

A COMPARATIVE EVALUATION OF BUTORPHANOL WITH PETHIDINE FOR TREATMENT OF POSTSPINAL SHIVERING.

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ABSTRACT

Background: Shivering is a common occurrence in anesthesia practice. It is an involuntary, rhythmic and intermittent muscle contraction beginning in the head & neck, extending to the extremities and culminating in generalized shaking. **Objective:** The present study was conducted with the aim of comparing response time and efficacy of pethidine and butorphanol for relief of postspinal shivering. We also compared the relapse of shivering and associated side effects. **Methods:** 60 patients of American Society of Anesthesiologist grade I and II, aged 18-60 yrs, belonging to either sex, scheduled for elective surgery under spinal anesthesia were included in the study. Patients were randomly allocated to three groups of twenty each to receive either pethidine 25mg (Group A), butorphanol 1 mg (Group B) or normal saline 0.9% (Group C) in equal volume, on occurrence of shivering. **Result:** It was observed that the mean response time was significantly less in Group B (1.59 ± 0.79 min) compared to Group A (3.83 ± 1.7 min) and Group C (13.53 ± 1.5 min). Success rate of butorphanol (Group B) was 95% compared to pethidine (Group A) 85% and saline (Group C) 15%. Relapse of shivering was observed more in patients of Group A (11.7%) as compared to Group B (5.3%) while shivering reappeared in all the patients who responded to saline treatment. Among the side effects, nausea was seen only in Group A (10%) while sedation was found more with group B (20%) compared to Group A (10%) and Group C (0%). **Conclusion:** Butorphanol is better than pethidine for control of postspinal shivering with more rapid response and lesser recurrence rate but is more sedating.

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INTRODUCTION

Perioperative hypothermia is a common problem in anesthesia. Both general and regional anesthesia influence the thermoregulatory process. Shivering is a frequent and serious consequence of hypothermia.^[1] The reported incidence is 67% following general anesthesia^[2] and 56.7% following regional anesthesia.^[3]

Regional anesthesia prevents peripheral vasoconstriction and impairs autonomic thermoregulation leading to intra-operative core hypothermia. The thresholds for vasoconstriction and shivering are decreased by 0.6° C, above the level of block^[4,4] and the reduction is proportional to the number of spinal segments blocked.^[5]

The legs constitute nearly half of the body surface area and the bulk of the peripheral thermal compartment. Prevention of vasoconstriction in legs by regional anesthesia markedly impairs regulatory ability to maintain core temperature.^[1,6] In addition, cold operating room environment and intravenous fluids also contribute to fall in body temperature and hence shivering. It not only adds to psychological stress to the patient but also

physiologically leads to an increase in O₂ consumption by 200-500%, increase in intraocular & intracranial pressures, and interferes with patient monitoring.^[7]

To overcome all the above mentioned consequences of shivering, several pharmacological agents have been used to prevent and treat it. Butorphanol tartrate is a centrally acting opioid analgesic with potent antishivering property mediated through kappa and μ receptors agonistic modulation^[8,9] while, pethidine exerts its effect through kappa receptors, N-methyl D-aspartate antagonism and stimulation of $\alpha 2$ adrenoreceptors.^[10,11] The aim of the present randomized double blind study was to compare the response time, efficacy and adverse effects of intravenously administered butorphanol and pethidine for relief of shivering.

METHODS

After institutional approval and written informed consent, 60 ASA grade I and II patients aged 18-60 yrs, belonging to either sex, scheduled for elective surgery under spinal anesthesia, who experienced shivering (\geq grade 3), were allocated randomly by draw of lots

method into three groups to receive either pethidine 25mg (group A), butorphanol 1mg (group B) or normal saline (group C, control). All the study drugs were prepared by blinded observer in equal volume (2 ml). Patients with coagulopathy, on anticoagulants, having systemic diseases like hypo or hyperthyroidism, cardiopulmonary diseases, anaemia, neuromuscular pathology, hepatic & renal insufficiency and with grades I and II of shivering were excluded from the study. On occurrence of shivering, the study drugs were given intravenously to the patients in a double-blind manner.

