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CONTROL OF SHIVERING UNDER SPINAL ANAESTHESIA- A PROSPECTIVE RANDOMIZED COMPARATIVE ANALYSIS OF BUTORPHANOL, TRAMADOL AND CLONIDINE

Anaesthesiology

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ABSTRACT

INTRODUCTION: Shivering that develops following spinal anaesthesia is a common problem and may occur in 40- 70% of patients .Perioperative hypothermia is the primary cause which occurs due to inhibition of thermoregulatory mechanism in the hypothalamus. It is detrimental to the patient hence effective control of shivering is mandatory.

AIM: To compare the relative efficacy of Butorphanol, Tramadol and Clonidine and find first line of management for the control of shivering during spinal anaesthesia in lower abdominal,lower limb and open gynaecological surgeries and study their side effects **MATERIALS AND METHOD:**114 (38 for each drug group) ASA 1 and 2 patients of either gender, aged between 18 to 65 yrs in the above mentioned surgeries who developed shivering after spinal anaesthesia were included in the study. Tab. Diazepam 10 mg was given the night before and morning of surgery. Baseline heart rate, SpO_2, Blood pressure, ECG and axillary temperature were recorded. Subarachnoid block was performed with Inj. Bupivacaine heavy 0.5% (3-4 ml) at L3-L4/L4-L5 interspace.Heart rate, SpO_2, NIBP and axillary temperature was recorded till 1 hour post operatively. For the patients who developed grade 2 and above of shivering , group B received 1mg Butorphanol ,group T 1mg /kg Tramadol and group C 1 µg/kg Clonidine randomly after diluting to 5 ml.The time and temperature at onset of shivering,time taken for control of shivering ,side effects- nausea, vomiting, hypotension, bradycardia,dry mouth,skin rash,sedation score,recurrence of shivering were noted.Statistical analysis was done using One way Anova and Chi square tests .**RESULTS:** There was a statistically significant difference in between the drug groups only for recurrence of shivering after drug. More recurrence was found with Clonidine. There was significant reduction in heart rate at 1 hour in Clonidine group compared to B and T groups. ASA-ps, grade of shivering, duration, time at onset of shivering, pre-op temp, temp at onset, time to control of shivering, SBP, DBP, MAP and SpO2 differences were not statistically significant.**CONCLUSION:** Clonidine caused more recurrence and more reduction in heart rate. Butorphanol had a faster control of post spinal shivering though not statistically significant. Tramadol and Butorphanol can be used with almost no side effects for post spinal anesthesia shivering,a higher dose of Clonidine may be required.

KEYWORDS

shivering spinal Anaesthesia Butorphanol Tramadol Clonidine

INTRODUCTION

Shivering that develops following spinal anaesthesia is a common problem and may occur in 40-70% of patients receiving spinal anaesthesia (1).Shivering, an involuntary oscillatory muscular activity, is a response to core hypothermia. It is a potentially serious complication resulting in metabolic heat production 600% above the basal level (2). There is also increased oxygen consumption and carbon dioxide production, catecholamine release; increased cardiac output, tachycardia, hypertension, lactic acidosis, and raised intraocular and intracranial pressure. Shivering may also decrease mixed venous oxygen saturation and interfere with patient monitoring (ECG,NIBP,SpO2) (3). It is detrimental to patients with low cardiopulmonary reserve. Therefore effective control of shivering is mandatory.

It has been found that perioperative hypothermia is the primary cause of shivering which occurs due to neuraxial anaesthesia induced inhibition of thermoregulatory mechanism in the hypothalamus. The initial hypothermia in regional anaesthesia results from redistribution of body heat from the core to the periphery. Patients given spinal anaesthetics cannot re-establish core temperature equilibrium, because peripheral vasoconstriction remains impaired, and hence shivering occurs (4). Increase in the muscle tone during shivering is due to temperature induced changes in the neuronal activity in the mesencephalic reticular formation.

Various methods are being used for the control of shivering; these may be non-pharmacological or pharmacological. Non pharmacological methods include passive and active strategies (3) that limit cutaneous heat loss to the surrounding. Cotton drapes, forced air warming, warming blankets, warm IV fluids may be used along with control of operating room environment. Many a times these may not be adequate and pharmacological intervention would be required.

