Original Article

Comparative Study Between Tramadol Hydrochloride and Pethidine for Control of Shivering Under Regional Anaesthesia in Obstetric Patients

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Abstract

Background: *Shivering is a common complication observed in post spinal anaesthesia. It can be very unpleasant and physiologically stressful for the patients. Different drugs are used for prevention and treatment of post spinal shivering.*

Materials & Methods: *This prospective, randomized, double blinded, comparative clinical study was conducted in the department of Anaesthesioloy, Bangladesh Medical College Hospital, Dhanmondi, Dhaka from 1st June '2016 to 30th November 2016. This study was designed to evaluate the efficacy and side effects of tramadol hydrochloride comparing with pethidine in the treatment of shivering of pregnant patients underwent cesarean section under spinal anaesthesia. Total 160 ASA grade-l & ll pregnant patients of cesarean section under Sub arachnoid block, who shivered, were included in this study. Patients were randomly allocated into two groups. Group-T (n=80) received tramadol hydrochloride 1mg/kg and Group-P (n= 80) received pethidine 0.5mg/kg body weight intravenously for treatment of shivering and side effects were recorded and subsequently analyzed.*

Results: *Disappearance of shivering after treatment was significantly earlier in Group-T (3.09±0.86 minutes) than in Group-P ((5.11±1.08 minutes) (p <0.01). Recurrence of shivering after treatment was significantly less in Group-T 2(2.5%) than Group-P 7(8.75%) (p<0.01). Adverse effects were significantly higher in Group-P than Group-T. Nausea in 5(6.25%) patients and vomiting in 4(5%) patients found in Group-P and nausea in 1(1.25%) patients and vomiting in 1(1.25%) patient found in Group-T. Differences were statistically significant in case of nausea (p<0.01) and vomiting (p<0.01). Dizziness and pruritus observed in no patient of Group-T and in Group-P dizziness observed in 5(6.25%) patients and pruritus observed in 4(5%). Differences were statistically significant in case of dizziness (p<0.001) & pruritus (p<0.001).*

Conclusion: *Both tramadol hydrochloride and pethidine effectively controlled shivering in patients during cesarean section under spinal anaesthesia, but tramadol hydrochloride offered rapid onset, less recurrence, and fewer side effects when compared to pethidine in obstetric patients.*

Key words:*Shivering,Regional Anesthesia, Tramadol Hcl, Pethidine.*

Introduction

Shivering is a common problem faced by anaesthesiologist during intraoperative as well as post-operative period. Shivering occurs after both the general and regional anaesthesia, but is more frequent and troublesome during regional anaesthesia especially spinal anaesthesia. The reported incidence of shivering during cesarean section performed under regional anaesthesia (neuraxial blockde) varies from 40-60%[1,2]. Mild shivering increases O_2 consumption to a level that is produced by light exercise, whereas severe

shivering increases metabolic rate and Oxygen consumption up to 100-600%. It may induce arterial hypoxemia, lactic acidosis, increased intra ocular pressure, intracranial pressure and interferes with ECG monitoring, pulse rate, blood pressure etc[3,4,5]. Shivering may be detrimental to the patients with low cardiorespiratory reserves[6.] It is uncomfortable to the parturients as well as to the operating room personnel, especially during regional anaesthesia[7]. Various non-pharmacological and pharmacological methods have been used to prevent body shivering. Non-pharmacological methods like electrical heaters, forced air warmers, blankets, radiant heat and warming the operating room suite. The use of warm I.V fluids are also effective to reduce shivering[8,9]. Pharmacological methods using ketanserine, nefopam, pethidine, alfentanyl, doxapram,tramadol,clonidine, etc have been tried and compared by many studies. Among them pethidine is a potent anti-shivering agent with few side effects and has no sufficient proof of not crossing the placenta or not being excreated in breast milk. Tramadol prevents shivering following spinal anaesthesia without any harmful effects on fetus.

