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Comparing Efficacy of Aprepitant, Ondansetron and Dexamethasone for Prevention of Postoperative Nausea and Vomiting in Patients Undergoing Surgery Under General Anaesthesia

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Abstract: ***Background and Aims**: Nausea and vomiting are one of the most common postoperative complications that causes an unpleasant feeling and delay in the discharge of patients. This study aimed to compare the effect of Aprepitant. Ondansetron, and Dexamethasone in preventing PONV inpatients undergoing surgery under general anesthesia. **Material and Methods**: This study was performed on 90 patients aged 18-60years undergoing surgery under general anesthesia of ASA grade 1 and 2. It was a single blinded randomized trial and patients were categorized into three groups of 30 patients each, who receive inj. Ondansetron 10mg IV and inj. dexamethasone 8mg iv both 10 min before induction and cap. Aprepitant 40mg orally 2hr before induction of anesthesia. After extubation patients were monitored for nausea, retching and vomiting for 30min, 60min, 2hr, 6hr 12hr, and 24 hr in the postoperative period. **Results**: The incidence rate for primary end point i.e complete response, no vomiting and no use of rescue drug over 0-24hour after surgery, which tested for effectivity of aprepitant, dexamethasone, and Ondansetron were not different across groups (96.7%aprepitant group,90.0% in ondansetron group and 93.3% in dexamethasone group at end of 24hour. However, the incidence of no vomiting at 12-24hour in both Aprepitant and dexamethasone both drugs were superior than ondansetron (10%). Although demand of rescue medicine and nausea control was not different. **Conclusion**: Aprepitant and Dexamethasone both have slightly lower prophylactic antiemetic efficacy in early phase after surgery but in delayed phase (12- 18hr) both were effective in preventing PONV as compared to Ondansetron. At the end of 24 hour all the three drugs were effective in reducing vomiting episodes and there was less need of any rescue medicine.*

Keywords: Aprepitant, complete response, anti-emetics, general anesthesia, PONV, VRS score.

1. Introduction

Postoperative nausea and vomiting is one of the most common and distresing complication related to surgery and anesthesia occurring within the first 24hr after surgery. The incidence of PONV ranges between 20-30% in general population and it increases up to 80% in high-risk surgical patients **[1].**

Treatment and prevention of PONV requires accurate risk stratification. The simplified Apfel's score includes the four factors female sex, non- smoker, postoperative use of opioids and previous PONV or motion sickness in past **[2].** If none, 1, 2, 3 or 4 of these factors are present, the incidence of PONV were 10%, 21%, 39%, 61% and 79% respectively **[3**].

General anaesthesia, use of inhalational gases, nitrous oxide increased intra-abdominal pressure during laparoscopic procedures, and long duration of surgery increases the risk of PONV [**4**].

A rate of 46%-75% has been reported for patients who did not receive antiemetic treatment after Laparoscopic cholecystectomy **[5].**

Surgical factors also include the effects of intra peritoneal CO2 insufflation on residual stretching and irritation of the peritoneum [**6**].

Ondansetron, a serotonin type 3 (5HT3) receptor antagonist is the most common antiemetic used for preventing PONV. **Dexamethasone a** glucocorticoid receptor agonist is an effective antiemetic at prophylactic dose of 8mg the longer onset of action of dexamethasone may result in relative less effective in preventing early PONV [**7**].

Aprepitant is equally effective in the prevention of post-operative nausea and has better control of vomiting at 24hr and 48hr when compared with conventional therapies and patients have reported less demand of rescue anti emetic. It is a selective, high-affinity NK- 1 receptor antagonist that blocks the binding of substance P. This new drug is also of added interest because of its mechanism of action via substance P, which other than nausea and vomiting is also involved in pain, anxiety and depression therapy adding to its potential applications. In patients having open abdominal surgical procedures and craniotomy, studies have shown that Aprepitant had more antiemetic effects than Ondansetron in preventing vomiting in the postoperative period. [**8**]. Using a 11-point Verbal rating scale, patients are graded as nausea from 0 (no nausea) to 10 (nausea as bad as could be) at 0-2hr; 2- 12hr and 12-28hr and 18-24hr after surgery. Verbal rating score of postoperative nausea between 1-3 is rated as mild; 4-7 as moderate; >8 as severe on a scale of 10.

