

Efficacy of Prophylactic Intravenous Ketamine Vs Tramadol for Prevention of Intraoperative Shivering in Spinal Anesthesia for Patient undergoing cesarean section

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ABSTRACT

Background: Shivering is a frequently occurring complication of spinal anaesthesia. It is more common in patients undergoing abdomen surgery, procedures of long duration and extremes of age. It has deleterious consequences on patient recovery unless prophylactic steps are taken to prevent this complication.

Aim: To compare the prophylactic use of I/V tramadol with I/V ketamine on the frequency of intraoperative shivering in spinal anesthesia for patients undergoing caesarean section.

Methods: A prospective randomized study was conducted in 400 parturients of ASA I and II status undergoing caesarean section. They were randomly divided into two groups n=200 each. Patients received prophylactic i/v 0.5mg Ketamine (K Group) and 2mg/kg i/v tramadol (T Group). Spinal anaesthesia was administered with injection bupivacaine. After assessment of adequacy of block, frequency of shivering was recorded.

Results: In this study of 400 patients, shivering was seen in 111 patients (27.75%). Shivering was seen not observed in 289(72.25%) patients. Frequency of shivering was seen in 72(36%) patients of tramadol group and 39 (19.5%) from ketamine group. This difference in two groups was statistically significant (P value 0.000).

Conclusion: It has been proved in our study that the use of prophylactic i/v low dose 0.5mg/kg Ketamine drug is significantly more effective as compared to i/v tramadol in the prevention of intraoperative shivering during spinal anesthesia in females undergoing caesarean section.

Keywords: Intraoperative, Shivering, Tramadol, Ketamine, Spinal Anesthesia

INTRODUCTION

Regional anaesthesia (spinal anaesthesia) is widely used as a safe anaesthetic technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70% of patients undergoing abdominal surgery under regional anaesthesia¹.

Shivering and vasoconstriction originate from hypothalamus in response to hypothermia related to neuraxial anesthesia. Hypothermia occurring in neuraxial anesthesia is due to vasodilatation and internal redistribution of heat. The accompanying thermo regulatory impairment from regional anesthesia that allow continued heat loss is due to altered perception by hypothalamus of temperature in anesthetized dermatome rather than a central drug effect as with general anesthesia². Shivering is frequent during the perioperative period and leads to variety of complication like increase heart rate, increase oxygen consumption, acidosis, enhance morbidity in CVS disease patients. It interferes not only in intraoperative monitoring but prolongs the recovery from anesthesia, poor wound healing and lengthen the period of hospital stay^{3 4 5}. Among drugs 5 HT3 receptor antagonist, alpha 2 receptor agonist, opioid and clonidine has been evaluated for prevention and treating shivering. However gold standard drug treatment has not been established because of unpredictable side effects respiratory depression hypotension, sedation, nausea and vomiting⁶.

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Ketamine, an NMDA receptor antagonist plays a role in the transmission of thermal signal to brain and spinal cord to avoid the hypothermia and shivering. Moreover it produces significant analgesic effect which rarely causes CVS or respiratory depression at the dose of 0.5mg / kg⁷.

Tramadol activates the monoaminergic receptor of descending neuraxial inhibiting pathway. This antishivering action of tramadol is probably mediated via opioid or serotonergic and non adrenergic activity or both⁸.

The purpose of this study was to compare the efficacy of prophylactic use of I.V ketamine and tramadol in decreasing intraoperative frequency of shivering in spinal anesthesia for patient undergoing caesarean section.

The objective of this study was to compare the efficiency of prophylactic i/v ketamine and tramadol in preventing intraoperative shivering after spinal anesthesia in females undergoing caesarean section.

Hypothesis: There is no difference in the frequency of reducing postspinal shivering with prophylactic i/v use of tramadol and ketamine after spinal anesthesia in females undergoing caesarean section.

