Original Paper

Effect of Tramadol and Pethidine on Shivering during Cesarean Section under Spinal Anaesthesia

Maruf AA[1], Islam MS[2], Hoq N[3]

Abstract

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

Objective: This study was designed to evaluate the efficacy and side effects of tramadol comparing pethidine in treatment of shivering on pregnant patients during cesarean section under spinal anaesthesia.

Methods: This prospective clinical type of study was conducted in the department of Anaesthesia and Intensive Care at Combined Military Hospital, Dhaka from July 2011 to June 2012. One hundred twenty American Society of Anaesthesiologist (ASA) grade I and II pregnant patients of cesarean section under spinal anaesthesia, who had shivering, were included in this study. Patients were divided into two groups. Group T(n=60) received tramadol 0.5mg/kg and Group P(n=60) received pethidine 0.5mg/kg body weight intravenously for treatment of shivering. Grade of shivering, disappearance 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 Group P (5.11±1.08 minutes) (P<0.01). Recurrence of shivering after treatment was significantly less in Group T 2(3,33%) than Group P 7(11.67%) (P<0.01). Side effects were significantly higher in Group P than Group T. Nausea in 5(8.33%) patients and vomiting in 4(6.67%) patients found in Group P and nausea in 1(1.67%) patient and vomiting in 1(1.67) patient found in Group T. Differences were statistically significant in case of nausea (P<0.05) and vomiting (P<0.05). Dizziness and pruritus observed in no patient of group of T and in Group P dizziness observed in 6(10%) patients and pruritus observed in 3(5%) patients. Differences were statistically highly significant in case of dizziness (P<0.001) and pruritus (P<0.001).

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

Key-words: Shivering, tramadol, pethidine, spinal anaesthesia.

Introduction

Spinal anaesthesia is widely used as a safe anaesthtic procedure for both elective and emergency cesarean section. Shivering is one of the most common complications of spinal anaesthesia reported 40 to 70% of the patients[1,2]. Shivering can be very unpleasent and physiologically stressful for the patients. Mild shivering increases oxygen consumption to a level that is produced by light exercise, whereas severe shivering increases metabolic rate and oxygen consumption upto 100-600% along with raised carbon di oxide production. It causes arterial hypoxaemia, lactic acidosis, increased intracranial pressure, intraocular pressure; and interfares with pulse rate, blood pressure and ECG monitoring[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 methods are available for the control of shivering during regional anaesthesia. Non pharmacological methods include

1. **Lt Col Abdullah Al Maruf** , MBBS, FCPS (Anaesthesiology), Classified Specialist in Anaesthesiology, CMH, Rangpur;
2. **Brig Gen Md Saiful Islam**, MBBS, FCPS (Anaesthesiology), Professor of Anaesthesiology, AFMC, Dhaka;
3. **Lt Col Naimul Hoq**, MBBS, DA, FCPS (Anaesthesiology), Graded Specialist in Anaesthesiology, CMH, Dhaka.

radiant heat warmers, warming the operation theatre, warm intravenous fluids and using anaesthetic drugs at body temperature[8,9]. Those are effective but may be expensive and not practicable in all settings. Pharmacological methods using various drugs like pethidine, clonidine, tramadol, doxapram, nefopam etc. have been tried, which are simple, cost effective and easily available[10]. The relative efficacy of these medications however, remains unclear. Tramadol has been used as an analgesic for labour pain without affecting the mother and newborn[11] and also effective in treatment of postoperative shivering[12]. Tramadol and pethidine are approximately equipotent with respect to analgesia. However, the anti shivering effects of these two agents may be mediated via different receptors. This prospective randomized clinical study was to designed to compare the efficacy, potency and the side effects between tramadol and pethidine for the treatment of shivering during spinal anaesthesia in cesarean section.

