

TO COMPARE THE EFFECTIVENESS OF PRE-EMPTIVE INTRAVENOUS ANTIEMETICS PALONOSETRON VS THE COMBINATION OF ONDANSETRON AND DEXAMETHASONE IN PREVENTING NAUSEA AND VOMITING IN CAESAREAN SECTIONS PERFORMED UNDER SPINAL ANESTHESIA

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Abstract

Background: The satisfaction of patients is a crucial result of hospital care after anesthesia. Postoperative nausea and vomiting (PONV) is a common side effect that may cause patient dissatisfaction and prolong the time it takes for a patient to be discharged from the surgical facility. The aim is to compare the effectiveness of pre-emptive intravenous antiemetics palonosetron vs the combination of ondansetron and dexamethasone in preventing nausea and vomiting in caesarean sections performed under spinal anesthesia. **Materials and Methods:** A total of 120 patients were chosen at random to participate in the study. They were divided into two groups, Group OD and Group P, with 60 patients in each group. The patients in the group got the injection prior to spinal anesthesia. Group P: Palonosetron 0.075mg and Group OD: Ondansetron 6mg + Dexamethasone 8mg. PONV grading was assessed using the following scale throughout the intra-operative and post-operative period, up to 24 hours: PONV score: 0 indicates the absence of nausea and vomiting, indicating full responders. The PONV score is a scale used to measure postoperative nausea and vomiting. A score of 1 indicates the presence of nausea alone, a score of 2 indicates vomiting once, and a score of 3 indicates vomiting more than once. **Result:** Among the patients in Group OD, 14 individuals (23.33%) had nausea throughout the intraoperative time. In Group P, 5 patients (8.33%) reported nausea during the same period. The incidence of intraoperative nausea was found to be significantly higher in Group OD compared to Group P (p Value = 0.03). Out of the 18 patients in Group OD, 33.33% had nausea throughout the post-operative period. Similarly, in Group P, 13.33% of the 8 patients reported experiencing nausea after the operation. Group OD exhibited a significantly higher incidence of post-operative nausea compared to Group P (p Value = 0.02). Out of the 14 patients in Group OD, 23.33% had vomiting during the intraoperative time. In Group P, 3 patients (5%) had vomiting during the same period. **Conclusion:** According to the results and analysis of the investigation, it can be concluded that giving female patients undergoing elective cesarean surgery a pre-emptive intravenous dose of 0.075mg palonosetron reduces the occurrence of nausea and vomiting during surgery, as well as the need for antiemetic medication, compared to using a combination of 6mg ondansetron and 8mg dexamethasone preemptively.

INTRODUCTION

The level of patient satisfaction after anesthesia is a crucial outcome of hospital care. Post-operative nausea and vomiting (PONV) is a prevalent adverse effect that occurs after surgery and leads to patient unhappiness and prolonged stay in the surgical

facility. This problem is associated with factors such as age, gender, medication use, changes in blood flow, and the administration of anesthesia. While the incidence of postoperative nausea and vomiting (PONV) is less common after spinal anesthesia (19%-22%) compared to general anesthesia (76%), people may still experience pain and need assistance.