In the operating room, temperature was maintained at 23-25°C and humidity 50-52%. Intravenous fluids and local anesthetic drug were maintained at room temperature and all the patients were preloaded with 10ml/kg of ringer lactate. Baseline vital parameters and rectal temperature were recorded using rectal temperature probe connected to monitor Drager Infinity Vista XL. All the patients were given spinal anesthesia with 25G Quincke spinal needle at L₃-L₄/L₄-L₅ level (midline approach) using 3ml of 0.5% (heavy) bupivacaine. Modified Bromage scale was used to evaluate motor blockade while the sensory blockade was assessed by pinprick method. All patients were covered with one layer of surgical drapes. No other warming device was used. Patients were closely observed for control of shivering and time taken to control shivering by an independent observer blinded to group allocation. Time of onset and grade of shivering after subarachnoid blockade (SAB) was recorded. On occurrence of shivering of grade ≥3, study drug was administered intravenously as per group allocation.

Response to drug was assessed as: Success-(absence of shivering), Null-(shivering intensity not changed). Response time i.e. the time to cessation of shivering after treatment was noted. It was defined as the time from the administration of the study drug to the time shivering stopped, as determined by an independent observer. Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO₂), and respiratory rate (RR) were recorded at the onset of shivering and then every 5 min for 30 min to monitor response to the treatment drug and side effects related to it. Rectal temperature was recorded at the onset of shivering. Patients were also observed for any relapse of shivering. No additional drug was given for null response or relapse cases. Warm saline bottles and cotton were used for these patients. Patients were monitored for side effects or any complications following drug administration, such as nausea, vomiting, pruritus, sedation, respiratory depression and bradycardia. Respiratory depression was defined as respiratory rate of less than 8/min and bradycardia as heart rate below 20% of baseline respectively. Nausea, vomiting and pruritus were assessed using four point scale: 0-None, 1-Mild, 2-Moderate, 3-Severe. Shivering and sedation were assessed according to gradation below:

Shivering Grades:¹²

0	-	No shivering
1	-	Piloerection or peripheral vasoconstriction but no visible shivering
2	-	Muscular activity in only one muscle group
3	-	Muscular activity in more than one muscle group but not generalised.
4	-	Shivering involving the whole body.

Only Patients with grade '3' and '4' of shivering were included in the study.

Sedation was assessed after 10min of treatment with study drug.

Gradation of Sedation:¹³

0	-	Awake
1	-	Drowsy
2	-	Asleep but arousable
3	-	Asleep but not arousable

STATISTICAL ANALYSIS

Assuming response time in group A 4.2±1.9 min and that in group B 2.3±1.4 min as observed in initial pilot observations with 80% power and 5% alpha error, sample size required was 19 cases per group. Therefore, we decided a sample size of 20 cases in each group.

Data was analysed using SPSS 15.0 statistical software (Illinois, Chicago). Demographic data and vital parameters were expressed as mean ± S.D. All the categorical data was analysed by using chi-square test/ Fisher exact test. Continuous data was analysed by using one way analysis of variance (ANOVA) test, followed by post hoc comparisons by Bonferroni's method. Besides this, change in hemodynamic parameters after treatment with the study drug was evaluated by repeated measure analysis (two way ANOVA). A p value of <0.05 was considered statistically significant.

