ORIGINAL RESEARCH

Comparative Study of Granisetron and Butorphanol To Control Intraoperative Shivering Under Spinal Anaesthesia

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ABSTRACT
Introduction: Shivering is a physiological response due to thermoregulatory mechanism to cold which is an involuntary, muscular twitching. It is usually observed during spinal and epidural anaesthesia administration. Surgery causes heat loss due to exposure to environment, evaporation of body heat and infusion of intravenous fluids which causes reduction in core body temperature. There is reduction in core body temperature due to altered afferent thermal input from the blocked region This study was done to evaluate the efficacy of granisetron and butorphanol to control shivering intraoperatively who undergo spinal anaesthesia**. Methods:** This study included 62 adult patients ,31 patients in group G and 31 patients in group B. Patients with American society of Anaesthesiologists (ASA) physical status I and II, aged 20-60 years, either gender who were scheduled for lower abdominal surgeries under spinal anaesthesia were included in the study. Vital parameters and grades of shivering were observed. **Results:** We observed onset of action of butorphanol was within 3-5 minutes while it took 5-7 minutes for granisteron to provide relief from shivering, making the time of onset of action statistically significant. There was significant statistical difference in Heart rate between two groups at 5mins 10mins and 30 mins. There was difference between Mean arterial pressure (MAP) between both groups at 10mins and 30mins was also found to be significant statistically. **Conclusion:** The incidence of tachycardia, hypotension and vomiting was significantly higher with butorphanol when compared to Granisetron. Butorphanol onset of action was faster with mild sedative effects .Thus Granisetron is superior to butarphanol in controll of shivering.
Keywords: Shivering, granisetron, butrophanol, spinal anaesthesia.

INTRODUCTION

Shivering is a physiological response due to thermoregulatory mechanism to cold which is an involuntary, muscular twitching. It is usually observed during spinal and epidural anaesthesia administration[1]. Surgery causes heat loss due to exposure to environment, evaporation of body heat and infusion of intravenous fluids which causes reduction in core body temperature. There is reduction in core body temperature due to altered afferent thermal input from the blocked region[2,3].Shivering is observed in more than 50% of the patients who undergo neuraxial blockade . Due to increase in oxygen consumption and increase in carbon dioxide production there is arterial hypoxemia. There is mismatch between oxygen supply and demand ratios causing lactic acidosis[4,5]. Hemodynamic are altered with heart rate variabilityand myocardial infarction in cardiac compromised patients. It also interferes in blood pressure, increases intracranial pressure, blood coagulopathy, decreased immunity and chances of surgical site infection which causes delay in wound healing. Shivering is unpleasant and increases anxiety in patients intraoperatively.

Serotonin (5-hydroxytryptamine), an amineis present in the brain and spinal cord which has an important role in neuronal transmission[6]. Few studies have found serotonergic system has some role in controlling shivering intraoperatively. A serotonin 5-HT3 receptor antagonist inhibits the uptake of serotonin in the preoptic anterior hypothalamic region, which influences both heat production and heat loss[7,8].

In our present study granisetron can reduce intra-operative shivering.

Butorphanol is a centrally acting opioid analgesic with kappa and mu receptors agonistic modulation has ant shivering property.

This study is done to evaluate the efficacy of granisetron and but orphanol to control shivering intraoperatively who undergo spinal anaesthesia.

MATERIALS AND METHODS

The study was done after obtaining institutional committee approval. Written consent was taken from all patients after explaining the study protocol.

This randomized prospectiveclinical study included 62 adult patients (31 in each group) and were allocated into two groups by computerized random number table.Patients with American society of Anaesthesiologists (ASA) physical status I and II, aged 20-60 years, either gender who were scheduled forlower abdominal surgeries under spinal anaesthesia were included in the study. Patients with any contraindication to spinal anaesthesia, thyroid disorders, morbid obesity, cardiopulmonary diseases, temperature >38^0 C and< 36^0 C and caesarean section were excluded from the study.

In group G patients received Granisetron 40mcg Intravenous(IV) and Group B patients received Butorphanol 0.01mg/kg IV when patient developed shivering intraoperativelywhich lasted more than two minutes.

