Comparison of Ondansetron and Pethidine for Prevention of Shivering after Spinal Anesthesia

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ABSTRACT
Shivering is one of the most common problems after anesthesia and spinal anesthesia. Though it occurs as a result of temperature reduction, it may occur in patients with a postoperative normal body temperature. Shivering can cause serious complications such as delay in recovery, increased blood pressure, increased effect of drugs, increased oxygen consumption, or haemostatic dysfunction especially patients with low cardiac reserve. The aim of this study is to determine and compare the effects of pethidine, ondansetron and placebo in prevention of shivering after spinal anesthesia in patients undergoing cesarean section. Sixty ASA I and II female patients were randomly selected. Patients were randomly divided into three groups of ondansetron (O), pethidine (P) and placebo (N).

All patients were given spinal anesthesia. All patients were hydrated with 500cc normal saline 30 minutes before spinal anesthesia. Immediately after spinal anesthesia, 4 mg ondansetron was administered intravenously to Group I, 25 mg pethidine was administered intravenously to Group II, 2cc normal saline as placebo was administered intravenously to Group III. The incidence of shivering was recorded 5 minutes prior to anesthesia and 5, 10, 15 and 30 minutes after anesthesia. The collected data was analyzed using SPSS 21, ANOVA and chi-square. There was no significant difference between the three groups in terms of age and mean duration of the surgery (p value>0.05). No significant difference was found in incidence of postoperative shivering in ondansetron and pethidine groups. Therefore, ondansetron is as much effective as pethidine in preventing postoperative shivering.

KEYWORDS: ondansetron, pethidine, shivering, spinal anesthesia,

INTRODUCTION:
Shivering is the rhythmic contraction of muscles with frequency of 4-8 Hertz[3] that increases the basal metabolism. It is characterized as a defense mechanism of the body to central hypothermia[4] with release of cytokines from surgical site. It is considered as the sixth most important problem of clinical anesthesiology with an estimated rate of 5-65%[1,2]. Postoperative shivering lasts 2 to 60 minutes. Almost all anesthetics impair autonomic control of body temperature. Shivering decreases mixed venous oxygen saturation as a result of impaired cardiopulmonary function. In addition, postoperative shivering can increase oxygen consumption up to 5 times, might increase carbon dioxide production, minute ventilation, and hence, cardiac output even in healthy adults[5]. It is a potentially serious complication that increases oxygen consumption roughly 100% in proportion to intraoperative heat loss. It might also be associated with increased blood pressure, intracranial pressure, metabolic rate lactic acidosis. Postoperative surgical wound pain[6,7]. Pharmacologic agents are still the most popular mode of treatment for postanesthetic shivering, such as meperidine, clonidine and physostigmine. Nonpharmacologic approaches remain as effective preventive measures for postoperative shivering[8]. Shivering also increases postoperative problems (complications), which consequently increases the cost of treatment. So it is necessary to treat and prevent shivering.

Acetaminophen, granisetron, nefopam, ketamine are the newer drug being evaluated for treatment of postop shivering.

Ketanserin, sufentanil, alfentanil, tramadol, physostigmine, clonidine, magnesium sulfate, Pethidine, and dexamethasone have been used for the treatment of postoperative shivering[9].

Fentanyl also used along with bupivacaine in spinal anesthesia prevents post-cesarean shivering[10].

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It is acknowledged that 0.5 mg/kg dose of ketamine reduces shivering in major surgeries\(^{[10]}\). Since pethidine is a typical opioid analgesic, it may interfere with other opioid analgesia used in spinal anesthesia that may eventually cause respiratory depression. In addition to depressive effect on the central nervous system, pethidine increases length of stay in the recovery room, nausea and vomiting, slows gastrointestinal motility and prolongs natural intestinal nutrition. Given that intrahypothalamic serotonin (5-hydroxytryptamine) greatly regulates body temperature, it is acknowledged that 5-hydroxytryptamine antagonist (ondansetron) also reduces postoperative shivering in anesthetized patients. Since ondansetron greatly reduces postoperative nausea and vomiting\(^{[12]}\) and pethidine is an opioid which can increase postoperative nausea and vomiting, it is necessary to find an ideal therapy simultaneously effective in postoperative nausea, vomiting and shivering. This study examined the incidence of postoperative shivering after prophylactic administration of ondansetron and pethidine.

