



# Intravenous Palonosetron for Attenuation of Hypotensive Response and Bradycardia during Spinal Anaesthesia

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## Abstract

**Aim:** This study was conducted to evaluate the role of intravenous (IV) palonosetron during spinal anesthesia. **Method:** A total of 100 patients undergoing elective lower limb and lower abdominal surgeries were randomly divided into two groups. Group P was given 0.25mg palonosetron diluted in 10 ml normal saline slowly before spinal anesthesia. Group S was given 10 ml of normal saline slowly before spinal anesthesia. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation (SpO<sub>2</sub>) were monitored at an interval of 2 minutes for the initial 20 minutes, then at an interval of every 5 minutes till the end of the surgery. Time to reach the maximum sensory level and its regression two levels below and then till S1 was noted. The incidence of nausea, vomiting, shivering, use of intravenous mephenteramine, level of motor block and its regression were also recorded. **Results:** Decreases in HR were more observed in Group S and the differences were statistically significant at 25 min [p=0.048] and 30 min [p=0.047]. The decrease in MAP were observed more in Group S and statistically significant difference noted at 20 min [p = 0.026], 25 min [p = 0.046] and at 30 min [p = 0.047]. The use of intravenous mephentermine [p = 0.009] and development of nausea [p = 0.049] were significantly more common in Group S, Sensory block regression was faster in group P. [p=0.054]. **Conclusion:** Premedication with 0.25mg IV palonosetron before spinal anesthesia reduces hypotension, bradycardia.

**Keywords:** Spinal Anesthesia, Hypotension, Bradycardia, Side effects.

## Introduction

Spinal anesthesia is among one of the most popular and widely used anesthetic technique. Its short learning curve and cost effectiveness makes it a unique procedure that provides complete sensory and motor block along with postoperative analgesia [1]. Various complications occur during and after administration of spinal anesthesia. Most common side effects associated is hypotension and bradycardia, occurring in 33% and 13% of cases, respectively [2,3]. Hypotension which develops after spinal anesthesia is attributed to various factors [4,5] one among which is Bezold-Jarisch Reflex [BJR] [6]. It is mediated through 5-HT<sub>3</sub> receptors. The HT<sub>3</sub> receptors are located centrally in the chemoreceptor trigger zone and peripherally on cardiac vagal afferent fibers along with in the wall of ventricles. These receptors cause an increased vagal output in efferent limb when stimulated by serotonin, which is released during hypovolemic states, causing an increased parasympathetic activity and finally precipitating as bradycardia and hypotension [7]. Palonosetron is a 5-HT<sub>3</sub> receptor

antagonist. It is currently approved for the treatment of nausea and vomiting caused by chemotherapy, radiation therapy and surgery. While going through the literature it was found that very few studies have been performed for evaluating the role of palonosetron in the dose of 0.25 mg, in attenuating hypotension and bradycardia after spinal anesthesia and a knowledge gap exists. Hence this study was planned to evaluate the effect of i.v. palonosetron used as premedication, to attenuate spinal anesthesia induced hypotension and bradycardia.

## Material and Method

It is a prospective, randomized double blind study. After obtaining approval of Ethical Committee of the institution and Drug Controller General of India, informed written consent from each patient was taken. A total of 110 patients of age group more than 18 years, belonging to ASA grade I and II physical status scheduled for elective lower limb and lower abdominal surgeries were enrolled for the study. Patients with unstable vital parameters,

deranged coagulation, history of allergic reaction to 5HT3 antagonist or local anesthetic agents, hypertensive patient, patients with cardiac diseases, patients on selective serotonin reuptake inhibitors and patients who refused for spinal anesthesia or had inadequate effect of spinal block were excluded from the study. A total of 10 patients were excluded and remaining 100 patients were randomized using slipped number opaque slips (SNOS). [Figure 1] All patients were kept fasting according to standard NPO guidelines. In the operating room, baseline values of heart rate, noninvasive blood pressure and pulse oximetry [SpO2] were recorded. A peripheral 18-G i.v. cannula was secured, and the patients were co-loaded with 10 ml/kg warm Ringer’s lactate solution. Patients were then randomized into two groups. Group P [Palonosetron group] had 50 patients and Group S [placebo group] also had 50 patients. The patients in Group P received 0.25 mg intravenous palonosetron hydrochloride diluted in 10 mL of saline, given over two minutes. The patients in Group S were administered 10 mL of normal saline [0.9% NaCl] over a period of two minutes. These drugs were given 15 minutes prior to administering spinal anesthesia. After injecting the drugs under all aseptic precautions, patient in sitting position, lumbar puncture was done via midline approach in L3-L4 intervertebral space with a 25 G Quincke type spinal needle. After confirmation of a clear and free flow of CSF, 3 mL of 0.5% hyperbaric bupivacaine was administered over 15

