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Original Research Article

Effects of Intravenous Ondansetron and Granisetron on Hemodynamic Changes and Motor and Sensory Blockade Induced by Spinal Anesthesia in Parturients Undergoing Cesarean Section

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Conflict of interest: Nil

Abstract:

Background: For caesarean section mothers, spinal anaesthesia provides several benefits, although hypotension is thought to be the most common consequence and can be treated with a variety of methods. Giving a serotonin receptor antagonist before spinal anaesthesia is one of these therapies. The study objectives are to investigate the effects of two serotonin receptor antagonists on the hemodynamics, sensory, and motor blockade brought on by intrathecal bupivacaine in caesarean section patients.

Methods: Twenty pregnant women in each group, with an ASA I-II physical state, underwent elective caesarean sections while receiving intrathecal bupivacaine spinal anaesthesia. Five minutes before spinal anaesthesia, group O was given an intravenous dose of 4 mg ondansetron diluted in 10 ml of normal saline, administered over a one-minute period. Group G was given the same dose of 1 mg granisetron, while group S received 10 ml of normal saline. We measured the average arterial blood pressure, heart rate, usage of vasopressors, sensory, and motor blockage.

Results: While there was considerably faster sensory recovery in group G than groups O and S ($P < 0.05$), decreases in mean arterial pressure were significantly smaller in group O than groups G and S with reduced vasopressor use. Actually, groups O and G experienced significantly lower rates of nausea than group S ($P = 0.008$).

Conclusion: In parturient females undergoing elective caesarean section, intravenous 4 mg of ondansetron given before subarachnoid block significantly reduced both the hypotension and the doses of vasopressor used, whereas intravenous 1 mg of granisetron given before subarachnoid block induced a faster rate of sensory recovery compared to both the ondansetron and the saline groups, with no significant differences between the latter two groups.

Keywords: Intrathecal Bupivacaine, Ondansetron, Granisetron, Parturients.

Introduction

Due to numerous benefits, such as minimising the risks of general anaesthesia, providing better postoperative pain relief, and allowing the patient to remain awake to witness the birth of her child, many anesthesiologists prefer to administer spinal anaesthesia to women who will have caesarean section[1]. Although spinal or epidural anaesthesia can be used to achieve this, spinal anaesthesia is a straightforward method with a low failure rate, quick onset, and low medication dose[2].On the other hand, the anaesthetist is having issues including hypotension, bradycardia, and block failure after administering spinal anaesthesia. However, hypotension is the most common consequence, with an incidence of roughly 55–100%[3,4]. Additionally, hypotension poses a risk to both the mother and the foetus because it can result in the woman's loss of consciousness, aspiration, and even cardiac death, as well as placental hypoperfusion, which can create foetal issues[5]. After spinal anaesthesia, there are numerous ways to reduce maternal hypotension, including fluids, drugs, and physical techniques like positioning, leg bindings, etc. [1]. This study focused on two drugs that can reduce the likelihood of post-spinal anaesthesia maternal hypotension. They are 5-hydroxytryptamine 3 (5-HT3) receptor antagonists that are selective for ondansetron and granisetron[6]. These receptors are situated centrally in the chemoreceptor trigger zone and

peripherally as cardiac chemoreceptors on the cardiac vagal afferent[7]. The Bezold-Jarisch reflex (BJR), on the other hand, is one of the mechanisms that explains why hypotension can occur following spinal anaesthesia through serotonin and decreased blood volume[7–10]. Reduced venous return stimulates cardiac chemo receptors in the heart, increasing parasympathetic activity while decreasing sympathetic activity, causing vasodilation and bradycardia[11]. A selective 5-HT3 receptor antagonist can block the antinociceptive effects of 5-HT3 receptors, which are also found in the spine [12]. On the other hand, prior research demonstrated that intrathecal bupivacaine significantly increased the amount of serotonin in cerebrospinal fluid, and intrathecal lidocaine's sensory block was counteracted by ondansetron [13,14]. This study compared the effects of ondansetron and granisetron, two serotonin receptor antagonists, on spinal-induced hypotension, bradycardia, sensory block, and motor block following intrathecal hyperbaric bupivacaine in expectant mothers undergoing caesarean sections.

