Ondansetron group compared with the Palonosetron group was significantly less. [Table 1]

The duration of Surgery is prolonged (>60 minutes) in both the study groups. Hence this prolonged duration of surgery is considered as a risk factor for PONV among these groups of patients (table-2). In all the post-operative duration of 72 hours (comprising3 periods), the incidence of nausea was found more in the Ondansetron group as compared to the Palonosetron group (table-3). The incidence of vomiting was significantly less with

Palonosetron group as compared with Ondansetron group in all the 3 periods of 72 hours post-operative duration. Though there was no statistical significance in the incidence of head ache, there was a moderate incidence of 57% and 40%among the Ondansetron and Palonosetron groups respectively in the post-operative period and this was caused by the prolonged duration, involvement of the vestibular system and parasympathetic nerve supply to the inner ear. There was no statistically significant difference in the incidence of the other side effects such as dizziness, abdominal discomfort and rash. From the above values the overall incidence of nausea is55.56% in Ondansetron and 7.78% in Palonosetron group while the overall incidence of vomiting is 31.11% in Ondansetron and3.33% in Palonosetron group. Thus, the risk of getting nauseaand vomiting is highest in Ondansetron and least in Palonosetron group. Only 10% of patients in the Palonosetron group needed rescue antiemetics, whereas nearly 53% in the Ondansetron group required rescue drug

Table 1: Demographic data

Variable	Ondansetron	Palonosetron
Age distribution in years		
20-29	12	12
30-39	9	10
40-49	2	3
50-59	7	5
Total	30	30
Mean	36.6± 11.57	35.28± 11.68
Sex distribution		
Male	17	14
Female	13	16
Weight distribution		
50-54	5	8
55-59	6	7
60-64	8	6
65-69	9	5
70-75	2	4
Mean	60.13± 6.23	58.97± 7.46
Total	30	30

Table 2: Duration of surgery

Variable	Ondansetron	Palesetron
Duration (mins)		
50 – 100	12	10
101 – 150	13	18
151 - 200	5	2

DISCUSSION

PONV is one of the main complaints in patients undergoing surgery under general anaesthesia and the incidence of its occurrence is 20-40%. It is one of the most important factors that determine the length of hospital stay after ambulatory anaesthesia. This can delay discharge and result in unplanned overnight hospital admission. In fact, its contribution to patient dissatisfaction is such that over 70% of patients have considered avoidance of PONV to be very important. This high incidence of PONV after general anaesthesia may justify the use of prophylactic antiemetic therapy. Various factors can affect PONV, such as age, gender, obesity, history of motion sickness and / or PONV, use of opioids, anaesthetic technique, duration and type of the surgical procedure and postoperative pain.

Numerous drugs have been used in the past in the prevention of post – operative nausea and vomiting, but they also have been associated with undesirable side effects. The 5 HT3 antagonists are very effective in preventing post-operative nausea and vomiting and do not produce any significant side effects.[5-7] This study compares the efficacy of Ondansetron and Palonosetron in the prevention of post – operative nausea and vomiting.

In the present study, majority of these factors (age, gender, weight, duration and type of the procedure) were not statistically significant between both the groups. The anaesthetic technique was standardized (general anaesthesia with controlled ventilation) in all patients.

The incidence of PONV was significantly less in the Palonosetron group (5.55%) as compared to the ondansetron group (43.33%), with a lesser need for rescue antiemetic in the Palonosetron group (10% vs. 53%).

This study is similar to the study conducted by Chatterjee et al,[8] found incidence of PONV was significantly less in the Palonosetron group (16.6%) as compared to the ondansetron group (40%).

Gan TJ et al,[9] found the overall incidence of post-operative nausea (PONV Score 1) in 24hrs was 56.66% in patients among group Ondansetron group and 30% in patients of Palonosetron group. The incidence is higher in ondansetron group and the difference between two groups was statistically significant (p=0.037) Both the study groups did not have significant adverse effects reflecting that both the drugs were well-tolerated. This was in accordance with the studies by Chatterjee,[8] and Gan TJ.[9]

CONCLUSION

PONV is one of the most distressing side-effects of anaesthesia and surgery with a high incidence following general anaesthesia. The quest for more effective antiemetic drugs without the potential for sedative or extra pyramidal. Side-effects have led to the development of a relatively new class of drugs, 5-HT3 antagonists of which ondansetron is a prototype. The need for drugs with improved performance within this group arose on account of relatively less potency and shorter duration of action, besides detectable binding to other 5-HT receptors by ondansetron. Palonosetron is a potent and highly selective 5-HT3 receptor antagonist that has little or no affinity for other 5-HT receptors.

In our study, we have compared the efficacy of ondansetron 4mg i.v and Palonosetron 1.5mcg/kg i.v given prophylactically. just before induction of anaesthesia in adult patients undergoing elective surgeries under general anaesthesia. Palonosetron is superior to the established first generation 5-HT3-Receptor Antagonists in respect of pharmacokinetic data such as a high receptor binding affinity (pKi 10.45) and a prolonged mean elimination half-life (40 hours) after intravenous administrationIn clinical trials Palonosetron 0.075 mg is statistically superior to Ondansetron in preventing PONV. Efficacy in the delayed period of 24–72 hours postoperatively is as overwhelming as expected. In conclusion, we have found that Palonosetron at a dose of 1.5mcg/Kg IV is safe and well-tolerated and proved more effective than Ondansetron 4 mg IV in the prevention of PONV. Though the side effects of Ondansetron and Palonosetron are comparable, till the further newer and better antiemetic drugs to be clinically evaluated, Palonosetron is one of the most effective anti-emetic drugs used for prevention of PONV in ENT surgeries.

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Table 3: Observations in both Ondansetron and Palonosetrongroups

Observation		Group				P-Value
		Ondansetron		Palonosetron		
		N	%	N	%	
Nausea Period - 1	No	15	50	28	93	13.9 0.0000(<0.05) Highly Significant
	Yes	15	50	2	7	
Nausea Period - 2	No	11	37	28	93	21.2

	Yes	19	63	2	7	0.0000(<0.05) Highly Significant
Nausea Period - 3	No	14	47	27	90	11.091 0.009(<0.05) Highly Significant
	Yes	16	53	3	10	
VomitingPeriod-1	No	22	73	29	97	6.41 0.01(<0.05) Significant
	Yes	8	27	1	3	
VomitingPeriod-2	No	18	60	29	97	11.9 0.001(<0.05) Highly Significant
	Yes	12	40	1	3	
VomitingPeriod-3	No	22	73	29	97	4.706 0.03(<0.05) Significant
	Yes	8	27	1	3	
Rescue	No	14	47	27	90	11.091 0.0009(<0.05) Highly Significant
	Yes	16	53	3	10	
Head ache	No	13	43	18	60	1.67 0.196(>0.05) Not Significant
	Yes	17	57	12	40	
Abdominal Discomfort	No	18	60	26	87	4.176 0.0410(<0.05) Significant
	Yes	12	40	4	13	
Rash	No	25	83	28	93	1.46 0.228(>0.05) Not Significant
	Yes	5	17	2	7	
Dizziness	No	20	67	28	93	5.104 0.0239(<0.05) Significant

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