Materials and Methods

This prospective clinical study was conducted at department of Anaesthesia and Intensive Care, Combined Military Hospital (CMH), Dhaka from July 2011 to June 2012. After approval from departmental review board and obtaining patient's written informed consent, 120 ASA grade I and II parturients, who subsequently developed shivering during elective or emergency cesarean section under spinal anaesthesia were included in the study. Patients with known hypersensitivity to tramadol or pethidine, known history of substance abuse, hyperthyroidism, cardiovascular diseases, psycological disorders or who recieved intramuscular pethidine for labour pain within one hour were excluded from the study. Spinal anaesthesia was administered with inj 0.5% bupivacaine (heavy) 2-3ml at L3,L4 or L4, L5 interspace using 25 gauge Quincke's needle. The volume of preloading intravenous fluid and the use of ephidrine for hypotension were determined by attending anaesthesiologist. Intravenous drugs and anaesthetic drugs were administered at room temperature. The operating room temperature was kept at 21-23º C and no means of active rewarming were used. Before begining of spinal anaesthesia, standard monitoring procedures were established. Patient's pulse rate, non invasive blood pressure (NIBP), ECG, oxygen saturation (SpO2) and body temperature (axillary) were recorded before the commencement of anaesthesia and thereafter at every 5 minutes interval till completion of surgery and transportation of patient to postoperative ward. Grading of shivering was done according to Wrench[13], which is as follows;

Grade 0 : No shivering.

Grade 1 : Piloerection or peripheral vasoconstriction but no visible shivering.

Grade 2 : Visible muscle activity confined to one muscle group.

Grade 3 : Visible muscle activity in more than one muscle group but no generalized shivering.

Grade 4 : Gross muscle activity involving whole body shivering.

Patients who developed either grade 3 or grade 4 shivering were divided into two groups, Group T and Group P. Group T (n=60) recieved inj tramadol 0.5 mg/kg body weight and Group P (n=60) recieved inj pethidine 0.5 mg/kg body weight for treatment of shivering after delivery of the baby. The attending anaesthesiologist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering), severity of shivering and response rate (shivering ceased after treatment in 15 minutes) and time elapsed from treatment. If shivering did not subside within 15 minutes, the treatment was considered to be not effective. Recurrence of shivering was also noticed until the patient left operation theatre. Patients who did not respond or in whom recurrence of shivering occured were treated with additional dose of tramadol (0.5mg/kg body weight) or pethidine (0.5mg/kg body weight) in the respective groups. Side effects like nausea, vomiting, dizziness, somnolence, pruritus and sedation were recorded. Sedation score was assesed with a four point scale as per Filos[14].

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

Nausea and vomiting were treated with inj metaclopromide when required. Statistical analysis was carried out using SPSS (Statistical Package for Social Sciences) 17.0 for windows. Student 't' test of the results. Results were considered statistically significant if P value was <0.5.

Results

Table-I: Patient's demographic and peroperative data.

Parameter	Group T (n=60)	Group P (n=60)	P value	Result
62 Age (Year)	25.67±5.15	26.17±4.87	0.12	NS(Student 't' test unpaired)
Weight (Kg)	62.41±6.21	61.23±5.78	0.28	NS(Student 't' test unpaired)
ASA Physical Status				
I	53(88.33%)	55(91.66%)	0.76	NS(Chi Square test)
II	7(11.67%)	5(8.34%)	0.97	NS(Chi Square test)
Amount of Intravenous Infusion(ml)	1932.86±198.12	1897±202.77	0.82	NS(Student 't' test unpaired)
Axillary Temperature (Celsius)	36.9±0.71	36.8±0.65	0.14	NS(Student 't' test unpaired)
Duration of Surgery (minute)	48.60±8.02	47.89±7.39	0.84	NS(Student 't' test unpaired)

Values are expressed in Mean±SD or percentage
NS – Not Significant

Patient's demographics and peroperative data were shown in Table-I. Both the groups were comparable with respect to age, bodyweight, ASA physical status, duration of surgery, volume of intravenous fluid administration and axillary temperature and differences were statistically not significant. Post spinal shivering related data were shown in Table-II.

