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COMPARISON BETWEEN INTRAVENOUS PALONOSETRON AND DEXAMETHASONE WITH ONDANSETRON AND DEXAMETHASONE FOR PREVENTION OF NAUSEA AND VOMITING IN PATIENTS POSTED FOR LAPAROSCOPIC SURGERIES UNDER GENERAL ANAESTHESIA

Clinical Research

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ABSTRACT

Background: PONV (post operative nausea & vomiting) is one of the most frightening post surgical complication for patients receiving general anaesthesia. It significantly impacts post operative care and recovery. It is challenging to quantify the risk of PONV in each patient due to the many factors that can contribute to its development. **Material & Method:** It was a hospital based single blinded prospective, randomized controlled study and was done (from June 2021 – May 2022) on 100 patients undergoing laparoscopic surgeries divided into 2 groups (Group P -Inj Palonosetron 75mcg + Inj Dexamethasone 8mg; Group O-Inj Ondansetron 4mg + Inj Dexamethasone 8mg), each containing 50 patients. All the patients were monitored for PONV, need for rescue antiemetics and complete response hourly for the first 6 hours and then on 12th and 24th hour post operative. **Results:** In Group O 14% patients complained of vomiting compared to only 2% un Group P. Only 8% patients in Group P needed rescue medication (Inj Metoclopramide) compared to 24% in Group O. Complete response (no incidence of nausea or vomiting) was seen in 34% of study subjects in Group O whearas it was 58% in Group P. **Conclusion:** From our study we concluded that Palonosetron in combination with Dexamethasone had decreased the incidence of PONV significantly providing patients with long tern relief with its prolonged duration of action. Hence Palonosetron was superior to Ondansetron in prevention of PONV in patients undergoing laparoscopic surgeries under general anaesthesia.

KEYWORDS

PONV, ondansetron, palonosetron & dexamethasone.

INTRODUCTION:

Despite numerous advancements in recent years and the use of nonpharmacological and pharmacological treatments to somewhat lessen the occurrence of PONV, it still ranks as the most unfavourable patient important outcome. Major predictors of PONV, according to Apfel and colleagues, include age, obesity[1] female patients, a history of PONV or motion sickness[2], the use of opiates[3] as an adjuvant to anaesthesia, and the non-smoker population[4]. Pre-operative anxiety, underlying medical conditions, hydration levels, use of volatile anaesthetics, kind and length of surgery, and type of anaesthesia[5] are additional pre- and post-operative factors that affect PONV.Incidence of PONV is extremely high in the general population (i.e., 30–40%), and it rises further in high-risk persons up to 80%. Along with this unpleasant sensation, PONV may have negative side effects that include pulmonary aspiration, hypovolemia, electrolyte imbalance, and wound dehiscence that lengthen post-operative recovery times and overall hospital stay[6] and raise hospital cost. The prevention of the aforementioned issues improve quality of life, decreases unplanned hospital admissions, and shortens hospital stay all of which minimise the patient's overall financial burden. Due to the involvement of several neurotransmitters at various sites, the pathophysiological process underlying PONV is complex.

The stimulation of the chemoreceptor trigger zone (CTZ), which is located at the floor of the fourth ventricle, is the primary cause of the vomiting center's activation. Dopamine, serotonin, opioids, acetylcholine, and neurotransmitter substance P are all receptors for CTZ. There appears to be no progress in lowering incidence of PONV despite substantial study and the introduction of new classes of anti-emetic medicines with superior safety and efficacy profiles. Recent research has expanded the use of combined anti-emetic therapy operating at more than one molecular location to regulate PONV because a single medication has not been proven to be a complete successful approach to combat this issue. Utilizing more than two antiemetic medications has its own drawbacks, including additional side effects and drug interactions. Therefore, it is urged to design single molecule with extended action and fewer adverse effects. The effectiveness of palonosetron and ondansetron in all types of surgical procedures are still under research and very little information is available uptil now. In order to compare the safety and effectiveness of Palonosetron and ondansetron in adult patients under going surgical procedures under general anaesthesia this study was conducted.

AIMS & OBJECTIVES:

The aim of our study is to compare the efficacy of the two drugs with respect to prevention of PONV when given as prophylaxis alongwith Dexamethasone during laparoscopic surgeries. Both ondansetron and palonosetron are 5HT3 receptor antagonists, ondansetron binds to receptor by competitive binding whereas palonosetron binds to its receptor site through positive co-operation and allosteric binding. This causes palonosetron to have 100 times more affinity than other 5HT3 receptor antagonists. Parameters used were vomiting, need of rescue medication and complete response (CR).

