



Original Research Article

Comparison of butorphanol and clonidine for control of intraoperative shivering under spinal anaesthesia

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ABSTRACT

Introduction: Shivering is a very common complaint in many patients intra-operatively after spinal anaesthesia. The reasons for shivering are multiple. Several measures are taken to prevent and control shivering under spinal anaesthesia. These measures include pharmacological and non-pharmacological intervention. Pharmacological intervention is an effective method to control shivering under spinal anaesthesia because the drugs for controlling shivering are easily available and it is cost effective. The present study was planned to compare effectiveness of two drugs: Butorphanol and Clonidine which were given intravenously to control shivering under spinal anaesthesia.

Material and Methods: The design of study was randomized and double blind. It included total of 60 patients of ASA I/II physical status. These patients were posted for elective surgeries under spinal anaesthesia; which included lower abdominal, urological and lower limb surgeries. Among these; patients who developed shivering of Grade 3 or 4 intra-operatively were included in our study. These patients were randomly divided into two groups: Group C and Group B. Each group included 30 patients. Group C patients were given Clonidine 1 µg /Kg and Group B patients were given Butorphanol 0.03 mg/Kg intravenously. The drugs were given after patient developed shivering of grade 3 / 4 intra-operatively during spinal anaesthesia. Time needed for control of shivering; whether complete or incomplete control of shivering, side effects of drugs and recurrence of shivering were observed and noted.

Results: The study groups were comparable with respect to demographic profile, duration of surgery and mean time for onset of shivering. Time required for control of shivering was more with Clonidine (331.33 ± 70.65 seconds) as compared to Butorphanol (81.17 ± 37.38 seconds). The incidence of recurrence was significantly more with Clonidine as compared to Butorphanol (P < 0.001). The percentage of side effects such as hypotension and bradycardia was significantly higher with Clonidine as compared to Butorphanol. The incidence of sedation was not statistically significant between two groups.

Conclusion: Butorphanol is better than Clonidine for control of shivering which occurs intra-operatively under spinal anaesthesia. The advantages of Butorphanol are faster control with lower incidence of recurrence of shivering and lower incidence of side effects such as hypotension and bradycardia.

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1. Introduction

Shivering is a normal thermoregulatory mechanism to increase heat production in response to hypothermia.¹ Shivering is one of the complications of spinal anaesthesia. It interferes with monitoring of ECG, oxygen saturation and blood pressure of the patient. Shivering under spinal

anaesthesia is due to impairment of thermoregulatory control.² Its reported incidence is 56.7%.³ Cold environment of operation theatre, infusion of cold fluids and impairment of temperature control mechanism of body under anaesthesia are responsible for decrease in core body temperature and shivering.^{1,4}

Regional anaesthesia leads to impairment of autonomic thermoregulation. It also prevents peripheral vasoconstriction and these two factors are responsible for decrease in

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core body temperature intraoperatively. The thresholds for vasoconstriction and shivering are decreased by 0.6°C above the level of block^{5,6} and reduction is proportional to number of segments blocked.⁷

Shivering under spinal anaesthesia can be very distressing for the patients. Mild shivering increases oxygen requirement to a level that is equivalent to requirement produced by light exercise while severe shivering may increase oxygen consumption to 200 to 500%. Shivering may increase intraocular and intracranial pressure and also interferes with patient monitoring.⁴ Shivering may also induce arterial hypoxemia rarely and is detrimental to the patients with low cardio-respiratory reserves.⁸ Considering the above mentioned facts, primary prevention and prompt control on occurrence of shivering is essential.

Shivering under regional anaesthesia can be controlled by various methods. Non pharmacological methods for control of shivering requires use of equipments like blanket warmer, fluid warmer etc. These equipments are expensive and it is also not possible to use them in each and every case due to lack of availability. Pharmacological methods for control of shivering includes use of drugs. The drugs like ondansetron, clonidine, doxapram, pethidine, ketanserine, nefopam etc have been tried but debate on ideal anti-shivering drug continues.