Materials & Methods

This was a prospective, randomized, double blinded, comparative study designed to evaluate the efficacy and side effects of tramadol hydrochloride comparing with pethidine in the treatment of shivering of pregnant patients underwent cesarean section under spinal anaesthesia. The study was conducted in the department of Anaesthesioloy, Bangladesh Medical College Hospital, Dhanmondi, and Dhaka from 1st June '2016 to 30th November 2016. After obtaining approval from ethical committee total 160 Parturients undergoing elective cesarean section with ASA grade l & ll that fulfilled the inclusion criteria enrolled in the study. Inclusion criteria's were ASA class I & II, Having consented to be in the study, Age 20-40years, Elective cesarean section under SAB, No history of hyperemesis gravidarum or motion sickness, No H/O hypertensive disorder. Exclusion criteria's were Patient unwilling to participate, Patients taking sedative, Significant cardiovascular ,liver or kidney disease, Age less than 18years or more than 40 years, Allergy or hypersensitivity to tramdol or pethedine, Severe bleeding, Unstable haemodynamics condition, Convert to operative procedure like hysterectomy, Weight heavier than 80kg and patient with a body mass index greater than 35kg/sqm, Inability to comply with the protocol.;i.e. a language barrier and obstetric patient with fever. The parturients who developed shivering during the process were included in the study. Patients were randomly allocated into two groups. Group-T (n=80) received tramadol hydrochloride 1mg/kg and Group-P (n= 80) received pethidine 0.5mg/kg body weight intravenously for treatment of shivering and side effects were recorded and subsequently analyzed. Two groups of participant of equal size made from the study population by card sampling method.

Statistical Analysis

Data analysis was carried out by using the statistical package for social science (SPSS) version 17.0 Continuous variables were presented as Mean±SD. Original variables were presented as numbers (%). Independent T test and chi square test were applied. P less than 0.05 ($p<0.05$) will be considered the minimum level of statistical significance.

Results and observations:

Patient characteristics, baseline demographics and peroperative data were similar between groups. Mean ages of the patients of group T and group P were 28.11±2.43 and 27.17±6.906 years respectively. Mean weights of the patients of group T was 68.05±5.41Kg and group P was 70.18±4.48Kg. Mean duration of surgery were 48.60±8.02 minutes in group T and 47.89±7.39 minutes in Group P. None of these differ statistically between groups.

Onset of shivering and severity of shivering (shivering grade) were almost similar in both groups and differences were statistically not significant. Shivering disappeared in 79(98.75%) patients who received tramadol and 78(97.50%) patients who received pethidine. Regarding responsiveness to treatment between two groups was almost similar and differences were not significant. Both the drugs were found to be effective in the treatment of shivering. Severity of shivering was unchanged in 1(1.25%) patient in Group T and 2(2.5%) patients in Group P. Recurrence of shivering occurred 2(2.5%) patients

in Group T and 7(8.75%) patients in Group P and the difference between two groups were statistically significant(P<0.01). The mean interval between the injection of drug (tramadol or pethidine) and complete cessation of shivering was (3.09±0.86) minutes in Group T and (5.11±1.08) minutes in Group P. The time interval between administration of drug after onset of shivering and disappearance of shivering was significantly shorter with tramadol (P<0.01).

Regarding adverse effect of treatment drugs we observed there were significantly higher in Group-P than Group-T. Nausea in 5(6.25%) patients and vomiting in 4(5%) patients found in Group-P and nausea in 1(1.25%) patients and vomiting in 1(1.25%) patient found in Group-T. Differences were statistically significant in case of nausea (p<0.01) and vomiting (p<0.01). Dizziness and pruritus observed in no patient of Group-T and in Group-P dizziness observed in 5(6.25%) patients and pruritus observed in 4(5%). Differences were statistically significant in case of dizziness (p<0.001) & pruritus (p<0.001).

