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Title- Shivering control with clonidine, butorphanol, and tramadol during spinal anaesthesia: a comparative study

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Abstract

Background: Shivering is a physiological response to core hypothermia to increase metabolic heat generation. Prolonged impairment of thermoregulatory autonomic function under anaesthesia, along with cool operating room temperatures and cold infusion fluids, causes shivering.

Methods: This prospective study included 90 individuals who shivered under spinal anaesthesia during abdominal or orthopaedic surgery. On shivering, patients received a 1 mL intravenous bolus dose of 50 mg tramadol, 1 mg butorphanol, or 150 mcg clonidine. All 3 groups were compared for shivering control, time to cessation, recurrence, hemodynamic changes, axillary temperatures, and side effects. Data was processed using statistical methods.

Results: Butorphanol and tramadol decrease shivering better than clonidine. Butorphanol, tramadol, and clonidine totally decreased rigours in 83%, 73%, and 53% of patients, respectively. Clonidine (3.3±0.9 minutes) took longer than butorphanol and tramadol (2.1±1.0 minutes and 1.8 ±0.5 minutes; P 0.001).

Conclusion: Butorphanol controlled shivering with fewer recurrences than tramadol, but both were better than clonidine with an early onset of action. Both opioids reduce rigours better than α-2 agonists.

Keywords: perioperative shivering, spinal anesthesia, tramadol, clonidine, butorphanol, thermoregulatory center

Introduction

Shivering is a physiological response to core hypothermia to increase metabolic heat generation. [1] Prolonged impairment of thermoregulatory autonomic function under

anaesthesia, along with cool operating room temperatures and cold infusion fluids, causes shivering. [1,2] Shivering can be caused by transfusion responses, medication reactions, high-grade fever, bacteremia, or contaminated intravenous fluids (fungal growth in dextrose containing fluids). Perioperative hypothermia is the most prevalent cause of shivering, however incidence is hard to measure. Shivering increases oxygen use by 200%–500% and carbon dioxide generation linearly. [3] Shivering may impair myocardial function in patients with insufficient oxygen reserve or coronary disease. [4] Shivering increases intraocular and intracranial pressure, wound discomfort, and postanesthetic care discharge. [2] Its harmful effects require primary prevention and rapid control. Various pharmaceutical interventions try to prevent or treat shivering, including opioids (pethidine, nalbuphine, or tramadol), ketanserin, propofol, granisetron, doxapram, physostigmine, clonidine, and nefopam. [2,5] In India, opioid licence restrictions and medicine scarcity worsen the problem. [6] Tramadol hydrochloride, a -opioid receptor agonist, inhibits the neuronal uptake of noradrenaline/serotonin and stimulates hydroxytriptamine production, which resets the body's temperature regulating centre. In clinical trials, it's been shown to reduce shivering. [6-8] Clonidine, an alpha-2 agonist, reduces noradrenaline release from hypothalamic axonal terminals to reduce shivering. [9] Butorphanol, a commonly available opioid, modulates k and receptors, however few studies have shown its anti-shivering benefits. [10] present observational study compared clonidine, butorphanol, and tramadol for perioperative shivering in spinal anaesthesia patients. Variations in hemodynamic parameters and deleterious effects were secondary outcomes.