Table-II: Post spinal shivering and response.

Parameter	Group T (n=60)	Group P (n=60)	P value	Result
Onset of Shivering (minute)	15.82±3.63	16.32±4.02	0.43	NS(Student 't' test unpaired)
Severity of Shivering (Grade)	3.2±0.8	3.09±1.1	0.92	NS(Student 't' test unpaired)
Response Rate	59(98.33%)	58(96.67%)	0.59	NS(Chi Square test)
Unresponsive	1(1.67%)	2(3.33%)	0.19	NS(Chi Square test)
Time Interval from Treatment to Cessation of Shivering(minute)	3.09±0.86	5.11±1.08	P<0.01	Sig(Student 't' test unpaired)
Recurrence of Shivering	2(3.33%)	7(11.67%)	P<0.01	Sig(Chi Square test)

Values are expressed in mean±SD or percentage
Sig - Significant, NS – Not Significant

Onset of shivering and severity of shivering (shivering grade) were almost similar in both groups and differences were statistically not significant. Shivering disappeared in 59(98.33%) patients who received tramadol and 58(96.67%) 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 treatment of shivering. Severity of shivering was unchanged in 1(1.67%) patient in Group T and 2(3.33%) patients in Group P. Recurrence of shivering occurred 2(3.33%) patients in Group T and 7(11.67) patients in Group P and the difference between two groups was 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).

Table-III: Side effects in both groups.

Parameter	Group T (n=60)	Group P (n=60)	P value	Result
Nausea	1(1.67%)	5(8.33%)	P<0.05	Sig(Chi Square test)
Vomiting	1(1.67%)	4(6.67%)	P<0.05	Sig(Chi Square test)
Dizziness	0	6(10%)	P<0.001	HS(Chi Square test)
Somnolence	2(3.33%)	3(5%)	0.39	NS(Chi Square test)
Pruritus	0	3(5%)	P<0.001	HS(Chi Square test)
Sedation (Scale)				
1	42(70%)	40(66.67%)	0.87	NS(Chi Square test)
2	18(30%)	20(33.33%)	0.79	NS(Chi Square test)

Values are expressed in percentage
Sig – Significant, HS – Highly Significant, NS – Not Significant

Side effects of treatment of shivering between two groups were shown in Table-III. Side effects were significantly higher in Group P than Group T. Nausea in 5(8.33%) patients and vomiting in 4(6.67%) patients were found in Group P and nausea in 1(1.67%) patient and vomiting in 1(1.67) patient were found in Group T. Differences were statistically significant in case of nausea (P<0.05) and vomiting (P<0.05). Dizziness and pruritus were observed in no patient of Group T and in Group P dizziness was observed in 6(10%) patients and pruritus was observed in 3(5%) patients. Differences were statistically highly significant in case of dizziness (P<0.001) and pruritus (P<0.001). Somnolence and sedation were almost same and similar in both groups and differences were statistically not significant. Desaturation was not observed in both groups. In addition NIBP, heart rate, respiratory rate, ECG and SpO2 were monitored in both groups after spinal anaesthesia and were not significantly different in both groups throughout peroperatively.

Discussion

The probable mechanism of shivering under regional anaesthesia could either be a result of decrease in core temperature or misinformation from the receptors[15]. The factors causing decrease in core body temperature include; sympathetic block causing peripheral vasodilatation, increased cutaneous blood flow resulting from heat loss through skin, cold operating room, rapid infusion of cold intravenous fluids and direct effect of cold anaesthetic solution upon thermostatic structures of spinal cord[7,15]. Shivering may represent an inappropriate programmed thermal response in body temperature[15].

