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ORIGINAL RESEARCH

Comparison of standard antiemetic characteristics to olanzapine to prevent post-discharge nausea and vomiting following propofol-based GA

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ABSTRACT

Background: PONV (Postoperative nausea and vomiting) is a consistent concern in subjects undergoing ambulatory surgery. Olanzapine is efficacious in preventing PONV in subjects undergoing highly emetogenic chemotherapy. However, existing literature data is scarce concerning the comparison of standard antiemetics to olanzapine to prevent PONV after general anesthesia. **Aim:** The present study aimed to comparatively assess the standard antiemetic characteristics of olanzapine to prevent post-discharge nausea and vomiting following propofol-based GA. **Methods:** The present study assessed 212 adult subjects aged 18-65 years undergoing highly emetogenic daycare surgeries under propofol-based general anesthesia. Group I subjects were given preoperative 10 mg oral olanzapine, and Group II served as a control and administered 4mg ondansetron and 8mg intravenous dexamethasone intraoperatively. Primary outcomes assessed were nausea (NRS >3) and/or vomiting 24 hours following discharge. Secondary outcomes were PACU nausea and vomiting, side effects, and vomiting and nausea. **Results:** The severity and incidence of postoperative nausea and vomiting were similar in both the study groups in PACU with eight subjects feeling nausea and vomiting and 6 subjects had severe symptoms in Group I (olanzapine) with p=0.06 and post-discharge, 6 subjects had nausea and vomiting in Group I (Olanzapine) compared to 10 subjects in the control group with eight depicted as severe with p=0.482. The side effects including lightheadedness, dizziness, and sedation were statistically comparable in the two study groups. **Conclusion:** The present study concludes that a single postoperative olanzapine can be an efficacious alternative to standard antiemetic prophylaxis involving ondansetron and dexamethasone for the prevention of PONV (pre-operative nausea and vomiting) in highly emetogenic daycare surgeries under propofol-based general anesthesia.

Keywords: Antiemetic, olanzapine, ondansetron, PONV, postoperative nausea and vomiting

INTRODUCTION

PDNV (post-discharge nausea and vomiting) signifies nausea and vomiting experienced following discharge from the healthcare facility extending to 72 hours following discharge. Ambulatory surgery has been increased globally including in India which can be attributed to the increase in its adoption for enhanced recovery following surgery protocols for optimization of patient outcomes. PDNV is a significant concern as post-surgery it increases patient's dissatisfaction, hindrance to resume daily activities, and increase sleep disturbances. Severe retching resulting from PDNV can lead to pneumothorax, increased intracranial pressure, esophageal rupture, and wound dehiscence. Unplanned readmission of the subjects from PDNV increases the healthcare costs which is a vital concern in healthcare settings with limited resources.[1]

Current guidelines for antiemetic prophylaxis utilize the use of ondansetron which is a 5-HT3 (serotoninergic) antagonist having a short half-life of nearly three hours. However, it is effective during the

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typical stay in PACU (post-anesthesia care unit), but its address of PDNV is inadequate. The shift from volatile anesthetic agents to propofol-based anesthesia results in similar advantages. With dexamethasone having an extended half-life, it has the benefit of decreasing PDNV.[2]

Olanzapine is an atypical antipsychotic agent having multiple receptors involved in the pathophysiology of PONV (postoperative nausea and vomiting) including histamine (HI), acetylcholine (muscarinic), serotonin (5-HT 2a, 2c, 3, and 6), and dopamine (D1-4). Peak action of Olanzapine at 6 hours and a prolonged half-life of 3-hour position, it is an ideal candidate to manage PDNV.[3]

The present study assessed the side effects and benefits of a single postoperative oral olanzapine for the prevention of PDNV. The primary objective of the present study was to assess the nausea incidence as NRS (numerical rating scale) >3 and vomiting within 24 hours following discharge after daycare surgery. A secondary objective was the incidence of severe post-discharge nausea (NRS >5) within 24 h post-discharge, PACU nausea or vomiting, the need for rescue antiemetics in PACU, and side effects such as lightheadedness, dizziness, and sedation post-discharge.

MATERIALS AND METHODS

This comparative clinical study aimed to assess the standard antiemetic characteristics of olanzapine to prevent post-discharge nausea and vomiting following propofol-based GA. The study subjects were from the Department of General Surgery of the Institute. Verbal and written informed consent were taken from all the subjects before study participation.