Butorphanol tartrate is a centrally acting opioid analgesic with potent anti-shivering property mediated through κ (Kappa) and μ (mu) receptors.⁹ Clonidine is an alpha-2 adrenoreceptor agonist, with antihypertensive, sedative, analgesic and antishivering properties. Clonidine exerts its antishivering effect by decreasing the release of nor adrenaline from the axonal terminals in the hypothalamus.¹⁰

Very few studies have been done to compare efficacy of Butorphanol and Clonidine for control of intra-operative shivering under spinal anaesthesia. Hence we conducted a study to compare effectiveness of Butorphanol and Clonidine for control of shivering under spinal anaesthesia and to find out of the two drugs as to which is better for control of intra-operative shivering.

2. Material and Methods

The design of this study was based on randomized double blind interventional study. The study was done in a teaching tertiary care hospital associated with a medical college and was approved by the institutional ethical committee. The study was carried in sixty ASA I/II patients who were aged between 18 to 60 years. All the patients underwent elective surgery. The surgeries included in study were lower limb fractures, infra-umbilical and urological surgeries. The patients were given spinal anaesthesia attaining T6 to T10 dermatome block. Sealed envelope technique was employed for grouping the patients into two groups; Group B (Butorphanol) and Group C (Clonidine). The patients were explained about the study

after which written informed consent was taken from them. Patients with fever, thyroid disorder, neuromuscular disease, compromised cardio-respiratory conditions, patients on long term phenothiazines & MAO inhibitors, patients with hepatic & renal insufficiency were excluded from the study. Patients having contraindication to spinal anaesthesia were also excluded.

In the operation theatre intravenous access was secured, standard monitors were attached and vitals were noted. The vitals observed included heart rate, systolic & diastolic BP, respiratory rate oxygen saturation, ECG and surface body temperature from axilla. Benzodiazapenes and Opioids were neither given preoperatively or intraoperatively. Temperature in operating room & post anaesthesia care unit was maintained at $20\text{--}23^{\circ}\text{C}$. Prior to neuroaxial blockade, patients were preloaded with intravenous fluid- Ringer Lactate @ 10ml/kg. The drugs and fluids administered were stored at room temperature.

Spinal anaesthesia was given in sitting position with a 25 G Quinke needle at L3-L4/ L4-L5 interspace with midline approach. Drug given was hyperbaric 0.5% Bupivacaine. T6-T10 dermatome level was attained as per surgical requirement with hyperbaric bupivacaine in a dose range of 15-20 mg. Post induction patients were observed intraoperatively for shivering, heart rate, blood pressure, oxygen saturation, surface body temperature and time required for shivering to disappear. The shivering intensity was graded on a scale of 0-4 as per Crossley & Mahajan scale.¹¹

Patients with intra-operative shivering of grade 3 or grade 4 which lasted for two minutes were included in the study. One of the study drug was given to these patients for control of shivering. Double blind randomization technique was used. The principal investigator who was administering the study drug and monitoring the patient was unaware of the type of drug handed over to him for administration to patient and patients were also unaware of the type of drug administered to them. Unblinding was done at the completion of study.

Patients who developed grade 3/4 shivering were given O_2 @ 6 liters/minute. This was followed by intravenous administration of one of study drug as per allocation- Group B: Butorphanol in dose of 0.03 mg/kg and Group C: Clonidine in dose of 1 μg /Kg intravenously. Both study drugs were diluted upto 10 ml and given slowly over 20 seconds. Patients were observed for the control of shivering and the time was noted for the control of shivering. The degree of remission of shivering was also noted. Accordingly complete control of shivering meant when shivering became grade 0, incomplete when shivering was not completely controlled after five minutes of drug administration though the grade of shivering decreased and failure when there was no change in grade of shivering after five minutes of study drug administration.

Table 1: Shivering grades (Crossley and Mahajan Scale)¹¹

Grade 0	No shivering
Grade 1	One or more of the following: Piloerection or peripheral vasoconstriction, with peripheral cyanosis 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 but not generalized
Grade 4	Gross muscular activity involving the whole body

Time taken for remission of shivering was recorded using stop watch and time in which shivering started after spinal anesthesia was also noted.