Drugs to treat shivering include opioids like pethidine, tramadol, butorphanol, also ketamine, ondansetron, nefopam etc. Recently clonidine is also being used to treat shivering. Of the study drugs, tramadol is an opioid analgesic with action mediated via mu receptor with modulatory effect on central mono-aminergic pathways whereas butorphanol acts through kappa and mu receptor agonistic modulation (5). Clonidine is a centrally acting selective alpha-2 agonist. The antishivering effects are exerted at three levels-hypothalamus, locus coeruleus and spinal cord (6).Although many drugs have been studied for control of this incapacitating symptom,the search for an ideal anti-shivering agent is still continuing because conclusions of most authors were relatively contradictory (7,8). Hence we are conducting this study in search of an ideal antishivering agent by comparing butorphanol, tramadol and clonidine.

AIMS AND OBJECTIVES

Aim of our study was to compare the relative efficacy of butorphanol, tramadol and clonidine and to find the first line of management for control of shivering during spinal anaesthesia in lower abdominal, lower limb and open gynaecological surgeries and to study the side effects of these drugs, if any.

MATERIALS AND METHODS

The study was a prospective randomized double blinded study conducted from the period October 2014 to September 2015(12 months), after getting Institutional Ethical Committee approval. Written informed consent after explaining in their vernacular language was obtained from each patient undergoing spinal anaesthesia for this study.

114 (38 for each drug group) ASA 1 and 2 patients of either gender, aged between 18 to 65 yrs, posted for lower abdominal, lower limb and open gynaecological surgeries, and who develop shivering after spinal anaesthesia, were included in the study.

Exclusion criteria included patients with fever (axillary temperature >38°C),hypo or hyperthyroidism,BMI > 40 kg/m^2,duration of surgery > 4 hrs,known allergy to study drugs,alcohol or substance abuse, psychiatric disorders and those requiring supplementation with GA.

All patients were given Tab. Diazepam 10 mg the night before and morning of surgery. After shifting the patient to OT, heart rate, SpO_2,

NIBP, ECG and axillary temperature monitoring was done and recorded.

Preloading was done with 10 ml/kg crystalloids. After sterile draping, subarachnoid block was performed at L3-L4/L4-L5 interspace with Inj. bupivacaine heavy 0.5% (3-4 ml) was injected. Ambient OT temperature was maintained between 20-23°C. Oxygen was administered to all patients with face masks at the rate of 5 L/min and they were adequately covered with drapes. All IV fluids and anaesthetic drugs was administered at normal body temperature. Heart rate, SpO_2, NIBP and axillary temperature were recorded every two minutes for the first 10 minutes, then every 5 minutes for 1 hour, followed by every 15 mins till 1 hour post operatively.

The patients who developed shivering after spinal anaesthesia were graded as per Wrench(27)

Grade 0: No Shivering
Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis without visible muscle acitivity.
Grade 2: Visible muscle activity confined to one muscle group
Grade 3: Visible muscle activity in more than one muscle group
Grade 4: Gross muscle activity involving the whole body

Randomization was done using SNOSE (Sequentially Numbered Opaque Sealed Envelopes) technique. The names of the three drugs and their doses were written as given below and put inside opaque envelopes, and they were sealed.The groups being:1mg Butorphanol (Group B),1 mg /kg Tramadol (Group T) and 1 µg/kg Clonidine (Group C).In this way, 114 envelopes (38 in each group) were prepared. One envelope was chosen randomly for the patients who developed grade 2 and above of shivering and the drug was given as mentioned above. The dose was rounded to nearest multiple of 10.

For double blinding, all study drugs were prepared by anaesthesia technician in identical syringes and in equal volume (5 ml) by diluting with distilled water, according to the drug and dose found in the envelope. The attending anaesthesiologist gave the drug as slow IV bolus injection and noted the various study parameters. Neither the observer nor the patient were aware of the nature of drug.

The following observations were recorded once shivering occurred .The time of onset of shivering after spinal anaesthesia (in minutes),the time taken, in seconds, for control of shivering (to Grade 0),temperature at onset of shivering,side effects- nausea, vomiting, hypotension (BP fall more than 20% of SBP at the time of shivering, bradycardia < 50 beats/minute), dry mouth, skin rash,Sedation score as per Filos(28),1.Awake and alert ,2.Drowsy-responsive to verbal stimuli,3.Drowsy-arousable to physical stimuli,and 4.Unarousable, and recurrence of shivering, in minutes.

