Original Research Article

To assess and evaluate effect of IV Ondansetron, Palonosetron and Ramosetron for prevention of PONV in patients posted for major elective surgery under General Anaesthesia

Anil Kumar Rajput[1],Preeti Goyal[2]

[1]Consultant Anaethesiologist,Department. of Anaethesiology, ChirayuMultispeciality Hospital, Gwalior, M.P.,India

[2]Designated Professor,Department. of Anaethesiology, JA Group of Hospitals and Gajra Raja Medical College, Gwalior, M.P.,India

Received: 21-04-2021 / Revised: 09-06-2021 / Accepted: 13-07-2021

Abstract

Background & Method: After obtaining approval from the ethical committee, the present study entitled " To assess and evaluate effect of IV Ondansetron, Palonosetron and Ramosetron for prevention of PONV in patients posted for major elective surgery under General Anaesthesia." was carried out on patients of ASA grade I and II in the Department of Anaesthesiology, J.A. Group of Hospitals of G.R. Medical College, Gwalior (M.P) from 2016- 18 after obtaining well informed written consent from the patients. Grouping: 120 patients of ASA grade I & II of either sex, scheduled for elective surgeries under general anaesthesia were divided into 4 groups, (n=30 each), randomly using closed envelope technique.**Result:** The statistical analysis of the number of patients who required rescue anti emetic till the time of the observation is shown above. The percentage of patients, requiring rescue drug, during observation period for group C, O, P, and R was 66.67%, 46.67%, 26.67%, and 23.0% respectively.The difference was statistically not significant while comparing group C&O (p=0.118); O&P (p=0.107); O&R (p=0.058); and P&R (p=0.76). However, the difference happened to be statistically significant when compared among groups C&P (p=0.0019); group C&R (p=0.0007).The statistical analysis of the number of patients who did not suffer from vomiting till the time of the observation is shown above.
The percentage of patients, free from vomitingduring observation period for group C, O, P, and R was 36.67%, 53.34%, 80.0%, and 76.67% respectively.The difference was statistically not significant while comparing group C&O (p=0.19); and P&R (p=0.754). However, the difference happened to be statistically significant when compared amonggroups C&P (p= 0.0006); group C&R (p= 0.001); O&P (p= 0.028); and O&R (p= 0.04).**Conclusion:**Palonosetron as well as Ramosetron are safe and equally effective in reducing the incidence of post operative nausea and vomiting up to 24 hours, when given prior to induction of general anaesthesia. Ondansetron is less effective than Palonosetron and Ramosetron in reducing the nausea and vomiting in post operative period.

Keywords: Ondansetron, Palonosetron, Ramosetron & PONV.

Introduction

Post operative nausea and vomiting(PONV) is common and distressing complication ofgeneral anesthesia ever since the ether and chloroform era, with an incidence up to75- 80% in high risk patients. It remains a problem despite an evident clinical perception that its severity has diminished with an estimated incidence of 20-50%[1].
Postoperative nausea and vomiting (PONV) are considered among the most common and feared postoperative complications and can occur after both general and regional anaesthesia. Many patients perceive PONV even more distressing than postoperative pain[2]. Over the last decade, some improvement is seen in our comprehension of the etiology, pathophysiology of PONV together with the introduction of newer effective anti-emetics for finding a solution to the problem. In today's world of cost-effective medicine, where there are ever-increasing pressures to avoid even minor side-effects of treatment, there has been an explosion of papers on the subject in which every aspect of risk, prevention, anaesthetic technique and management strategies have been examined[3]. A number of factors have emerged, which are associated with the problem. These include age, sex, history of motion sickness, previous PONV, duration and type of surgery, pre-anaesthetic medication, the use of nitrous oxide, facemask ventilation, the use of opiates, early postoperative ambulation, the timing of oral intake and postoperative pain. There may be infinite number of combinations which may lead to an unfavourable outcome. Therefore, there have been attempts to define those variables and in particular, those fixed patient factors that may be used to quantify more meaningfully the extent to which an individual may be at risk[4].The vomiting center lies in the medulla oblongata and comprises the reticular formation and nucleus of tractussolitarius. The vomiting reflex has got two main detectors: GIT and chemoreceptor trigger zone (CTZ) in area postrena[5]. Vomiting and nausea are natural reflexes which insure the expulsion of toxins from GIT and prevent further intake of such substances and toxins containing them[6]. The vomiting reflex is triggered in GIT by chemo receptorspresent in mucosa of upper part of GIT which are sensitive to noxious chemicals. Mechanoreceptors are also therein muscular wall of gut and get activated by contraction and distension of the same, physical damage and manipulation e.g. during abdominal surgery[7]. The afferent vagus nerve mainly gets activated (80%-90%) and relays the information to CTZ in area postrena.

**Correspondence*
Dr. Preeti Goyal
Designated Professor, Department. of Anaethesiology, JA Group of Hospitals and Gajra Raja Medical College, Gwalior, M.P.,India
E-mail:

Material & Method

After obtaining approval from the ethical committee, the present study entitled **"To assess and evaluate effect of IV Ondansetron, Palonosetron and Ramosetron for prevention of PONV in patients posted for major elective surgery under General Anaesthesia."** was carried out on patients of ASA grade I and II in the Department of Anaesthesiology, J.A. Group of Hospitals of G.R. Medical College, Gwalior (M.P) from 2016- 18 after obtaining well informed written consent from the patients.

Criteria for selection:

- Patients of ASA grade I & II
- Patients of age group 20 to 60 years of either sex.
- Patients of body weight between 40-80 kg selected after pre anesthetic check up .

Exclusion Criteria:

Patients with following are excluded from the study:

1. ASA grade III and onwards.
2. Patients under 20 year and above 60 year of age.
3. Known history of sensitivity to study drugs.
4. Prone to nausea vomiting and motion sickness.
5. Already received opioid analgesic or anti-emetics within 24 hours before anaesthesia.
6. Requiring continuous gastric suction for 24 hours in postoperative period.
7. Emergency surgeries
8. Airway more than Mallampatti class- 1.

Methodology

Grouping: 120 patients of ASA grade I & II of either sex, scheduled for elective surgeries under general anaesthesia were divided into 4 groups, (n=30 each), randomly using closed envelope technique.

Results

Table 1: Showing Demographic Distribution

Variables	Group C	Group O	Group P	Group R	P- value
Age (yrs)	39.10 ± 15.16	38.96 ± 12.56	39.0 ± 12.23	41.9 ± 11.89	0.77
Weight (kg)	59.53 ± 7.91	62.56 ± 9.92	62.94 ± 5.42	60.67 ± 6.72	0.28
Duration of surgery (min)	101 ± 48.48	103 ± 27.96	110 ± 36.74	105 ± 37.26	0.76

Demographic data such as mean age, mean weight, and mean duration of surgery, in all four groups were well comparable to each other and they were statistically insignificant (p>0.05).

Table 2: Showing Sex Distribution

Sex	Group C		Group O		Group P		Group R	
	No.	%	No.	%	No.	%	No.	%
Male	15	50	14	46.7	17	56.7	14	46.7
Female	15	50	16	53.3	13	43.3	16	53.3
Total	30	100	30	100	30	100	30	100

Sex distribution in all four groups was well comparable and both sexes were equally distributed.

Table 3: Drug response to prevent nausea (nausea free patients)

Duration	Group C		Group O		Group P		Group R	
	No.	%	No.	%	No.	%	No.	%
30 min.	18	60	20	66.67	27	90.0	27	90.0
60 min.	18	60	22	73.34	27	90.0	26	86.67
2 hours	20	66.67	22	73.34	28	93.34	28	93.34
6 hours	22	73.34	24	80.0	27	90.0	27	90.0
12 hours	23	76.67	25	83.34	27	90.0	28	93.34
24 hours	24	80.0	25	86.67	28	93.34	28	93.34
p value	0.39		0.58		0.99		0.92	

Above table shows drug response to prevent Nausea at different time intervals in each group.In group C, the percentage of nausea free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 60, 60, 66.67, 73.34, 76.67, and 80.0 respectively. They were statistically insignificant from each other during the period of 24 hour (p>0.05).

In group O, the percentage of nausea free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 66.67, 73.34, 73.34, 80.0, 83.34, and 86.67 respectively. They were statistically insignificant from each other during the period of 24 hour (p>0.05).

In group P, the percentage of nausea free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 90.0, 90.0, 93.34, 90.0, 90.0, and 93.34 respectively. They were statistically insignificant from each other during the period of 24 hour (p>0.05). In group R, the percentage of nausea free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 90.0, 86.67, 93.34, 90.0, 93.34, and 93.34 respectively. They were statistically insignificant from each other during the period of 24 hour (p>0.05). These findings of our study revealed higher response in group P and in group R, in comparison to group C and O.

Table 4: Drug response to prevent vomiting (vomiting free patients)

Duration	Group C		Group O		Group P		Group R	
	No.	%	No.	%	No.	%	No.	%
30 min.	23	76.67	26	86.67	28	93.34	29	96.67
60 min.	23	76.67	25	83.34	29	96.67	28	93.34
2 hours	24	80.0	27	90.0	28	93.34	29	96.67
6 hours	25	83.34	27	90.0	29	96.67	29	96.67
12 hours	26	86.67	27	90.0	29	96.67	29	96.67
24 hours	26	86.67	28	93.34	29	96.67	29	96.67
P value	0.83		0.87		0.95		0.98	

Above table shows drug response to prevent vomiting at different time intervals in each group.

In group C, the percentage of vomiting free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 76.67, 76.67, 80.0,

83.34, 86.67, and 86.67 respectively.They were statistically insignificant from each other during the period of 24 hour (p>0.05).
In group O, the percentage of vomiting free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 86.67, 83.34, 90.0, 90.0, 90.0,and 93.34 respectively.They were statistically insignificant from each other during the period of 24 hour (p>0.05).
In group P, the percentage of vomiting free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 93.34, 96.67, 93.34, 96.67, 96.67, and 96.67 respectively. They were statistically insignificant from each other during the period of 24 hour (p>0.05).
In group R, the percentage of vomiting free patients at 30 min, 60min, 120min, 6 hrs, 12hrs, and 24 hrs were 96.67, 93.34, 96.67, 96.67, 96.67, and 96.67 respectively. They were statistically insignificant from each other during the period of 24 hour (p>0.05).
It was quite explicit from above explained statistics that drug response to prevent vomiting was higher and equal in group P and R, in comparison to group C and O.

Table 5: Statistical Analysis - Nausea free patients

Groups	No.	%	χ^2	P value	Significance
C O	05 11	16.67 36.67	3.07	0.07	**NS**
C P	05 20	16.67 66.67	15.43	0.00008	**S**
C R	05 21	16.67 70	17.38	0.00003	**S**
O P	11 20	36.67 66.67	5.41	0.02	**S**
O R	11 21	36.67 70	6.70	0.009	**S**
P R	20 21	66.67 70	0.08	0.78	**NS**

The statistical analysis of the number of patients who did not suffer from nausea till the time of the observation is shown above. The percentage of patients, free from nausea during observation period for group C, O, P, and R was 16.67%, 36.67%, 66.67%, and 70% respectively.
The difference was statistically not significant while comparing group C&O (p=0.07); and P&R (p=0.78). However, the difference happened to be statistically significant when compared amonggroups C&P (p= 0.00008); group C&R (p= 0.00003); O&P (p= 0.02); and O&R (p= 0.009).

Table 6: Statistical Analysis - Vomiting free patients

Groups	No.	%	χ^2	P value	Significance
C O	11 16	36.67 53.34	1.67	0.19	**NS**
C P	11 24	36.67 80.0	11.59	0.0006	**S**
C R	11 23	36.67 76.67	9.77	0.001	**S**
O P	16 24	53.34 80.0	4.8	0.028	**S**
O R	16 23	53.34 76.67	3.59	0.04	**S**
P R	24 23	80.0 76.67	0.1	0.754	**NS**

The statistical analysis of the number of patients who did not suffer from vomiting till the time of the observation is shown above. The percentage of patients, free from vomitingduring observation period for group C, O, P, and R was 36.67%, 53.34%, 80.0%, and 76.67% respectively.
The difference was statistically not significant while comparing group C&O (p=0.19); and P&R (p=0.754). However, the difference happened to be statistically significant when compared amonggroups C&P (p= 0.0006); group C&R (p= 0.001); O&P (p= 0.028); and O&R (p= 0.04).

Table 7: Statistical Analysis – patients requiring rescue drug

Groups	No.	%	χ^2	P value	Significance
C O	20 14	66.67 46.67	2.44	0.118	**NS**
C P	20 8	66.67 26.67	9.64	0.0019	**S**
C R	20 7	66.67 23.34	11.38	0.0007	**S**
O P	14 8	46.67 26.67	2.58	0.107	**NS**
O R	14 7	46.67 23.34	3.59	0.058	**NS**
P R	8 7	26.67 23.34	0.09	0.76	**NS**

The statistical analysis of the number of patients who required rescue anti emetic till the time of the observation is shown above. The percentage of patients, requiring rescue drug, during observation period for group C, O, P, and R was 66.67%, 46.67%, 26.67%, and

23.0% respectively.The difference was statistically not significant while comparing group C&O (p=0.118); O&P (p=0.107); O&R (p=0.058); and P&R (p=0.76). However, the difference happened to be statistically significant when compared among groups C&P (p=0.0019); group C&R (p=0.0007).

Discussion

120 patients of ASA grade I and II of either sex and aged between 20- 60 years were enrolled. All the patients were posted for surgeries under general anaesthesia and got randomly divided into 4 groups according to the drug, they received. 120 patients of ASA grade I & II of either sex, aged between 20-60 years, scheduled for major elective surgeries under general anaesthesia, were randomly divided into 4 groups, (n=30 each), using closed envelop technique. In group C, Normal Saline 2 ml IV; in group O, Ondansetron 4 mg (2ml) IV; in group P, Palonosetron 0.075 mg (1.5 ml diluted up to 2ml) IV; and in group R, Ramosetron 0.3 mg (2ml) IV were injected, 10 minutes prior to induction of anaesthesia.

As shown in table - 1 and 2, the mean age, mean weight, and mean duration of surgery for each group were comparable with that of others. The young age, obesity, duration of surgery, female sex etc. are well known risk factors for PONV and since we used placebo in this study, patients with high risk factors were not given priority in the study, because it was not ethical to let them experience such a distracting complication.

The drug response in preventing nausea and vomiting, was maximum in group P, which was almost similar to that of group R, followed by group O and group C. The number of patients free from nausea and vomiting was observed to be increasing with advance in duration of study; however, it was statistically not significant (p>0.05). These findings were in accordance with the study conducted by Won-Suk Lee et al[8], which was probably due to reduced intensity of surgical and anaesthetic factors.The statistical analysis shown in tables, revealed that Ondansetron was not superior to placebo in prevention of nausea and vomiting. This finding was supported by a study done by M K Koivuranta et al[9] which proved that 4 mg Ondansetron was not effective in prevention PONV. No difference was found in need of rescue drug between Ondansetron and placebo[10]. The number of patients free from nausea and vomiting was significantly higher with Palonosetron than with placebo. This result of our study is supported by a study conducted by Keith A. Candiottiietal[11] which showed that single dose of 0.075mg Palonosetron was effective in preventing nausea and vomiting when compared to the placebo from 0-24 hours. In our study, Palonosetron was also proved to be superior to Ondansetron which was upheld by a study done by J. SambasivaRao et al[12]. The longer half life (40 hours), binding with receptor to an allosteric site, in a positive cooperative manner, and internalization of 5HT3 receptors, make Palonosetron long lasting and more effective as compared to Ondansetron as per study conducted by Soo Kyoung Park et al[13]. The need of rescue drug was much lower with Palonosetron than with placebo and Ondansetron, but the difference between Palonosetron and Ondansetron was statistically insignificant (p>0.05).

Conclusion

Palonosetron as well as Ramosetron are safe and equally effective in reducing the incidence of post operative nausea and vomiting up to 24 hours, when given prior to induction of general anaesthesia. Ondansetron is less effective than Palonosetron and Ramosetron in reducing the nausea and vomiting in post operative period.

Conflict of Interest: Nil
Source of support:Nil

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