Pre-operative evaluation included history of underlying medical illness, previous history of surgery, anesthetic exposure and hospitalization

Physical examination included general condition of the patient, Vital signs- heart rate (HR), blood pressure, respiratory rate, height and weight. Cardiovascular system, respiratory system, central nervous system, spine examination and airway assessment by Mallampati grading was done.

Investigations such as complete blood count, bleeding time, clotting time, blood glucose, blood urea, serum creatinine. Chest x-ray and electrocardiography (ECG) were done if required.

All patients were kept nil by mouth the night before surgery for 8 hours.

On day of surgery baseline vital parameters were recorded in the preoperative room.

On the operating table all monitors were attached like pulse oximeter, non-invasive blood pressure (NIBP) and ECG. IV line was secured with 20 G cannula.. All patients were preloaded with 500ml Ringer lactate solution at room temperature.. Baseline temperature was recorded using a mercury thermometer placed in the axillary region. Operatingtheatre temperature was maintained at 22-25 C.

Under aseptic precautions all patients were administered spinal anaesthesia in left lateral or in sitting position with 26 G Quincke needles in L3-L4 lumbar space. Hyperbaric bupivacaine 0.5% was injected with dose of 15-20mg according to the type and duration of the surgery.Surgical drapes were used to completely wrap all patients. Other warming methods were not employed.

In our study, patients who began to shiver for two minutes after receiving spinal anaesthesia such patients data were collected.

Grade -0 -No shivering, grade -1- piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause but without visible muscular activity, grade-2 -Visible muscular activity confined to one muscle group, grade-3- visible muscular activity in more than one muscle group, grade-4-gross muscular activity involving the entire body

According to the 5 item Shivering scale, shivering with grades two or more medical intervention was carried out.

Patients were randomly assigned to one of the two study groups,. Granisetron 40 mcg/kg in Group G and Butorphanol 0.01 mg/kg in Group B. When patients experienced shivering of the above mentioned grades for a minimum of two minutes from the commencement of the shivering axillary temperature was recorded.

The study medication was then injected slowly over a 30-second period. A timer was used to precisely record the period of time between administration of the drug and the patient's shivering cessation.. Initial action of the patient to the drug was graded as either Success (shivering absent) or Nil (shivering intensity not controlled).

All patients where observed for grades of shivering , heart rate , oxygen saturation , NIBP, temperature for a period of 1 minute for the first 5 minutes and later it was observed for 10, 20 and 30 minutes till shivering stopped.

All patients where observed for reappearance of shivering, sedation score, failure of drug action and adverse reactions such as nausea, vomiting, pruritus, respiratory depression, bradycardia, and hypotension. Bradycardia was taken as a heart rate below 60bpm, and respiratory depression as a respiratory rate less than 10 cycles per minute.

Modified Ramsay's sedation scale was used to measure the level of sedation.

Score 1- Awake and alert, no cognitive impairment.

Score 2- Awake but tranquil, purposeful responses to verbal commands at conversation level.

Score 3- Appears asleep, purposeful responses to verbal commands at the conversation level.

Score 4- Appears asleep, purposeful responses to verbal commands but at louder than usual conversation level or requiring light glabellar tap.

Score 5- Asleep, sluggish purposeful responses only to loud verbal commands or strong glabellar tap.

Score 6- Asleep, sluggish purposeful responses only to painful stimuli.

Score 7- Asleep, reflex withdrawal to painful stimuli only.

Score 8- Unresponsive to external stimuli, including pain.

Above 5 and 6 are considered as satisfactory sedation levels

Drug which was administered stopped shivering that particular drug was considered to be effectiveintreatment of shivering. Reappearance of shivering or incomplete cessation of shivering was treated with other modalities like warm fluid therapy and drug therapy such as Injection tramadol 50mg IV and Injection Dexamethasone 8mg IV , and the test medication was deemed ineffective in these cases.

STATISTICAL ANALYSIS

On the basis of a study conducted by AsthaPalan et al[9], anticipated mean± SD of butorphanol and tramadol for shivering is 98.36+ or – 0.40 and 98.44 = and – 0.38respectively. 62 patients of both gender were randomly divided into two groups of 31in eachgroup. Sample size calculation was done.