seconds. Patients were immediately turned to supine position. A resident anesthesiologist blinded to the study drug solutions given intravenously prior to the spinal anesthesia, measured and recorded the hemodynamic parameters, presence of nausea, vomiting, shivering, level of sensory and motor block and its regression and the use of i.v. mephentermine. Vital signs were measured at 2 min intervals up to 20 min after intrathecal injection and changed to 5 min interval until the end of surgeries. The primary outcome variables were HR and MBP after spinal anesthesia. The secondary outcome variables were changes of SBP, DBP, level of sensory and motor block, amount of mephentermine used, incidence of nausea and vomiting. The upper level of sensory block was assessed using a short beveled 26-gauge needle by bilateral loss of pinprick sensation every 2 min till the sensory level became fixed at two consecutive times, thereafter, the patients were evaluated every 15 min till the sensory level regressed to two level below the maximum level reached and then till S1. Also, motor block was assessed every 2 min by the modified Bromage scale till the complete motor block achieved, then every 15 minutes till complete motor recovery occurred. Hypotension was defined as a decrease in MAP <20% of the baseline, which was treated immediately with intravenous mephentermine 3 mg. Bradycardia [heart rate <50 beats/min] was treated with intravenous atropine 0.5 mg.

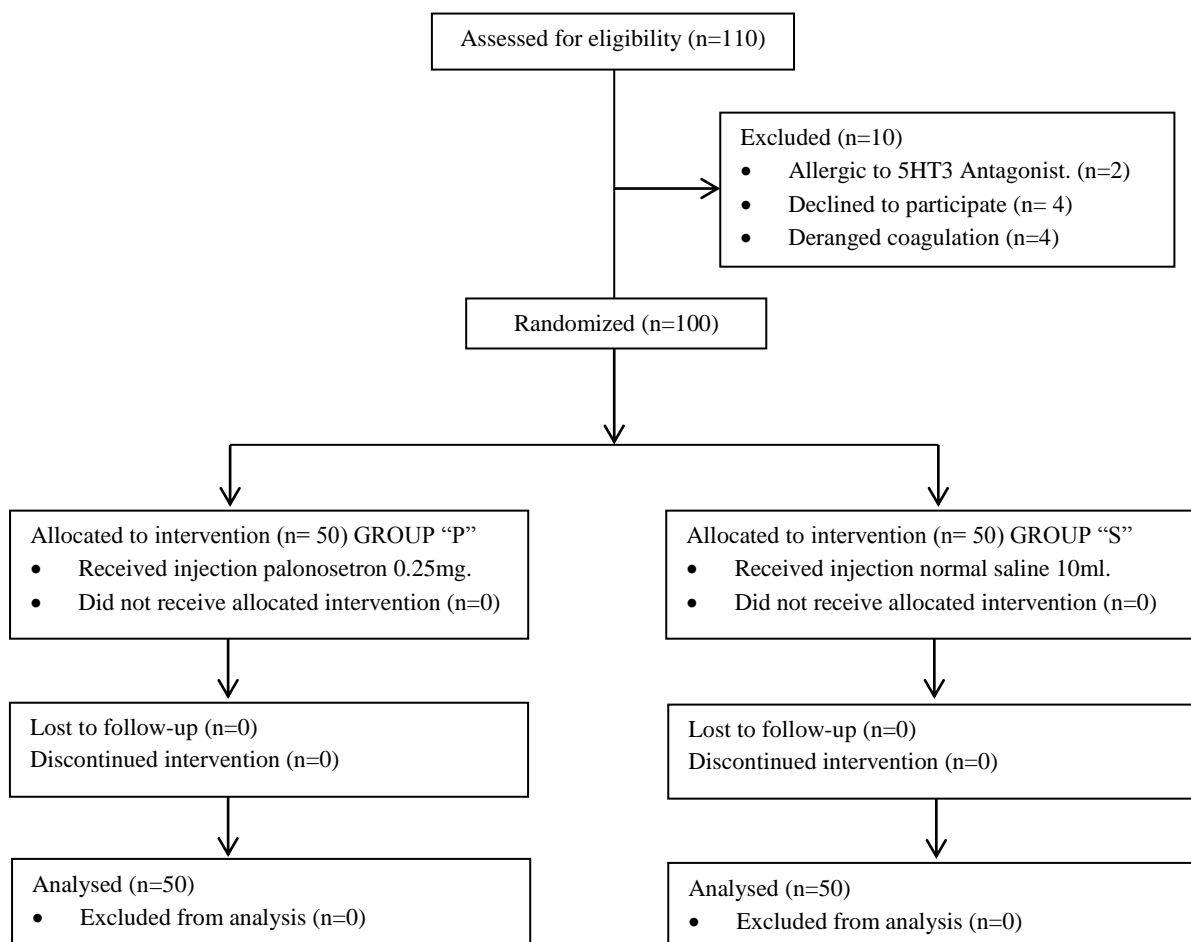


Figure 1: Consort diagram showing patient flow.

## Results

In the present study, there were no significant differences between the two groups in regards to the demographic profile of the patients [age, weight, and height] and the procedure duration. [Table 1]. There were significant differences noted among the groups as

regard the basal MAP and HR. Decreases in HR were more common in Group S as compared to Group P and the differences was statistically significant at 25 min [Group P: 88.42 ± 15.57 vs. Group S: 73.76 ± 12.28 beats/min, p=0.007] and 30 min post

administration of spinal anesthesia [Group P: 84.06 ± 16.69 vs. Group S: 71.92 ± 13.38 beats/min, p=0.043]. [Table 2].