The study included adult male and female subjects aged 18-65 years in ASA (American Society of Anesthesiologists) physical status I and II and were undergoing highly emetogenic daycare surgeries under propofol-based general anesthesia. These surgeries were assessed from Apfel score as the threshold of ≥4 risk factors- female gender, age <50 years, history of PONV or motion sickness, anticipated use of opioids in PACU, and anticipated nausea in PACU.[4] Nausea anticipation in PACU was assessed when the subject was a smoker, surgical approach as laparoscopy, endoscopy, or arthroscopy, >125 µg fentanyl dose intraoperatively, surgeries of > 1-hour duration, and surgery type as knee arthroplasty, upper extremity surgeries, prostrate, hernia, otorhinolaryngology, and/or cholecystectomy. The exclusion criteria for the study were surgeries of >2 hours duration from incision time, contraindication to olanzapine use such as neurological disorders, Lewy body dementia, and/or Parkinson's diseases, congestive heart failure, arrhythmias, unstable angina, myocardial infarction, patients having torsade de pointes arrhythmia or QTc >450 ms, pregnant/lactating patients, and need for hospitalization.

The subjects were randomly divided into two groups where Group I subjects were given preoperative 10 mg oral olanzapine and Group II served as control and administered 4mg ondansetron and 8mg intravenous dexamethasone intraoperatively. In Group I, subjects were given 10mg single per oral (PO) olanzapine dose 1 hour before surgery with water sips in the preoperative area. A similar placebo as Olanzapine was given in Group II control subjects. In the intraoperative phase, Group II (controls) received standard antiemetic prophylaxis- intravenous 8mg dexamethasone Immediately following anesthesia induction and 4mg IV ondansetron nearly 30 minutes before emergence. Group I was given saline injections as a placebo.

Endpoints of the study were assessed including follow-up after 24 hours of the discharge, monitoring of subjects in PACU, and completion of preformed structured proforma. Demographic and clinical data were gathered in all the subjects including opioid use and nausea, total propofol use, surgery duration, incision time, risk factor score for PDNV, planned surgery, diagnosis, QTc interval, ASA status, weight, gender, and age. Anesthesia induction was done with 1.5–2.5 mg/kg propofol 1-2 µg/kg fentanyl and 0.5mg/kg IV atracurium for neuromuscular blockade as bloused at the discretion of the anesthesiologist. IV propofol infusion titration was done to attain a bispectral index/entropy value of 40–60. IV glycopyrrolate and neostigmine were administered for the reversal of neuromuscular blockade before tracheal extubation. Side effects and PONV were assessed with NRS. Vomiting/nausea with NRS>3 was taken as significant and rescue antiemetics use was noted. In PACU, IV 4mg ondansetron was used as rescue antiemetic. Subjects were advised for oral ondansetron following discharge, as needed. Follow-up was done telephonically 24 hours after discharge. The severity of side effects, vomiting, and nausea was assessed with NRS.

Primary study outcomes assessed were nausea occurrence with NRS >3 and vomiting in 24 hours postoperative and discharge in subjects undergoing daycare surgeries. Secondary outcomes assessed were nausea and vomiting occurrence in PACU, side effects such as lightheadedness, dizziness, and sedation, severe PDNV within the initial 24 hours following discharge, and the necessity for rescue antiemetics in PACU.

The data gathered were analyzed statistically using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk. NY, USA) for assessment of descriptive measures, one-way ANOVA (analysis of variance), Pearson correlation, and chi-square test. The results were expressed as mean and standard deviation and frequency and percentages. The p-value of <0.05 was considered statistically significant.

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RESULTS

This comparativeclinical study was aimed to comparatively assess the standard antiemetic characteristics of olanzapine to prevent post-discharge nausea and vomiting following propofol-based GA. The present study assessed 212 adult subjects aged 18-65 years undergoing highly emetogenic daycare surgeries under propofol-based general anesthesia. Group I (n=108) subjects were given preoperative 10 mg oral olanzapine and Group II (n=104) served as control and administered 4mg ondansetron and 8mg intravenous dexamethasone intraoperatively. All demographic parameters at baseline were statistically comparable in the two groups. The mean age of the study subjects was 35.35±8.98 and 35.17±19.74 years respectively. There were 16 males and 92 females in Group I and 16 males and 88 females in Group II. ASA status was comparable in the two groups (p>0.05). PONV risk scores were 4.02±0.17 and 4.02±0.26 in Groups I and II (Table 1).

