Effect of Systemic Granisetron in the Clinical Course of Spinal Anesthesia with Hyperbaric Bupivacaine for Outpatient Cystoscopy

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Abstract

Background: The goals of this study are evaluation the effect of intravenous (IV) granisetron on the duration of sensory and motor block produced by intrathecal hyperbaric bupivacaine and also post-operative nausea and vomiting in patients undergoing outpatient cystoscopy.

Methods: 62 patients, undergoing cystoscopy received either 3 mg IV granisetron or placebo 15 minutes before the spinal block. Sensory and motor block were assessed after the intrathecal injection of bupivacaine every 2 minutes until the maximum block was achieved and thereafter every 15 minutes until recovery from the sensory and motor block.

Results: Demographic data were not statistically different in the study groups. Duration of sensory and motor block were also not statistically different between the study groups (P = 0.060 and P = 0.070 respectively). No patient in either group had vomiting. Seven patients in saline and zero patient in granisetron group had nausea that was statistically significant (P = 0.040). Time to discharge after surgery was 243 ± 21 and 239 ± 24 minutes in granisetron and control group respectively (P = 0.150).

Conclusions: Systemic granisetron had no effect on the duration of sensory and motor block produced by spinal anesthesia with hyperbaric bupivacaine.

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Introduction

Several factors can influence the height and intensity of spinal block including the injected drug, technical aspects, level of injection, needle type, patient position, and patient characteristics, such as age, height, weight, pregnancy, and spinal anatomy (1).

The 5-hydroxytryptamine Type 3 (5-HT3) antagonists are a class of drugs frequently used to prevent and treat nausea and vomiting. It has been shown that a 5-HT3 receptor exists in the spinal nerves and affects pain control in animals. The 5-HT3 binding sites are abundant at the spinal level (2). These receptors are located in the superficial laminae and substantia gelatinosa of the spinal cord (3). Although the spinal serotonergic mechanisms in pain modulation are complex, several studies have confirmed the role of 5-HT3 receptors in antinociception. In humans, the cerebrospinal fluid serotonin levels increased three-fold after spinal bupivacaine administration. Also, ondansetron antagonized the sensory blockade of spinal lidocaine (4-6).

In a study by Fassoulaki et al. systemic administration of ondansetron, a selective 5-HT3 antagonist, enhanced regression time of sensory block produced by intrathecal injection of lidocaine (7).

However, in a study by Paraskeva et al. on 50 male patients undergoing transurethral surgery received either 8 mg oral ondansetron the evening before surgery plus intravenous (IV) 8 mg ondansetron 15 minutes before subarachnoid anesthesia or placebo; it had no effect on the subarachnoid sensory or motor block produced by ropivacaine (8).

Cystoscopy is usually an outpatient surgery, and patients should ambulate as early as possible; they should not have any motor or sensory block and also nausea and vomiting during discharge. So we conducted a study to evaluate the effect of systemic granisetron, a selective 5-HT3 antagonists, on the duration of sensory and motor block after spinal anesthesia with hyperbaric bupivacaine in this group of patients.

The hypothesis of this study was that granisetron can enhance the regression time of sensory and motor block in patients who undergoing spinal anesthesia

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with bupivacaine for outpatient cystoscopy.

The primary aim of our study is to evaluate the effect of granisetron on the duration of sensory or motor block in spinal anesthesia with bupivacaine for cystoscopy that is evaluated by measuring sensory level regression time. The secondary aim is to evaluate the efficacy of granisetron on reducing nausea and vomiting in this group of patients.

Materials and Methods

This randomized double-blinded controlled trial was performed in Shariati Hospital of Tehran University of Medical Sciences since March to September of 2013. The study protocol conformed to the ethical guidelines of the 1989 Declaration of Helsinki and ethical approval was provided by the Ethical Committee of Tehran University of Medical Sciences, Tehran, Iran.