The purpose of this study was to determine the antiemetic efficacy of Aprepitant against Ondansetron and Dexamethasone for preventing postoperative nausea and vomiting in patients undergoing surgery under general anaesthesia.

2. Material and Methods

This study was conducted in a tertiary care hospital from the period November 2020 to October 2021 with prior approval from the ethical committee of the institution. Informed consent was obtained from 90 patients between age group of

18-60 years as physical status Class 1 and 2 according to ASA, scheduled for elective surgery under general anaesthesia. Exclusion criteria were patients with ASA III and above, pregnant and lactating women, patients with history of motion sickness and past history of Post-operative nausea and vomiting, and patients who had received anti emetics within 24hour before surgery.

All the patients were kept fasting for 8 hours prior to surgery. A peripheral intravenous line was established with 18 gauge cannula and preloaded with 7- 10ml /kg of ringer lactate and monitors were connected and baseline heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SPO2) by pulse oximeter were recorded.

Patients were randomly assigned using computer-generated block randomization schedule, to compose three groups of thirty patients each.

1) Group A receiving capsule Aprepitant (40mg) orally, 2hr before induction of anaesthesia.
2) Group B receiving Ondansetron (4mg) IV, 10 minutes before induction and
3) Group C receiving injection Dexamethasone (8mg) IV, 10 minutes before induction of anaesthesia.

After pre oxygenation for 3min, all the patients were induced within Propofol (2-2.5mg/kg) IV and inj. Atracurium (0.5-1mg/kg) to facilitate intubation. Anaesthesia was maintained with 33% O2, 66% N2O, Isoflurane, Atracurium (0.06-0.1mg/kg) and Paracetamol 1gm iv is given for analgesia. Patients did not receive any more opioids during surgery. Adequate monitoring was done intra-operatively. At the end of surgery residual neuromuscular blockade reversed using inj. Glycopyrrolate 0.01mg/kg and inj. Neostigmine, 0.05mg/kg at the end of surgery. The trachea was extubated after meeting extubation criteria and then transferred to the post anaesthesia care unit (PACU) where in addition to hemodynamic monitoring the patients were assessed for pain and PONV. Apart from the incidence of PONV, the number of emetic episodes, severity of postoperative nausea, timing of the first vomiting episode, and use of rescue antiemetic and complete response was also noted.

Using **11 point verbal rating scale**, nausea was graded from 0 (no nausea), to 10 (worst nausea), at 0-2, 2-6, 6- 12, 12- 18 and 18-24 h after the operation.

Verbal rating score between 1-3 rates as mild; 4-7 as moderate and >8 was considered as severe on a scale of 0- 10. The results were statistically analysed to determine the efficacy of drugs for preventing postoperative nausea and vomiting. Rescue therapy, if required inj. Metoclopramide 10mg was offered intravenously on patient request, presence of persistent nausea (>5cm), or any vomiting episode.

Statistical analysis:
Baseline comparability was assessed by using chi square/test as deemed appropriate using SPSS 20.0 software. Continuous variables are summarized in the form of means and standard deviation and categorical variables were summarized as percentages.

3. Results

The three groups were comparable with respect to age, sex, and ASA status. In early hours there were incidence of mild nausea in all three groups but in late hours i.e18-24hour incidence of nausea in aprepitant group (3.3%) and dexamethasone group (6.7%) were less than ondansetron group (10%) However the results were statistically insignificant.

At 12- 18 hour, there is statistically significant difference of Group O (10%) with Group A and Group D with no vomiting episodes. (P-value<0.05). This could be attributed to the short duration of action of Ondansetron. At 18- 24hours, in Aprepitant group no patients (0%) had vomiting, and both in Group A and Group D no patient had required antiemetic.

At 18-24 hour, in all the three groups; Group A, Group O, and Group D, no patient had needed rescue antiemetic. In immediate period i.e. 0-2hours, in Group A 25 patients (83%) showed complete response, in Group O, 26 patients (86.7%) showed complete response, and in Group D, 27 patient (90%) had shown complete response (Complete response=No nausea, no vomiting).

In delayed period i.e. 18-24hours, in Group A, 29 patients (96.7%) showed complete response, in Group O, 27 patients (90.0%) showed complete response, and in Group D, 28 patients (93.3%) have shown complete response. However, there is no statistically significance between the three groups in complete response at anytime interval.