To conduct the comparative study of Granisetron versus Butorphanol in controlling intraoperative shivering under spinal anesthesia, 62 patients (31 in each group) are required to have a 90% chance of detecting, a decrease in relief of shivering from 63% in the G group to 23% in the B group, at 5% significant level.

All characteristics are summarized descriptively. The summary statistics of n, mean, and standard deviation (SD) will be utilised for continuous variables. In the data summaries for categorical data, the number and percentage will be utilised, and the data will be examined using the Chi-Square test for association, the t test to compare means, the ANOVA, and diagrammatic presentation. All data was entered in a Microsoft Excel sheet, and for analysis SPSS 22 version software was used. Frequencies and proportions were used to represent categorical data. For qualitative data, the chi-square test was utilised as a significance test. Standard deviation and mean were used to describe continuous data. Independent t test was used as a test of significance to determine mean difference between two quantitative variables.

RESULTS

In this study, there was no statistically significant difference between the groups with respect to demographic data and body temperature(Table-1)

Table 1: Demographic Data

	GROUP G (n=31)	GROUP B(n=31)	p value
Age (Mean±SD)	37.965±9.861	36.258±10.84	0.519
Gender Female	11(35.48%)	12(38.7%)	-
Male	20(64.51%)	19(61.29%)	-
ASA Grading -1	20(64.52%)	18(58.06%)	-
ASA Grading -2	11(35.48%)	13(41.94%)	-
Body temperature(Mean±SD)	37.051±9.841	38.038±10.841	0.708

Data is represented as numbers and n(%),*p value- <0.05 significant, Group G- Granisetron, Group B- Butrophanol.

The grade of shivering were found to be comparable between the two groups with 58.06% in Group G and 48.39% in group B demonstrating grade 3 shivering. It was found that onset of action of butorphanol was within 3-5 minutes while it took 5-7 minutes for granisteron to provide relief from shivering, making the time of onset of action statistically significant(Table-2).

Table 2: Grade and time of onset of shivering

	GROUP G(n=31)	GROUP B(n=31)	P Value
Time of onset of shivering(Mean±SD)	6.06±0.83	3.31±0.86	<0.01*
Grade of Shivering			
GRADE- 1	0	0	-
GRADE 2	3(9.68%)	5(16.13%)	
GRADE 3	18(58.06%)	15(48.39%)	
GRADE 4	10(32.26%)	11(35.48%)	

Data is represented as numbers and n(%),*p value- <0.05 significant, Group G- Granisetron, Group B- Butrophanol.

There was significant statistical difference in Heart rate between two groups at 5mins 10mins and 30 mins (Table-3).

Table 3: Mean heart rate

TIME Mean±SD	GROUP G n=31	GROUP B n=31	p Value
1 min	96.02±2.36	97.45±8.58	0.374
3 mins	95.18±2.37	94.87±3.47	0.682

4 mins	96.18±2.37	97.7±8.63	0.348
5 mins	92.09±0.43	93.18±2.11	0.006
10 mins	85.74±6.55	88.66±2.11	0.021
20 mins	87.83±5.49	88.66±2.11	0.435
30 mins	87.74±4.67	89.66±1.11	0.029

Data is represented as Mean±SD, * p-value- <0.05 significant, Group G- Granisetron, Group B-Butrophanol

There was difference between Mean arterial pressure (MAP) between both groups at 10mins and 30mins was also found to be significant statistically. Slight dip in heart rate was found immediately after the administration of butorphanol while hypotension was only observed 10 min after the administration(Fig 1). No such notable variations in the HR and MAP were observed after the administration of granisteron.