RESULTS

Patient characteristics and duration of surgery in all the three groups were comparable (Table 1). Level of sensory blockade and degree of motor blockade achieved was also similar between the groups. Mean rectal temperature decreased significantly after SAB, at the onset of shivering in all the groups compared to preoperative values, however, on comparison no significant intergroup difference was found. All the groups were comparable with regard to time of onset and grading of shivering. Shivering was controlled in 95% of patients in butorphanol group compared to 85% of patients in pethidine group and 15% in normal saline group. A statistically significant difference (p value <0.001) in success rate was observed when group A and group B were compared to group C (Figure 1). It was observed that mean response time to the cessation of shivering after injection of drug was 3.83±1.7min in group A while it was 1.59±0.79 mins in group B and 13.53±1.5 min in group C which was statistically significant (p value <0.001) on intergroup comparison (Figure 2). Out of patients who were successfully treated after the injection of study drug, relapse of shivering was observed in two patients (11.7%) in group A, one patient (5.3%) in group B and three patients (100%) in group C. This difference in relapse rate was insignificant (p value 0.59) when pethidine group was compared to butorphanol group, however, statistical significant difference (p value <0.001) was observed when these groups were compared to control group.

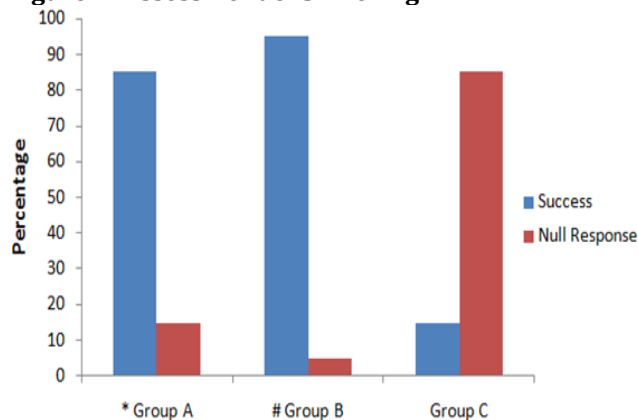
No statistically significant difference was noted in vital parameters i.e. PR, SBP, DBP, SpO₂, RR in all the three groups compared to pretreatment values (p>0.05). Among the side effects, two patients (10%) experienced mild nausea in group A while it was not observed in group B and group C. This was not found to be statistically significant. One patient (5%) in group A and two patients (10%) in group B had sedation grade I while one patient (5%) in group A and two patients (10%) in group B had sedation

grade II after 10 minutes of treatment. None of the patients was sedated in group C. Although difference in degree of sedation was found between the groups, this was not statistically significant.

Table 1: Patient Characteristics and Duration of Surgery

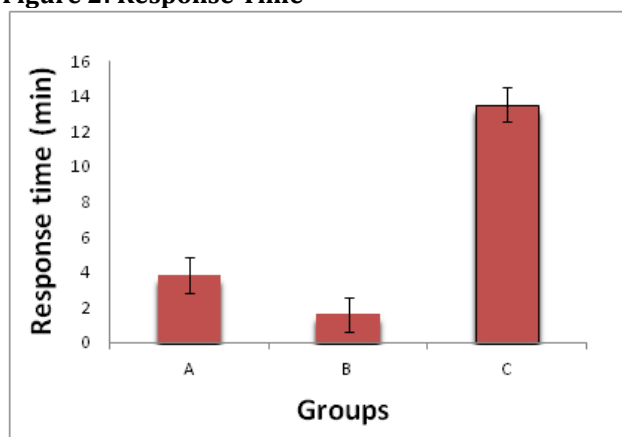
Parameters	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Age(yrs)	33.8±6.84	34.4±10.4	35.6±10.1	0.83
Weight(kg)	64.65±9.0	65.60±8.9	64.05±8.6	0.86
Height (cms)	162.45±6.97	164.35±6.15	164.35±5.87	0.49
Sex(M/F)	14/6	15/5	15/5	0.92
ASA Grading(I/II)	15/5	15/5	15/5	1.0
Duration of surgery (minutes)	81.2±24.7	80.7±30.7	82.5±29.4	0.98

Figure 1: Assessment of Shivering



Note: *Group A vs C; # Group B vs C; symbols indicate points where *P* value < 0.001 on intergroup comparison

Figure 2: Response Time



Note: *P* value < 0.001 on intergroup comparison.