Material and Methods

This comparison study was carried out in Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, from October 2022 to March 2023 after receiving written consent from each patient. This prospective study included 60 pregnant women with ASA I-II physical status who were 20 to 40 years old and planned for elective caesarean sections. Women who had a neuraxial block contraindication (such as abnormal hemodynamics, coagulation defects, a history of hypersensitivity to granisetron or local anaesthetic agents, hypertensive disorders of pregnancy, cardiovascular insufficiency, on selective serotonin reuptake inhibitors or migraine medications), or who refused to participate in the study, were not included in the study.

All patients were asked to fast for 6 to 8 hours before to surgery during the preanesthetic appointment. A peripheral 18-gauge intravenous cannula was placed before noninvasive blood pressure (BP), pulse rate, and pulse oximetry (SPO2) values were taken. All patients received lactated Ringer's solution (20 mL/kg/h) preloaded over 30 minutes and intravenous ranitidine (1 mg/kg). Three equal groups of twenty patients each were created by randomly dividing the patients. Groups G and S each got intravenous injections of 1 milligramme of granisetron diluted in 10 ml of normal saline five minutes before to the start of the subarachnoid block, while Group O received an intravenous injection of 4 mg of ondansetron diluted in 10 ml of normal saline. Noninvasive blood pressure, electrocardiogram, and pulse oximetry baseline readings were taken in the operating room. Ondansetron, granisetron, or saline in the amount of 10 ml was administered intravenously. Five minutes later, the patient was placed in the sitting position and given spinal anaesthesia at the level of L3-4 or L4-5 using a 25-gauge Quincke needle to administer 2 ml of 0.5% hyperbaric bupivacaine. This was done after the cerebrospinal fluid was allowed to flow freely without barbotage. Till the end of the operation, intravenous lactated Ringer's solution was administered at a rate of 15 ml/kg/h.

The haemodynamics, presence of nausea, vomiting, shivering, or insufficient analgesia were monitored and documented by a resident anesthesiologist who was blinded to the study medication solutions. From the beginning of spinal anaesthesia, mean arterial pressure (MAP), heart rate (HR), and oxygen saturation (SPO2) were monitored at 2-min intervals for 20 minutes, then every 5 minutes until the end of the procedure. Additionally, the midclavicular line was pinprick-tested bilaterally every two minutes with a short, bevelled 25-gauge needle to determine the upper sensory level, which is the highest sensory level. The patients were then assessed every 15 minutes to determine when the upper sensory level had returned to S1. Additionally, motor block was measured using the modified Bromage scale every 2 minutes until it was fully blocked, and again every 15 minutes until it was fully recovered.

Modified Bromage scale [15]:

- 0 = able to move hip, knee, ankle, and toes.
- 1 = unable to move hip, able to move knee, ankle, and toes.
- 2 = unable to move hip and knee, able to move ankle and toes.
- 3 = unable to move hip, knee and ankle, able to move toes.
- 4 = unable to move hip, knee, ankle and toes.

Decrease in MAP more than 20% of the preoperative value was treated with i.v. 6 mg ephedrine. Decrease in HR to less than 50 beat/min was treated with 0.5 mg atropine intravenous. Shivering was treated with i.v. 25 mg tramadol. Nausea and vomiting were treated with i.v. 10 mg metoclopromide. Fentanyl 50 mg intravenously was used to relieve pain, but if it continued the patient was regarded to have failed spinal anaesthesia and was removed from the trial. Using SPSS version 19, data were verified, inputted, and analysed. For comparison across groups, data were presented as mean±SD for quantitative variables, number and percentage for categorical variables, chi-squared (X2) or fisher exact tests, ANOVA (F test), and LSD (where ANOVA was significant). Statistics were deemed significant at $P < 0.05$.