For the surgeries done in the study subjects, Ophthalmology (orbital mass excisions, pars plana vitrectomy) surgeries were done in 3.7% (n=4) and 3.8% (n=4) subjects from Groups I and II. Orthopedics (core biopsy, implant removal) surgeries in 3.7% (n=4) and 5.7% (n=6) subjects from Groups I and II. Plastic surgery (isolated nerve repairs, contracture release) in 5.5% (n=6) and 1.9% (n=2) subjects from Groups I and II. Hysteroscopic polypectomy, and tubal ligation in 9.2% (n=10) and 13.4% (n=14) study subjects from Groups I and II. Hernioplasty in 14.8% (n=16) subjects from Group I and 19.2% (n=20) subjects from Group II. Lumpectomy/mastectomy was done in 18% (n=20) and 17.3% (n=18) subjects from Groups I and II. Laparoscopic cholecystectomies in 44% (n=48) and 17.3% (n=18) subjects from Groups I and II (Table 1).

It was seen that for the comparison of intraoperative characteristics in two groups of study subjects, surgery duration was 66.55±27.05 and 68.63±27.51 minutes in Groups I and II which was non-significant with p=0.683. Total propofol use was 468.87±205.52 and 511.71±188.41 mg in Groups I and II which was non-significant with p=0.213. Intraoperative fentanyl use (µg) was also statistically comparable in the two groups with p=0.677. In PACU characteristics, rescue antiemetics and severe vomiting/nausea in PACU were seen in 5.6% (n=6) subjects from Group I and no subject from Group II (p=0.241). NRS for nausea/vomiting in PACU was 4.58±1.54 in Group I.Fentanyl dose in PACU was statistically comparable in Group I and II with p=0.897 and Fentanyl use in PACU was seen in 20.4% (n=22) and 23.1% (n=24) subjects from Group I and II respectively (p=0.733) (Table 2).

The study results showed that concerning the comparison of post-discharge characteristics in two groups of study subjects, side effects were seen in 16.7% (n=18) and 13.5% (n=14) subjects from Groups I and II which were statistically non-significant with p=0.643. Severe vomiting/nausea post-discharge was seen in 5.6% (n=6) and 7.7% (n=8) subjects from Groups I and II which were statistically non-significant with p=0.711. NRS for vomiting/nausea post discharge was 6.02±1.00 and 5.58±1.12 from Groups I and II which was statistically non-significant with p=0.731. Vomiting/nausea post-discharge was seen in 5.6% (n=6) and 9.6% (n=10) subjects from Groups I and II which were statistically non-significant with p=0.482 (Table 3).

Table 1: Demographic and disease data in two groups of study subjects

Characteristics	Group I (n=108)	Group II (n=104)
Mean age (years)	35.35±8.98	35.17±19.74
Gender		
Males	16	16
Females	92	88
Mean weight (kg)		
ASA		
I	94 (87%)	84 (80.8%)
II	14 (13)	20 (19.2)
PONV risk score	4.02±0.17	4.02±0.26
Surgeries done n (%)		
Ophthalmology (orbital mass excisions, pars plana vitrectomy)	4 (3.7)	4 (3.8)
Orthopedics (core biopsy, implant removal)	4 (3.7)	6 (5.7)
Plastic surgery (isolated nerve repairs, contracture release)	6 (5.5)	2 (1.9)
Hysteroscopic polypectomy, tubal ligation	10 (9.2)	14 (13.4)
Hernioplasty	16 (14.8)	20 (19.2)
Lumpectomy/mastectomy	20 (18)	18 (17.3)
Laparoscopic cholecystectomies	48 (44)	40 (38.5)

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Table 2: Comparison of perioperative characteristics in study subjects

Intraoperative characteristics	Group I (n=108)	Group II (n=104)	p-value
Surgery duration (mins0	66.55±27.05	68.63±27.51	0.683
Total propofol use (mg)	468.87±205.52	511.71±188.41	0.213
Intraoperative fentanyl use (µg)	97.02±24.90	98.83±25.62	0.677
PACU characteristics			
Rescue antiemetics	6 (5.6)	0	0.241
Severe vomiting/nausea in PACU	6 (5.6)	0	0.241
NRS for vomiting/nausea in PACU	4.58±1.54	-	-
Vomiting/nausea in PACU	10 (9.3)	0	0.06
Fentanyl dose in PACU (µg)	38.16±18.86	35.81±10.82	0.897
Fentanyl use in PACU	22 (20.4)	24 (23.1)	0.733

Table 3: Comparison of post-discharge characteristics in two groups of study subjects

Post-discharge characteristics	Group I (n=108)	Group II (n=104)	p-value
Side-effects	18 (16.7)	14 (13.5)	0.643
Severe vomiting/nausea post-discharge	6 (5.6)	8 (7.7)	0.711
NRS for vomiting/nausea post-discharge	6.02±1.00	5.58±1.12	0.731
vomiting/nausea post-discharge	6 (5.6)	10 (9.6)	0.482