Intraoperatively recurrence was treated with intravenous Clonidine 0.5 µg /Kg in group C or Butorphanol 0.015mg/ kg in group B. Hemodynamic parameters were also noted during recurrence along with time taken for control of recurrence. In case of significant hypotension intraoperatively (Mean arterial pressure of less than 65 mmhg), Ephedrine 6 mg IV was given in incremental doses to correct hypotension and Atropine sulphate 0.64 mg was given intravenously for bradycardia (heart rate less than 60 beats/minute).

Sedation was observed in patients after the administration of study drug and scored as per filios.¹²

2.1. Statistical analysis^{13,14}

The entire data is statistically analyzed using statistical package for social sciences (SPSS Version 21.0 IBM Corporation, USA) for MS Windows. The inter-group comparison of categorical variables is done using chi-square test or Fisher's exact probability test for 2x2 contingency table. The statistical significance of inter-group difference of means of normally distributed continuous variables is tested using independent sample t test or unpaired t test. In entire study, the p-values less than <0.05 were considered statistically significant.

3. Results

With regards to ASA physical status, Body mass index, Sex and Age, the two groups were comparable.

The two groups were comparable with regards to duration of surgery and baseline axillary temperature ($P > 0.05$). Shivering grade in two groups were not significantly different ($P > 0.05$).

No significant difference ($P > 0.05$) was found between two groups regarding mean time for onset of shivering. However, the two groups showed statistically significant difference regarding mean time taken for control of shivering ($P < 0.05$). Compared to Group B; it is significantly higher in Group C ($P < 0.001$).

Statistically significant difference was also found between the two study groups with respect to control of shivering ($P < 0.05$); In Group B the control of shivering was better than Group C.

Group C showed significantly higher rate of recurrence of shivering as compared to Group B ($P < 0.05$).

Incidence of sedation was comparable in two Groups and was statistically insignificant ($P > 0.05$).

The Hemodynamic parameters were significantly altered from their respective baseline values in the Group C throughout the procedure.

Of 30 cases studied in Group B, one patient (3.3%) had nausea /vomiting. None of the patient in Group B had itching, respiratory depression, bradycardia or hypotension.

Of 30 cases studied in Group C none of the patient had itching, none had respiratory distress. 4 patients (13.3%) had nausea/vomiting.

In Group C, 11(36.7%) patients had hypotension and 11(36.7) had bradycardia. Statistically significant difference was noted with regards to incidence of bradycardia and hypotension between two study Groups ($P < 0.001$). Bradycardia and hypotension was found to occur significantly higher in Group C in comparison with Group B ($P < 0.001$). However with regards to other side effects, two groups did not show statistically significant difference.

4. Discussion

The safety profile of Spinal anaesthesia compared with General anaesthesia makes it the anaesthesia of choice whenever possible. The most common surgical procedures done under spinal anaesthesia include inguinal hernias, lower limb fractures, infra-umbilical and urological surgeries. Shivering is a very common complaint in many of the patients intra-operatively after spinal anaesthesia. Several measures are taken to prevent and control shivering during surgery under spinal anaesthesia. Pharmacological method including drugs is an effective measure to control shivering under spinal anaesthesia because these drugs are easily available at all centers and they prove to be practical in many settings.

The shivering under spinal anaesthesia could be due to decreased in core body temperature or misinformation from receptors.¹⁵ It has been found that the neurotransmitter pathways are involved in the initiation of shivering. These pathways involves opioids, alpha 2 adrenergic agonists, anticholinergic and serotonergic receptors. Hence the drugs acting on these pathways (pethidine, clonidine, tramadol, ondansetron) have been used in controlling shivering.^{1,16}

Table 2: Demographic profile of patients.