Results

Regarding demographic information (age, weight, and height) and the length of the procedure, there were no appreciable variations between the two groups in the current investigation (Table 1).

Table 1: Demographic data and Procedure duration

	Age (years)	Height (cm)	Weight (kg)	Procedure duration (mm)
Group O (n=20)	32±5	167±5	79±10	63±7
Group G (n=20)	30±5	165±5	75±11	63±9
Group S (n=20)	31±7	167±6	74±13	60±8
p-value	0.56	0.45	0.43	0.47

Data represented by Mean±SD, No significant differences between the 3 groups, Group O = Ondansetron, Group G = Granisetron, Group S = Saline.

Regarding the baseline MAP and HR, there were no significant differences between the groups. However, there was a significant difference between group O and both groups G and S at 5, 10, 15, 20, and 25 minutes with regard to the decrease in MAP.

After 25 minutes, there were no significant differences among the three groups, while there were negligible differences between groups G and S (Table 2).

Table 2: Changes in Mean Atrial Pressure (MAP) in 3 groups

	BP (mmHg) Basal	BP (mmHg) 5 min	BP (mmHg) 10 min	BP (mmHg) 15 min	BP (mmHg) 20 min	BP (mmHg) 25 min
Group O (n=20)	100±10	82±12	84±4	84±4	92±6	93±5
Group G (n=20)	98±10	75±8*	74±9*	78±3*	86±6	87±6
Group S (n=20)	99±8	80±12*	82±6*	80±5*	90±9	90±8
p-value	0.8	0.03	0.02	0.001	0.002	0.013

*Compared with group O ($P < 0.05$).

The three groups' HR did not significantly differ from one another. Between the three groups, there was no discernible change in the sensory level's fixation time.

However, group G saw two substantial segment regressions more quickly than groups S and O (64±20 vs. 80±24 min and 73±27 min, respectively). Additionally, group G experienced faster regression to T10, T12, and S1 than groups O and S, while there were no discernible differences between groups O and S.

The time to the maximum motor block, the time to motor recovery by one level, and the time to complete motor recovery were not significantly different between the three groups, as shown in (Table 3).

Table 3: Spinal block timing course

	Group O	Group G	Group S	p-value
Time to upper sensory level block (min)	12.1±2.3	11.2±2.9	11.9±3.8	0.6
Time to two segment regression (min)	72.8±17.1*	64.3±20.2	79.8±23.5*	0.05
Time to sensory regression to T10 (min)	102.9±25.0*	98.2±21.1	115.7±20.1*	0.037
Time to sensory regression to T12 (min)	126.2±26.3*	107.8±18.6	124.8±15.6*	0.007
Time to sensory regression to S1 (min)	181±31.9*	159.8±21.4	179.5±24.6*	0.005
Time to modified Bromage scale = 4 (min)	10.1±1.9	10.9±2.0	9.8±1.8	0.2
Time to modified Bromage scale = 3 (min)	113.4±21.9	109.3±27.2	119.0±15.1	0.5
Time to modified Bromage scale = 0 (min)	168.2±28.4	159.3±33.8	170.2±25.4	0.32

*Significant compared with group G ($P < 0.05$).

Oxygen saturation did not change significantly in all groups. Table 4 shows that there were no statistically significant variations in the frequency of discomfort, bradycardia, or shivering. However, 10% of patients in group S and 15% of patients in group G experienced bradycardia, which was managed with atropine (0.5 mg, which can be repeated as often as every 3–5 minutes if necessary, up to a maximum total dose of 3 mg). Despite the fact that no patients in any group experienced vomiting, group S had a significantly higher percentage of cases of nausea than groups G and O (40% vs. 10% and 5%, respectively), but there were no other noteworthy differences between groups G and O.

Additionally, groups S and G significantly more

frequently used ephedrine than group O (35% and 25% vs. 5%, respectively). Two cases of unsuccessful spinal anaesthesia were generalised anaesthetized and excluded from the study.