Peroperative and post-operative hemodynamic parameters were almost similar in both groups measured at different time period starting from after positioning of the patient to operating table to 8hrs post-operatively. The mean changes of heart rate per minute varied in group-T from 76.54 ±6.56 to 100.39±5.15 in group-P from 70.89±6.89 to 90.54. Significant change were observed at 20th minute, 30th minute (p<0.05). In other time no significant changes were observed. The mean changes of Systolic Blood Pressure varied in Group-T from 105.51±6.82 to 122.82 ±5.56 and in Group-P from 99.1±7.45 to 121.85 ±4.89. Significant changes were observed at 10mins during operation (p<0.05). In other period no significant changes were observed. The mean changes of Diastolic Blood Pressure varied in Group-T from 63.54 ±5.32 to 70.84 ±5.74 and in Group-P from 60.94 ±4.629 to 71.09 ±5.313. No significant changes were observed throughout the intra operative and post-operative period. The mean changes of Mean Blood Pressure varied in Group-T from 74.01 ±5.98 to 90.63 ±6.67 and in Group-P from 70.54 ± 4.76 to 88.56 ±6.38. No significant changes were observed throughout the intra operative and post-operative period.

Table-1 *Post spinal shivering and response.to treatment. Statistical significance at p<0.05*

Parameter	Group-T (n=80)	Group-P (n=80)	*p*- value
Onset of shivering(minutes after SAB)	15.82±3.63	16.32±4.02	0.43
Severity of shivering(Grade)	3.2±0.8	3.09±1.1	0.92
Response rate	79(98.75%)	78(97.50%)	0.59
Unresponsive rate	1(1.25%)	2(2.50%)	0.19
Time interval from treatment to cessation of shivering(minute)	3.09±0.86	5.11±1.08	*p*<0.01
Recurrence of shivering	2(2.5%)	7(8.75%)	*p*<0.01

*Independent sample t-test was done to measure the level of significance

Table-2: *Side effects in both groups. Statistical significance at p<0.05. *Independent sample t-test was done to measure the level of significance*

Parameter	Group-T (n=80)	Group-P (n=80)	*p*-value
Nausea	1(1.25%)	5(6.25%)	<0.05
Vomiting	1(1.25%)	4(5%)	<0.05
Dizziness	0	5(6.25%)	<0.001
Somnolence	2(2.5%)	3(3.75%)	<0.39
Pruritus	0	4(5%)	<0.001
Sedation(Scale)			
1	62(77.5%)	60(75%)	<0.87
2	18(22.5%)	20(25%)	<0.79

Discussion:

Regional anaesthesia including central neuraxial blockade and peripheral nerve blockade is a safe and popular technique for various surgeries. The probable mechanism under regional anaesthesia would either be a result of decrease in core body temperature or misinformation from receptors[10]. The factors causing decrease in core body temperature include sympathetic block causing peripheral vasodilation, increased blood flow resulting in increase heat loss through skin, cold operating room, rapid infusion of cold intravenous fluids and direct effect of cold anaesthetic solution upon the thermosensitive structure of spinal cord[7,10]. Shivering may represent an inappropriate programmed thermal response to rise in body temperature[9]. Even local anaesthetic introduced into the extradural space might modify environmental thermal clues, with resultant inappropriate thermal responses to false information[11]. The parturients experienced it to be uncomfortable after enjoying the benefits of modern anaesthesia.

In our study we compared synthetic opioid tramadol with pethidine, which was gold standard for control of shivering. Tramadol is a synthetic opioid agonist prevents shivering by inhibiting the reuptake of norepinephrine and serotonin, hence activating the descending inhibitory spinal pathways. It also modulates the activity of nucleus median raphe acting centrally on the μ(mu) opioid receptors predominantly with minimal effects on κ (kappa) and δ(delta) receptors whereas pethidine acts mainly through opioid receptors namely ê (kappa) receptors. The mechanism of action of tramadol is different from that of pethidine. Tramadol has minimal effect on ê (kappa) receptors. The anti-shivering effect of Tramadol is mediated via serotonergic or noradrenergic receptors or both [6,12]. Pethidine controlled shivering better than fentanyl and Morphine[14]. Therefore we undertook a study to compare a newer agent with a time-tested drug.

In this study, we observed tramadol is as effective as pethidine in treating post spinal anaesthesia shivering. The response rate of treatment of shivering found satisfactory with both tramadol and pethidine & was almost similar. But the time interval from commencement of treatment to cessation of shivering was quite less with tramadol (3.09±0.86 minutes) than with pethidine (5.11±1.08 minutes) and the difference was statistically significant ($p< 0.01$). About recurrence of shivering, it was more with pethidine; 2(2.5%) patients with tramadol had recurrence while 7(8.75%) suffered recurrence with pethidine and difference was statistically significant ($p< 0.01$). The findings were in condolence with other studies which noted 8% with Tramadol group[12] and 13-50% in pethidine group[8,12]. Thus various studies including ours there was higher rate of recurrence with pethidine in comparison to tramadol. Our results are in accordance with that of Bhatnagor[3] study on higher efficacy of tramadol in controlling the postoperative shivering.