If shivering did not subside for 15 minutes, treatment was be considered as failed and IV dexamethasone 8 mg was administered .Bradycardia, hypotension and vomiting were treated with Inj. atropine, mephentermine, and metaclopramide respectively in titrated doses whenever required and recorded.

DATAANALYSIS

The data were analysed using SPSS for WINDOWS (Statistical Package for Social Sciences, SPSS Inc, Chicago, Illinois) Software. Three groups were compared using One way ANOVA(Analysis Of Variance). Post hoc intergroup comparison was done with Tukey test. Nominal data was analysed by Chi square test. p value <0.05 was considered significant.

RESULTS

The mean age of Group B was 33.61 yrs, Group C was 39 yrs and Group T was 35.92 yrs with p value of 0.2 in our study.23 male and 15 female patients were studied in Group B whereas in Group C and T had 24 male and 14 female patients each.There were more ASA I than ASA II patients studied in all three groups. C group 28/10, T group 30/8 and B group 31/7 ASA I/II patients.

In our study, 21 patients underwent lower abdominal surgeries, 7 patients lower limb surgeries and 10 patients open gynaecological surgeries in group B, in group C the numbers were 23, 6, 9 and Group T 22, 8, 8 respectively. The mean duration of surgery in the three groups B (73.16 mins), C (71.76 mins) and T (69.08 mins), p value=0.839.The mean time at onset of shivering was found to be 34.08 mins in group T, 31.53 mins in group B and 31.37 mins in group C, (p value 0.860) .The mean grade of shivering was B group(2.58), C group(2.53) and T group(2.68) with p=0.367 which is not statistically significant.The mean temperature at onset of shivering was found to decrease the most in T group compared to B and C groups in our study. B group had the fastest onset of control of shivering (90.55 secs) compared to C group (102.67 secs) and T group (103.92 secs), but p value was not statistically significant . Treatment was successful in all patients in B group, in 97.36% patients in T group and 94.73% patients in C group.In clonidine group there was complete cessation of shivering in 2.54 ± 0.76mins whereas in tramadol group it took 5.01 ± 1.02 mins. Heart rate is decreased significantly in clonidine group at 1 hour in our study. The butorphanol group showed highest reduction in mean systolic blood pressure compared to C and T groups. The mean diastolic blood pressure and mean arterial pressure were also found to decrease the most in butorphanol group than C and T groups.

Sedation score of 2 was higher in butorphanol group (29/76.3%) than C (19/50%) and T (23/60.5%) groups with p =0.059.Clonidine group had 16 patients with recurrence of shivering after mean duration of 14.13 mins. In tramadol group there were 6 recurrences after 9 mins and in butorphanol group there were 5 recurrences after 6.8 mins. Hence C group had maximum recurrences,p value=0.021 is statistically significant. Post hoc Tukey test confirmed significant difference.There were 2 patients who developed nausea in group T,1 patient in group B and none in group C. 1 patient each developed vomiting,hypotension and bradycardia in Tramadol group. There was no statistical significance found in any of the sideeffects (Table 27 and Figures 12,13,14,15). No statistics are computed because of the side effect dry mouth and skin rash are constant.

Bradycardia occurred in 2 patients of group C and 1 patient of group T. In group C, 3 patients suffered from hypotension and 1 patient had dry mouth ,but none in group T.

Table1 .Heart rate (per min)

	Drug group			P value
	B Mean (SD)	C Mean (SD)	T Mean (SD)	
HR- at shivering	83.7(16.5)	81.7(14.1)	79.5(17.7)	0.532
HR- after control of shivering	79.7(13.9)	77.3(11.8)	78.0(18.4)	0.775
HR-after 15 mins	79.0(13.0)	74.4(11.9)	77.7(17.4)	0.367
HR-after 30 mins	77.6(12.0)	71.6(11.6)	76.7(16.1)	0.115
HR-after 1 hour	75.3(11.3)	68.0(11.1)	76.2(14.1)	0.008

Table 2.Time from drug to control of shivering

	N	Mean	Std. Deviation	Std. Error	p value
B	38	90.55	68.270	11.075	
C	36	102.67	65.267	10.878	0.713
T	37	103.92	95.463	15.694	
Total	111	98.94	77.089	7.317	