Postoperative vomiting and nausea refers to the occurrence of nausea and/or vomiting within 24 hours after a surgical procedure. The stimulation of the vomiting center is complicated by the involvement of seven neurotransmitters and three neurons, which poses challenges for treatment and prevention. Administering antiemetic premedication may decrease the occurrence of postoperative nausea and vomiting. Numerous pharmaceutical remedies, techniques, and methods have been developed throughout time, although their effectiveness is often hindered by adverse effects.^[1-3] PONV is more prevalent in certain surgical procedures, such as laparoscopic cholecystectomies and gynaecological surgeries. Spinal anesthesia (SA) for cesarean births often leads to the most frequent and troubling side effect. When antiemetic medicine is not used as a preventative measure, Caesarean sections performed under regional anesthesia are linked to a higher likelihood of experiencing nausea and vomiting (ranging from 50% to 80%) during and after the procedure. PONV may result in gastrointestinal toxicity, as well as pneumothorax, oesophageal rupture, subcutaneous emphysema, and suture dehiscence. Postoperative nausea and vomiting (PONV) occurs in 30-40% of the overall population, although the prevalence increases to 75-80% in certain high-risk populations. Due to the use of less emetogenic anesthetic techniques and the introduction of novel medications for the prevention of postoperative nausea and vomiting (PONV), the occurrence of PONV has decreased by 50%. This decline is especially evident when non-opioid medicine is used for pain management. Although significant efforts are being made to mitigate postoperative nausea and vomiting (PONV), it still persists in around 20% to 30% of patients during the first day. Postoperative nausea and vomiting (PONV) prevention and management are crucial after surgery. Several variables, including patient-related factors, surgical factors, and anesthetic, might influence the occurrence of postoperative nausea and vomiting (PONV). The risk variables associated with surgery, anesthesia, and patient characteristics have been identified. The patient's risk factors include her gender, non-smoking status, and history of motion sickness or postoperative nausea and vomiting (PONV).^[4-6]

The administration of volatile anesthetics during surgery, as well as the use of opioids both during and after surgery, are identified as risk factors associated with anesthesia and the use of nitrous gas. Factors to be taken into account while assessing surgical risk may include the kind and length of the surgical procedure. In order to prevent postoperative nausea and vomiting (PONV), a variety of antiemetic drugs from different pharmacological classes are used, either alone or in combination. These include antihistamines, phenothiazine derivatives, anticholinergic drugs, dopamine receptor antagonists, and 5-HT₃ antagonists. 5-hydroxytryptamine receptor antagonists (5-HT₃) are

currently regarded the primary choice for avoiding PONV because to their high effectiveness and minimal adverse effects. Unlike other medications, they do not elicit extrapyramidal, dysphoric, or sedative effects. Ondansetron is often regarded as the most effective treatment among various antiemetics. Due to its lower cost, it is the first 5-HT₃ receptor antagonist and may be given either alone or in combination for prophylaxis.^[7] The efficacy of this substance as an antiemetic is well recognized. The half-life of this substance is rather short, ranging from three to five hours.

MATERIALS AND METHODS

A hospital-based prospective, double-blinded, randomized experiment was done. All patients classified as ASA II who had cesarean section while under spinal anesthesia and met the inclusion criteria. A total of 120 patients were chosen at random to participate in the study. They were divided into two groups, Group OD and Group P, with 60 patients in each group. The allocation of patients to each group was done by selecting a number from a computer-generated random number table, which was only done after obtaining approval from the Institutional Ethics Committee and receiving written informed consent from each patient, who was fully informed about the study procedure.

The patients in the group got the injection prior to spinal anesthesia.

Group P: Palonosetron 0.075mg

Group OD: Ondansetron 6mg + Dexamethasone 8mg

This research included individuals who met the following criteria: ASA grade II, age between 18-45 years, body mass index ranging from 18.5 to 30, and undergoing elective cesarean delivery under spinal anaesthesia. The trial excluded patients with severe cardio-respiratory illness, hepatic and renal disease, subarachnoid block failure, and medication allergy to the study medicines. PONV grading was assessed using the following scale throughout the intra-operative and post-operative period, up to 24 hours: PONV score: 0 indicates the absence of nausea and vomiting, indicating full responders. The PONV score is a scale used to measure postoperative nausea and vomiting. A score of 1 indicates the presence of nausea alone, a score of 2 indicates vomiting once, and a score of 3 indicates vomiting more than once.