Nausea	Group A		Group O		Group D		P-value
	No.	%age	No.	%age	No.	%age	
0-2 Hours	5	16.7	4	13.3	3	10.0	0.749
2-6 Hours	3	10.0	2	6.7	1	3.3	0.585
6- 12 Hours	0	0.0	1	3.3	1	3.3	0.599
12- 18 Hours	1	3.3	2	6.7	1	3.3	0.769
18-24 Hours	1	3.3	3	10.0	2	6.7	0.585

Table 9: Incidence of vomiting in three groups at various intervals of time

Vomiting	Group A		Group O		Group D		P-value
	No.	%age	No.	%age	No.	%age	
0-2 Hours	4	13.3	3	10.0	2	6.7	0.691
2-6 Hours	1	3.3	2	6.7	1	3.3	0.769
6- 12 Hours	1	3.3	2	6.7	0	0.0	0.355
12- 18 Hours	0	0.0	3	10.0	0	0.0	0.045*
18-24 Hours	0	0.0	1	3.3	1	3.3	0.599

Table 10: Need of Antimetic in the Three Groups at Various

Need of antiemetic	Group A		Group O		Group D		P-value
	No.	%age	No.	%age	No.	%age	
0-2 Hours	3	10.0	1	3.3	1	3.3	0.429
2-6 Hours	0	0.0	0	0.0	0	0.0	-
6- 12 Hours	0	0.0	1	3.3	0	0.0	0.364
12- 18 Hours	0	0.0	2	6.7	0	0.0	0.129
18-24 Hours	0	0.0	0	0.0	0	0.0	-

Table 11: Complete response in three groups at various intervals of time

Complete Response	Group A		Group O		Group D		P-value
	No.	%age	No.	%age	No.	%age	
0-2 Hours	25	83.3	26	86.7	27	90.0	0.749
2-6 Hours	27	90.0	27	90.0	29	96.7	0.538
6- 12 Hours	29	96.7	28	93.3	29	96.7	0.523
12- 18 Hours	29	96.7	27	90.0	29	96.7	0.429
18-24 Hours	29	96.7	27	90.0	28	93.3	0.585

4. Discussion

Despite the introduction of newer anti emetic drugs, shorter acting anesthetic agents and minimal invasive surgical techniques the incidence of postoperative nausea and vomiting has remained largely unchanged. Use of antiemetic prophylaxis has become the standard approach to minimize the nausea and vomiting post-operative.

Ondansetron, a serotonin type 3 receptor antagonist which is the most common anti emetic drug used for preventing postoperative nausea and vomiting and is more effective in preventing early but not late PONV due to its shorter duration of action i.e. 5-7hours.Dexamethasone a glucocorticoid receptor agonist is an effective anti-emetic at prophylactic dose of 5-8mg IV. Longer onset of action of Dexamethasone may result in relative less effective in preventing early PONV but is more effective in preventing delayed postoperative nausea and vomiting. **Aprepitant** is a highly selective, central acting neurokinin- 1 inhibitor antagonist with a long half-life and good preclinical efficacy against opioids induced emesis. It is commonly used in patient receiving chemotherapy, however it is not commonly used for preventing PONV till now. Aprepitant is also effective in the prevention of postoperative nausea and has better control in vomiting at 24hr and 48hr when compared with conventional therapies. This drug is of added interest in relieving pain, anxiety and depression therapy adding to its potential applications.

The current study was undertaken to compare and to determine the antiemetic efficacy of Ondansetron, Aprepitant and Dexamethasone in patients undergoing surgeries under General anesthesia. We have also studied the side effects and safety profile of these drugs. Ninety patients of American society of Anesthesiologist (ASA) grade 1 and 2, aged 20-60 years, of either sex scheduled for elective surgeries under general anesthesia were included in the study. Our study did not have a control group receiving placebo since we thought that the placebo controlled trials may be unethical if so many antiemetics are available because postoperative nausea and vomiting is a common and distressing symptom against which effective treatment should be given to all the patients.