CONCLUSIONS

Butorphanol had a faster control of post spinal shivering than tramadol and clonidine though not statistically significant .Butorphanol had more sedation compared to tramadol and clonidine which was not significant statistically .Side effects like nausea and vomiting were observed with tramadol and only nausea with butorphanol and none with clonidine.There was statistically significant reduction in heart rate at 1 hour with clonidine but pharmacological intervention was not required. More recurrence of shivering was found with clonidine. Hence a higher dose of clonidine is required for better efficacy at the cost of increased side effect like hypotension. Demerits of our study are that although sample size was calculated based on a previous study, the sample size was relatively small in proportion to the burden of this perioperative problem. Most of the findings in our study were not statistically significant, hence cannot be extrapolated to similar cases done under spinal anaesthesia in general population. Core temperature was not measured during the study as the probe placement was uncomfortable for the patient. Core temperature measurement could have given a better idea about the temperature changes occurring after spinal anaesthesia.The environmental conditions in the operation theatre were maintained in a similar range but exact conditions for all patients was not possible.The drug doses were chosen based on the best response rates and least side effects to find the best drug, this may effect the results of the study.

DISCUSSION

Various pharmacological agents along with the studied drugs tramadol, butorphanol and clonidine, have been used for prophylaxis and treatment of post spinal anaesthesia shivering . These include meperidine (intrathecal and intravenous), nalbuphine, fentanyl, nefopam, ondansetron, granisetron , ketamine, MgSO4 and dexmedetomidine .

The drug clonidine has been used by oral, epidural and intrathecal route apart from intravenous route of administration. Oral clonidine 150mcg given 90 mins before spinal anaesthesia has shown to be effective to prevent shivering in patients undergoing elective urological surgeries (9). When clonidine 150mcg was compared with meperidine 50mg epidurally, it was found to be as effective in controlling shivering in 60 caesarean delivery patients,with greater reduction in heart rate (10). But the same 150mcg clonidine through intrathecal route failed to prevent post spinal shivering compared to 1 mcg/kg given intravenously in orthopaedic surgery patients (11). Foroushzadeh et al (12) in 2006 compared Clonidine 30 mcg, meperidine 25 mg and fentanyl 50 mcg in 60 ASA- I elective caesarean section patients. Their study showed that clonidine offers better thermodynamics along with modest failure rate but meperidine was effective with more serious side effects.

Tramadol has been extensively studied for the prevention and treatment of post spinal anaesthesia shivering and has been found to be very useful. Tramadol at two different doses, 0.5mg/kg and 1mg/kg did not show any difference in response rate or incidence of side effects (13).

Talakoub et al (14) in 2006 studied 73 ASA-I pregnant patients undergoing cesarean section under spinal anaesthesia who developed post operative shivering with tramadol 0.5 mg/Kg and meperidine 0.5 mg/Kg and found that tramadol is more effective in control of shivering but results in more frequent nausea,vomiting and somnolence.

Dhimer et al (15) in the year 2007, compared tramadol with pethidine in a randomised prospective study in 60 ASA I – III patients with dose of 1 mg/kg IV of each drug, after appearance of shivering under regional anaesthesia and noted that tramadol and pethidine were equally efficacious but tramadol was more potent with respect to control of shivering and its recurrence.

Butorphanol at a dose of 1 mg has also been found effective in treating shivering after spinal anaesthesia (16). Even shivering induced by epidural anaesthesia in parturients has been controlled using butorphanol (17).

Joshi S S et al(18) in 2013 studied 150 ASA I and II patients for elective surgery under spinal anaesthesia to compare anti shivering qualities of Tramadol 1 mg/Kg, butorphanol 0.03 mg/Kg and ondansetron 0.06 mg/Kg. Ondansetron is not much effective, butorphanol and tramadol are equally effective with butorphanol having quicker onset.

Charuluxanan et al (7) in year 2009, did a review of the pharmacological treatment of post anaesthetic shivering in 32 randomised control studies and concluded that meperidine 20-50 mg and tramadol 0.5-1 mg /kg are effective in the treatment of post operative shivering at 15 minutes and both of them had no statistically significant difference in efficacy. Also, clonidine 30-150 µg, ketanserin 10 mg , Doxapram 25-100 mg and nalbuphine 0.05- 0.1 mg/kg can be used as therapeutic alternatives. Side effects of each regimen were mostly non-hazardous.