RESULTS

The duration of operation between Group OD (66.54 ± 5.63) and Group P (66.41 ± 7.38) was compared. The P-value obtained was 0.14, indicating that there is no statistically significant difference. Being female, a nonsmoker, having postoperative opioid consumption, and having a history of motion sickness or postoperative nausea and vomiting (PONV) are all risk factors for PONV. A comparison of these risk variables was conducted between Group OD and

Group P using the Apfel Score. The computed P-value was 0.26, indicating statistical comparability. Among the patients in Group OD, 14 individuals (23.33%) had nausea throughout the intraoperative time. In Group P, 5 patients (8.33%) reported nausea during the same period. The incidence of intraoperative nausea was found to be significantly higher in Group OD compared to Group P (p Value = 0.03). Out of the 18 patients in Group OD, 33.33% had nausea throughout the post-operative period. Similarly, in Group P, 13.33% of the 8 patients reported experiencing nausea after the operation. Group OD exhibited a significantly higher incidence of post-operative nausea compared to Group P (p Value = 0.02). Out of the 14 patients in Group OD, 23.33% had vomiting during the intraoperative time. In Group P, 3 patients (5%) had vomiting during the same period. The incidence of vomiting during surgery was substantially higher in Group OD compared to Group P (p Value = 0.04). Out of the 15 patients in Group OD, 25% had vomiting during the post-operative period. Similarly, in Group P, 8.33% of the 5 patients had vomiting after the operation. Group OD had a considerably higher incidence of post-operative vomiting compared to Group P (p Value = 0.02). In the intraoperative time, the antiemetic rescue was administered to 15 patients (25%) in Group OD and to 5 patients (8.33%) in Group P. The use of rescue antiemetic during surgery was considerably higher in Group OD compared to Group P (p-value = 0.03). In the post-operative period, a rescue antiemetic was administered to 17 patients (28.33%) in Group OD and 5 patients (8.33%) in Group P. The analysis of post-operative usage of rescue antiemetic showed that Group OD had a significantly greater value compared to Group P (p-value = 0.02). The PONV score was compared

between two groups. A PONV score of 0 was assigned to patients who had no nausea or vomiting throughout the post-operative period, indicating full response. Patients with just nausea were assigned a PONV score of 1, patients who had vomiting once were assigned a PONV score of 2, and patients who vomited more than once during the post-operative period were assigned a PONV value of 3. There were a greater number of complete responders with a PONV score of 0 in Group P compared to Group OD. The number of patients experiencing postoperative nausea and vomiting (PONV) with a score of 1 and 2 was lower in Group P compared to Group OD. None of the patients in Group P had PONV score 3, indicating vomiting occurring more than once, but 6 patients in Group OD did. The computed P value (0.03) obtained from the chi-square test was found to be statistically significant. Group OD had a significantly higher occurrence of nausea compared to Group P throughout both the intraoperative and postoperative periods (p values < 0.05). The occurrence of vomiting was substantially higher in Group OD compared to Group P both throughout the intraoperative and postoperative periods (p values <0.05). The use of rescue antiemetic was much higher in Group OD compared to Group P during the intraoperative and postoperative periods (p values <0.05). The occurrence of headaches was examined between Group OD and Group P throughout both the intraoperative and postoperative periods. The P values were more than 0.05, indicating that the results were statistically equivalent. The occurrence of dizziness was examined between Group OD and Group P throughout both the intraoperative and post-operative periods. The P values were more than 0.05, indicating comparability.

Table 1: Duration of Surgery and Apfel Score

	Group OD		Group P		P-Value
	Mean	Sd	Mean	Sd	
Duration of Surgery	66.54	5.63	66.41	7.38	0.14
Apfel Score	2.33	0.56	2.45	0.35	0.26

Table 2: Intra-operative Nausea and Post-operative Nausea

Nausea				
		Number	Percentage	P-value
Intra-operative Nausea	Group OD	14	23.33	0.03
	Group P	5	8.33	
	Total	19	15.83	
Post-operative Nausea	Group OD	18	33.33	0.02
	Group P	8	13.33	
	Total	26	21.67	