MATERIALS & METHODS

After obtaining institutional ethical clearance and written informed consent from patients a comparative study was undertaken in the department of Anaesthesiology at Silchar Medical College and Hospital.

Duration Of Study : 12 months.

Period Of Study : 1 st June 2021-31 st May 2022.

Sample Size: A total of 100 patients were taken and were randomly divided into 2 groups, each containing 50 patients. Sample size was calculated with the assumption of alpha error 5% i.e confidence level 95% with margin of error 5%. The study population was selected from the patients who were posted for elective laparoscopic surgeries under general anaesthesia.

The study was conducted on 100 patients of both sexes aged between 18-60 years, of ASA class I or II which were randomly selected and allocated into two groups.

1. Group P- Inj Palonosetron 75 mcg + Inj Dexamethasone 8mg iv 5 min before intubation.
2. Group O- Ind Ondansetron 4mg + Inj Dexamethasone 8 mg iv 5 mins before intubation.

Inclusion Criteria:

1. Patients between age 18-60 years.
2. Patients of both sexes.
3. Patient of ASA grade I and II.
4. Patients scheduled for elective laparoscopic surgical procedure under general anaesthesia.

Exclusion Criteria:

1. Age <18 and >60 years
2. ASA III and IV.
3. Patient refusal.
4. Patients with anticipated difficult airway.
5. History of hypersensitivity to study drugs.
6. Patients having cardiovascular, respiratory, hepatic, renal, and central nervous system disorders.
7. History of motion sickness.
8. GERD

Pre Anaesthetic Assessment:

On the day prior to surgery a thorough clinical examination of the patient was performed, including General physical examination and systemic examination. All patients were explained about the anaesthesia technique and written informed consent was taken. Patient was kept nil per oral for 8 hours prior to surgery. All patients were given tablet alprazolam 0.5mg orally at bed time on the previous night of the surgery.

Technique Of Anaesthesia:

On arrival of the patient in the operation theatre, patient's body weight, consent and preoperative evaluation done previously was checked. An 18 gauge iv cannula was secured and connected to iv fluid(Ringer Lactate) premedicted with Inj Ranitidine 100mg. The patient was connected to standard monitor to record heart rate, non invasive measurement of SBP and DBP, MAP and continuous ECG monitoring and oxygen saturation.

All patients were pre-medicated with inj. glcopyrrolate0.004mg/kg iv and Inj fentanyl 1mcg/kg

- In group O(n=50): Inj Ondansetron 4mg +Inj Dexamethasone 8 mg IV slowly over 5 minute.
- In group P(n=50): Inj Palonosetron 75 mcg + Inj Dexamethasone 8 mg IV slowly over 5 minute.

The patients were preoxygenated for 3mins via a face mask and anaesthesia was induced with Inj Propofol 2mg/kg, followed by succinylcholine 1mg/kg to facilitate endotracheal intubation. Laryngoscopy and intubation was performed approx 1 min after the administration of succinylcholine.

All the patients were intubated with Mcintosh curved blade laryngoscope of appropriate size within a period of 30 seconds and the patients who needed more than 30 seconds for intubation were excluded. Anaesthesia was maintained using 4:2 nitrous oxide:oxygen with sevoflurane and Inj. Atracurium after connecting the patient to the anaesthesia workstation till the end of surgery.

Before skin closure, the port site infiltration was done with 10–12 ml of 1% lignocaine for postoperative analgesia. Reversal of residual neuromuscular blockade was done with neostigmine 50 µg/kg and glycopyrrolate 10 µg/kg. The trachea was extubated once the patient fulfilled the extubation criteria.

Method Of Collection Of Data:

The patients were observed for PONV during 24 h follow-up with 1 hr interval in the first 6 h and then at 12th and 24th hour. The hemodynamicparameters were also noted for the same time intervals. Rescue antiemetic metoclopramide 10 mg i. v. was given for VAS ≥4 score in case of nausea and any vomiting episode which was repeated whenever necessary. The need for rescue medication was also observed. Patients who were free of nausea, retching and vomiting during the first 24 hours post surgery were considered as complete responders. Any adverse effects related to drugs such as dizziness, headache, and arrhythmia was noted.

Stastical Evaluation:

All recorded data was analyzed using SPSS version 20 for determining the statistical significance. The chi square test for continuous variables and independent T/Mann whitney categorical variables was done for analysis of data. "P value of <0.05 was considered to be statistically significant in this study.

RESULT AND OBSERVATION:

Demographic variables including age, sex, blood pressure and heart rate were comparable in both groups and were statistically not signicant.