Material and methods-

After getting written/informed consent from patients, we conducted this observational study on both sexes between 18 and 65. The study comprised patients with American Society of Anesthesiologists physical status I–III who shivered intra or postoperatively (up to 2 hours). Hypo or hyperthyroidism, morbid obesity, fever, and cardiopulmonary impairment were excluded. Group A received 50 mg (1 mL) tramadol, Group B received 1 mg butorphanol, and Group C received 150 mcg (1 mL) clonidine. All operating rooms had standard monitors and baseline values collected. The surgery room and recovery room were kept at 22°C–28°C. Spinal anaesthesia was delivered with a 25- or 26-gauge Quincke spinal needle, in a sitting position, at the L 3–4/4–5 interspace (midline approach with 0.5%, heavy) at a dose of 3.2–3.5 mL, to obtain an acceptable level at T8–10 dermatome. Patients were monitored for shivering after spinal anaesthesia until postoperatively. 0 = no shivering; 1 = shivering in face and head (mild); 2 = apparent tremors involving more than one muscle group (moderate); 3 = extensive muscular activity involving the entire body, bed shaking (severe). Only cases with grade 2 or 3 perioperative shivering were treated. At grade 2 or 3 shivering, all patients received 6 L/min of oxygen via face mask and 1 mL of the study medication. Complete shivering control was defined as scores dropping to 0 post-treatment, incomplete as scores dropping but not abolishing shivering, and unsuccessful as no change in scores. Grade 0 = Alert; 1 = Arouse to voice; 2 = Arouse with modest tactile stimulation; 3 = Arouse with intense tactile stimulation; 4 = No awareness. At 5-minute intervals up to 15 minutes, rigours and hemodynamic changes were recorded. Recurring (any rise in shivering scores post-

treatment) episodes of rigour and axillary temperatures were observed in each group, as were probable study drug side effects. Recurrences or incomplete control were treated with convection heaters, moderately warm fluids, multimodal therapy (propofol [50 mcg/kg] and/or pethidine [0.5 mg/kg]), or both.

Results

During the study period, 340 spinal anaesthetics were delivered; 90 patients had grade 2 and 3 shivering. The study groups had similar demographics, ASA health status, and surgical duration (Table 1).

Table 1 Demographic profile of patients in all groups

Patient variables	Group C	Group B	Group A
Age (years)	34 ± 12	38 ± 16	33 ± 14
Sex (M/F)	21/9	23/7	25/5
Weight (kg)	49 ± 13.5	53 ± 11.0	54 ± 15.8
ASA status (I/II/III)	21/7/2	25/2/3	22/5/3
Duration of Surgery (min)	64 ± 23	66 ± 16	72 ± 27
IV fluid infused (mL)	1103.82 ± 125.9	1153.82 ± 151.6	1146.87 ± 170.8

Though axillary temperatures fell at both data points, no significant differences were seen across groups. All 3 groups had equivalent hemodynamic characteristics at shivering onset. In all 3 groups, hemodynamic measures tended to fall, but the clonidine group had a considerably larger fall in systolic and diastolic blood pressure and rise in pulse rate at various time intervals. A significant decline in mean axillary temperatures (1.2ºC to 1.4 ºC) was observed in all 3 groups during rigors and at post-treatment interval (after 15 minutes) compared with their baseline values (Figure 4). The response rate (complete cessation of shivering after treatment) was 53%, 73%, and 83% for Groups C, A and B, respectively, which was significantly low for patients treated with clonidine compared with tramadol and butorphanol (Table 2). The time taken for complete cessation of shivering was also significantly higher (3.3 ±0.9 minutes) in Group C than in Group A (2.1 ± 1.0 minutes) and B (1.8 ± 0.5 minutes) (*P* , 0.001), though the difference between tramadol and butorphanol was insignificant (*P* = 0.13). The degree of recurrent shivering was significantly less in butorphanol (2) treated cases as compared with those receiving clonidine (8) and tramadol (9). Five cases in Group A and 4 each in Group B and Group C (total 13) had nausea and vomiting at different time intervals, though the difference was non-significant in each group (*P* . 0.05). A comparatively higher incidence of grade 1 and 2 sedation was observed in butorphanol-treated cases (12/7) compared with Group A (3/0) and Group C (8/3) respectively. The incidence of grade 2 sedation was significantly higher (*P* = 0.023) in 26% (7) of butorphanol-treated cases, compared with 10% (3) in clonidine-treated cases and 0% in tramadol-treated cases. Episodes of oxygen desatura-tion or respiratory depression were not detected in any patient of any group during the study (*P* . 0.5), probably due to oxygen supplementation during shivering.