62 patients with American Society of Anesthesiologists (ASA) Class I to III, aged 50-75 years who were scheduled for diagnostic or therapeutic cystoscopy conducted as outpatient surgery under spinal anesthesia, were included and written informed consent was obtained separately before surgery. Patients with contraindications to spinal anesthesia, difficulty in communicating, chronic pain, neurological diseases, and those receiving opioids, α2 agonists and drugs that act on serotonin receptors or affect the level of serotonin were excluded. Patients were randomly allocated into two groups, granisetron (n = 31) or control saline group (n = 31). Randomization was done by means of computer-generated codes. All members of the surgical team, nursing staff, patients and the anesthetist were unaware of the allocation. Study drugs were prepared, according to the randomization code, by an anesthesia staff who was not involved in the study and envelopes containing the information of the randomization were sealed and kept in the patient's folder until the end of the study period. Then prepared drugs with the same volume and shape were given to the anesthesiologist who was blinded to the allocation.

On arrival to the operating room, standard monitoring was applied to all patients including pulse oximeter, electrocardiogram, non-invasive arterial blood pressure. An 18-gauge IV catheter was placed on the dorsum of the non-dominant hand of the patients, and 5 ml/kg lactate Ringer's solution was infused before spinal anesthesia. Patients received 3 mg granisetron (Kytril, Roche, 1 mg/ml) or the same volume of 0.9% normal saline solution IV, according to the allocation 15 minutes before performing spinal anesthesia.

All patients received no premedication and were blocked in the lateral position in which a 25 gauge Quincke needle was inserted by midline approach into the L3-4 or L4-5 interspaces and after ensuring the correct position of the needle, 12 mg of hypertonic 0.5% bupivacaine was injected. Patients were immediately placed in the supine position after the block.

In the operating room and in the recovery room, an anesthesiologist who was unaware of the patient's group assignment recorded the following variables: cephalad sensory level by loss of pinprick sensation bilaterally at the midclavicular line using a short-beveled 25-gauge needle, every 2 minutes until the sensory block remained at the same level at two consecutive times and was recorded as maximal sensory block.

Motor block was assessed every 2 minutes until maximal motor blockade using the modified Bromage scale, and scored as: 0 = no motor block, 1 = being unable to move the hip, 2 = being unable to move the knee, and 3 = being unable to move the ankle (8).

Sensory and motor block were then assessed every 15 minutes after the subarachnoid injection for 3 hours or until recovery from the motor block or regression of sensory block by two dermatomes. Patient's age, sex, weight, height, ASA class, duration of surgery and also post-operative nausea and vomiting were all recorded and compared between the study groups.

Until completion of measurements, no sedatives, analgesics, or other adjuvants were given perioperatively except for the drugs determined by the study protocol. Patients requiring sedatives or analgesics before or during the measurement of sensory or motor block for any reason were excluded.

We included 31 patients in each group to detect a 10 minutes difference in two segment regression time of sensory block between the study groups with standard deviation = 1.2, assuming a power of 90% and a significance level 0.05. If consecutive patients do not fulfill the inclusion criteria or were excluded, they are substituted by another one until sample size completion. Statistical analysis was performed using SPSS package (version 19, SPSS, Chicago, IL). Normality of distribution of data was tested by the Kolmogorov–Simirnov test. Data were analyzed with independent sample t-test, chi-square and repeated measured ANOVA when appropriate.

Results

In total, of 74 patients scheduled consecutively for cystoscopy, 10 were excluded due to fulfilling the exclusion criteria and two others for spinal block failure. Finally, 62 patients were allocated for statistical analysis (Figure 1).

Demographic data were not statistically different in the study groups. None of the patients was in ASA Class I (Table 1).

There was no statistical difference in the maximum level of sensory and motor block and their regression time between the study groups (Table 2).

Time to discharge after completion of surgery was 203 ± 24 minutes in granisetron group and 205 ± 21

minutes in control group (P = 0.150). No patient in either group had vomiting (P = 0.060). Seven patients in saline group and no patient in granisetron group had nausea (P = 0.040).

No patient required IV rescue medication for pain, sedation or nausea.