Table 3: Intra-operative Vomiting and Post-operative Vomiting

Vomiting				
		Number	Percentage	P-value
Intra-operative Vomiting	Group OD	14	23.33	0.04
	Group P	3	5	
	Total	17	14.17	
Post-operative Vomiting	Group OD	15	25	0.02
	Group P	5	8.33	
	Total	20	16.67	

Table 4: Intra-operative Rescue antiemetic use and Post-operative Rescue antiemetic use

Rescue anti- emetic required				
		Number	Percentage	P-value
Intra-operative Rescue antiemetic use	Group OD	15	25	0.03
	Group P	5	8.33	
	Total	20	16.67	
Post-operative Rescue antiemetic use	Group OD	17	28.33	0.02
	Group P	5	8.33	
	Total	22	18.33	

Table 5: Comparison of Incidence of Nausea and Vomiting

		Group OD	Group P	P-value
Nausea	Intra-operative	14	5	0.03
	Post-operative	18	8	0.02
Vomiting	Intra-operative	14	3	0.03
	Post-operative	15	5	0.02
Rescue antiemetic use	Intra-operative	15	5	0.03
	Post-operative	17	5	0.02
Headache	Intra-operative	14	3	0.23
	Post-operative	15	5	0.14
Dizziness	Intra-operative	18	5	0.18
	Post-operative	14	8	0.21

Table 6: Comparison of PONV Score

PONV Score	Group OD	Group P	Total
0	39	52	91
1	5	3	8
2	9	5	14
3	7	0	7

DISCUSSION

Due to its cost-effectiveness and ease of administration, spinal anesthesia is the most often used method for performing cesarean sections. In comparison to general anesthesia, it reduces the mortality risk associated with cesarean sections by a factor of sixteen. Spinal anesthesia eliminates the risks often associated with general anesthetic, including the possibility of inhaling stomach contents, difficulties in airway management, respiratory distress in newborns, and the potential for moms to be conscious throughout the process. Another advantage of this method is that it maintains awareness and provides an excellent surgical environment, long-lasting pain relief, a low occurrence of thromboembolism, and a prompt restoration of gastrointestinal function. Additionally, it serves a crucial role in reducing acute post-operative pain and facilitating outpatient anesthesia. Inadequate pain management post-surgery leads to a patient's recovery being prolonged, resulting in an extended hospitalization period and ultimately increasing healthcare costs while also hindering the bonding between mother and child.

Spinal anesthesia has distinct effects on pregnant women compared to non-pregnant women. The distribution of the anesthetic drug into the cerebrospinal fluid is less predictable in pregnant women due to changes in the protein contents and acid-base balance of the cerebrospinal fluid, as well as increased pressure on the spinal canal caused by physiological changes related to pregnancy. In addition, parturient women who get spinal anesthetic for a caesarean section are at risk of feeling emetic

symptoms both during and after the surgery. This might be associated with post-induction hypotension, which can stimulate the vomiting center and lead to brainstem hypoxia.

There are other categories of receptors and their mediators that have been associated with PONV, and the pathophysiology of PONV is complex. The receptors mentioned are: (1) serotonin 5HT3 receptor, (2) dopamine type 2 receptor, (3) histamine type 1 receptor, (4) muscarinic cholinergic type 1 receptor, (5) hormone receptor, and (6) neurokinin type 1 receptor (NK1).

Historical studies indicate that 60-80% of persons who have a cesarean section and are given neuraxial opioids without antiemetic prophylaxis have postoperative nausea and vomiting (PONV). Given the intricate causes and several receptor sites involved in PONV, no treatment can completely prevent or cure the condition, despite the advancement of new antiemetic medications. Instead than using only one antiemetic medicine, it is recommended to use combination treatment with numerous antiemetics that target different receptor sites for patients who are at a high risk for postoperative nausea and vomiting (PONV). Hence, the most recent consensus recommendations advocate for the use of either a solitary, potent antiemetic medicine or a combination of two medications from distinct categories to proactively mitigate postoperative nausea and vomiting (PONV) in people at high risk. In order to assess the efficacy of combining palonosetron with ondansetron and dexamethasone, as well as monotherapy, in preventing postoperative nausea and vomiting (PONV) in patients following caesarean sections, we