**MATERIALS AND METHODS:**

After obtaining approval from the institutional ethical committee at Rama Medical College Kanpur, a randomised controlled study was formulated. The study was conducted from August 2017 to March 2018. The study population comprised 60 female patients with ASA I and II aged 20-40 years. Those patients with hypertension, difficulty in breathing, asthma, sensitivity to pethidine and ondansetron and cardiovascular problems were excluded from the study.

All patients were randomly divided into three groups of ondansetron, pethidine and control. All participants were hydrated 30 minutes before spinal anesthesia with 500 cc of normal saline. Temperature at operating and recovery rooms was kept constant within 23-25ºC range for all the patients. Then, all patients were given spinal anesthesia by an anesthesiologist using 53.5 mg xylocaine 5% at the L4-5 interspace with 25 gauze spinal needle. Immediately after spinal anesthesia, 4 mg ondansetron was administered intravenously to Group I, 25 mg pethidine was administered intravenously to Group II, 2 cc normal saline as placebo was administered intravenously to Group III. Five minutes before spinal anesthesia, hemodynamic status of the patients (blood pressure and heart rate) and incidence of shivering were examined and recorded.

After spinal anesthesia, hemodynamic status of the patients and incidence of shivering were examined and recorded every 5 minutes for 30 minutes. The patients would be treated with 10 mg ephedrine if blood pressure was below 90 systolic or MAP below 60 and 0.6 mg atropine in case that heart rate was below 50 beats per minute. After the patients were transferred to the recovery room, the incidence of shivering was recorded within 45 minutes of stay in the PACU (post-anesthesia care unit). The incidence of shivering referred to physical contractions lasting for at least 15-30 seconds. If necessary, shivering was treated with 25 mg pethidine. Finally, the incidence of shivering was expressed as percentage in each group at different times. The collected data was entered in SPSS. The incidences of postoperative shivering were compared with chi-square test (K) and t test.

**RESULTS:**

The study was conducted on 60 patients undergoing spinal anesthesia. All participants were selected from those women undergoing caesarean section in order to reduce confounding error attributed to type of surgery. The participants were divided into three groups including ondansetron, pethidine and control (normal saline). Twenty patients were included in each group. Mean age of the participants was 28. Mean age was 28 in Group I (ondansetron), 27.5 in Group II (pethidine), 28.2 in Group III (control).

The relationship of mean age with changes in systolic and diastolic blood pressure was not significant in each group (p-value = 0.34). No significant relationship was also found between mean age of the participants and the incidence of shivering in each group (p-value = 0.13). Mean systolic blood pressure was 123 within five minutes before the surgery and mean diastolic blood pressure was 69 within five minutes before the surgery in different groups. Mean systolic blood pressure was 109 within five minutes after the surgery and mean diastolic blood pressure was 64 within five minutes after the surgery.
pressure was 66 within five minutes after the surgery in every three group. Mean systolic blood pressure was 105 within ten minutes after the surgery and mean diastolic blood pressure was 63 within ten minutes after the surgery in every three group. Mean systolic blood pressure was 110 within fifteen minutes after the surgery and mean diastolic blood pressure was 64 within fifteen minutes after the surgery in every three group. Mean systolic blood pressure was 124 within thirty minutes after the surgery and mean diastolic blood pressure was 64 within thirty minutes after the surgery in every three group.