Dhimer et al[14] found that shivering disappeared at 1 minute with tramadol 1mg/kg body weight and in 5 minutes with pethidine 1mg/kg body weight.

In Talakoab et al[15] study; efficacy and harm of tramadol for treatment of post spinal anaesthesia shivering in cesarean section were evaluated. They compared tramadol (0.5mg/kg body weight) with pethidine (0.5mg/kg body weight) to control of shivering and concluded tramadol was more effective to control of shivering but results in more nausea, vomiting. De Witte et al[16] published that both tramadol and pethidine have nearly similar properties on post-operative shivering. The second dose of the drug controlled the shivering completely but the possibility of respiratory depression with pethidine should be borne in mind. The probable reason for recurrence of shivering could be result of low plasma concentration of the active drug, when hypothermia is still persisting and individual variations in the core temperatures. Till date it is not clear whether higher shivering grades requires a higher dose of drug[12].

In our study both the drugs gave good and better haemodynamics stability throughout the course of the study in all the patients. No repiratory depression was observed in any of the cases. Only in 5(6.25%) cases nausea and 4(5%) vomiting in pethidine group which was easily treated with antiemetic drug. Earlier studies have found that use of 1mg/kg of tramadol was associated with higher incidence of nausea and vomiting and also

sedation, which was not observed in our study[10]. Some others have suggested that slow injection of tramadol over 2 minutes, reduces and prevent nausea and vomiting[6].

Dizziness and pruritus observed in 5(6.25) & 4(5%) patients respectively with pethidine but no patient had pruritus or dizziness with tramadol. About somnolence and sedation incidences were almost similar and no patient had grade 3 or 4 sedation with tramadol or pethidine. Ali Seifi et al[17] showed pethidine was associated with more nausea, vomiting and sedation than tramadol in control of per-operative shivering.

Mathews et al[6] have also shown that use of low dose of tramadol to be superior to pethidine without incidences of severe side effects in control of post anaesthetic shivering (PAS). Others studies documented that side effects of tramadol were dose dependent and considering more likely to appear if the loading dose is higher[18,19,20]. The literature supports a higher incidence of emesis with opioids, though the doses used by us were frequently associated with this adverse effect. A limitation of this study was that we could not measure the body core temperature, the probe needs to be put in the esophagus, rectum or near tympanic membrane, but those are uncomfortable and unacceptable who had been given spinal anaesthesia.

Conclusion:

The study was done with a view to acquire an idea about the effects of tramadol and pethidine for control of shivering under spinal anaesthesia in elective cesarean section. We can derive at a conclusion that tramadol is effective in treating shivering under spinal anaesthesia due to its rapid onset, effective control, less recurrence rate, minimum side effects like nausea, vomiting, dizziness and pruritus in a dose of 1mg/kg when compared to pethidine.

Limitations of the study:

This study was conducted in one hospital only and may not reflect the actual situation of the country. It was done within a short period of time. Sample size was small, a larger sample size can give a better conclusion. The study was conducted in a tertiary hospital which may not represent primary or secondary center.

References:

1. De Whitte, Sessler DI, et al. Perioperative shivering: Physiology and Pharmacology. Anaesthesiology 2002; 96(2): 467-84.
2. Sessler DI, Jose Ponte, et al. Shivering during epidural anaesthesia. Anesthesiology 1990; 72: 816-21
3. Bhatnagar S, Saxena A et al.Tramadol for postoperative shivering: a double blind comparison with Pethidine. Anesth Intensive care 2001; 29: 149-54
4. Katyal Sunil, Tewari Anurag et al. Shivering: Anesthetic Considerations. J Anaesth Clin Pharmacol 2002; 18(4):363-76
5. Sessler Daniel I.Temperature Monitoring. Textbook of Anaesthesia; Ronald D Miller 5Th edition, Churchill Livingstone Inc. 1994: 1367-89
6. Mathews S, Al Mulla A et al. Postanaesthetic shivering-a new look at Tramadol. Anaesthesia 2002; 57: 387-403
7. Anne Miu Han Chan, Kwok Fu et al. Control of shivering under regional anaesthesia in obstetric patients with Tramadol.Can J Anesth 1999; 46(3): 253- 58
8. Wrench J Cavill et al. Comparison between Alfentanil, Pethidine, and placebo in the treatment of postoperative shivering. Br J Anaesth. 1997; 79: 541-42
9. Takehiko I, Sessler Daniel I et al. Meperidine and Alfentanyl do not reduce the gain or maximum intensity of shivering. Anaesthesiology 1998; 88(4): 858-65
10. Chaturvedi S, Domkondwar G. Control of shivering under regional anaesthesia using Tramadol. Asian Archives of Anaesthesiology and Resuscitation 2002; 57: 491-96
11. Pamela J, Webb et al. Shivering during epidural analgesia in women in labour. Anaesthesiology 1991; 55: 706-07
12. Write J De Deloof, T et al. Tramadol in the treatment of post anesthetic shivering. Acta Anaesthesiol Scand 1997; 41:506-10
13. Singh P, Dimitriou V et al. Double blind comparison between Doxapram and Pethidine in the treatment of postanaesthetic shivering

. Br J Anaesth 1993; 71: 685-88

14. Maheshwari BS, Shah SK, Chadha IA. Tramadol and Butorphanol for control of shivering : Randomised double blind comparative study. J Anaesth Clin Pharmacol 2008;24(3):343-46
15. Kelsaka E, Sibel B, Deniz K, Binnur S. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. Reg Anesth Pain Med 2006;31:40-45
16. De witte J,Kim JS,Sessler DI,Bastanmehr H,Bjorksten AR, Tramadol reduces the shivering,vasoconstriction and sweating threshold.Anaesth Analg 1998;87:173-9
17. Seifi A, Avestmehr S, Mowla A, Kamalipour H. A comparative study of the effect tramadol and pethidine on post-operative shivering. The Internet Journal of Anaesthesiolgy 2008;Vol 16(2)
18. Kranke P, Eberhart LH, Roewer N, Tramer MR. Pharmacological treatment of postoperative shivering: a quantitative systematic review of randomized controlled trials. Anesth Analg. 2002;94:453–4
19. Buggy DJ, Crossley AWA,Gann et el, Thermoregulation, mild perioperative hypothermia, and post-anaesthetic shivering. Br J Anaesth 2000;84:615–628
20. Mathews S, Al Mulla A, Varghese PK, Radim K, Mumtaz S. Post-anaesthetic shivering: A new look at tramadol. Anesthesia 2002;57:387-403
21. Bansal P, Jain G. Control of shivering with clonidine, butorphanol, and tramadol under spinal anesthesia: a comparative study. Local and Regional Anesthesia 2011;4:29–34
22. Ebru Kelaska, Korakaya D. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. Regional anesthesia and pain medicine 2006;31(1):40-45
23. Atashkhoyi S, Negargar S. Effect of tramadol for prevention of shivering after spinal anesthesia for cesarean section. Research Journal of Biological Sciences 2008;3:1365–1369
24. Dhimar AA, Patel MG, Swadian VN. Tramadol for control of shivering: comparison with Pethidine. Indian J Anesthesia 2007;51:28–31
25. Gangopadhyay S, Gupta K, Acharjee S, Nayak SK, Dawn S, Piplai G. Keatmine, tramadol and pethidine in prophylaxis of shivering during spinal anaesthesia. J Anaesth Clin Pharmacol 2010;26(1):59-63
26. Maheshawri BS, Shah SK, Chadha M. Tramadol and butrophenol for control of shivering: randomized double blind comparative study. J Anaesth Clin Pharmacol 2008;24:343-6
27. Emadi A. Comparison postanesthetic shivering between tramadol & pethidin. Mazandaran University of Medical Sciences.2011; 20: 78