Decreases in MAP were observed in both groups but more so in Group S. Statistically significant differences were observed at 20 min [Group P 89.30 ± 10.90 mmHg vs. Group S 76.78 ± 8.83 mmHg, p = 0.031], 25 min [Group P 88.88 ± 10.96 mmHg vs. Group S 78.76 ± 9.16 mmHg, p = 0.001] and at 30 min [Group P 88.94 ± 10.52 mmHg vs. Group S 77.85 ± 9.65 mmHg, p = 0.003]. [Table 3].

The mean time to reach maximum sensory level was slightly longer in group P [16.42 ± 2.91 min] as compared to group S [15.48 ± 3.84 min] but this difference was not statistically significant [p>0.05]. Also the two segment regression of block level that is time between the maximum sensory level reached to its

regression to two level below was faster in Group P [68.3± 21.2] as compared to Group S [83.8±21.5]. [Table 4]

The number of times ephedrine was given in response to drop in B.P over different phases of the study after spinal block was higher among patient in group S as compared to that in group P. [p value 0.009][Table 5] The development of nausea [P = 0.049] were significantly more common in Group S. Time to reach modified Bromage 3 motor block and time to motor regression to modified Bromage 0 was statistically comparable among both the groups . There were no significant changes in oxygen saturation in either group. There were no significant differences noted in the occurrence of shivering. No patient experienced vomiting or underwent conversion to general anesthesia.

**Table 1: Demographic data**

	Age(years)	Height(cm)	Weight(kg)	Procedure duration(minutes)
Group S	42.36±11.79	157.26±9.23	59.42±9.83	58.9±12
Group P	40.8±10.91	157.9±9.17	58.22±9.57	56.7±13.06
p Value	0.49	0.4	0.54	0.39

**Table 2: Heart Rate**

	Group S (beats/min)	Group P (beats /min)	p value
0 minutes	94.26 ± 14.40	92.64 ± 12.73	0.5526
25 minutes	73.76 ± 12.28	88.42 ± 15.57	0.007
30 minutes	71.92 ± 13.38	84.06 ± 16.69	0.043

**Table 3: Mean Arterial Pressure (mmhg)**

	Group P (mmHg)	Group S (mmHg)	p Value
0 min	100.55 ± 11.10	99.58 ± 6.81	0.602
20 min	89.30 ± 10.90	76.78 ± 8.83	0.031
25 min	88.88 ± 10.96	78.76 ± 9.16	0.001
30 min	88.94 ± 10.52	77.85 ± 9.65	0.003

**Table 4: Block timings**

	Group S (minutes)	Group P(minutes)	p Value
Time to reach maximum sensory level block (min)	15.48 ± 3.84	16.42 ± 2.91	0.175
Time to two segment regression of block (min)	83.8±21.5	68.3± 21.2	0.054

**Table 5: Cumulative doses of ephedrine used in both the groups**

Group	N	Mean ± Standard Deviation (Mg)	p Value
S	50	20.03±4.608	0.009
P	50	8.16±2.425	

## Discussion

Spinal anesthesia is an excellent technique to implement intra-operative anesthesia and a safe alternative to general anesthesia in many situations. Though it has numerous advantages, spinal anesthesia does have adverse effects, which mainly include unwanted cardiovascular effects like hypotension and bradycardia. Hypotension is mainly due to decreased vascular resistance caused by blockade of sympathetic nerves, bradycardia due to relative dominance of the parasympathetic system. In our study a significant difference between heart rate among both the groups S & P was found. Decrease in heart rate was more significant in group S as compared to group P, with mean heart rate in the group S always lower than mean heart rate in group P over a period of 60 minutes. Similar findings were elucidated by Martinek RM and Heesen M where a decrease in heart rate was attenuated by use of a 5HT3 antagonist [8,9]. In contrast Samarah WK et al in their study on effect of ondansetron administration prior to spinal anesthesia in

patients undergoing elective caesarean section, found that heart rate at minute 1 was significantly more in control group than in ondansetron group. This difference in findings from ours could be due to difference in the study population as they included only pregnant women [10].

In 1998 White CM et al in his study on a hemorrhagic rabbit model concluded that granisetron was significantly more effective at preventing inappropriate heart rate slowing as compared to normal saline [11]. Similar findings were reported by Eldaba AA et al in their study on granisetron in caesarean section [12].

In a study done by Jung Ju Choi et al on palonosetron use before spinal anesthesia in patients undergoing orthopedic surgery concluded that intravenous palonosetron [0.075 mg] given prior to administration of spinal anesthesia may not decrease hypotension and bradycardia occurring after spinal anesthesia. They attribute it to palonosetron having different structure with allosteric binding so that its effects persisted beyond its binding to the 5-HT3 receptor at

the cell surface [13,14]. However the dose of palonosetron used in their study was much smaller as compared to our study which could be the probable reason for the difference in the results. Similarly, in a study by Choudhary J et al on comparison of i.v palonosetron and iv granisetron concluded that premedication in form of granisetron 1 mg and Palonosetron 0.075 mg before spinal anesthesia does not attenuate the hemodynamic changes in patients undergoing abdominal hysterectomy [15].

In our study, a statistically significant difference was observed in mean arterial pressure between group P and group S. The decrease in blood pressure was more profound in group S as compared to group P. This is similar to the findings of Sahoo T et al, who in their study concluded that ondansetron 4 mg, given 5 min prior to subarachnoid block decreases hypotension and vasopressor use in patients undergoing elective caesarean section. Tatikonda CM et al and Palmese S et al also found that the minimal values of mean arterial pressure obtained were significantly higher in the ondansetron group as compared to the placebo group [16,17,18].

In this study, we found that palonosetron given i.v before spinal anesthesia resulted in faster sensory level regression. This is in contrast to results found by Kim MH et al, who studied effects of i.v. palonosetron on spinal anesthesia and concluded that i.v palonosetron in dose 0.075mg had no effect on sensory block level and recovery from it. These findings may be attributable to the smaller dose of palonosetron used in their study which is having a sufficient effect on chemoreceptor trigger zone but being insufficient to affect the bupivacaine in the intervertebral space [19]. Effects similar to our study were concluded by Mowafi et al. who studied the effects of IV granisetron on the sensory and motor blockade produced by intrathecal bupivacaine [20] and with Fassoulaki et al and Rashad MM et al who studied the effects of IV ondansetron on the spinal anesthesia [21,22].

We also found that the amount of ephedrine used was significantly more in group S as compared to group P. Similar results were found by Xiao F et al where i.v ondansetron significantly reduced the dose of phenylephrine infusion in cesarean deliveries [23].

## Conclusion

Based on our observations and in comparison with prior studies in the literature we submit that Intravenous palonosetron given in the dose of 0.25 mg prior to induction of spinal anesthesia reduces fall in heart rate and mean arterial pressure. There was also significant decrease in ephedrine consumption and in the incidence of postoperative nausea and vomiting. No major side effects were seen after administration of palonosetron. However, we recommend more studies with larger sample size to substantiate the current findings.

## Ethics approval and consent to participate

Ethical committee approval was taken from the institute ethical board. Reg No ESIPGIMSR-IEC/2012010.

## List of abbreviations

HR Heart Rate  
B.P Blood Pressure  
MM HG Milli meter of Mercury  
MG Milli Gram  
I.V Intravenous

## Data Availability

All the data compiled in the manuscript is with the medical record department of the institute where the study has been done.

## Conflicts of Interest

None

## Funding Statement

None

## Authors' contributions

SS supervised the work and gave important intellectual inputs.

YR did data collection and compilation.

AS did paper drafting and editing.

All authors read and approved the final manuscript.

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