Demographic Characteristics	Mean \pm SD		P value
	Group B	Group C	
Age (years)	35.6 \pm 13.5	40.7 \pm 10.9	0.359
Sex Male Female	19 \pm 63.3 11 \pm 36.7	20 \pm 66.7 10 \pm 33.3	0.787 0.787
BMI (Kg/m ²)	21.81 \pm 1.99	21.66 \pm 2.03	0.999
Physical status ASA I/II	20/10	23/7	0.567

Table 3: Comparison of duration of surgery, baseline temperature and shivering grade in both groups

Variables	Mean \pm SD		P- value
	Group B	Group C	
Duration of surgery (minutes)	88.0 \pm 23.9	92.7 \pm 24.7	0.999
Baseline axillary temperature (^o C)	36.8 \pm 0.22	36.8 \pm 0.25	0.999
Shivering grade Grade III Grade IV	15(50%) 15(50 %)	14(46.7 %) 16(53.3 %)	0.999

Table 4: Comparison of anti-shivering effects of drugs in both groups

Variables	Group B		Group C		P- Value
	n	%	n	%	
Mean time for onset of shivering (minutes)	13.27 \pm 2.32		12.73 \pm 2.45		0.999
Time for control of shivering (seconds)	81.17 \pm 37.38		331.33 \pm 70.65		0.001
Control of Shivering Complete	27(90%)	2(6.7%)	15(50%)	10(33.3%)	5(16.7%)
Incomplete Failure Recurrence rate	1(3.3%)	3(10%)	15(50%)		

Table 5: Incidence of Sedation

Incidence of Sedation	Group B	Group C	P- Value
Present Absent	13(43.3%) 17(56.7 %)	14(46.7%) 16(53.3%)	0.999

Table 6: Comparison of side effects

Side effects	Group B		Group C		P-value
	n	%	n	%	
Itching	0	0.0	0	0.0	0.999
Nausea/Vomiting	1	3.3	4	13.3	0.353
Respiratory depression	0	0.0	0	0.0	0.999
Hypotension	0	0.0	11	36.7	0.001
Bradycardia	0	0.0	11	36.7	0.001

This study was planned to compare Butorphanol and Clonidine (given intravenously) for control of shivering which occurred intra-operatively under spinal anaesthesia.

The mean time for onset of shivering after spinal anaesthesia was 13.27 \pm 2.32 minutes in group B and 12.73 \pm 2.45 minutes in group C. Thus it was comparable in both groups. Similar observations were present in a study conducted by Koay CK, Chan WY *et al* in 1991.¹⁷

The mean time taken to control shivering was 81.17 \pm 37.38 seconds in group B and it was 331.33 \pm 70.65 seconds in group C. Time taken for control of shivering was significantly more in group C than group B. The findings were similar with the study done by Bansal P, Jain G in 2011.¹⁸

In our study, control of shivering was not good with Clonidine as compared to Butorphanol. This finding is similar to study done by Bansal P, Jain G in 2011.¹⁸

The incidence of recurrence was also higher with Clonidine than Butorphanol. This observation was exactly opposite to observations of study done by Schwarzkopf *et al*¹⁹ and Horn *et al*.²⁰

We observed in our study that mean axillary temperature at the onset of shivering was 36.2 \pm 0.25^o c in Group B and 36.2 \pm 0.29^o c in Group C which was similar to study done by Dhimar AA, Patel MG *et al*²¹ in 2007 and Bansal P, Jain G¹⁸ in 2011.

The incidence of sedation was statistically insignificant between Group B and Group C. (P>0.005)

In our study Group C, 11(36.7%) patients had hypotension and 11(36.7%) had bradycardia while none of the patient in group B had bradycardia or hypotension. Thus incidence of hemodynamic variations was significantly higher in group C as compared to group B ($P < 0.001$).

In group B, one patient had nausea/vomiting while four patients in group C had nausea/vomiting ($P > 0.005$). None of the patients in group B or group C had itching or respiratory depression. Thus incidence of side effects such as nausea/vomiting, itching, respiratory depression was not statistically significantly between two groups.

Limitation of our study was small sample size. Another limitation was that we were not able to measure core body temperature. The temperature probe needed to be put in oesophagus or near tympanic membrane. Both of them are not comfortable for patients under spinal anaesthesia.

5. Conclusion

From our study we can conclude:

1. Control of shivering is faster and better with Butorphanol than Clonidine.
2. The incidence of recurrence is significantly less with Butorphanol than Clonidine.
3. The incidence of hemodynamic variations (bradycardia / hypotension) is significantly higher with Clonidine as compared to Butorphanol.

6. Source of Funding

None.

7. Conflict of Interest

None.

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