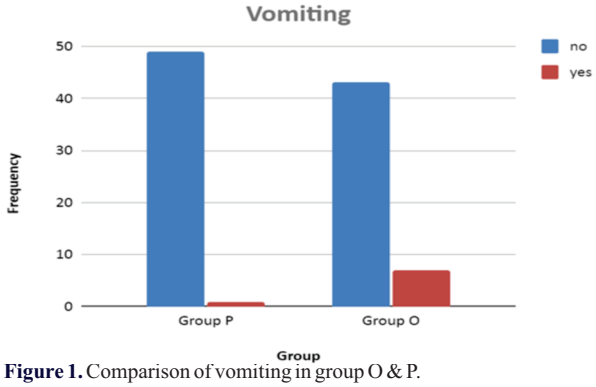

Figure 1. Comparison of vomiting in group O & P.

Figure 1 shows the comparison between group O & P during the 24 hrs study period. It showed 98% patients in group P did not have any episodes of vomiting when compared to 86% in group O. The p value is 0.027 which was statistically significant.

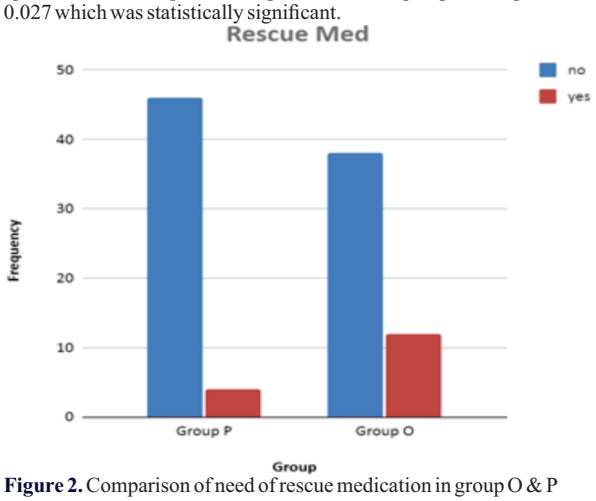

Figure 2. Comparison of need of rescue medication in group O & P

Figure 2 compared the need of rescue medication between both groups. 92% in group P did not need any rescue medication compared to 76% in group O with p value of 0.029 which was statistically significant.

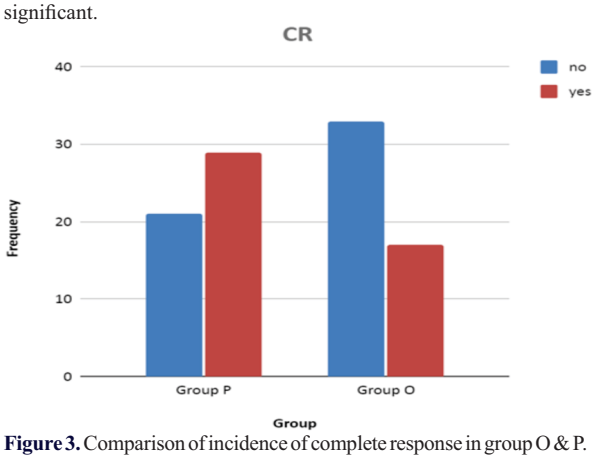

Figure 3. Comparison of incidence of complete response in group O & P.

Figure 3 compared complete response (no incidence of nausea & vomiting) between the two groups. In group O, 34% study subjects showed complete response compared to 58% in group P. Since the p value is 0.016 it was statistically significant.

DISCUSSION:

The postoperative period is associated with variable incidence of nausea and vomiting depending on many factors including the duration of surgery, the type of anesthetic agents used, smoking habit, gender etc. The major trigger for the vomiting reflex is the stimulation of the 5-HT3 receptor. The central 5-HT3 receptors in the medullary chemoreceptive trigger zone (CTZ) are stimulated by anaesthetic drugs, and serotonin is also released from the small intestine's

enterochromaffin cells, triggering the 5-HT3 receptors on the vagus nerve afferent fibres[7].

After laparoscopic surgery, PONV is very common. Age, obesity, a history of prior PONV, surgical method, anaesthetic technique, and postoperative discomfort are some of the variables that can affect the aetiology, which is complicated. When there are no risk factors present, the incidence of PONV is 10%; when there are four risk factors present, it is 79%. Because abdominal gas insufflation may stretch intestine mechanoreceptors and then activate 5-HT3 receptors by releasing serotonin[7], laparoscopic surgery is also very prone to PONV. The usage of fentanyl is another explanation for the frequent PONV in our findings. In this study, the patient demographics, the type and length of surgery, the anaesthetic regimen, and the postoperative usage of antibiotics and analgesics were equivalent between the groups.