MATERIALS AND METHODS

This randomized controlled trial was conducted in the Department of Anesthesiology, Service Hospital, Lahore for a period of 6 months. Sample size of 400 cases; 200 cases in each group is calculated with 80% power of test, 5% level of significance and taking expected percentage of shivering i.e. 3.03% with ketamine and 0% with tramadol in spinal anesthesia in females undergoing caesarean section. Non probability, consecutive sampling technique was used.

Data collection procedure: After ethical committee approval and informed consent from patients, 400

parturients of American society of Anesthesiology (ASA) grade I-II pregnant patients (18-40 yr) scheduled for elective cesarean section parity < 6, more than 37 week as per LMP were included in study. Pregnant patient with coexisting disease like thyrotoxicosis, cardiopulmonary disease, bleeding disorder, ASA III & IV were excluded from study.

Patients were randomly divided in two groups (n=200 each group), by using Lottery method. In group K, Patients were given intravenous ketamine 0.5mg/Kg, in group T, patients were given i/v Tramadol 2mg/kg. Both drugs were diluted to volume 5ml with N/S and were given slowly prophylactically.

After insertion of 18G 1/v Cannula on fore arm, secured with adhesive tape. Baseline Heart rate, Blood pressure, O2 saturation & temperature were recorded by using noninvasive monitor and mercury thermometer kept under Axilla. Patient in each group was preloaded with 10 ml/kg Ringer lactate solution (preheated to 37.5°C) Patient shifted to operating table with attached monitor operating room temperature was adjusted at 25-26°C. Under aseptic measure, Spinal anesthesia was given using hyperbaric Bupivacain (1.8ml). At L3-4 or L4-5 interspace. Adequacy of Sensory and motor blockade was assessed. Injection ketamine / Tramadol respected doses administered by an assistant. After adequacy of block, Oxygen Supplement 4 L/min via face mask given. Surgery is proceeded for delivery of baby. Patients were monitored for Heart Rate, Blood Pressure and temperature at different interval during surgery. Presence of intra operative shivering was graded by using scale validated by Tsai & Chu.

1. No shivering,
2. piloerection or peripheral vasoconstriction but no visible shivering,
3. muscular activity in only one muscle group,
4. muscular activity in more than one muscle group,
5. whole body shivering.

Grade 1-4 was considered as shivering during cesarean section after 15 minutes of administration of spinal anesthesia. If shivering occurred, prophylaxis was regarded as ineffective, i/v 20mg Ketamine was given. Hypotension (Systolic BP less than 20% of Base line) were treated with Phenylephrine 25-50µg, nausea vomiting with 10mg i/v metaclopramide.

Data analysis: Data was entered and analyzed by SPSS version 20. Quantitative variables like age and gestational age were calculated as mean and standard deviation. Qualitative variables like parity and shivering were calculated as frequency and percentage. Both groups were compared for shivering by chi-square test. p-value ≤ 0.05 was taken as significant. Data was stratified for age (18-30, 31-40 years), gestational age, and parity. Chi-square test was applied post stratification taking p-values ≤ 0.05 as significant.

RESULTS

In this present study total 400 cases were enrolled. The mean age of the patients was 29.21±6.75 years with minimum and maximum ages of 18 & 40 years respectively (Table 1).

In our study the mean age of the tramadol group patients was 28.53±6.61 years and its mean age in ketamine group was 29.90±6.84 years (Table 2).

Study Result showed in Ketamine group (n=200) shivering was seen in 39(19.5%) patients and in 161(80.5%) patient no shivering was seen. In Tramadol group (n=200) shivering occurred in 72(36%) patients but 128(64%) patients had no shivering. Statistically significant difference was seen in frequency of shivering among the groups (p=0.000) (Table 3, Fig.1).

