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Comparative Study of Intravenous Butorphanol and Intravenous Tramadol for Control of Intra-operative Shivering Under Spinal Anesthesia

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Abstract

Background: Shivering is one of the complications of central neuraxial blockade due to impairment of thermoregulatory control. Control of post spinal anesthesia shivering is essential for optimal peri-operative care which can be achieved by non-pharmacological and pharmacological means. *Aim:* The present study was designed to evaluate and compare the efficacy of intravenous Butorphanol and Tramadol for control of intra-operative shivering under spinal anesthesia. *Material & Methods:* In this prospective, interventional double blind, randomized study, 60 ASA I/II patients, aged 18–60 years, undergoing elective lower abdominal, urological and lower limb surgeries under spinal anesthesia, who subsequently developed shivering of grade 3 or 4, were randomized into two groups, to receive Tramadol 1 mg/kg or Butorphanol 0.03 mg/kg. Time taken to control shivering, response rate, recurrence rate and side effects such as nausea, vomiting, dry mouth, respiratory depression and sedation were observed. *Results:* Butorphanol had rapid onset of action for control of shivering as compared to Tramadol ($p<0.05$). The incidence of recurrence was significantly higher with Tramadol compared to Butorphanol while as sedation was found to be significantly higher with Butorphanol as compared to Tramadol. Side effects such as nausea, vomiting was significantly higher with Tramadol. *Conclusion:* Both Intravenous Butorphanol and Tramadol are effective treatment for control of shivering following spinal anaesthesia. Butorphanol is superior to Tramadol for control of shivering post spinal anaesthesia in several respects like rapid onset of action, lesser recurrence and lesser incidence of nausea and vomiting.

Keywords: Spinal anaesthesia; Shivering; Butorphanol; Tramadol.

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Introduction

Shivering is a common problem during the intra-operative period under regional anaesthesia. The reported incidence of shivering is 55% following regional anaesthesia [1]. Shivering is an oscillating involuntary muscular activity that increases basal metabolic rate for heat production. It is a physiological response to core hypothermia [2]. Shivering is caused by a lowering of core body temperature which is due to several factors like

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impairment of thermoregulatory autonomic control under anaesthesia, cold temperature of operating rooms and infusion of crystalloids [3].

Shivering can be very distressful and unpleasant for the patients. Mild shivering increases the consumption of oxygen which may be increased by 200 to 500% in severe shivering. Intraocular and intracranial pressures may be raised by shivering. Involuntary muscular activity in shivering interferes with monitoring of parameters like blood pressure, heart rate, oxygen saturation and ECG [4]. Shivering may also contribute to increased wound pain, delayed wound healing and delayed discharge from Post anaesthesia care3. These all factors prompt primary prevention and control of shivering once it occurs.

Effective and prompt treatment for control of shivering is achieved by non-pharmacological and pharmacological methods. Various drugs used for control of shivering include Pethidine, Clonidine, Ketamine, Nalbuphine, Butorphanol, Tramadol etc. However debate for an ideal anti- shivering continues [2,3].

Butorphanol Tartrate is a centrally acting opioid analgesic with potent antishivering property mediated through κ (kappa) and μ (mu) receptors agonistic modulation [5]. Tramadol Hydrochloride is a synthetic opioid with opioid action preferably mediated via μ (mu) receptor and has been effective in controlling post spinal shivering [6].

This clinical study was set out to compare the efficacy of Butorphanol and Tramadol for controlling peri-operative shivering of surgical patients under spinal anaesthesia as primary outcome. Secondary outcomes included peri-operative variations in hemodynamic parameters and incidence of adverse effects among the groups.

Methodology

This randomized, prospective double blind study was conducted in a multi-specialty tertiary care Hospital associated with a medical college from September 2016 to May 2018 and was approved by institutional ethical committee. 60 patients aged between 18 to 60 years with American Society of Anaesthesiologists physical status I/II, posted for elective Lower abdominal, Urological and Lower limb surgeries under spinal anaesthesia were taken up for the study. These patients were divided in two groups of 30 patients each (Group B and Group T) by sealed envelope technique. Group B – Patients were administered Inj. Butorphanol 0.03 mg/kg while Group T – Patients were administered Inj Tramadol 1 mg/kg.

Written informed consent was obtained from all patients. Patients having fever, thyroid disease, neuromuscular diseases, compromised cardio-respiratory conditions, patients on long term phenothiazines and MAO inhibitors and patients with hepatic, renal insufficiency and any contra-indication to spinal anaesthesia were excluded from study.