The relationship of mean systolic and diastolic blood pressure with the incidence of shivering in each group was not significant (p-value = 0.2). The incidence of shivering five minutes after the surgery was zero in Group I (ondansetron), zero in Group II (pethidine) and in zero Group III (saline). The incidence of shivering five minutes after the surgery was zero in Group I, 2.2% in Group II and zero in Group III. The incidence of shivering 10 minutes after the surgery was zero in Group I, 2.3% in Group II and 9.1% in Group III. The incidence of shivering 15 minutes after the surgery was 2.2% in Group I, 4.5% in Group II and 23.1% in Group III. The incidence of shivering 30 minutes after the surgery was 2.4% in Group I, 9.2% in Group II, 39.3% in Group III. The incidence of shivering in Group I did not significantly differ from Group II (p-value > 0.05). The incidence of shivering in Group I and II significantly differed from Group III (p-value < 0.05).

**DISCUSSION:**

Postoperative shivering increases recovery length of stay and cost and is an additional burden to both the patients and hospitals. Prevention and treatment of postoperative shivering is an important part of postoperative patient care.

Ondansetron, a 5-HT3 antagonist, is generally used as an antiemetic but its efficiency and safety in the prevention of PAS remains controversial. This study examined the incidence of postoperative shivering after prophylactic administration of ondansetron and pethidine. The results of the study showed that 4 mg dose of ondansetron can be effective in reducing the incidence of postoperative shivering. Mean incidence of shivering in ondansetron and pethidine groups was less than placebo group. The results showed that the incidence of shivering in Group I was less than Groups II and III. In addition, mean incidence of shivering in pethidine group was less than control. However, no statistically significant difference was found between ondansetron and pethidine groups. However, no statistically significant difference was found between those who received ondansetron and those who took pethidine. Therefore ondansetron is as much effective as pethidine in preventing postoperative shivering.

The results of this study were similar to results of several studies as mentioned here. Asl ME et al, compared meperidine with ondansetron with placebo & found shivering 50% in placebo, 13.3% in ondansetron group & 20% in meperidine group. Tie HT et al, also compared ondansetron with meperidine & placebo they
found similar results. These results were consistent with the results of this study. Klaska et al. compared a 4mg dose of ondansetron and an 8mg dose of meperidine in reducing shivering after spinal anesthesia. The incidence of shivering reduced from 36% in control to 8% in meperidine group and 8% in ondansetron group. No significant difference was found between the two groups of meperidine and ondansetron. These results were consistent with the results of this study. Piper et al. compared Dolestron 12.5 mg, clonidine 3µ/kg & saline. In the clonidine group, no shivering in 86.6% patients, whereas Dolestron & placebo group only 63.3% ,66.6% were symptom free. It may be due to inadequate dosage. Shhaky S et al compared ketamine 0.25 mg/kg with ondansetron 4 mg and saline they found that ketamine and ondansetron produces anti shivering effect in comparison to placebo in patients undergoing spinal anaesthesia.

Powell et al. compared prophylactic administration of ondansetron with normal saline. The results showed that incidence of postoperative shivering was 57% in the saline group, which was reduced to 33% in the ondansetron group. Thereby, postoperative shivering reduced in the ondansetron group compared to normal saline group.

Marashi SM et al, compared different dose of ondansetron with placebo, they found that there were no significant difference in MAP & HR b/w the ondansetron group. Incidence of shivering were 4% in 6 mg & 2% in 12 mg ondansetron group while 45% in placebo group. Many researchers have used Alfentanyl, fentanyl, tramadol, ketamine, clonidine, dexame-thasone, dexmedetomidine, acupuncture, granisetron, pentazocine for Prevention of Postoperative Shivering.

CONCLUSION:
No significant difference was found in incidence of postoperative shivering in ondansetron and pethidine groups. Since pethidine is narcotic, there is the risk of respiratory depression although a small dose of pethidine was used to reduce shivering. As a result, pethidine cause more complications than ondansetron. Thereby, ondansetron should be used to reduce postoperative shivering since it is a new drug with minimal complications during pregnancy and lactation.

REFERENCES: