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Original Research Article

Randomized Clinical Comparative Assessment of Granisetron Versus Pethidine for the Prevention of Perioperative Shivering Under Spinal Anesthesia

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Abstract

Aim: The aim of the present study was to compare the efficacy of prophylactic granisetron on post anaesthetic shivering in comparison to pethidine an agent which is known to be effective in the treatment and prevention of post anaesthetic shivering.

Methods: The present study was conducted in the Department of Anaesthesia for six Months and we selected 100 patients aged 20–50-year, American Statistical Association (ASA) physical Status I and II, scheduled for lower abdominal surgery under spinal anesthesia. The patients were randomly allocated to Group P (n = 50) receiving pethidine 0.4 mg/kg and Group G (n = 50) receiving granisetron 40 mcg/kg intravenous (IV) as study drug before spinal anesthesia.

Results: The three groups were comparable regarding distribution of age, weight, height, gender, duration of anaesthesia, duration of operation and ASA physical status. The number of patients with postoperative shivering on arrival in the recovery room, 15 minutes after arrival, were significantly less in Group G and Group P than in Group S ($p<0.05$). There was no statistically significant difference between Group P and G ($p > 0.05$). However, in Group G and Group P only 4 and 10 patients reached grade 3 shivering respectively. However, there were no significant differences in the core temperature amongst the patients before and after the anaesthesia.

Conclusion: Prophylactic granisetron 40 mcg/kg IV is equally effective as pethidine 0.4 mg/kg in the prevention of perioperative shivering following spinal anesthesia, maintains core temperature and oxygen saturation levels above that of pethidine. Prophylactic granisetron also reduces the need of antiemetics.

Keywords: Shivering; Postoperative; Granisetron; Pethidine.

Introduction

During perioperative period, shivering is one of the commonest challenges (the incidence ranges between 20 and 80.0%). Different studies reported that, shivering increase oxygen consumption and CO2 production. It also affects monitoring and increase intraocular and intracranial pressure. [1,2] Perioperative shivering remains common irrespective of rigorous efforts to prevent peri-operative hypothermia. [3,4] The main etiologies for intra/postoperative shivering are loss of temperature, reduced sympathetic tone and pyrogenic release. [5] In a previous trial, risk factors for developing perioperative shivering include but not limited to younger age, endoprosthetic surgery, long surgery duration and low core body temperature. [6]

There are pharmacological and non-pharmacological interventions to control perioperative shivering. Non-pharmacological maneuvers include fluid warmers, monitoring ambient temperature of operating theatre, space blankets, and surgical drapes. However, its effectiveness is questioned. [7] As pharmacological intervention could decrease the incidence of perioperative shivering, many drugs were tried. The list of drugs with anti-shivering effects included dexmedetomidine [8], 5-hydroxytryptamine-3 receptor antagonists [9], meperidine [10], fentanyl, buprenorphine, doxapram, clonidine. [11] However, these drugs were not widely used due to its high cost and their safety is disputed. [12]

Among the pharmacological agents, pethidine has been shown to be one of the most effective treatment. [13,14] Although its mechanism of action is not completely understood, it probably acts directly on the thermoregulatory centre [15] or

via opioid receptors.1 Serotonin (5-Hydroxytryptamine), a biological amine found in the brain and spinal cord, has a role in neurotransmission and studies suggest that the serotonergic system has a role in control of postanaesthetic shivering.[16] Granisetron, 5-HT3 receptor antagonist, has been shown to be effective in the prevention of emetic symptoms. [17,18]

The aim of the present study was to compare the efficacy of prophylactic granisetron on postanaesthetic shivering in comparison to pethidine an agent which is known to be effective in the treatment and prevention of postanaesthetic shivering.

Materials and Methods

The present study was conducted in the Department of Anaesthesia, Shri Krishna Medical College, Muzaffarpur, Bihar, India for six months and we selected 100 patients aged 20–50 year, American Statistical Association (ASA) physical Status I and II, scheduled for lower abdominal surgery under spinal anesthesia. The patients were randomly allocated to Group P (n = 50) receiving pethidine 0.4 mg/kg and Group G (n = 50) receiving granisetron 40 mcg/kg intravenous (IV) as study drug before spinal anesthesia. Patients with cardiopulmonary disease, psychological disorder, and thyroid disorders, patients who are likely to receive blood transfusion intraoperatively and with body temperature more than 38°C or <36.5°C were excluded from the study.

Standardized monitoring was done throughout the perioperative period. Heart rate, NIBP, respiratory rate, and oxygen saturation were recorded during the surgery. Core body temperature was measured by tympanic thermometer, and skin temperature was measured using skin probe. Operation room temperature was maintained at 24°C by air-conditioning. Peripheral IV access is secured using 18 gauge cannula. All patients preloaded with warm Ringer's lactate solution of 10 ml/kg before spinal anesthesia. Patients received respective drugs intravenously before spinal anesthesia. Patients from both the groups received 0.5% hyperbaric bupivacaine 15 mg intrathecally with the help of 26 or 27 G Quincke's spinal needle at L3–L4 interspace in the lateral position. After subarachnoid block, the patients were turned to the supine position. Patients received oxygen 6 L/min by face mask throughout the procedure. Except surgical field patients were properly covered with cotton drapes. The hypotension if following spinal injection was treated by increasing the rate of IV fluid administration and by injection of Mephentermine 3–6 mg

IV. An anesthesiologist blinded for the study drug observed the patients for shivering, pain, nausea, and vomiting. Heart rate, NIBP, oxygen saturation, and temperature were measured and recorded on admission and every 15 min up to 6 h. The shivering was graded using a 5-item scale.[19] The possible side effects of the study drug (i.e., nausea, vomiting, hypotension, tachycardia, dry mouth, and dizziness) were recorded. In the recovery room also all patients were monitored, received oxygen through facemask and were covered with woolen blanket. Patient with nausea and vomiting were treated with metoclopramide 10 mg. Tramadol 1 mg/kg was kept as rescue medication to treat the shivering more than Grade II on 5-item scale.

Statistical analysis of data was done using IBM corp. Released 2013. IBM SPSS statistics for windows. Version 22.0. Armonk, NY.

Results

Table 1: Patient characteristics of the three treatment groups

Variables	Group G	Group P	P value
Age	42.58	41.39	0.4634
Sex (M/F)	10/40	0/50	0.1224
Weight	54.66	52.88	0.1544
Height	152.58	153.57	0.9350
ASA (I/II)	40/10	42/8	0.9944

The three groups were comparable regarding distribution of age, weight, height, gender, duration of anaesthesia, duration of operation and ASA physical status.

Table 2: Number of patients with different grades of shivering in the three treatment groups after arrival in recovery room in 15 minutes

Grades of shivering	Group G	Group P	P value
0	40	34	<0.05
1	3	4	<0.05
2	3	2	<0.05
3	4	10	<0.05
4	0	0	<0.05

The number of patients with postoperative shivering on arrival in the recovery room, 15 minutes after arrival, were significantly less in Group G and Group P than in Group S ($p<0.05$). There was no statistically significant

difference between Group P and G ($p > 0.05$). However, in Group G and Group P only 4 and 10 patients reached grade 3 shivering respectively.

Table 3: Variation in core temperature (°c)

	OR temperature	Group G	Group P	P Value
Pre-operative	21-22°C	35.5±0.44	36.4±0.36	>0.05
Post-operative	21-22°C	34.46±0.16	34.56±0.24	>0.05

However, there were no significant differences in the core temperature amongst the patients before and after the anaesthesia.

Discussion

Shivering, the "big little problem," has an incidence of 60% following general anesthesia and up to 33% following regional anesthesia. [19] Shivering is unpleasant and causes several undesirable physiologic consequences such as increase in oxygen consumption, carbon dioxide production, increased chances of myocardial ischemia, infection, bleeding, and increase in the minute ventilation. It also induces hypoxemia, lactic acidosis, increased intraocular pressure, intracranial pressure (ICP), and interferes with patient monitoring such as electrocardiogram (ECG), noninvasive blood pressure (NIBP), and SpO2. Spinal anesthesia is known to decrease the shivering threshold, preceded by core hypothermia and vasoconstriction above the level of block. [20] Various methods are available for the control of shivering such as nonpharmacological or pharmacological. Nonpharmacological preventing measures such as fluid warmers, maintaining ambient operating room temperature, space blankets, surgical drapes, and active circulating water mattress have been used. Pharmacological methods include various drugs such as opioids (pethidine, pentazocine, and tramadol), α2 agonists (clonidine, ketansarin), others such as doxapram, neofam, neostigmine, and magnesium sulfate have been tried. [21]

The three groups were comparable regarding distribution of age, weight, height, gender, duration of anaesthesia, duration of operation and ASA physical status. The number of patients with postoperative shivering on arrival in the recovery room, 15 minutes after arrival, were significantly less in Group G and Group P than in Group S ($p<0.05$). There was no statistically significant difference between Group P and G ($p > 0.05$). Pethidine has been shown to be one of the most effective treatments to prevent postoperative shivering at a dose of 0.4 mg/kg. The antishivering effect of pethidine is due to stimulation of kappa receptors and drug‐induced decrease in the shivering threshold. In addition, pethidine is a potent alpha two receptor agonist which contributes to antishivering effects. Butorphanol – a kappa receptor agonist – antagonist stops shivering more effectively than opioids with a predominant mu‐opioid receptor agonist effect. Evidence for a role of kappa receptors in the antishivering effects of meperidine and butorphanol is the failure of naloxone to completely inhibit this drug‐induced effect. A disadvantage of pethidine is that it can cause respiratory depression in the presence of previously administered opioids or anesthetics. Moreover, nausea and vomiting are also important adverse effects of pethidine. [22,23]

Powell and Colleagues [24] reported that after general anaesthesia, shivering was determined in 57%, 33% and 15% of patients in control, ondansetron 4mg and 8mg respectively. Similarly, Bock and colleagues [25] mentioned in their study report that dolasetron 1mg.kg-1 decreases the incidence of shivering from 62% to 27%. However, in Group G and Group P only 4 and 10 patients reached grade 3 shivering respectively. However, there were no significant differences in the core temperature amongst the patients before and after the anaesthesia. Cutaneous warming is also the most effective means of preventing intraoperative hypothermia, so patients are covered with cotton drapes. [20] Saito et al. reported that hypothermia is likely to develop faster during spinal anesthesia due to impairment of thermoregulation. A natural consequence of the rapid temperature decreases during spinal anesthesia is that the shivering threshold will be reached sooner and that more shivering will be required to prevent further hypothermia. [26]

Conclusion

Prophylactic granisetron 40 mcg/kg IV is equally effective as pethidine 0.4 mg/kg in the prevention of perioperative shivering following spinal anesthesia, maintains core temperature and oxygen saturation levels above that of pethidine. Prophylactic granisetron also reduces the need of antiemetics.

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