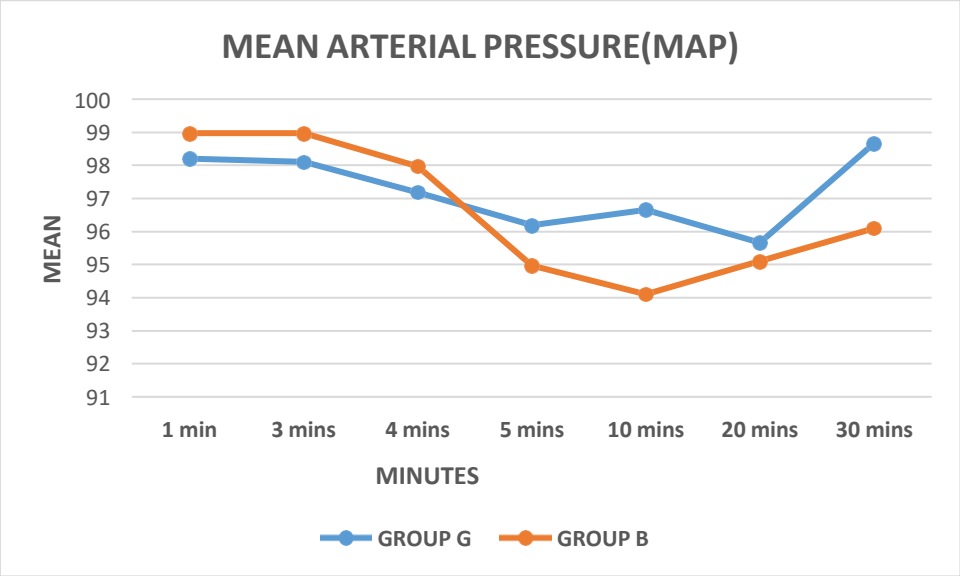

Figure-1- Line diagram showing Mean arterial pressure

However, there was difference in Oxygen saturation (SPO2) at 10 mins and 30mins was found to be significant ststistically between the two groups(Fig 2).

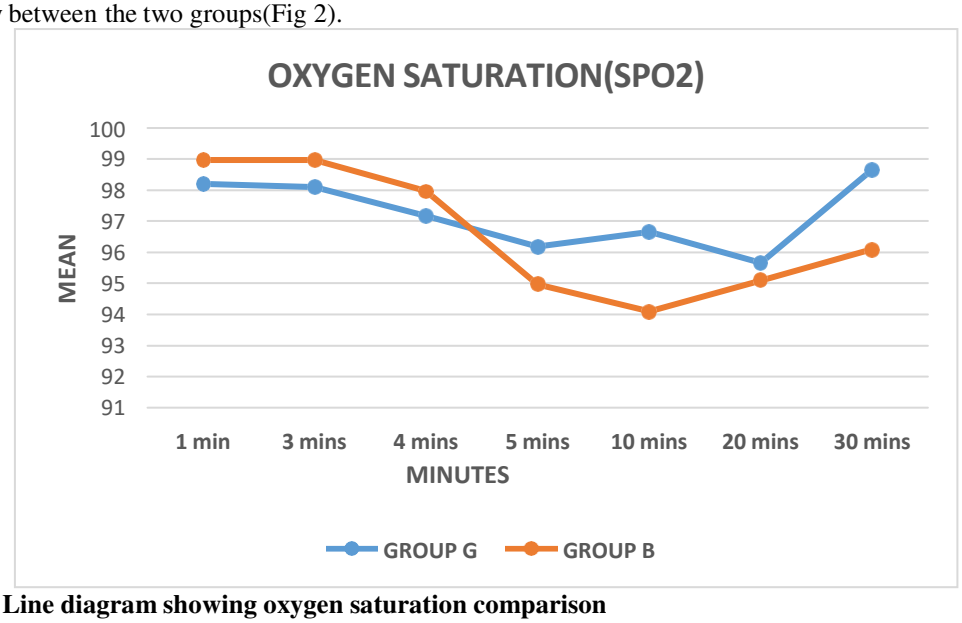

Figure-2 - Line diagram showing oxygen saturation comparison

Grade 3 sedation was observed in all the patients receiving butorphanol whereas grade 2 sedation was noted with granisetron.

Twelve patients who received butorphanol experienced nausea and vomiting during the intra-operative period, while patients who received granisteron had no such complaints. Hence making comparison of the incidence of

side effects between the two groups statistically significant. However, no other side effects wereobserved(Table-4).

Table 4: Adverse effects

Complications	GROUP G n=31	GROUP B n=31
Nausea and vomiting	-	12(0.001%)
Sedation	6(20%)	14(45%)
Pruritis	-	-
Recurrence of shivering	-	-
Respiratory depression	-	-

Data is represented as numbers and n(%),*p value- <0.05 significant.
Group G- Granisetron, Group B-Butrophanol.