A combination of antiemetic medications, each with a unique mechanism of action to give greater prophylaxis and fewer side effects, is required for patients with a high risk of PONV. Because numerous authors have confirmed that this combination is more successful than other combinations, we employed dexamethasone in combination with 5-HT3 receptor antagonists (ondansetron or palonosetron) in our study.

The dose of ondansetron selected for this study is 4mg which is within its known effective dose range. However, the dose of palonosetron used i.e 75mcg is not firmly established and is extrapolated from the doses used in earlier studies. **Kovac and colleagues**[8] showed that palonosetron 75 mcg is the more effective dose for the prevention of PONV after major laparoscopic surgery than 25 mcg and 50 mcg[8]. We did not include a control a placebo group. **Aspinall and Goodman** have suggested that if active drugs are available, placebo controlled trials may be unethical because PONV episodes are very much distressing for patients after a laparoscopic surgery.

It's crucial to consider when to administer preventive antiemetics. We administered these combinations before induction of anaesthesia because dexamethasone has been demonstrated to be more effective when administered at that time. Because metoclopramide has a different mechanism of action from the study medications, we chose it as a rescue antiemetic in our trial for patients who complained of PONV.

After the sixth hour of the study interval, we discovered that the palonosetron and dexamethasone group had overall less vomiting than the ondansetron and dexamethasone group. Overall nausea was equivalent between the two groups, however during study intervals of 12 and 24 hours, group O's VAS values for nausea were significantly higher. Similar results were observed by **Bajwa et al**[9] in their study where 6.66% had nausea and 3.33% had vomiting in the palonosetron group while 20% observed nausea and 13.33% observed vomiting in the first 6 hrs after surgery in the ondansetron group which was statistically significant. Consistent results were also found in a previous study conducted by **Kim and associates**[10] on female patients undergoing laparoscopic surgeries where PONV incidence in the palonosetron group was 22.2% and 77% in ondansetron group within the study period of 48hrs.

Our study correlates well with a systemic review and meta-analysis by **Xiong et al**[11]. The study compared palonosetron and ondansetron for prevention of PONV within 24 hours after surgery. Their primary outcomes were postoperative nausea, postoperative vomiting in early (0–6 hours) or late (0–24 hours) postoperative period. They found that palonosetron provided an effective prophylaxis against early postoperative nausea (RR = −0.51), late postoperative nausea (RR = −0.41), and late postoperative vomiting (RR = −0.77) in comparison to ondansetron.

In our study, the number of rescue medications used in the palonosetron group and ondansetron group were 4 and 12 respectively. In the ondansetron group, more patients required rescue Inj Metoclopramide as compared to palonosetron group and the difference was statistically significant. **Sharma and colleagues**[12] study also showed higher (20%) use of rescue medication in the ondansetron group versus palonosetron group (4%). **Kim and associates**[13] found less use of rescue antiemetics in the palonosetron group compared to ondansetron or ramosetron group.

Complete response was evaluated as no nausea or vomiting and also no need of rescue antiemetics i.e metoclopramide. Out of the 100 patients, 46 were complete responders among which 29 were from the palonosetron group and 17 were from the ondansetron group. The difference of numerical value of 12 among the groups was statistically significant. Similar results were seen in a study conducted by **Musso and colleagues**[14] which was a prospective study done on cancer patients undergoing chemotherapy. They showed 80% complete response for CINV(chemotherapy induced nausea & vomiting) in the palonosetron group compared to 60% in the ondansetron group respectively. **Mattiuzzi et al**[15] also showed higher complete response in the palonosetron group when compared to the ondansetron group. In another study for prevention of CINV, **Schwartzberg and colleagues**[16] showed an overall complete response 51% in the palonosetron group and 40% in ondansetron, dolasetron or granisetron group.

This study has its own share of limitations, the most important limitation is that a double blind comparison would have been more significant, but we were forced to settle with single blinding due to logistical issues. All subjects needed to have participated in the experiment without taking any concurrent medications that might have affected the risk of PONV. We did not, however, exclude all concurrent medications, such as antihypertensives and antidiabetics, even though we did exclude patients receiving drugs that definitely could affect emesis, such as psychiatric medication. The biochemical indicators of PONV, such as C-reactive protein, aldehydes, and ketones, were also not measured. Finally, all patients should have received the same postoperative antibiotic and analgesic regimen. In actuality, this was generally comparable but not always exactly the same.

CONCLUSION:

Based on our study, it was observed that palonosetron (75mcg) which is a 2nd generation 5HT3 receptor antagonist had prolonged duration of action and had decreased the incidence of PONV significantly in combination with dexamethasone (8mg) when compared to ondansetron (4mg) with dexamethasone (8mg), providing patients with better relief of PONV. Hence palonosetron was found to be better than ondansetron in prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries under general anaesthesia.

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