have undertaken this randomized double-blind experiment. Due to the higher efficacy of palonosetron alone in reducing the occurrence of postoperative nausea and vomiting (PONV) compared to its combination with dexamethasone, we chose to use palonosetron monotherapy in our study. The FDA has authorized a dosage of 0.075 mg of palonosetron, which has been shown to effectively reduce postoperative nausea and vomiting (PONV) in previous clinical studies. Palonosetron has an onset time of 30 minutes, thus we administered 0.075 mg of the medicine prior to doing the subarachnoid block at the beginning of the procedure.

A dosage of 6 mg of ondansetron, a first-generation 5HT₃ antagonist, was chosen due to its equivalent efficacy in treating and preventing post-operative nausea and vomiting compared to a higher dosage. Moreover, at this specific dose, there will be no adverse consequences. Pearman et al. proposed that pregnant women who are prone to experiencing nausea and vomiting may get more benefits from a dosage of 6 mg ondansetron compared to a dosage of 4 mg ondansetron.^[8] Dexamethasone has been proposed as an effective antiemetic for use after general and pediatric surgery. Moreover, dexamethasone has been proposed as a means to reduce the likelihood of postoperative nausea and vomiting (PONV) after the administration of neuraxial opioids.^[9] According to the research conducted by Tzeng et al., it was hypothesized that dexamethasone might potentially alleviate the nausea and vomiting caused by epidural morphine after a caesarean section.^[10]

Metoclopramide is a benzamide derivative that acts by antagonizing serotonin and dopamine 5-HT₃ receptors. Metoclopramide, a commonly used medicine to prevent nausea and vomiting (antiemetic), is typically and securely given at a dose of 10 mg to those experiencing postoperative nausea and vomiting (PONV). A total of 120 patients were randomly assigned to either Group P or Group OD. There were fifty patients in each group. Group P received intravenous palonosetron at a dose of 0.075mg, whereas group OD received intravenous ondansetron at a dose of 6mg together with dexamethasone at a dose of 8mg, immediately before to spinal anesthesia. The demographic data, including age and weight, were carefully matched across the research groups and were determined to be equivalent.

The current investigation revealed that 25% of patients in group OD and 8.33% of patients in group P required intra-operative rescue antiemetic. Additionally, post-operative rescue antiemetic was needed by 28.33% of patients in group OD and 8.33% of patients in group P. The data clearly indicates that the occurrence of post-surgical nausea and vomiting after surgery is considerably higher in group OD (33.33% and 23.33% respectively) compared to group in P (13.33% and 8.33% respectively). The data also indicate that the same trend is seen in post-operative nausea and vomiting (PONV), with a

significantly greater occurrence in group OD compared to group P. The study conducted by Singh et al compared the effectiveness of granisetron, ondansetron, and palonosetron in reducing nausea and vomiting during surgery. The results indicated that patients in the ondansetron group had a higher incidence of postoperative nausea and vomiting (PONV) within 24 hours compared to the palonosetron group for middle ear procedures under general anesthesia.^[11]

A comparative study conducted by Swaro et.al. investigated the effectiveness of palonosetron, dexamethasone, and a combination of both in preventing postoperative nausea and vomiting (PONV). The study found that 40% of patients in Group D received an intravenous dose of 8 mg of dexamethasone, which was significantly higher than the 27% of patients in Group P who received an intravenous dose of 0.075 mg of palonosetron, and the 20% of patients in Group PD who received an intravenous dose of 4 mg of dexamethasone along with 0.075 mg of palonosetron. In addition, they showed that Group D (30%) needed a higher amount of rescue antiemetic compared to Group P (6%) and Group PD (3%).^[12] Although multiple studies indicate that the occurrence of postoperative nausea and vomiting (PONV) is significantly reduced when palonosetron is used as an antiemetic compared to other antiemetics such as ondansetron, granisetron, and dexamethasone, a study conducted by Kim et al,^[13] demonstrates that palonosetron and ondansetron have similar effectiveness in preventing PONV in high-risk patients undergoing gynecological laparoscopic surgery and receiving IV-PCA with opioids. While opioid-based patient-controlled analgesia was administered to these people, our research did not use opioid-based analgesia.