Table 4: Incidence of side effects of the spinal anesthesia in 3 groups

	Shivering n (%)	Pain n (%)	Nausea n (%)	Bradycardia n (%)	Ephedrine use n (%)
Group O (n=20)	2(10.0%)	2(10.0%)	1(5.0%)*	0(0)	1(5.0%)*
Group G (n=20)	2(10.0%)	3(15.0%)	2(10.0%)*	3(15.0%)	5(25.0%)
Group S (n=20)	5(25.0%)	3(15.0%)	8(40.0%)	2(10.0%)	7(35.0%)
p-value	0.3	0.86	0.008	0.21	0.05

*Significant compared with group S ($P < 0.05$).

Discussion

One regional approach frequently used with caesarean section patients to decrease the hazards associated with general anaesthesia is spinal anaesthesia [2]. The most common risk associated with this procedure is hypotension brought on by practically total sympathetic block, as the level of block needs to be at T4 for effective coverage, as well as the impact of a gravid uterus on venous return [2,16,17].

Hypotension, which is regarded as one of the most dangerous outcomes of spinal anaesthesia, was studied in several ways in a trial to prevent it[2]. However, because both drugs have the same mechanism of action, this study compared the effects of ondansetron and granisetron, two potent antiemetics, on blood pressure fluctuations, sensory block, and motor block caused by spinal anaesthesia given to C.S. parturients. Subarachnoid block causes a reduction in systemic vascular resistance, which in turn causes blood to pool causing hypotension. The systemic response to hyper- and hypovolemia is caused by BJR, which is initiated by cardiac mechanoreceptors[18–20]. As a result, vasodilatation, hypotension, and bradycardia caused by serotonin-induced BJR contribute to the systemic response to spinal anaesthesia [10,21].

Our results were consistent with those of Sahoo et al.[22], who conducted research on ondansetron and found that it decreased spinal-induced hypotension when administered intravenously to C.S. patients prior to spinal anaesthesia. Contrarily, Tsikouris et al [23] investigation of granisetron revealed that it reduced heart rate and blood pressure changes brought on by BJR during the head-up tilt table test. This study inspired the authors of the current investigation to compare granisetron and ondansetron with regard to their hemodynamic effects on C.S. parturients under spinal anaesthesia. Granisetron, however, was shown to have no effects on the hemodynamic variables, which is in accordance with Mowafi et al. [12]. According to animal research, serotonin inhibits excitatory transmitters and increases inhibitory transmitters in the spinal cord, which has an antinociceptive effect[24,25]. According to Giordano and Dyche [26], serotonin antagonists lower the nociceptive threshold as a result. It was discovered that IV ondansetron did not affect the sensory or motor block of intrathecal bupivacaine, contrary to the findings of Fassoulaki et al.[14], who discovered that systemic ondansetron enhanced the sensory block regression after intrathecal lidocaine. This finding was made when the effects of ondansetron and granisetron on sensory regression and motor block of subarachnoid anaesthesia were studied.

Contrarily, we discovered in this trial that administering IV granisetron before intrathecal bupivacaine sped up the sensory regression but had no impact on the motor block. This finding was in line with that of Mowafi et al.[12] who investigated the effects of IV granisetron on the sensory and motor blockade brought on by intrathecal bupivacaine as well as Fassoulaki et al.[14] who investigated the effects of IV ondansetron on the spinal anaesthesia brought on by lidocaine. Despite belonging to the same class and having a similar mechanism of action, ondansetron and granisetron have different effects. This could be because ondansetron acts on mixed receptors while granisetron has a high affinity for 5-HT3 receptors but a low affinity for other 5-HT receptors, adrenergic, histaminic, dopaminergic, or opioid receptors [6,28].

Conclusion

In parturient females undergoing elective caesarean section, intravenous 4 mg of ondansetron given before subarachnoid block significantly reduced both the hypotension and the doses of vasopressor used, whereas intravenous 1 mg of granisetron given before subarachnoid block induced a faster rate of sensory recovery compared to both the ondansetron and saline groups, with no significant differences between the latter two groups.

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