In the operation theatre, Intravenous access was secured, standard monitors were attached and baseline heart rate, blood pressure, respiratory rate, electrocardiograph (ECG), oxygen saturation (SpO_2) and base line axillary temperature were noted. Sedatives and hypnotics inclusive of opioids were avoided in premedication as well as intra operatively. Ambient temperature of the operating room and recovery room were maintained at 20-23^{0}C. All the patients were preloaded with ringer lactate 10 ml/kg before administration of neuro-axial blockade. All the fluids and drugs were stored and administered at room temperature. Spinal Anesthesia was performed with a 25 gauge quincke spinal needle in a sitting position, at L3-L4/ L4-L5 interspace (midline approach) with bupivacaine (hyperbaric 0.5%) in a dose range of 15-20 mg to achieve a desirable level of T6-T10 dermatome, in accordance with surgical procedure. After induction of spinal anesthesia, patients were observed for the occurrence of shivering, its disappearance, hemodynamic status, axillary temperature and complications (if any) until the post-operative period and parameters were observed and noted. The intensity of shivering was graded on a scale of 0-4 as per Crossley and Mahajan scale.

Shivering grades (Crossley and Mahajan scale)

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 muscle activity involving the whole body.

All the patients who developed intra operative shivering post-spinal anesthesia of grade 3 or grade 4, lasting for a minimum period of two

minutes were included in the study and were given treatment on an intention to treat basis. A double blind technique was used. The principal investigator, who was administering the drug and monitoring the patient, was not aware of the type of drug handed over to him by a senior faculty member of the department. Patients were also unaware of the type of drug administered to them for control of shivering. A record sheet was maintained by the faculty member where in details of patient along with drug administered was maintained. At the end of study un-blinding was done.

At the onset of shivering (grade 3 or 4), all the patients were given oxygen via face mask at six litre/minute and study drug was diluted up to ten ml as per group allocation, in the dose of Tramadol 1 ml/kg and Butorphanol 0.03 ml/kg given over 20 seconds. Shivering control was defined as complete when the shivering grade declined to grade 0, incomplete when the grade was decreased but shivering was not abolished completely after five minutes of drug administration and failed if no change in grades were observed after five minutes of drug administration.

The time taken for complete control of shivering after drug administration was accurately noted in seconds with a stop watch. Patients were monitored for failure of drug, incomplete control, and recurrence of shivering. Time taken for onset of shivering following spinal anesthesia was observed and noted.

Recurrence of shivering was observed until patient left the operation theatre and was treated with tramadol 0.5 mg/kg or butorphanol 0.015 mg/kg. diluted in ten ml normal saline and given over 20 seconds. Hemodynamic parameters were noted during recurrence along with time taken for control of recurrence.

Significant hypotension (MAP < 65 mmhg) would have been treated with intravenous ephedrine six mg in increments and significant bradycardia (HR< 60 beats/minute) with atropine sulphate 0.64 mg intravenously.

Sedation was observed in patients after the administration of study drug and was assessed with a sedation score as per Filos.

Sedation score as per "Filos":

Grade 1	Awake and alert.
Grade 2	Drowsy, responsive to verbal stimulus.
Grade 3	Drowsy, arousable to physical stimuli.
Grade 4	Unarousable.

Statistical Analysis

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 2 x 2 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 the entire study, the p-values less than 0.05 are considered statistically significant.

Results

Table 1: Demographic profile of patients

Demographic Characteristics	Mean ± SD		p-value
	Group B	Group T	
Age (years)	35.6 ± 13.5	39.0 ± 13.6	0.335
Sex			
Male	19 ± 63.3	20 ± 66.7	0.787
Female	11 ± 36.7	10 ± 33.3	0.787

In our study both the groups were comparable with regards age and sex (Table 1).

Table 2: Comparison of duration of surgery, baseline temperature and shivering grade in both groups

Variables	Mean ± SD		p-value
	Group B	Group T	
Duration of surgery (Minutes)	88.0 ± 23.9	90.3 ± 26.4	0.721
Baseline axillary temperature (^{0}C)	36.8 ± 0.22	36.8 ± 0.25	0.741
Shivering Grade			
Grade III	15 (50%)	13 (43.3%)	0.605
Grade IV	15 (50%)	17 (56.7%)	

Duration of surgery and baseline temperature were comparable between two study groups (p>0.05). The distribution of grade of shivering among the cases studied did not differ significantly between two study groups (p>0.05) (Table 2).

Table 3: Comparison of anti-shivering effects of drugs in both groups.

Variables	Mean ± SD		p-value
	Group B	Group T	
Mean time for onset of shivering (Minutes)	13.27 ± 2.32	13.03 ± 2.53	0.711
Time to control shivering (Seconds)	81.17 ± 37.38	170.23 ± 48.15	0.001
Control of shivering			
Complete	27 (90%)	22 (73.3%)	0.226
Incomplete	2 (6.7%)	4 (13.3%)	
Failure	1 (3.3%)	4 (13.3%)	
Recurrence rate	3 (10%)	12 (40%)	0.015

The distribution of mean time for onset of shivering did not differ significantly between two groups (p>0.05). Mean time for control of shivering is significantly higher in Group T compared to Group B (p<0.001). The distribution of control of shivering among the cases studied did not differ significantly between two study Groups (p>0.05). Incidence of recurrence was significantly higher in Group T as compared to Group B (p<0.05) (Table 3).