In this study we have compared recently introduced synthetic opioid tramadol with pethidine, which used traditionally for control of shivering. Tramadol's opioid action preferably mediated via mu receptor with minimal effect on kappa and delta binding sites. Tramadol has a modulatory effect on central mono-aminergic pathways; this inhibits the reuptake of noradrenalin/serotonin and encourages hydroxy-tryptamine secretion which resets the body temperature regulation centre. The anti shivering action of tramadol is probably via its opioid or serotonergic and noradrenergic activity or both[6,16,17]. Pethidine controlled shivering most likely mediated via receptors other than mu receptor in particular the kappa receptor. This is supported by observations that pethidine controlled shivering better than morphine and fentanyl[18,19]. Therefore we undertook a study to compare a newer agent tramadol with time tested drug pethidine. 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 and was almost similar. But the time interval from commencement of treatment to cessation of shivering was quite less with tramadol (3.09±0.86minutes) than with pethidine(5.11±1.08 minutes)and difference was statistically significant (P<0.01). About recurrence of shivering, it was more with pethidine; 2(3.33%) patients with tramadol had recurrence while 7(11.67%) suffered recurrence with pethidine and difference was statistically significant (P<0.01). Earlier studies supported less recurrence with tramadol, which noted 8% recurrence with tramadol and 15% with pethidine[8,20]. Our results are in accordance with that of Bhatnagor[3] study on higher efficacy of tramadol in controlling the postoperative shivering. Dhimer et al[21]. found that shivering disappeared in 1 minute with tramadol 1mg/kg bodyweight and in 5 minutes with pethidine 1mg/kg bodyweight. In Talakoab et al[22] study; efficacy and harm of tramadol for treatment of post spinal anaesthesia shivering in cesarean section were evaluated. They compared tramadol(0.5mg/kg bodyweight) with pethidine(0.5mg/kg bodyweight) to control of shivering and concluded tramadol was more effective to control of shivering but results in more nausea, vomiting. Angral R et al[23]. found that tramadol significantly reduced incidence and severity of postoperative shivering following open and laparoscopic cholecystectomy. Zahidi H et al[24] found tramadol terminates post anaesthetic shivering faster than pethidine during elective cataract surgery with less recurrence rate. De Witte et al[25]. published that both tramadol and pethidine have nearly similar properties on postoperative shivering.

The side effects were found to be higher in cases of pethidine compared to tramadol. In the present study, the incidences of nausea and vomiting were significantly higher with pethidine than tramadol (P<0.05). Dizziness and pruritus observed in 6(10%) and 3(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[26] showed pethidine was associated with more nausea, vomiting and sedation than tramadol in control of post operative shivering. Study conducted by Gangopadhyay et al[27] reported higher incidences of vomiting with tramadol than pethidine, while Maheshari et al[28] showed a higher a higher incidences of vomiting with buterophanol compared to tramadol. 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. Other studies documented that side effects of tramadol were dose dependant and considering more likely to appear if the loading dose is higher[17,18,29]. 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. For measurement of core body temperature, the probe needs to be put in the oesophagus, rectum or near tympanic membrane. But those are uncomfortable and unacceptable who has been given spinal anaesthetics.

Conclusion

In conclusion both tramadol (0.5mg/kg bodyweight) and pethidine(0.5mg/kg bodyweight) effectively control shivering in parturient during spinal anaesthesia. But tramadol offered rapid onset, less recurrence rate and less side effects like nausea, vomiting, dizziness and pruritus when compared to pethidine.

References

1. De Whitte, Sessler DI. Perioperative shivering: Physiology and pharmacology. Anaesthesiolgy 2002; 96:467-84.

2. Sessler DI, Ponte J. Shivering during epidural anaesthesia. Anaesthesiology 1990; 72:816-21.

3. Bhatnagor S, Saxena A, Kannan TR, Punj J, Panigrahi M, Mishra S. Tramadol for postoperative shivering: A double blind comparison with pethidine. Anaesth Intensive Care 2001; 29:149-54.

