ORIGINAL ARTICLE

Randomized control trial of tramadol versus ketamine in the prevention of shivering during spinal anesthesia

Mohammad Ilyas, Ambreen Naz, Fazal Wadood, Neelum Halimi, Zaid Jawaid, Parhaizghar Khan

Received:
7th November, 2018

Accepted:
22nd August, 2019

Abstract:
Objective: The aim of this study was to compare the efficacy of ketamine and tramadol in the prevention of shivering during spinal anesthesia.
Material and Methods: This randomized controlled trial was conducted for a period of six months at Anesthesia Department, Khyber Teaching Hospital, Peshawar. A total of 92 patients of both gender between the age of 18 to 60 were observed. All patients were randomly allocated in two groups (46 in each). Patients in group-A were subjected to low dose ketamine while patients in group-B were subjected to tramadol. Conduct and maintenance of subarachnoid block was same in both groups. Grade of shivering was noted down intra-operatively and up to 40 minutes after the surgery, at 15 minutes' intervals, using Crossley and Mahajan scale. All the data was analyzed with SPSS version 23.
Results: 5-patients in ketamine group and 11-patients in Tramadol group have significant shivering. So ketamine was more effective in preventing shivering compared to tramadol.
Conclusion: Our study concluded that low dose ketamine was superior to tramadol in preventing shivering during spinal anesthesia.

Keywords: spinal anesthesia, shivering during spinal anesthesia, ketamine and tramadol, Crossley and Mahajan scale

Khyber Teaching Hospital, Peshawar
M Ilyas
A Naz
F Wadood
N Halimi
Z Jawad
P Khan

Correspondence:
Dr. Ambreen Naz,
Khyber Teaching Hospital, Peshawar
Cell: 0333-9116410
Email: umbarinnaz1@yahoo.com

Pak J Surg 2019; 35(4):311-15

Introduction:
Shivering is an unpleasant and frequent problem during and after spinal anesthesia and post-operatively after general anesthesia. Its prevention is important not because it is a life threatening event, but is very distressing for the patient and some of its complications may adversely affect the patients with cardio-respiratory disease.[1-3] It is defined as spontaneous, involuntary and rhythmic muscular contractions at rate of 4-8 hertz and is a physiological method of heat production in humans.[4] Its frequency has been reported 40-70% in the literature during and after spinal anesthesia (SA) and is extremely unpleasant for the patient.[5] Vasodilation due to sympathetic block in spinal anesthesia facilitates rapid heat loss and core to peripheral re-distribution of body heat, resulting in hypot-hermia that lowers the threshold for shivering.[1,6] Its adverse effects include increased oxygen consumption up to five times that leads to hypoxemia, increased carbondioxide production, increase in minute ventilation and hence cardiac output and lactic acidosis.[7,8] Moreover, it increases intra-cerebral and intra-ocular pressure, can be uncomfortable for patients, aggravates wound pain and interferes with electrocardiography monitoring, blood pressure and pulse oximetry, which may pose a patient safety issue.[9]

Both non-pharmacological and pharmacological agents have been used to prevent and treat shivering. Non-pharmacological methods include forced air warmers, blankets, radiant heat

and increasing the operating room ambient temperature. By decreasing heat loss these measures maintain core body temperature thus preventing shivering.[10] However, these methods are expensive and cumbersome to use.[11] Different pharmacologic agents including opioids, N-methyl D-aspartate receptor antagonists, α2-agonists, cholino mimetics, bio-genic amines (serotonin 5-HT3 receptor antagonist), dexamethasone, Doxapramand magnesium sulphate have been used for prevention of shivering.[12]

Tramadol, a centrally acting analgesic drug with μ-opioid agonist effects with minimum effect at kappa (κ) and delta (δ) receptors, has been shown to be effective in the prevention of post-spinal shivering.[13] The mechanism of action is proposed to act through the modulatory effect on central mono-aminergic pathways, inhibiting the neuronal uptake of noradrenaline and serotonin in the spinal cord and increasing hydroxyl-tryptamine secretion, which resets the body temperature regulation center.[14] Katamine is a competitive receptor antagonist of N-methyl D-aspartate which modulates thermo regulation at multiple levels. It modulates serotoninergic and noradrenergic neurons in the locus caeruleus.[14] Ketamine, has also been shown to inhibit post-operative shivering in many reports.[16-19]

Prevention and control of shivering is important as it also affects the outcome of surgeries and can play a role in delaying the surgeries. No standard pharmacological treatment has been recommended in the past as all the drugs used for prevention and control of shivering has been associated with various side effects. So the present study was designed to compare the efficacy of low dose ketamine with tramadol in prevention of shivering during and after spinal anesthesia and to recommend a better and economical agent for future use.

Objective: To compare the efficacy of ketamine and tramadol in the prevention of shivering during and after spinal anesthesia.

Material and Methods:

This study was conducted at Anesthesia Department, Khyber Teaching Hospital Peshawar for a period of six months from September 2017 to March 2018. After approval from ethical committee of the hospital a total of 92 patients were recruited into the study. This was a double blind randomized controlled trial in which both the patients and the investigators were blinded to the study. After taking informed consent the patients were divided into two groups of 46 patients each. All patients of both gender with American Society of Anesthesiologists class 1 and 2 between the age of 18-60 years undergoing lower abdominal procedures (appendectomy, vaginal or abdominal hysterectomy, hernioplasty) were selected. While pregnant patients, procedures requiring transfusion of blood or blood products, obese patients, patients with coagulopathy, abscess at the site of injection, hemo-dynamically unstable patients, cardiovascular disease and allergy to local anesthetics were excluded. Block randomization was done to allocate two groups in such a way that first block of 10 was allocated to group-A (Ketamine) second block to group-B (Tramadol) and so on until the group allocation was complete. Consecutive non probability technique was used for sampling.

Patients in group-A were subjected to low dose ketamine while patients in group-B were subjected to tramadol. No pre-medication was given. Both drugs were prepared in same 10 ml syringes. Both the patients and the anesthesiologist responsible for injecting drugs and recording the data were blinded to the study drugs. All patients were preloaded with 15 ml per kg of Lactated Ringers solution. Sub-arachnoid block was performed at L 3-4 interspace with 15 mg of 0.5 % heavy bupivacaine using 25G pencil point spinal needle. Operation room temperature was recorded with a wall thermo-meter and was maintained between 24-26°C and all intravenous fluids were warmed to this temperature before infusion. After injection of local anesthetic solution the level of sensory and motor block was assessed. Then patients in group-A were injected with 0.05mg per kg of Ketamine

Table-1: Shivering grade accroding to Crossley and Mahajan scale

Shivering grade	Clinical symptoms
0.	No shivering
1.	Piloerection or peripheral vasoconstriction but no visible shivering
2.	Muscular activity in only one muscle group
3.	Muscular activity in more than one muscle group but not generalized
4.	Shivering involving the whole body

Table-2: Efficacy (n=92)

Efficacy	Group-A (low dose ketamine)	Group-B (Tramadol)
Effective	41(90%)	35(76%)
Not effective	5(10%)	11(24%)
Total	46(100%)	46(100%)

P value 0.000

intravenously and patients in group-B received 1mg per kg of injection tramadol intravenously. Grade of shivering was noted intra-operatively and up to 40 minutes after surgery at 15 minutes intervals using 5 point Crossley and Mahajan scale as shown in table-1.

Pethidine 25mg I.V. was given as a rescue drug and metoclopramide 10mg I.V. was given to control nausea and vomiting. All the data was analyzed with SPSS version 23. Frequency and percentages was computed for categorical variables while numerical data was described as Mean±SD. Chi square test was used to compare the efficacy between the two groups and P-Value <0.05 was considered significant.

Results:

Demographic data such as age, gender was not statistically different among both groups. In group-A 31(68%) patients were in the age range 18-40 years and 15(32%) patients were in the age range 41-60 years. Mean age was 38 years with SD±2.77. Where as in group-B in 32(70%) patients were in the age range 18-40 years and 14(30%) patients were in age range 41-60 years. Mean age was 40 years with SD±3.12. Gender distribution among two groups showed 19(42%) patients were male and 27(58%) patients were female in group-A. Where as in group-B 21(45%) patients were male and 25(55%) patients were female.

In Ketamine group 3 patients in the age range 18-40 years and 2 patients in the age range 41-60 years developed significant shivering. While in Tramadol group 8 patients in age range 18-40 years and 3 patients in age range 41-60 years developed significant shivering. Thus prophylactic Ketamine was more effective in preventing shivering than tramadol as only 10% of patients in group-A developed significant shivering compared to 24% in group-B (table-2).