DISCUSSION

The present study assessed 212 adult subjects aged 18-65 years undergoing highly emetogenic daycare surgeries under propofol-based general anesthesia. Group I (n=108) subjects were given preoperative 10 mg oral olanzapine and Group II (n=104) served as control and administered 4mg ondansetron and 8mg intravenous dexamethasone intraoperatively. All demographic parameters at baseline were statistically comparable in the two groups. The mean age of the study subjects was 35.35±8.98 and 35.17±19.74 years respectively. There were 16 males and 92 females in Group I and 16 males and 88 females in Group II. ASA status was comparable in the two groups (p>0.05). PONV risk scores were 4.02±0.17 and 4.02±0.26 in Groups I and II. These data were comparable to the previous studies of Grigio TR et al[5] in 2023 and Apfel CC et al[6] in 2012 where authors assessed subjects with demographic data comparable to the present study.

The study results showed that for the surgeries done in the study subjects, Ophthalmology (orbital mass excisions, pars plana vitrectomy) surgeries were done in 3.7% (n=4) and 3.8% (n=4) subjects from Groups I and II. Orthopedics (core biopsy, implant removal) surgeries in 3.7% (n=4) and 5.7% (n=6) subjects from Groups I and II. Plastic surgery (isolated nerve repairs, contracture release) in 5.5% (n=6) and 1.9% (n=2) subjects from Groups I and II. Hysteroscopic polypectomy, and tubal ligation in 9.2% (n=10) and 13.4% (n=14) study subjects from Groups I and II. Hernioplasty in 14.8% (n=16) subjects from Group I and 19.2% (n=20) subjects from Group II. Lumpectomy/mastectomy was done in 18% (n=20) and 17.3% (n=18) subjects from Groups I and II. Laparoscopic cholecystectomies in 44% (n=48) and 17.3% (n=18) subjects from Groups I and II. These results were consistent with the findings of Wang J et al[7] in 2020 and Kolesnikov Y et al[8] in 2013 where surgeries done by present study subjects were comparable to the results reported by authors in their respective studies.

Concerning the comparison of intraoperative characteristics in two groups of study subjects, surgery duration was 66.55±27.05 and 68.63±27.51 minutes in Groups I and II which was non-significant with p=0,683. Total propofol use was 468.87±205.52 and 511.71±188.41 mg in Groups I and II which was non-significant with p=0.213. Intraoperative fentanyl use (µg) was also statistically comparable in the two groups with p=0.677. In PACU characteristics, rescue antiemetics and severe vomiting/nausea in PACU were seen in 5.6% (n=6) subjects from Group I and no subject from Group II (p=0.241). NRS for nausea/vomiting in PACU was 4.58±1.54 in Group I.Fentanyl dose in PACU was statistically comparable in Group I and II with p=0.897 and Fentanyl use in PACU was seen in 20.4% (n=22) and 23.1% (n=24) subjects from Group I and II respectively (p=0.733). These findings were in agreement with the results of Klenke S et al[9] in 2018 and Laugsand EA et al[10] in 2011 where intraoperative characteristics reported by the authors in their studies were comparable to the results of the present study.

It was also seen that concerning the comparison of post-discharge characteristics in two groups of study subjects, side effects were seen in 16.7% (n=18) and 13.5% (n=14) subjects from Groups I and II which were statistically non-significant with p=0.643. Severe vomiting/nausea post-discharge was seen in 5.6% (n=6) and 7.7% (n=8) subjects from Groups I and II which were statistically non-significant with p=0.711. NRS for vomiting/nausea post discharge was 6.02±1.00 and 5.58±1.12 from Groups I and II which was statistically non-significant with p=0.731. Vomiting/nausea post-discharge was seen in 5.6% (n=6) and 9.6% (n=10) subjects from Groups I and II which were statistically non-significant with p=0.482.

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These results were in correlation with the studies ofHayase T et al[11] in 2015 and Rueffert H et al[12] in 2009 where post-discharge characteristics reported by the authors in their studies were similar to the results of the present study.

CONCLUSIONS

Within its limitations, the present study concludes that single postoperative olanzapine can be an efficacious alternative to standard antiemetic prophylaxis involving ondansetron and dexamethasone for prevention of PONV (postoperative nausea and vomiting) in highly emetogenic daycare surgeries under propofol-based general anesthesia. Further studies must be done in the future with a larger sample size and considering wider arena of surgeries.

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