DISCUSSION

Shivering is an uncontrollable, oscillatory muscle movement and is a physiological response to hypothermia in an effort to increase metabolic heat generation[2]. Shivering is caused by a reduction in core body temperature, which is caused by a sustained disruption of thermoregulatory autonomic function when under anaesthesia, in addition to infusion of intravenous fluids and low operating roomtemperature[10,11]. The most frequent cause of shivering is perioperative hypothermia[12], however it is difficult to determine the precise incidence of each.

When shivering occurs, oxygen demand may rise by 150% to 500%, and carbon dioxide production may also rise linearly[13,14]. In patients who have decreased myocardial reserve or pre-existing coronary disease shivering exaggerates the condition. Shivering may cause higher wound pain, slower wound healing and a longer recovery time after anaesthesia. It also raises intraocular and intracranial pressure.

Perioperative shivering is a frequent problem that can lead to tachycardia, hypertension, and increased metabolic needs. It impedes with ECG, blood pressure, and oxygen saturation during the intraoperative period[15]. Other risk factors for shivering include the type and length of anaesthesia, the degree of sensory blockage, the temperature of the operating room, and fluid infusion. In comparison to propofol, thiopentone was found to cause higher shivering in females and when used after general anaesthesia. Despite the possibility of rigours in the context of normothermia, it typically happens as a physiological response to maintain the core body temperature.

Although it is possible that shivering frequently develops as a defensive mechanism to hypothermia. In our study we observed reduction in temperature during shivering and after treatment of shivering when compared to baseline values. We observed that there was no significant difference in temperature during and after treatment of shivering, indicating that the cessation of shivering was likely caused by the study drugs resetting thermoreceptors at a lower threshold rather than by a change in body temperature.

Pharmacological intervention lowers the shivering threshold rather than raising body temperature, reducing rigours. Opioids, α-2 adrenergic, serotonergic, and anticholinergic receptors are all implicated in the intricate neurotransmitter pathways that cause shivering. Drugs that affect these systems are used to treat this ailment as a result of this fact.

In our study we observed granisetron to be more effective in controlling shivering over butorphanol. Granisetron and butorphanol both had comparable results in complete suppression of shivering which accords with observations made by D kabade et al[16]concluded that prophylactic granisetron 40ug/kg IV is very effective in control of perioperative shivering following spinal anaesthesia and also reduces the need for antiemetic.

Similar studies by Saito et al[17],showed that impaired thermoregulation under spinal anaesthesia makes hypothermia more likely to occur quickly. The shivering threshold will be achieved earlier and more shivering will be needed to prevent additional hypothermia as a result of the rapid temperature drops that occur during spinal anaesthesia.

We also observed in our study the sedation caused by butorphanol was 20% more compared to granisetronwhich was 6%.In our study we found 12 patients had nausea /vomiting in group B when compared to no nausea/vomiting in Group G. Some studies showed that ondansetron and granisetron are very effective in treatment of nausea,vomiting in caesarean section patients under spinal anaesthesia which correlated with our study[18,19,20].

Similar studies done by Wang Y et al[21]studied on different doses of butrophanol and found to effectively prevent recurrence of shivering in post operative period which provided good postoperative analgesia and recovery.

AsthaPalan et al[9] compared butorphanol with tramadol to control intraoperative shivering under spinal anaesthesia and concluded that butorphanol is better in treatment of shivering during regional anaesthesia when compared to tramadol due its fast onset of action and less adverse reactions.

Krithika V et al[22]compared tramadol and butorphanol for control of shivering and concluded that butorphanol is effective compared to tramadol in treatment of postoperative shivering due to fast onset of action, high success rate and less recurrence.

LIMITATIONS OF THE STUDY

A large sample size can predict more accurate results .Due to differences in body habitus and individual tolerance to temperature differences, the findings of our study might not be congruent with those of studies conducted on other ethnic communities.

CONCLUSION

The incidence of tachycardia, hypotension and vomiting was significantly higher with butorphanol when compared to Granisetron. Butorphanol onset of action was faster with mild sedative effects .Thus Granisetron is superior to butarphanol in control of shivering.

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