Nausea and Retching:
In our study it was found that both in Aprepitant and Dexamethasone group in the early phase i.e.0-2hr after administration of drug, the incidence of nausea was slightly more, however in delayed phase the incidence of nausea significantly decreased in both these groups. The early incidence on nausea in Aprepitant and Dexamethasone group is due to longer onset of action of both these drugs as compared to Ondansetron which has a short onset but it was observed that once the peak effect is achieved, the incidence of nausea is significantly decreased in both Aprepitant and Dexamethasone group. Also, it has to be noted that another reason for this could be that the dose of Aprepitant used in our study is less i.e. 40mg and in other studies higher doses have been used i.e. 80mg and 125 mg Aprepitant **[9]**. Also, the route of administration of Aprepitant is oral whereas, Ondansetron and Dexamethasone have been given intravenously which leads to its shorter onset and higher bio-availability and peak effect. Also it has been seen that in delayed phase more number of patients in Ondansetron group, complained of episodes of nausea as compared to other two groups due to its short duration of action of Ondansetron. However it has been found that there has been reduction of nausea episodes in all the three groups, but the difference in the incidence of nausea in the three groups is not statistically significantly at anytime interval (P>0.05).

In a study by **Tsutsumi MY et al,2011[10]** it was found that PONV incidence at acute phase i.e. 0-2 hours was present in both control and Aprepitant groups which was 63% and 43%, respectively. At delayed phase PONV was present in the control group, but was absent in the NK1 group ((27%) and (0%) respectively. And also the severity of nausea was significantly less in the Aprepitant group. Our results are also in accordance with observation of **Maitra S et al., (2016)** [7] that showed that the incidence of post-operative nausea was significantly lower at 4-6 hours when Dexamethasone was used instead of Ondansetron in laparoscopic surgeries.

Vomiting:
In the immediate post-operative period i.e. within the first 0-2hrs, 4 patients (13.3%) in Aprepitant group, whereas 3 patients (10%) in Ondansetron group and 2 patients (6.7%) in Dexamethasone group had vomiting episodes. Although, it was found that in 12- 18 hours interval all patients were emesis free in both Aprepitant and Dexamethasone group but in Ondansetron group, 3 patients (10.0%) have shown mild episodes of vomiting. And the difference between the incidence of vomiting between the three groups is statistically significant (P=0.045%).

However, it has been seen that at 18-24hours, both in Ondansetron and Dexamethasone group 1 patient (3.3%) had mild episodes of vomiting while in Aprepitant group all patients were emesis free. Patients in Ondansetron group have shown more incidence of vomiting in delayed phase due to short duration of action of this drug as compared to other two drugs. **Safarnejad F et al., (2021**) [**11**] had observed that the highest severity of nausea and vomiting had occurred in the Ondansetron group and the lowest was in the group receiving the combination of Aprepitant plus Ondansetron. In a study by **B Subramaniam et al., (2001) [12]** found that the incidence of PONV in 0- 6hours (early) was comparable but in 6-24hours period (late phase) PONV was significantly lower in Dexamethasone group than in Ondansetron and placebo group

Erhan Y et al., (2008) [13] concluded that the patients of Dexamethasone group showed better efficacy in preventing vomiting episodes than the patients of Ondansetron group in the first 24 hour.

Need for Rescue Antiemetics:
After 2 hours it was found that both in Aprepitant and Dexamethasone group there was no requirement of rescue antiemetic. However, in Ondansetron group, in 6- 12hrs 1 patient (3.3%) and in 12- 18 hrs 2 patients (6.7%) had required rescue anti emetics. **Tsutsumi YM et al., (2011) [10]** performed a study and it was consistent with the finding of our study.

Complete Response
It has been observed that and all the three drugs were comparatively effective in achieving complete response in 0-24 hour postoperative period, however the difference was not statistically significant. **Gan TJ et al., (2007) [14]**, who concluded that Aprepitant was superior to Ondanstron for prevention of vomiting in the first 24hour and 48hr, but no significant difference were observed between Aprepitant and Ondansetron for nausea control, use of rescue, or complete response. Also, **Jeyabalan S et al., (2019) [15]** observed that single dose of oral Aprepitant has comparable effects to inj. Ondansetron in preventing PONV, the severity of nausea, number of rescue antiemetics, and the time to first emetics episodes in the first 24hour postoperative period.

5. Conclusion

Thus, in this study we concluded that single dose of injection Dexamethasone 8mg IV and oral 40mg Aprepitant was more effective in reducing the post- operative vomiting episodes and the need of rescue anti emetic as compared to injection Ondansetron 4mg IV in patients undergoing surgery under general anesthesia. Also it is concluded that Aprepitant and Dexamethasone have shown slightly lower prophylactic antiemetic effects in early phase but in delayed phase both drugs were better in preventing PONV as compared to Ondansetron. At the end of 24hrs vomiting episodes were effectively reduced in all the patients in three groups and also there was reduction in need of rescue antiemetic. However, in control of nausea, need for rescue anti emetic and to achieve complete response, all the three drugs were comparable. As far as safety profile is concerned all three drugs are equally safe and devoid of any clinically important adverse effects when used in this manner. However, further studies are needed for combination of anti-emetics and determining the adequate dosage of anti-emetics which have been used in our study.