Table 1: Descriptive statistics of age (years)

N	400
Mean	29.21
SD	6.75
Minimum	18
Maximum	40

Table 2: Comparison of age with study groups

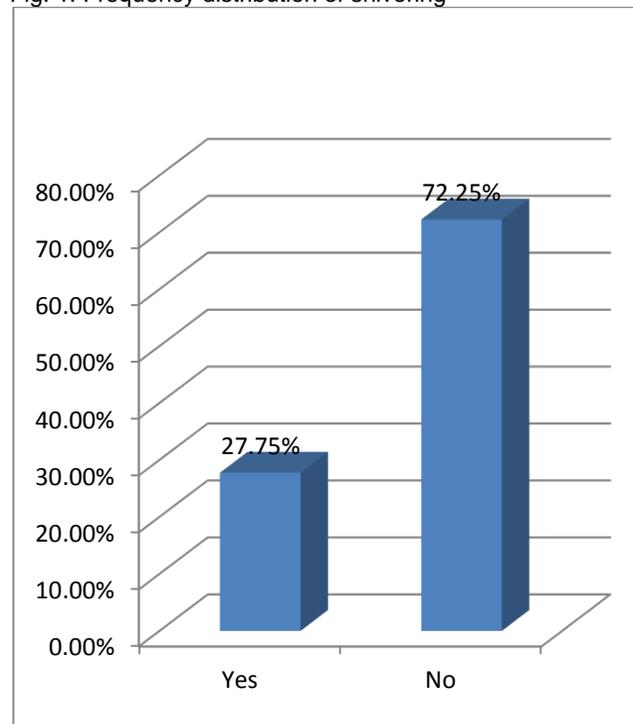
Age (years)	Study group	
	Tramadol	Ketamine
n	200	200
Mean	28.53	29.90
SD	6.61	6.84

Table 3: Comparison of shivering with study groups

Shivering	Study groups		Total
	Tramadol	Ketamine	
Yes	72	39	111
No	128	161	289
Total	200	200	400

Chi value=13.57 p-value=0.000 (Significant)

Fig. 1: Frequency distribution of shivering



DISCUSSION

Shivering is an unpleasant and stressful phenomenon that can occur during perioperative period. Shivering has multiple deleterious physiological effects, like increase PVR, left shift of Hb Oxygen saturation curve, alter mental status, impaired renal function, delay drug metabolism and impairment in wound healing, increase risk of infection. Perioperative shivering may increase Oxygen consumption as much as five fold and may decrease arterial oxygen saturation and may be associated with increase myocardial ischemia^{2 9 10}.

Various treatments like warming of intravenous fluid, radiant heat application, controlling operation theater temperature or pharmacological agents like ketamine, clonidine, tramadol & pethidine have been used to control intraoperative shivering to avoid the deleterious consequences of shivering^{11 12}.

Our study Result have shown ketamine to be a better drug in controlling intraoperative shivering rather tramadol. Intraoperative shivering frequency was seen in 39 patients (19.5%) ketamine group vs 72 patients (36%) in tramadol group. This difference in shivering was statistical significant ($p=0.000$).

Several studies evaluated the frequency of perioperative shivering under neuraxial block with use of low dose of prophylactic i.v ketamine Vs tramadol and found better result with ketamine than tramadol in preventing intraoperative shivering.

Similar to our study results Akram Muhammad et al compared the efficacy of prophylactic low dose ketamine 0.05mg/kg (group K = 32 patients) and tramadol 1mg/Kg (group T = 32 patients) for prevention of shivering during spinal anesthesia for patient under going lower abdomen surgery (obstetric and non-obstetric pts) and showed significant difference in incidence of shivering between Ketamine (18.7%) and tramadol group (46.88%) (P value = 0.01)¹³.

Reda S Rehman et al compared five groups - group C (n=20) control received saline, group M (n = 20) received midazolam 75µg/kg, MK(n=20) received midazolam 37.5 µg/kg plus ketamine 0.25 mg / kg, group T (n=20) received tramadol 0.5mg and Group TK (n = 20) received tramadol 0.25mg/kg+ ketamine 0.25mg / kg prophylactically after the adequacy of spinal anesthesia for orthopedic patients. The incidence of shivering in group C, M, MK, T, TK were 55%, 45%, 5%, 30% & 15% respectively. Midazolam+Ketamine (MK) combination was superior in prevention of post spinal shivering than other groups¹⁴.