Discussion:

Treatment and relief of patients' symptoms have long been the priority of health professionals. Shivering is a major complication during and following sub-arachnoid block and can be sometimes very distressing for the patient. Its frequency has been reported up to 40-70 % in literature.[5] Although shivering is not a life-threatening event, it may cause almost 100-200% increase in metabolic oxygen demand and Carbon dioxide production with lactic acidosis.[7] Thus as a result both minute ventilation and cardiac output increase leading to an imbalance in oxygen demand and supply ratio of the myocardium. These effects are often poorly tolerated by patients with cardio-respiratory disease. Furthermore, shivering resulting from hypothermia also interferes with monitoring techniques such as pulse oximetry, electro-cardiography and non-invasive measurement of blood pressure. The cause of shivering during and after sub-arachnoid block is many fold. Vaso dilatation during sub-arachnoid block facilitates rapid heat loss and core to peripheral re-distribution of body heat resulting in hypo-thermia that lowers the threshold for shivering. Furthermore, there is altered thermo-regulatory response under sub-arachnoid block and thus reducing shivering threshold.[1]

Of various pharmacological agents which have been used for prevention of shivering pethidine is the most effective agent in preventing post-operative shivering. Although its mechanism of action is not completely understood, it probably acts through opioid receptors or directly on the thermo-regulatory center in the brain. However, it is avoided because of its un-wanted effects such

as nausea, vomiting, drowsiness, delayed gastric emptying and increase hospital stay. Ketamine is a phencyclidine derivative and is a competitive antagonist of N-methyl D-Aspartate (NMDA) receptors. Its action through multiple levels, modulates thermo-regulatory center in brain. Tramadol on the other hand acts centrally and resets the body temperature regulation center.[14]

Several studies have been done in the past to find a better therapeutic agent for prevention and treatment of shivering with variable results. Some of the investigators could not find any difference in efficacy between the two drugs. Lema et al compared Ketamine and tramadol with control (saline) group in patient undergoing cesarean section under spinal anesthesia and found Tramadol and Ketamine more effective than saline.[20] In their study shivering was seen in 22(53.7%) patients in Tramadol group, 17(41.5%) patients in the Ketamine group and 29(70.7%) patients in the normal saline group. However, grade-III shivering was more in Ketamine group than Tramadol group, 09 vs 08 patients. Thus they concluded both drugs to be more effective than control (Saline). Ansari and his colleagues found Tramadol to be more effective and potent than Ketamine in preventing shivering. These studies showed that both drugs were equally effective in decreasing frequency of shivering.

Our sample size was also small but p-value was 0.000 which was statistically significant. Thus in our study Ketamine was found to be superior compared to Tramadol in preventing shivering during and after sub-arachnoid block. Results in our study have been supported by various other studies. In a study conducted by Muhammad Akram and associates, only 6 patients in ketamine group developed shivering compared to 15 patients in Tramadol group, concluding superiority of Ketamine over tramadol in preventing shivering. In their study the frequency of shivering after spinal anesthesia for elective surgery was 18.75% in Ketamine (group) while 53.12% in Tramadol (group). They concluded that the prophylactic administration of low-dose I.V. Ketamine or I.V. tramadol is effective for reducing the incidence and intensity of shivering.[23]

Ketamine has also been compared with saline (placebo) and in combination with midazolam in the past with results in favor of use of Ketamine for prophylaxis and treatment of shivering.[1,19] Laiq N et al compared Ketamine with Saline and found Ketamine to be more effective than control in preventing post-operative shivering. Similar results were obtained in another study done by Tariq and associates.[24]

However, majority of Anesthesiologists are reluctant to use ketamine due to its undesirable side effects such as sedation, hallucinations, nausea, vomiting and night mares. We recommend low-dose I.V. ketamine prophylaxis for patients undergoing lower abdominal surgeries under spinal anesthesia till the development of newer pharmacological agents with more desirable safety profile and fewer side effects.

Conclusion:
Our study concludes that low dose ketamine and tramadol are both effective in preventing shivering. However, Ketamine is superior to Tramadol for reducing the frequency and intensity of shivering during and after spinal anesthesia.

Conflict of interest: None

Funding source: None

Role and contribution of authors:
Dr. Mohammad Ilyas, collected the data, references and helped in initial writeup.

Dr. Ambreen Naz, collected the referenes and did the initial writeup

Dr. Fazal Wadood, helped in colleting the data and introduction writing

Dr. Neelam Halimi, helped in collecting the referecns and also helped in discussion writing

Dr. Zaid Jawad, collected the references and

helped in tabulation of result

Dr. Parhaizghar Khan, critically review the article and made the final changes.