Table 2 Effect of studied drugs in all 3 groups and their significance

Variable	Group C (%)	Group B (%)	Group A (%)	*P* value
Shivering control				0.10*, 0.34**, 0.012#
Complete	16 (53.3)	25 (83.3)	22 (73.3)	
Incomplete	7 (46.6)	4 (16.6)	5 (26.6)	0.51*, 0.71**, 0.31#
Time taken for cessation (min)	3.3 ± 0.9	1.8 ± 0.5	2.1 ± 1.0	﹥0.001*, 0.13**, ﹥0.001#
Recurrence of shivering	8	2	9	0.77*, 0.01**, 0.03#
Nausea and vomiting	4	4	5	0.71*, 0.71**, 1#
Sedation score: 1/2	8/3	12/7	3/0	0.03*, ﹥0.001**, 0.10#

Discussion

Shivering causes hypertension, tachycardia, and higher metabolic demands. It interferes with intraoperative ECG, BP, and SpO2 monitoring. [5] Type and length of anaesthesia, sensory blockage, age, and operating room and infusion fluid temperatures might cause shivering. [11] Postoperative shivering occurred in 5%–65% of general anaesthesia patients and 30% of regional anaesthesia volunteers, but no additional investigation supports this observation. 3 After general anaesthesia, thiopentone and females shivered more than propofol. [12] Rigor is a protective reaction to core hypothermia, however it can occur in normothermia. During shivering and post-treatment, all 3 groups' axillary temperatures fell significantly (P 0.001) compared to their baseline values. A non-significant temperature difference was identified between cases during shivering and post-treatment, indicating that cessation of rigours was not connected to modulation in body temperature, but was likely due to resetting thermoreceptors at a lower threshold by the examined medications. Pharmacological intervention doesn't enhance body temperature, but lowers the shivering threshold, reducing rigours. Shivering involves opioids, -2 adrenergic, serotonin, and anticholin-ergic receptors. Drugs targeting these systems are used to treat this disorder. [1,2] Butorphanol trumped tramadol and clonidine in our tests. Tramadol and butorphanol both completely suppressed shivering, confirming Atashkhoyi and Negargar, Dhimar et al, and Bhatnagar et al. [15] In our study, tramadol-treated patients had a higher incidence of rigours recurrence than butorphanol-treated patients (8% vs 25%). Clonidine-treated patients had decreased efficacy and increased recurrence in controlling shivering. This observation contradicts Schwarzkopf et al1[6]and Horn et al[17], who found 100% response rates in control or prevention of rigours with clonidine after general anaesthesia, however they also saw recurrences. Clonidine took longer than tramadol and butorphanol to control shivering. Most experiments utilising opioids to control rigours took less than 5 minutes, proving opioids' advantage against -2 agonists or other classes of medications. [7–10,14–16]

All 3 groups had a similar incidence of nausea and vomiting. Previous investigations have found a higher incidence of nausea and vomiting with tramadol than clonidine or butorphanol. Gangopadhyay et al[18] found a higher incidence of vomiting with tramadol than pethidine, while Maheshwari et al[10] found a higher incidence of vomiting with

butorphanol than tramadol. Literature suggests opioids cause more emesis, although our doses rarely caused this side effect. Tramadol overdosing causes emesis, butorphanol sedation and respiratory depression, and clonidine hypotension and somnolence. In other studies, following repeated medication dosing to eliminate rigours, these side effects were more common, which may explain why they were less common in ours. [10,14,15,19] Pethidine has an 80%–85% effectiveness rate in preventing and controlling rigidity under regional anaesthesia or following general anaesthesia. Butorphanol (83% of instances) was superior to tramadol (73%) and clonidine (63%) as an anti-shivering medication due to its early beginning of action, higher rate of shivering cessation, and lower recurrence.

Conclusion- We find that butorphanol and tramadol are preferable to clonidine for postoperative shivering treatment due to higher success rates, earlier onset of action, and lower recurrence with equivalent levels of safety. Opioids currently have a strong reputation as dependable anti-shivering medicines, however the quest for an ideal alternative is ongoing.

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