Kose et al compared and documented the effectiveness of prophylactic administration of 0.25mg/kg and 0.5mg/kg of i/v Ketamine in Cesarean Section under spinal anesthesia. Similar to our study results, they found significant less incidence of shivering in both group of ketamine when compare to control group⁵.

Hidaych MN et al, recorded incidence of shivering among three drugs given after intrathecal, hyperbaric Bupivacain 2.5ml (12.5mg) and 25µg fentanyl for surgeries under spinal anesthesia. Each group patient receive either prophylactic Ketamine 0.05mg/kg (group K), i.v tramadol 0.5mg/kg (group T) or normal saline as control (group P).

Comparable to our study, the incidence of shivering was significantly lower in group K (8%) than in group T (16%)¹⁵.

Sri Kanta G et al also documented the result in favor of our study. He concluded the superiority of low dose of ketamine over tramadol. Incidence of shivering recorded with ketamine (13%) Vs tramadol group (40%) ($P<0.05$)¹⁶.

Various studies failed to demonstrate decrease in frequency of intraoperative shivering with prophylactic i.v low dose ketamine.

Results of Lemaet al were different from our study. He administered prophylactic (group K n=41) ketamine 0.2mg/kg, (group T n=41) tramadol 0.5mg/kg, (group S n=41) control group Saline for patients undergoing cesarean section in spinal anesthesia. Incidence of shivering was found higher in ketamine (41.5%) and Tramadol (53.7%) in comparison to our study result Ketamine (19.5%) Vs Tramadol (36%). Reason of difference could be use of cold IV fluids and no control of operation theater temperature¹⁷.

Wason et al studied 200 patients for control of shivering under neuraxial anesthesia in lower abdominal and limb surgeries and divided into four groups (50 patients in each group) I.V ketamine 0.5mg/kg, clonidine 75µg, tramadol 0.5mg/kg and placebo group before the block. He concluded no drug showed any significant advantage over the others¹⁸.

Result by Ansari Mohammad U et al were not consistent with our study result, though he used 0.5mg/ kg IV ketamine in 30 patients and 0.5mg IV tramadol in 30 patients, after appearance of shivering under neuraxial block for lower abdominal surgery. He found tramadol to be more potent than ketamine. The difference in results could be due to lower plasma concentration of active drug tramadol in our study¹⁹.

Study by A. Musarat et al differ from our study results, he used, prophylactic tramadol 0.5mg/kg, ketamine 0.5mg/kg just before spinal anesthesia and found equal decrease in incidence of shivering. The reason of difference may be due to different timing of administration of study drug²⁰.

L. Gajal et al used ketamine 0.25mg/kg and tramadol 0.5mg after the adequacy of spinal block in lower abdominal and limb surgery. Both drug were significantly effective in preventing post spinal shivering. The reason of difference may be due to smaller sample size. The study 30 patients in each group in comparison to our study of 200 patients in each group²¹.

Limitation of our study was lack of constant monitoring of intravenous fluid temp during intraoperative period. Another limitation of our study was that we did not use any adjuvant with bupivacaine for intrathecal injection. Future studies may be proceeded by adding intrathecal fentanyl along with hyperbaric bupivacain and monitoring of intravenous fluid temperature during intraoperative period for incidence of intraoperative shivering.

CONCLUSION AND RECOMMENDATION

We recommended the prophylactic administration of low-dose of IV ketamine 0.5 mg/kg IV after spinal anesthesia was significantly better in reducing the incidence of intraoperative shivering in patient undergoing Cesarean Section than tramadol.