REFERENCES

1. Sessler DI, Ponte J.Shivering during epidural Anaesthesia.Anaethesiology 1999; 72: 816-821.
2. De White, Sessler D I. Perioperative shivering: Physiology and Pharmacology. Anaesthesiology 2002;96: 464-484.
3. Buggy D J, Crossley A W A. Thermoregulation, mild perioperative hypothermia and post anaesthetic shivering. Br. J Anaesth 2000; 84: 615-28.
4. Bhattacharya P K, Bhattacharya L, Jain R K, Agarwal R C. Post anaesthetic shivering(PAS): A Review. Indian J Anaesth. 2003; 47(2):88-93.
5. Bhatnagar S , Saxena A,Kannan T R, Punj J, Panigrahi M ,Mishra S. Tramadol for post operative shivering-a double blind comparison with Pethidine.Anaesth Intensive care 2001;29:149-154.
6. Bansal P, Jain G. Control of shivering with Clonidine, Butorphanol, and Tramadol under spinal anesthesia: a comparative study. Local and regional Anaesthesia 2011;4: 29-34.
7. Charuluxannanan S, Trakulthong C, Areejunthawat J, Koonanthukul C, Jarukasetrporn C,Patradul C. Pharmacological treatment of post-anesthetic shivering: a systemic review and meta analysis. Asian Biomedicine 2009; 3 (4): 351-363.
8. Park S M,Mangat H S,Berger K,Rosengart A J.Efficacy spectrum of anti shivering medications:Meta-analysis of randomized controlled trials. Crit care med 2012;40(11):3070-82.
9. Dhorigol MG,Dhulkhed VK,Biyani A,Desai N.Randomized controlled;Double blind study to evaluate oral Clonidine to prevent post-subarachnoid block shivering in patients undergoing elective urological surgery.J Anaesth clin Pharmacol 2010;26(1):15-18.
10. Mercadante S,DeMichele P,Letterio G,Pignataro A,Sapio M,Villari P.J pain symptom manage 1994 July;9(5):294-97.
11. Jeon YT,Jeon YS,Kim YC,Bahk JH,Do SH,Lim YJ.Intrathecal Clonidine does not reduce postspinal shivering.Acta Anaesthesiologica Scandinavica 2005 Nov;49(10):1509-13.
12. Foroushzadeh F J,Pipelzadeh M R,Bagherybarma F.Comparison of clonidine,pethidine and fentanyl for post-spinal anesthesia shivering in elective caesarean sections.Armaghan Danesh 2006;11(3);60-67.
13. Chan AM,Ng KF,Tong EW,Jan GS.Control of shivering under regional anesthesia in obstetric patients with Tramadol.Can J Anaesth 1999 Mar;46(3):253-58.
14. Talakoub R, Noori Meshakati Sh. Tramadol versus meperidine in the treatment of shivering during spinal anesthesia in caesarean section.Journal of Research in Medical Sciences 2006;11(3):151-5.
15. Dhimer A A, Patel M G , Swadia V N . Tramadol for control of shivering (comparison with Pethidine). Indian J Anaesth 2007;51(1) :28-31.
16. Sheng-an L,Zu Liang W,Qing-Hong M.Effect of treating shivering after intraspinal anaesthesia with Butorphanol.Jilin medical Journal 2010;35
17. Juneja M,Ackerman WE,Heine MF,Cases-Cristobal V,Urella RP,Rigor BM.Butorphanol for relief of shivering associated with extradural anesthesia in parturients.J Clin Anesth.1992;4(5):390-93.
18. Joshi S S,Arora A,George A,Shidhaye R V.Comparison of intravenous butorphanol, ondansetron and tramadol for shivering during spinal anaesthesia: A prospective randomized double- blind study. Anaesth Pain & Intensive care 2013;17(1):33-39. 19.
19. Wrench I J, Singh P, Dennis A R, Mahajan R P, Crossley A W. The minimum effective dose of pethidine and doxapram in the treatment of post operative shivering. Anaesthesia 1977;52:32-6.
20. Filos K S, Goudas L C, Patroni O, Polyzou V. Hemodynamic and analgesic profile after intrathecal Clonidine in humans. A dose response study, Anaesthesiology, 1994;81: 591-601.