DISCUSSION

Body temperature is centrally regulated, primarily by hypothalamus, which integrates the information from all other organs. Body responds to thermal perturbations by activating the efferent mechanisms which maintain a normal core temperature. Major factors contributing to hypothermia and shivering during regional anesthesia are: internal redistribution of heat from core to peripheral compartment, heat loss to the environment because of vasodilation below the level of block, impairment of centrally mediated thermoregulatory control because of alteration in afferent thermal input from legs (the blocked region)^[1,6] and due to exposure to cold operating room environment and intravenous fluids. Principal defences against hypothermia include skin vasomotor activity, non-shivering thermogenesis and shivering. Thermoregulatory vasoconstriction decreases cutaneous heat loss and maintains body temperature. Spinal anesthesia inhibits

vasoconstriction and shivering in lower extremities through sympathetic and somatic neural blockade.^[14] Since, shivering in these patients is restricted to the small muscle group cephalad to block, resulting in heat loss in excess of heat production, causing hypothermia. Even, in our study we observed mean rectal temperature decreased significantly after SAB, at the onset of shivering compared to the preoperative value.

Several groups of drugs have been used till date to treat post-anesthetic shivering. In this study we used pethidine and butorphanol in the doses used by most authors.^[2,9,13,15-18] We found that butorphanol (1mg) and pethidine (25mg) given through intravenous routes are effective in treating postspinal shivering while normal saline did not show any significant effect. Butorphanol (group B) was effective in 95% patients compared to success rates of pethidine (group A) in 85% of patients and normal saline (group C) in 15% of patients only.

Our results were similar to those of Wang JJ et al^[16], Vogelsang J et al^[17,19] and Wrench IJ et al^[20] but in contradiction with the observations made for butorphanol by Maheshwari et al^[8] where they found it to be effective only in 28% of patients.

Present study demonstrated that butorphanol has significantly less mean response time (1.59±0.79min) when compared to pethidine (3.83±1.7min) and control group (13.53±1.5min). Our findings for mean response time are similar to observations made by Bansal P et al^[9] with butorphanol (1.8±0.5min) and Chuan Yu sai et al^[21] with pethidine (4.2± 2.3 min). We found that 90% of patients in group B, experienced cessation of shivering in less than 5 min and 95% patients in less than 10 min, while in group A 75% patients were relieved of postspinal shivering (PS) in 5 min and 85% patients within 10 min. Our findings are in accordance with the studies done by Bansal P et al^[9], Vogelsang J et al^[17,19], Chuan Yu sai et al,^[21] and Macintyre et al.^[22] In group C only 15% patients responded to treatment, out of which 5% experienced cessation of PS within 15 min and 15% of them within 20 min. Wang Jhi Joung et al^[16] and Wrench et al^[20] also found similar results.

In our study relapse of shivering was seen more with group A (11.7%) compared to group B (5.3%) while shivering reappeared in all the patients who responded to saline treatment, group C. This observation for pethidine was consistent with observation made by Vogelsang J et al^[17], Wrench et al^[20] and Alfonsi P et al^[23]. Our results for recurrence of shivering with butorphanol were similar to findings observed by Bansal P et al^[9] but it was in contradiction with the findings by Bhaarat S Maheshwari et al^[8]. No significant difference in HR, SBP, DBP, RR and SpO2 was found in any of three groups after injection of treatment drug. Among the side effects, we observed mild nausea in 10% of patients treated with pethidine and no nausea with butorphanol or saline similar to the previous reports^[2,17] but in contradiction to the observations made by Maheshwari et al^[8]. In our study we found butorphanol to be more sedating compared to pethidine, consistent with the findings by Maheshwari et al^[8] and Bansal P et al^[9]. None of the patients in any of the groups experienced hypotension, bradycardia, respiratory depression, pruritus, vomiting or any other side effect.

CONCLUSION

To conclude both butorphanol (1mg) and pethidine (25mg) are effective treatment for shivering following

subarachnoid block. However, Butorphanol is better than pethidine for suppression of postspinal shivering in several respects like more rapid action, fewer treatment failures and absence of nausea or vomiting but it causes more sedation than pethidine.

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