References:

1. Abdelrahman RS. Prevention of shivering during regional anesthesia: comparison of midazolam, midazolam plus ketamine, tramadol, and tramadol plus ketamine. Life Sci J. 2012;9(2):132–9.
2. Entezariasl M, Isazadehfar K. Dexamethazone for prevention of Postoperative Shivering:Randomized Double-Blind comparison with Pethidine. International J of Preventive Medicine.2013; 4(7): 818-24.
3. Jabari M, Soltani G, Hoosmandi F, Amini S. Effect of intravenous, ketamineonprevention of postoperative shivering: A comparison with intravenous pethidine. J of Surj and trauma. 2014; 2(1): 1-5.
4. Eydi M, Golzari SE, Aghamohammadi D, Kolahdouzan K, Safari S, Ostadi Z. Postoperative management of shivering. A comparison of pethidinevs ketamine. Anesth. Pain Med. 2014;4(2): 1-5.
5. AasimSA,Reddy S, Reddy V, Reddy M and Chandarkanth C. Randomised double-blind Comparativestudy of Tramadol and Dexmedetomidine for post spinal Anesthesia shivering. J ofChalmedaAnandRaoInstitute of Med. Sciences. 2016; "(1): 18-21
6. Kranke P, Eberhart LHJ, Roewer N, Tramer MR, Pharmacological Treatment of Postoperative Shivering: A Quantitative Systematic Review of Randomized Controlled Trials. Anesth. Analg. 2002;94:453-60.
7. Kim YA, Kweon TD, Kim M, Lee HI, Lee YJ, Lee KY. Comparison of meperidine and nefopam for prevention of shivering during spinal anesthesia. Korean J Anesthesiol. 2013;64(3):229–33.
8. Zhang Y, Wong KC. Anesthesia and postoperative shivering: its etiology, treatment and prevention. Acts Anesthesiol Sin. 1999; 37(3): 115-20.
9. Kaparti L. A randomised trial 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):07-09.
10. Al Maruf A, Isltam MS, Hoq N. Effect of tramadol and pethidine on shivering during cesarean section under spinal anaesthesia. J Armed Forces Med Coll Bangladesh. 2015;10(2):27–32.
11. Elmawgood AA, Rashwan S, Rashwan D. Efficacy of prophylactic use of hydrocortisone and low dose ketamine for prevention of shivering during spinal anesthesia. Eg J Anaesth. 2012;28(3):217–21.
12. Kose EA, Honca M, Dal D, Akinci SB, Aypar U. Prophylactic ketamine to prevent shivering in parturients undergoing cesarean delivery during spinal anesthesia. J ClinAnesth. 2013;25(4):275–80.
13. Eydi M, Golzari SE, Aghamohammadi D, Kolahdouzan K, Safari S, Ostadi Z. Postoperative management of shivering: a comparison of pethidine vs. ketamine. Anesth Pain Med. 2014;4(2):e15499.
14. Ejiro B, Edomwonyi N, Imarengiaye C. Ondansetron versus tramadol in the prevention of postanaesthesia shivering following caesarean section under spinal anaesthesia. African J Anaesth Intensive Care. 2014;14(1):6–11.
15. Hasannasab B, Banihashem N, Khoshbakht A. Prophylactic effects of doxapram, ketamine and meperidine in postoperative shivering. Anesth Pain Med. 2016; 6(1): e27515.
16. Shakya S, Chaturvedi A, Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. J AnaesthesiolClinPharmacol. 2010;26(4):465–9.
17. Kose EA, Honda M,Dal D,Akinci SB, Aypar U. Prophylactic ketamine to prevent shivering in parturients undergoing cesarean delivery during spinal anesthesia. J ClinAnesth. 2013;25(4): 275-80.
18. Park SM, Mangat HS, Berger K, Rosengart AJ. Efficacy spectrum of antishivering medications: meta-analysis of randomized controlled trials. Crib Care Med. 2012; 40(11):3070-82.
19. Laiq N, Khan MN, Nasir N, khans. Prevention of postoperative shivering by prophylactic Ketamine in patients undergoing major surgeries under General Anesthesia. Ann Pak Inst med Sci2006; 2/3): 163-6.
20. Lema GF, Gebremedhn EG, Gebregzi AH, Desta YT, Kassa AA. Efficacy of intravenous tramadol and low dose Ketamine in the prevention of post-spinal anesthesia shivering following cesarean section. International J of women's health. 2017; 9: 681- 88.
21. Ara M, Shamim A. Comparison of prophylactic Ketamine, clonidine and tramadol for the control of shivering under neuraxial anesthesia: A prospective randomized study. International Journal of Advanced Research. 2015; 10 (3): 1136-42.
22. Wason R, Jain N, Gupta P and Gogra AR. Randomized double blind comparison of prophylactic Ketamine, Clonidine and Tramadol for the control of shivering under neuraxial anesthesia. JPBMS 2013; 28(28); 677-82.
23. Akram M, Raza H, Imam SM. Efficacy of Prophylactic low dose Ketamine and Tramadol for prevention of shivering during spinal anesthesia in patients undergoing lower abdominal Surgeries. PJMHS 2017; 11(1): 378-380.
24. Tariq MA. Use of ketamine plus midazolam versus ketamine alone in prevention of shivering during spinal anesthesia: A randomized control trial. Khyber Med Univ J 2014; 6(1): 5-8.