References

[1] **Murakami C, Kakuta N, Tsutumi YM et al. A** comparison of Fosaprepitant and Ondansetron for preventing postoperative nausea and vomiting in moderate to high risk patients: A retrospective database analysis. Biomed Research Int.2017;(5703528):1-5.
[2] **Weilbach C, Raymonds K, Mayer NR et al**. Postoperative Nausea and vomiting (PONV): Usefulness of the Apfel's score for identification of high risk patients for PONV. Acta Anaesth Belg.2006 Jan;57(4):361-36.
[3] **Apfel CC,Laara E, Koivauranta et al.** A simplified risk score for Predicting postoperative nausea and vomiting. Anesthesiol. 1997;91(3):693-700.
[4] **Shaikh SI, Nagarekha D, Hagede G et al.** Postoperative nausea and vomiting: A simple yet complex problem. Anesth Essays Res.2016 Sep Dec;10(3):388-396.
[5] **Arsalan M.** Preventing Postoperative Nausea and Vomiting after laparoscopic cholecystectomy: A prospective, Randomised. Double Blind study. Elsevier HS Journal 2011 Feb;72(1):1- 12.
[6] **Sharma D, Mishra AK, Sharma N et al.** Postoperative nausea and vomiting: A Review. IJCRR 2014 Oct;20(6):48-54.
[7] **Maitra S, Bhattacharjee S, Baidya DK *et al.*** Comparison of Ondansetron and Dexamethasone for Prophylaxis of Postoperative Nausea and vomiting in Patients Undergoing Laparoscopic surgeries: A Meta-Analysis of Randomised Controlled Trials. *Anesthesiology Research and Practice* 2016; 2016(7089454):1-8.
[8] **Habib AS, Keifer CJ, White WD et al.** A comparison of the combination of Aprepitant and Dexamethasone versus the combination of Ondansetron and Dexamethasone for the prevention of postoperative Nausea and Vomiting in Patients undergoing craniotomy.Anesth Analog2011;112(4):813- 18.
[9] **Jung WS, Kim YB, Park HY et al.** Oral administration of Aprepitant to prevent postoperative nausea in highly susceptile patients after gynaecological laparoscopy. J Anaesthesiol.2013 Jun;27(3):396-401.
[10] **Kakuta N, Tsutsumi YM, Horikawa YT et al.** Neurokinin-1 receptor antagonism, aprepitant, effectively diminishes post-operative nausea and vomiting while increasing analgesic tolerance in laparoscopic gynecological procedures. J Med Invest. 2011 Aug;58(3-4):246-51.
[11] **Safarnejad F, Nasseri K, Karami R *et al.*** Comparison of the effects of Aprepitant and Ondansetron individually and combining of Postoperative Nausea and Vomiting after Laparoscopic Cholecystectomy. *World J Lap Surg.* 2021; 14(1):39-42.
[12] **Subramaniam B, Madan R, Sadhasivam S *et al*.** Dexamethasone is cost effective alternative to Ondansetron in preventing PONV after paediatric strabismus repair British Journal of Anaesthesia 2001;86:84-89
[13] **Erhan Y, Yentur A, Aydede H et al.** Ondansetron, Granisetron, and Dexamethasone compared for the prevention of Post operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: A randomised Placebo- controlled study. Surg. Endosc.2008 Jun;22(6):1487-92.
[14] **Gan TJ, Apfel CC, Kovac A et al.** A randomized, double -blind comparison of the NK1 antagonist, Aprepitant, versus Ondansetron for the prevention of postoperative nausea and vomiting. Anesth Analg.2007 May; 104(5)1082-9.
[15] **Jeyabalan S et al, Thampi Sampi SM** et al. Comparing the efficacy of Aprepitant and Ondansetron for the prevention of postoperative nausea and vomiting (PONV): A Double -blinded, randomized control trial in patients undergoing breast and thyroid surgeries. Indian J Anesth.2019 April; 63 (4):289-94.