Table 4: Incidence of sedation

Incidence of Sedation	Group B	Group T	p-value
Present	13 (43.3%)	4 (13.3%)	0.020
Absent	17 (56.7%)	26 (86.7%)	

The incidence of sedation was significantly higher in Group B compared to Group T. (p<0.05).

Mean heart rate, mean systolic and diastolic blood pressure along with mean arterial pressure did not significantly alter from their respective baseline values in both the groups, throughout the procedure, barring a few statistically insignificant changes. (p>0.05) (Table 4).

Table 5: Comparison of side effects

Side effects	Group B		Group T		p-value
	n	%	n	%	
Itching	0	00	2	6.7	0.492
Nausea/Vomiting	1	3.3	8	26.7	0.026
Respiratory depression	0	0.0	0	0.0	0.999
Hypotension	0	0.0	0	0.0	0.999
Bradycardia	0	0.0	0	0.0	0.999

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

In Group T, two patients (6.7%) had itching, eight patients (26.7%) had nausea/vomiting, none had hypotension, bradycardia or respiratory depression.

Incidence of nausea/ vomitting was significantly higher in Group T as compared to Group B. (p< 0.05). Incidence of other side effects did not differ significantly between two groups (Table 5).

Discussion

The safety profile of spinal anesthesia compared with general anesthesia makes it the anesthesia of choice whenever possible. Shivering is a very distressing complaint in many of patients intra-operatively after spinal anesthesia. The probable mechanism of shivering under regional anesthesia could be either a result of decreased core body temperature or misinformation from receptors [7].

Various pharmacological and non-pharmacological methods have been used to prevent and control shivering. Pharmacological intervention is an effective measure to control shivering under spinal anesthesia because these drugs are easily available at all centers and they prove to be practical in many settings.

This study was formulated with an aim to compare the efficacy of two drugs; Butorphanol and Tramadol given intravenously for control of shivering under spinal anesthesia.

The mean time for onset of shivering following spinal anesthesia was comparable in both groups. In group B it was 13.27 ± 2.32 minutes while in group T it was 13.03 ± 2.53 minutes. Similar observations were made in a study conducted by Koay CK, Chan WY et al. in 1991. They observed that if shivering under spinal anesthesia occurs, it usually occurs within ten minutes after administration of spinal anesthesia [8].

Time taken for control of shivering was significantly lower in group B than group T. While the mean time taken to control shivering was 81.17 seconds ± 37.38 seconds in group B, it was 170.23 ± 48.15 seconds in group T. The results were in accordance with studies conducted by Joshi SS, Arora A et al. [9] in 2013 and Krithika V, Selvarajan R et al. [10] in 2017. However a study by Maheshwari BS, Shah SK et al. [11] in 2008 showed contrasting results.

In our study, control of shivering was comparable in both groups after the administration of study drugs which accords with the observation made by Joshi SS, Arora A et al. [9] and Bansal P, Jain G [12] in their studies. However we observed that the incidence of failure rate and incomplete control of shivering was higher in Tramadol group.

We observed in our study that the mean axillary temperature at onset of shivering was 36.2 in group B and 36.1 in group T which was similar to a study by Dhimar AA, Patel MG et al. [13] in 2007.

Recurrence of shivering was higher in group T (40%) as compared to group B (10%). This was in accordance with the conclusion of a study by Bansal P, Jain G [12] in 2011 while Maheshwari BS, Shah SK et al. [11] has contrasting findings/results.

The incidence of sedation was significantly higher in group B (43.3%) than group T (13.3%). This finding was similar to finding of the study by Bansal P, Jain G [12] in 2011.

In our study both the drugs gave good hemodynamic stability throughout the course of the study in all the patients. The incidence of nausea/ vomiting as a side effect was significantly higher in group T (26.7%) compared to group B (3.3%). Similar observations were made by Joshi SS, Arora A et al. [9] in their study. None of the cases in both groups had hypotension, bradycardia or respiratory depression.

In our study a dose-response using a single drug may have delineated its antishivering profile and corresponding increase in side effects. Further studies can investigate these aspects or compare the efficacy of combination of drugs for control of shivering under spinal anesthesia.

The limitation of our study includes a relatively small sample size in proportion to the burden of this peri-operative problem.

Conclusion

From our study we can conclude:

1. Both intravenous butorphanol and tramadol are effective treatment for control of shivering following spinal anesthesia.
2. Butorphanol is superior to tramadol for control of post spinal shivering in several respects like more rapid onset of action, lesser recurrence and less incidence of nausea and vomiting with comparable level of safety.
3. Butorphanol causes more sedation than tramadol.

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