4. Katyal S, Tewari A. Shivering: Anaesthetic considerations. J Anaesth Clin Pharmacol 2002; 18:363-76.

5. Sessler DI. Temperature monitoring. In: Miller RD, 5th ed. Textbook of Anaesthesia. Churchill Livingstone Inc, New York 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 bstetric patients with tramadol. Can J Anesth 1999;46():253-8.

8. Wrench IJ, Cavill G, Ward JE, Crossly AW. Comparison between alfentanil, pethidine and lacebo in the treatment of post operative shivering. Br J Anaesth 1997; 79:541-2.

9. Ikeda T, Sesslar DI, Tayefeh F, et al. Meperidine and alfentanyl do not reduce the gain or maximum intensity of shivering. Anaesthesiology 1998;88:858-65.

10. Bhattcharya PK, Bhattcharya L, Jain RK, Agarwal RC. Post anaesthesia shivering (PAS): A Review. Indian J Anaesth 2003;47(2):88-93.

11. Viegas OA, Khow B, Ratnam SS. Tramadol in labour in primiparous patients: A prospective comparative clinical trial. Eur J Obstet Gynecol Repord Biol 1993;49(1):131-5.

12. Pausawasdi S, Jirasiritham S, Phaoaric C. The use of tramadol hydrochloride in the treatment of post anasesthetic shivering. J Med Assoc Thai 1990; 73(1):16-20.

13. Wrench IJ, Singh P, Dennis AR, Mahajan RP, Crossly AW. The minimum effective doses of pethidine and doxapram in the treatment of post anaesthetic shivering. Anaesthesia 1977;52:32-6.

14. Filos KS, Goudas LC Patroni O, Polyzou V. Haemodynamic and analgesic profile after intrathecal clonidine in humans: A dose-response study. Anaesthesiology 1994; 81:591-601.

15. Chaturvedi S, Domkondwar G. Control of shivering under regional anaesthesia using tramadol. Asian Archives of Anaesthesiology and Resuscitation 2002; 57:706-7.

16. Tsai YC, Chi KS. A comparison of tramadol, amitryptyline and meperidine for post epidural naesthetic shivering in parturients. Anaesth Analg 2002; 93:1288-92.

17. Bilotta F, Pietropaoli P, Sanita R, Libertori G, Rosa G. Nefopam and tramadol for the prevention of shivering in parturients. Anaesth Analg 2002; 93:1288-92.

18. Pauca AL, Savage RT, Simpson S, Roy RC. Effect of pethidine, fentanyl and morphine on post operative shivering in man. Acta Anaesthesiol Scand 1984;28(2):138-43.

19. Kurz M, Belani KG, Sessler DI, Kurz A et al. Naloxone, meperidine and shivering. Anaesthesiology 1993;79(6):1193-1201.

20. De witte J, Deloof T, Deyelder J, Housmans PR. Tramadol in the treatment of post anaesthetic shivering. Acta Anaesthesiol Scand 1997;41:506-10.

21. Dhimer AA, Patel MG, Swadia VN. Tramadol for control of shivering (comparison with pethidine). IIndian J Anaesthesia 2007;51(1):28-31.

22. Talakoub R, Noorimeshakti S. Effect of tramadol in post spinal shivering in cesarean section. Canadian J of Anaesthesia 2005;5:A132.

23. Angral R, Wani AA, Kapoor BB. Tramadol and postoperative shivering in patients undergoing open and laparoscopic cholecystectomy under general anaesthesia. South Afr J Anaesth Analg 2012;18(2): 111-14.

24. Zahedi H. Comparison of tramadol and pethidine for post anaesthetic shivering in elective ataract surgery. Journal of Research in Medical Sciences 2004;5:234-9.

25. 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.

26. 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). DOI:10.5589/1817.

27. 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.

28. 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.

29. Horn EP. Post operative shivering: Aetiology and treatment. Curr Opin Anaesthsiol 1999;12(4):449-53.