REFERENCES

1. De Whitte, Sessler DI, et al. Perioperative shivering: Physiology and Pharmacology. *Anaesthesiology* 2002; 72: 816-21
2. Morgan GE, Mikhail MS, Murray MJ. *Clinical Anaesthesiology* fourth edition. 2006. 148-150
3. Witte J, Sessler DI. Perioperative shivering. *Anesthesiology*. 2002;96(2):467-484
4. Sessler DI. Temperature Monitoring and Perioperative Thermoregulation. *Anaesthesiology* 2008; 109(2) 318-338
5. S. Mathews, A. Al Mulla et al. Postanaesthetic shivering – a new look at tramadol . *Anaesthesia* 2002;57:387-403.
6. Kose EA, Honca M, Dal D, Akinci SB, Aypar U. Prophylactic ketamine to prevent shivering in parturients undergoing Cesarean delivery during spinal anesthesia. *ClinAnesth*, 2013 : 25(4): 275-80.
7. Eydi M, Golzari SE, Aghamohammadi D, Kolahdozan K, Safari S, Ostadi Z, Postoperative Management of shivering: a comparison of pethidine Vs ketamine, *anesth Pain Med* 2014;4(2).
8. T M, Kaparti L.A randomised trail comparing efficacy, onset and duration of action of pethidine and tramadol in abolition of shivering in the intra operative period. *J. ClinDiagn Res*, 2014;8(11)
9. Alfonsi P. ,Postanesthetic shivering: epidemiology, path physiology and approaches to prevention and management, *Drugs*, 2001;61:2193-2205.
10. Norouzi M, Doroodian MR, Salajegheh S. Optimum Dose of ketamine for prevention of postanesthetic shivering; a randomized double – blind placebo controlled clinical trial *anesthesiolBelg* 2011;62:33-36.
11. Wrench J Cavill et al. Comparison between Alfentanil, pethidine, and placebo in the treatment of postoperative shivering. *Br J Anaesth*. 1997; 79:541-42.
12. Takehiko I, Sessler Daniel et al. Meperidine Alfentanil do not reduce the gain or maximum intensity of shivering *Anesthesiology* 1998;88(4):858-65.
13. Akram M, Raza H. Efficacy of low dose ketamine and tramadol for prevention of shivering during spinal anaesthesia in patients undergoing lower abdominal surgeries. *PJMHS* 2017; 11 (1).
14. Reda S. Prevention of shivering during regional anaesthesia: Comparison of Midazolam, Midazolam plus ketamine, Tramadol and Tramadol Plus Ketamine. *Life Science Journal*, 2012; 9(2)
15. Hidayah MN, Liu CY, Joanna OS. Ketamine and Tramadol for the prevention of shivering during spinal anaesthesia. *Clin Ter*. 2014;165(4):193-8.
16. Srikanta G, Krichna G, Smita A, Sushil KN, Satrajit D, Gautam P, et al. Ketamine, Tramadol and Pethidine in prophylaxis of shivering during spinal anaesthesia. *J AnesthesiolClinPharmacol*. 2010;26(1):59-63.
17. Lema GD. Efficacy of intravenous tramadol and low dose ketamine in the prevention of post-spinal anesthesia shivering following caesarean section: *International Journal of women's health* 2017;9 681-688.
18. Rama Wason, Nikhil Jain, Poonam Gupta, and Anoop R Gogia. Tandomized double-blind comparison of prophylactic ketamine, clonidine and tramadol for the control of shivering under neuaxial anaesthesia. *Indian J Anaesth*. 2012 : 56(4): 370-375
19. Ansari Muhammad U, Porwal Sanjay K. Post anaesthesia shivering during neuraxial anaesthesia. *J PBMS* 2013 ;28(28):677-682
20. Dr. Ara M, Dr. Shamim A. Comparison of prophylactic ketamine, clonidine and tramadol for the control of shivering under neuraxial anaesthesia: a prospective randomized study. *International Journal of Advanced Research*. 2015; 10 (3); 1136-1142
21. GajalLakhe, Krishna MurariAdhikari. Prevention of shivering during spinal Anaesthesia: Comparison Between Tramadol, Ketamine and Ondenstron. *J Nepal Med Assoc* 2017;56(208):395-400.