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Original Research Article

Comparison of palonosetron with placebo for preventing post operative nausea and vomiting in patients undergoing surgeries under spinal anaesthesia

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Abstract: Postoperative nausea and vomiting (PONV) is the most common complication of surgery and anesthesia. The incidence of PONV is much higher when spinal anesthesia is administered with intrathecal morphine. Palonosetron is a newer generation 5HT3 antagonist used in the management of Chemotherapy induced Nausea & vomiting. We undertook the study to compare the efficacy of Palonosetron, with placebo in preventing PONV, to assess the severity of PONV, to observe side effects if any and to assess the requirements of rescue antiemetic in the post operative period. 100 ASA 1&2 patients were randomly allocated in 2 groups P & C. Group P received Inj. Palonosetron 1.5ml(0.075mg) iv and Group C received Inj. Saline 1.5ml iv15 minutes before Spinal Anaesthesia. Patients were administered Spinal Anaesthesia in the L3-L4 or L4-L5 space.2.5ml of 0.5% Hyperbaric Bupivacaine with Inj. Morphine 200µg (0.2ml) as per protocol. They were monitored using Nausea score & Vomiting.The Nausea score showed significant differences in the group that received palonosetron as compared to the control group which was more in all through the 24 hour observation period. The severe cases of nausea were significantly more in Group C as compared to Group P.A single intravenous dose of 0.075mg Palonosetron significantly reduces PONV & reduces the need for rescue anti-emetics in first 48hrs, compared to placebo, in patients undergoing infraumbilical surgeries under spinal anaesthesia with Bupivacaine & Morphine.
Keywords: PONV, Palonosetron, intrathecal, morphine.

INTRODUCTION:

Postoperative nausea and vomiting (PONV) is the most common complication of surgery and anesthesia. Both health care professionals and patients rate its avoidance and control of similar importance to that of alleviating pain [1-4]. In addition to patient dissatisfaction [5]. PONV may have adverse consequences such as delayed recovery, unexpected hospital admission and delayed return to work of ambulatory patients. Rarely postsurgical morbidities such as wound dehiscence, pulmonary aspiration, surgical site bleeding and dehydration occur [6]. Nausea occurs in approximately 20%of patients in the recovery room and in 50% thereafter, with vomiting in 5% and 25%respectively [7]. Although children more than 3 years of age are at higher risk than adults,[8]in some high-risk adult populations the incidence of PONV is 80% or more [9,10].

The incidence is up to 25% in regional anaesthesia [11]. This Increases to 35%-75% with intrathecal morphine and it seems to be dose dependent. Intrathecal Morphine (100 to 200mcg) as an adjuvant can provide safe and effective post operative analgesia for up to 24 hours [12]. The most common adverse effects of intrathecal Morphine are PONV, pruritus and urinary retention.

Palonosetron is a unique 5-HT3 receptor antagonist approved for use in the prevention of chemotherapy induced nausea and vomiting. Palonosetron can be distinguished from older 5-HT3 receptor antagonists (ondansetron, dolasetron and granisetron) by its unique chemical structure, greater binding affinity, and substantially longer half-life of approximately 40 h [13, 14].

We undertook the study to compare the efficacy of Palonosetron, with placebo in preventing PONV, to assess the severity of PONV, to observe side effects if any and to assess the requirements of rescue antiemetic in the post-operative period.

METHODOLOGY:

After obtaining the approval from research review board, informed consent was obtained from 100 Adult patients aged between 18 to 50 years of pphysical status ASA I & II undergoing surgery under spinal anaesthesia. Demographic data like age, gender and weight were recorded. The patients were randomly allocated to 2 groups of 50 each. Group P received Inj. Palonosetron 1.5ml (0.075mg) iv and Group C received Inj. Saline 1.5ml iv15 minutes before Spinal Anaesthesia. All patients were administered Tab. Alprazolam 0.5mg on the previous night and were kept nil orally for 6 hours. Patients were administered Spinal Anaesthesia in the L3-L4 or L4-L5 space.2.5ml of 0.5% Hyperbaric Bupivacaine with Inj. Morphine 200µg (0.2ml) as per protocol. The patients were monitored sequentially throughout the surgical procedure using SpO2, ECG, and NIBP.

Postoperatively the following observations were recorded in all the patients. The complete responders (no emesis, no rescue antiemetic). Four point nausea score [Table1]. Number of episodes of vomiting post operatively over 48hrs. Pain (Verbal Analogue Scale)[Table 2].Sedation by Ramsay sedation scale[Table 3]. Complications and side effects if any were noted. Rescue antiemetic Inj. Ondansetron 4mg iv was administered in patients with Nausea > 2 score, Vomiting

Table 1: Four Point Nausea score

0	None
1	Mild
2	Moderate
3	Severe

Table 2: Pain Verbal Analogue Score

0	No Pain
2-4	Mild pain
5-7	Moderate pain
8-10	Worst pain

Table 3: Ramsay sedation Score

1	Anxious or Restless or both
2	Co-operative, oriented and tranquil.
3	Responding to commands.
4	Asleep, brisk response to light, Glabellar tap stimuli or loud auditory stimuli.
5	Asleep, sluggish response to stimuli.
6	Asleep and unarousable.

RESULTS:

The groups were comparable with respect to age, weight and duration of type of surgery [Table 4]

Table 4: Demographic Data

	GROUP P(N=50)	GROUP C (N=50)
Gender		
Male	19	17
Female	31	33
Age		
18-29	16	15
30-39	18	21
40-50	16	14
Mean± SD	36.1 ±11.03	33.82 ±9.58

The duration of surgeries was significantly longer in the group P than C [Table 5]

Table 5: Duration of surgery

Duration of surgery(min)	Group P	Group C	P value
Mean± SD	81.82±21.50	79.62±18.58	0.052

The heart rate and mean arterial blood pressure was comparable in both the groups in the perioperative period. The Pain scores were comparable in both the groups in the perioperative period. The Sedation scores were comparable in both the groups.

The incidence of a complete response (no PONV, no rescue medication) during 0-6 hour in the postoperative period was significantly more in group with palonosetron ($p<0.03$), the incidence during 6-24 hour postoperatively was also significantly more in the group that received palonosetron ($p<0.021$) [Table 6].

Table 6: Complete Responders

Complete Responders	Group P	Group C	P Value
0-6 Hrs	38	24	0.03
6-24 hrs	40	31	0.021
24-48 Hrs	47	45	0.031

The Nausea score showed significant differences in the group that received palonosetron as compared to the control group which was more in all through the 24 hour observation period. The severe cases of nausea were significantly more in Group C as compared to Group P. [Table 7]

Table 7: Nausea Score

NAUSEA	0-6hrs Grp P	0-6hrs Grp C	Pvalue	06-24hrsGroup P	06-24hrsGroup C	Pvalue	24-48Hrs Group P	24-48Hrs Group C	Pvalue
MILD	03	01	0.02	04	02	0.011	02	02	0.523
MODERATE	02	03	0.05	03	06	0.012	01	01	0.502
SEVERE	02	09	0.01	00	04	0.01	00	01	0.602

The incidence of vomiting also was more in the control group as compared to the group P especially during 0-6 hr period. [table8]

Table 8: Vomiting (No. of Episodes)

Vomiting	Grp P	Grp C	P Value
0-6 hrs	5	13	0.02
6-24hrs	3	7	0.04
24-48 hrs	1	1	0.86

The rescue antiemetic requirement at 48 hrs was also significantly more in group C as compared to Group P [table 9]

Table 9: Rescue antiemetics at 48 hrs

Rescue antiemetics	Group P	Group C	P Value
Total No	11	30	<0.05

The incidence of minor side effects like urinary retention, pruritis, and headache was comparable in both the groups. [Table 10]

Table 10: Side effects

Side effects	Group P	Group C
None	26	30
Urinary retention	6	9
Pruritis8	8	8
UR+ Pruritis	5	3
Headache	4	0

DISCUSSION:

Postoperative period is associated with variable incidence of nausea and vomiting depending on the duration of surgery, the type of anaesthetic agents used (dose, inhalational drugs, opioids), smoking habit etc[15]. 5-HT3 receptor stimulation is the primary event in the initiation of vomiting reflex [16]. These receptors are situated on the nerve terminal of the vagus nerve in the periphery and centrally on the chemoreceptor trigger zone (CTZ) of the area postrema [17]. Anaesthetic agents initiate the vomiting reflex by stimulating the central 5-HT3 receptors on the CTZ and also by releasing serotonin from the enterochromaffin cells of the small intestine and subsequent stimulation of 5-HT3 receptors on vagus nerve afferent fibres [17].

According to Candiotti *et al.;* a dose-dependent increase in complete response was observed in 0-24hrs for the placebo, Palonosetron 0.025mg, 0.05 mg, and 0.075 mg groups of 26%, 33%, 39%, and 43% respectively in day care laparoscopy [18].

Dhurjoti Prosad Bhattacharjee *et al.;* compared Palonosetron & Granisetron in preventing PONV for laparoscopic Cholecystectomy under GA in female patients. Complete response rates of Palonosetron & Granisetron over 0-3hrs, 3-24hrs , 24-48hrs were 90%, 90%, 90% & 82.9% 74.3 & 97.1% respectively [19].

Kovac *et al.;* concluded a single iv dose of 0.075mg Palonosetron effectively reduces severity of PONV compare to Placebo & lower doses were not so effective (0.025, 0.050mg) [20].

Our study demonstrate that the antiemetic efficacy of palonosetron for preventing PONV after Spinal anaesthesia with intrathecal morphine is very effective for getting a complete response (no PONV, no rescue medication) for 24-48 hours. This suggests that palonosetron has an antiemetic effect which lasts significantly longer than no medication. The reason for the better effectiveness of palonosetron may be related to the half-lives(palonosetron 40 hrs) and/or the binding affinities of 5-HT3 receptor antagonists (palonosetron interacts with5-HT 3 receptors in an allosteric, positive cooperative manner)7,8.

CONCLUSION:

A single intravenous dose of 0.075mg Palonosetron significantly reduces PONV & reduces the need for rescue anti-emetics in first 48hrs, compared to placebo, in patients undergoing infraumbilical surgeries under spinal anaesthesia with Bupivacaine & Morphine.

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