The research found that the total occurrence of post-operative nausea (PONV Score 1) within 24 hours was 8.33% in patients from group OD and 5% in patients from group P. The prevalence is greater in group OD and the disparity between the two groups was statistically significant. The incidence of vomiting once (PONV Score 2) during a 24-hour period differed considerably between the ondansetron and palonosetron groups, with rates of 15% and 8.33% respectively. The incidence of vomiting more than three times in a 24-hour period (PONV Score 3) was 11.67% in the ondansetron group and 0% in the palonosetron group. This is consistent with the research conducted by Y.E. Moon et.al,^[14] T. Singh et al,^[11] and N. Chakravarty and S.K. Raghuvanshi.^[15]

Our research demonstrates that using palonosetron, a 5-hydroxytryptamine subtype 3 (5-HT₃) antagonist, as an antiemetic prophylactic is a clinically superior method for reducing postoperative nausea and vomiting. Their efficacy and duration of impact exhibit statistically significant differences compared to the combination treatment of ondansetron and dexamethasone.

Research conducted by Tiwari et al,^[16] and Swaro et al,^[17] has determined that both palonosetron alone and palonosetron in conjunction with dexamethasone are effective in treating postoperative nausea and vomiting. However, it was shown that palonosetron alone is not superior to the combination of palonosetron and dexamethasone in this regard. In comparison to previous antagonists, palonosetron, a second generation 5HT3 antagonist, has a higher affinity for the 5HT3 receptor and has a longer plasma half-life of over 12 hours. As a result, it extends the duration of receptor function suppression. Palonosetron distinguishes itself from first-generation antagonists by the following features: Palonosetron has a distinct chemical composition. Unlike previous drugs that had a resemblance to serotonin with their three substituted indole structures, this particular medication has a quinuclidine moiety connected to a fused tricyclic ring structure. Upon binding to the 5HT3 receptor, it exhibits allosteric binding and positive cooperativity, resulting in receptor internalization and a prolonged inhibition of receptor function. Palonosetron effectively inhibits substance P-induced responses, which are the primary cause of delayed emesis resulting from chemotherapy. This is achieved by specifically suppressing the crosstalk between 5HT3 and NK1 receptors. The pharmacologic features of palonosetron may reduce the need for combination treatment, which is often essential for preventing postoperative nausea and vomiting (PONV) in patients at high risk.

Kovac et al. demonstrated that palonosetron 0.075 mg, when compared to a placebo, effectively reduced postoperative nausea and vomiting (PONV) for a duration of up to 72 hours.^[18] During their analysis to determine the appropriate dosage, they found that 0.075 mg of palonosetron was the most effective amount. In high-risk women who received fentanyl-based intravenous PCA, palonosetron 0.075 mg was more effective than ondansetron 4 mg and ramosetron 0.3 mg in preventing PONV during the first 48 hours following lap surgery. This clearly demonstrates that palonosetron alone is superior to the combination of dexamethasone and ondansetron as a prophylactic treatment for managing nausea and vomiting during an elective cesarean surgery performed under spinal anesthesia.

CONCLUSION

According to the results and analysis of the investigation, it can be concluded that giving female patients undergoing elective cesarean surgery a pre-emptive intravenous dose of 0.075mg palonosetron reduces the occurrence of nausea and vomiting during surgery, as well as the need for antiemetic medication, compared to using a combination of 6mg ondansetron and 8mg dexamethasone preemptively.

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