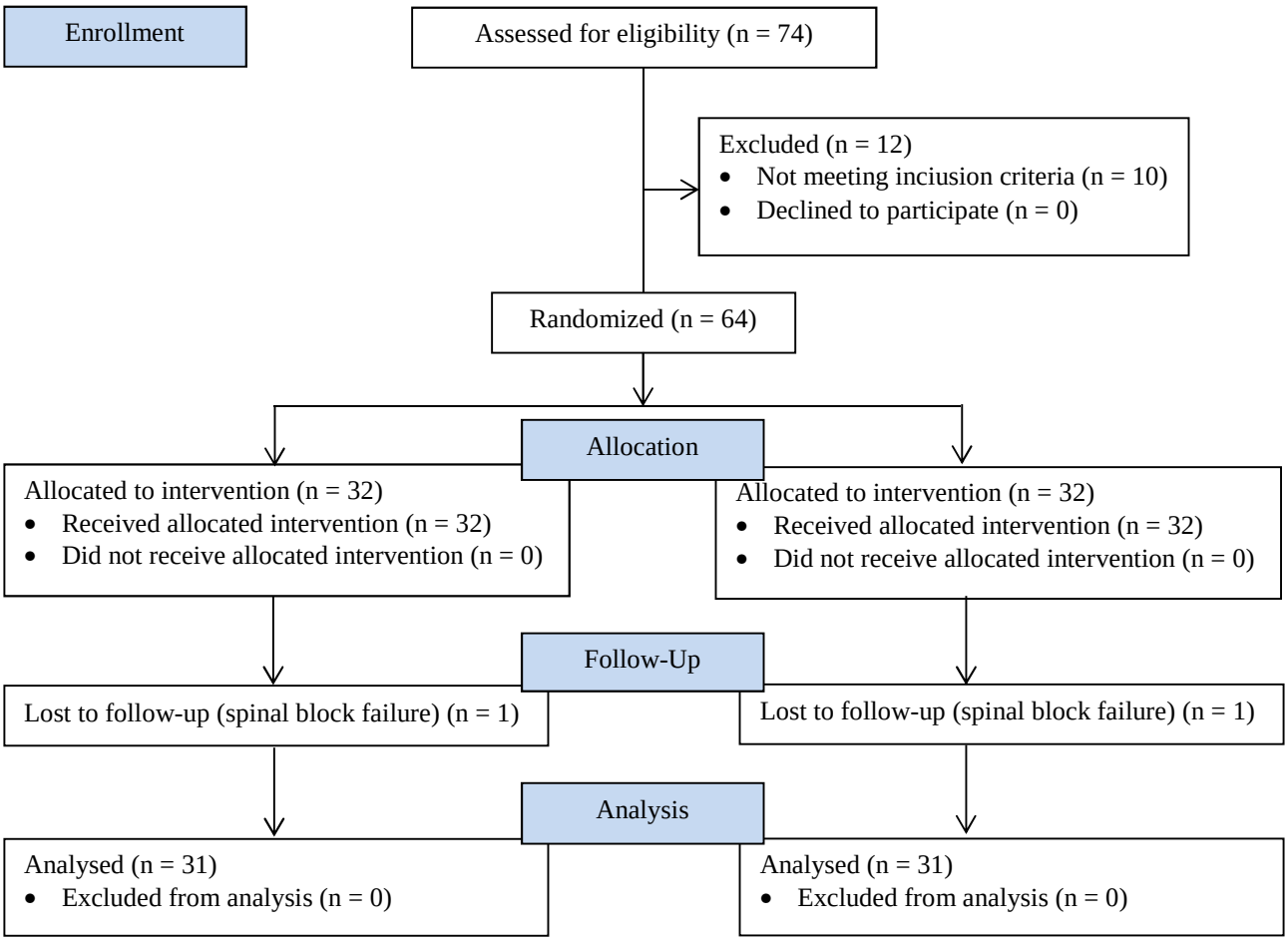

Figure 1. Consort flow diagram

Table 1. Comparing demographic data and surgery time between the study groups

Variable	Granisetrone group (n = 31)	Saline group (n = 31)	P-value
Age (year)	59.0 ± 9.3	57.5 ± 12.1	0.500
Sex (male/female)	20/11	18/13	0.200
Weight (kg)	73.6 ± 8.1	71.4 ± 9.5	0.300
Height (cm)	169.1 ± 7.6	169.1 ± 6.4	0.900
ASA Class II/III (n)	29/2	28/3	0.300
Duration of surgery (minutes)	63.9 ± 11.7	60.8 ± 8.1	0.200

Data are presented as mean ± SD, number of patients (n), P < 0.050. SD: Standard deviation

Table 2. Comparing time course of sensory and motor block between the study groups

Variable	Granisetrone group (n = 31)	Saline group (n = 31)	P-value
Time to maximum sensory block (minutes)	12.4 ± 2.1	12.5 ± 1.9	0.120
Time to maximum motor block (minutes)	16.6 ± 2.0	16.1 ± 1.9	0.230
Time to regression of sensory level by two dermatomes	68.3 ± 8.9	68.4 ± 7.3	0.240
Time to motor recovery by one level (minutes)	109.9 ± 14.4	112.9 ± 14.5	0.310
Time to complete motor recovery (minutes)	161.7 ± 32.4	164.3 ± 37.1	0.520
Maximum level of sensory block (dermatome)	T10-T12	T10-T12	0.510

Data are presented as mean ± SD, P < 0.050. SD: Standard deviation

Discussion

This study showed that IV granisetron had no effect on the maximum level and regression time of sensory and motor block produced by spinal anesthesia with hyperbaric bupivacaine.

Our results disagree with those of Fassoulaki et al., who reported that systemic ondansetron, caused a faster regression of the sensory block after spinal lidocaine (7).

However, our results correlated with those of Paraskeva et al. in which 50 male patients undergoing transurethral surgery received either 8 mg oral ondansetron the evening before surgery plus IV 8 mg ondansetron 15 minutes before subarachnoid anesthesia or placebo. They found that ondansetron had no effect on the subarachnoid sensory or motor block produced by ropivacaine (8).

In a study by Mowafi et al., 40 unpre-medicated patients scheduled for elective knee arthroscopy under spinal anesthesia were randomly allocated to receive either IV granisetron 1 mg or saline on arrival to the operating room. They found that IV granisetron facilitated a faster recovery of the sensory block but not motor block after bupivacaine subarachnoid anesthesia which partially correlated with our study (9).

Granisetron, in contrast to ondansetron, which acts on mixed receptors, strongly and selectively binds to the 5-HT3 receptors with minimal or no affinity for other 5-HT receptors, or dopaminergic, adrenergic, histaminic, and opioid receptors (10).

The role of 5-HT3 receptors in pain modulation is conflicting, as they could mediate excitatory and inhibitory effects, depending on variables such as the concentration of 5-HT or the state (sensitized/desensitized) of the spinal cord (11).

IV granisetron was also effective in preventing post-operative nausea in our study which correlated with previous studies (12,13).

In a study by Samra et al. on 60 patients undergoing transurethral resection of bladder tumors, patients received 4 mg ondansetron or saline 15 minutes prior to the administration of subarachnoid block. They found that IV ondansetron does not affect the intensity or duration of sensory and motor block after spinal anesthesia with hyperbaric bupivacaine. They results were similar to ours however their drug, patients and surgeries were different (14).

In another study by Rashad and Farmawy on 60 patients undergoing elective cesarean section under spinal anesthesia by intrathecal bupivacaine, they randomly divided patients into three groups. Group O received IV 4 mg ondansetron 5 minutes before spinal anesthesia, Group G given IV 1 mg granisetron by the same route and Group S given 10 ml normal saline. They concluded that in parturient females undergoing elective cesarean section, IV 4 mg ondansetron before subarachnoid block significantly decreased both the hypotension and the doses of vasopressor used, while IV 1 mg granisetron prior to subarachnoid block induced faster sensory recovery compared to both the ondansetron and saline groups, with no significant differences between the latter two groups. Their finding was similar to ours in regard to enhanced sensory recovery with granisetron however we used 3 mg granisetron and we also did not compare hemodynamic responses between the study groups. They also found a significant decrease in the incidence of nausea in Groups O and G than Group S ($P = 0.008$) that was correlated with our study (15).

In this regard, the difference of our study to mentioned studies may be explained by different doses of 5-HT3 receptors antagonists and discrepancies between the type, baricity and duration of the local anesthetics used and the different time intervals between block assessments. The dose of hyperbaric bupivacaine that was selected in our study was also not the best for outpatient surgery.

Conclusion

IV administration of 3 mg granisetron before intrathecal bupivacaine had no effect on recovery of sensory and motor block for cystoscopy as outpatient surgery. However, patients in granisetron had less nausea compared to control group.

Further study are recommended with different doses of granisetron and bupivacaine on regression time of the spinal block in outpatient surgeries in order to reduce hospital staying time and also post-operative nausea and vomiting with only one drug.

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References

1. Hocking G, Wildsmith JA. Intrathecal drug spread. Br J Anaesth. 2004; 93(4): 568-78.
2. Boess FG, Martin IL. Molecular biology of 5-HT receptors. Neuropharmacology. 1994; 33(3-4): 275-317.
3. Giordano J, Schultea T. Serotonin 5-HT(3) receptor mediation of pain and anti-nociception: implications for clinical therapeutics. Pain Physician. 2004; 7(1): 141-7.
4. Xu W, Qiu XC, Han JS. Serotonin receptor subtypes in spinal antinociception in the rat. J Pharmacol Exp Ther. 1994; 269(3): 1182-9.
5. Eide PK, Hole K. The role of 5-hydroxytryptamine (5-HT) receptor subtypes and plasticity in the 5-HT systems in the regulation of nociceptive sensitivity. Cephalalgia. 1993; 13(2): 75-85.
6. Bardin L, Lavarenne J, Eschalier A. Serotonin receptor subtypes involved in the spinal antinociceptive effect of

5-HT in rats. Pain. 2000; 86(1-2): 11-8.
7. Fassoulaki A, Melemeni A, Zotou M, Sarantopoulos C. Systemic ondansetron antagonizes the sensory block produced by intrathecal lidocaine. Anesth Analg. 2005; 100(6): 1817-21.
8. Paraskeva A, Chatziara V, Siafaka I, Zotou M, Fassoulaki A. Ropivacaine spinal anesthesia is not antagonized by ondansetron pretreatment. Anesth Analg. 2009; 109(5): 1684-7.
9. Mowafi HA, Arab SA, Ismail SA, Al-Ghamdi A. The effects of intravenous granisetron on the sensory and motor blockade produced by intrathecal bupivacaine. Anesth Analg. 2008; 106(4): 1322-5, table.
10. Blower P. A pharmacologic profile of oral granisetron (Kytril tablets). Semin Oncol. 1995; 22(4 Suppl 10): 3-5.
11. Lopez-Garcia JA. Serotonergic modulation of spinal sensory circuits. Curr Top Med Chem. 2006; 6(18): 1987-96.
12. Wilson AJ, Diemunsch P, Lindeque BG, Scheinin H, Helbo-Hansen HS, Kroeks MV, et al. Single-dose i.v. granisetron in the prevention of postoperative nausea and vomiting. Br J Anaesth. 1996; 76(4): 515-8.
13. Taylor AM, Rosen M, Diemunsch PA, Thorin D, Houweling PL. A double-blind, parallel-group, placebo-controlled, dose-ranging, multicenter study of intravenous granisetron in the treatment of postoperative nausea and vomiting in patients undergoing surgery with general anesthesia. J Clin Anesth. 1997; 9(8): 658-63.
14. Samra T, Bala I, Chopra K, Podder S. Effect of intravenous ondansetron on sensory and motor block after spinal anaesthesia with hyperbaric bupivacaine. Anaesth Intensive Care. 2011; 39(1): 65-8.
15. Rashad MM, Farmawy MS. Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section. Egyptian Journal of Anaesthesia. 2013; 29(4): 369-74.