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**ORIGINAL ARTICLE**

# Compare the Effect of Addition of Low Dose Ketamine to Tramadol for the Prevention of Shivering Under Spinal Anesthesia

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## ABSTRACT

**Objective:** To see if adding a mild dosage of ketamine to tramadol can help avoid shivering when under spinal anaesthesia.
**Study Design:** Randomized study
**Place and Duration:** The study was conducted at the department of Anesthesia, Sindh Government Liyari General Hospital Karachi and Shiekh Khalifa Bin Zayed Hospital, Quetta for the duration of six-months from December 2020 to May 2021.
**Methods:** There were one hundred and seventy patients of both genders undergoing inguinal hernia were included in this study. Informed permission was obtained before to calculating demographic information such as age, sex and BMI. Patients were divided equally into two groups. Group A had 85 patients and received low dose ketamine 0.25 mg/kg (K) into tramadol and group B had 85 patients and received tramadol 0.5 mg/kg (T) alone. Post-treatment effectiveness among both groups was compared in terms of shivering control. We used SPSS 19.0 version to analyze complete data.
**Results:** In group I the mean age of the patients was 33.9±9.76 years and mean age in group II was 31.5±3.23 years. There were 55 (64.7%) males and 30 (35.3%) females in group I while in group II 65 (70.6%) were males and 30 (29.4%) females. HTN and diabetes mellitus were the most common comorbidities found among both groups. 50 (58.2%) patients in group I had ASA class II and in group II 54 (63.2%) had ASA class II. We found that low dose ketamine to tramadol was effective in reduction of shivering in 33 (38.9%) as compared to tramadol alone shivering found in 41 (48.2%) cases.
**Conclusion:** We concluded in this study that low dose ketamine into tramadol under spinal anesthesia is an effective and useful in terms of reduction in shivering as compared to tramadol alone in patients undergoing surgery.
**Keywords:** Spinal Anesthesia, Ketamine, Tramadol, Shivering

## INTRODUCTION

Shuddering encompasses all types of muscle activity, including spontaneous, involuntary, and recurring muscle motion. Spinal anaesthesia (SA) can result in hypothermia that reduces the threshold for shivering owing to vasodilation, which can lead to fast heat loss and core to peripheral redistribution of body heat. [1,2]

Though it is rarely life-threatening, excessive shivering can have serious side effects in individuals with a history of cardiorespiratory illness. These include hypoxia, an increase in carbon dioxide in the blood, as well as lactic acidosis and other issues. Patients may also experience discomfort, exacerbate wound pain, and interfere with vital signs monitoring, such as ECGs, blood pressure, and pulse oximetry, which might represent a risk to their health. [3,4]

Shivering can be reduced by a variety of non-pharmacological means, including the use of blankets, radiant heat, forced air warmers, and raising the temperature in the operating room. These methods, however, are expensive and time-consuming to implement. [5] N-methyld-aspartate receptor antagonists, opioids, magnesium sulphate, dexmedetomidine, biogenic amines (serotonin 5-HT3 receptor antagonists), and cholinomimetics have all been used to reduce post-spinal anaesthesia shivering, but the most commonly utilised pharmacological drug is magnesium. [6]

Postoperative shivering has been shown to be prevented by ketamine, a competitive antagonist of (NMDA) N-methyl D-aspartate.[7]

A centrally acting analgesic, Tramadol, is effective in the suppression of post-spinal anaesthetic shivering because it has little effects on kappa (k) and delta receptors. The mechanism of action is designed to function within the modulatory impact on central monoaminergic pathways, inhibiting the neuronal absorption of serotonin and norepinephrine in the spinal cord and raising hydroxytryptamine production, and thereby resetting the body's temperature control centre. [8]

Reducing shivering with tramadol combined with ketamine was much more effective than tramadol alone, according to Reda S. Abdelrahman, who compared the two medications (15 percent vs. 30 percent ). [9] A study of the literature shows that the combination of ketamine and tramadol has not been examined for the same goal as the solo functions of these two drugs in various dosages.. As of this writing, there isn't a clear gold standard for treatment and prevention. Pharmacological therapies and procedures for reducing post-operative shivering, such as meperidine and alfentanil, tramadol, magnesium sulphate, ondansetron, and dexmedetomidine have been employed. [10]

Tramadol and ketamine were compared in this study to see if they might be used to minimize shivering under spinal anaesthesia, as opposed to tramadol alone.

## MATERIAL AND METHODS

This randomized study was conducted at the department of Anesthesia in Sindh Government Liyari General Hospital Karachi and Shiekh Khalifa Bin Zayed Hospital, Quetta for the duration of six-months from December 2020 to May 2021 and consisted of 170 patients undergoing inguinal hernia. Informed permission was obtained before to calculating demographic information such as age, sex and BMI. Patients with unstable heart illness, other systemic conditions, and preoperative hypothermia or hyperthermia were not allowed to participate in this study.

Included patients were aged between 25-65 years. A scale similar to that used by Lema was used to grade shivering: 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 generalised; and 4 = shivering involving the entire body.

No nausea or vomiting was evaluated as 0, 1 was simply sickness, 2 was once nausea and vomiting, and 3 was a multiple incident of both.

As the name suggests, this measurement measures the amount of time it takes from when local anaesthetic is injected into your subarachnoid area at time zero to when you start shivering (time s).

In terms of heart rate, bradycardia is less than 60 beats per minute, while hypotension is less than 90 millimetres of mercury.

On arrival in the operation room (OR), NIBP, O2 saturation, and ECG were measured and baseline values were recorded. Iv infusion rates ranged from 10 to 15mm/kg/h in this study. Every five minutes, until the patient was discharged from recovery, hemodynamic data were monitored and recorded. A temperature of 24 degrees Celsius was fixed as per institution regulation for OR. $T_o$ was measured using a mercury axillary thermometer prior to intrathecal injection. When shivering began, a second reading of the body temperature was obtained (T1). Using either the L3/4 or L4/5 interspaces, subarachnoid anaesthesia was administered. A 25G Quincke spinal needle was used to administer 15 mg of 5 mg/ml hyperbaric bupivacaine. randomization was performed using a sealed opaque envelope approach. The intravenous bolus of all medications was administered immediately following the intrathecal injection. There were five syringes each of the study medicines, each containing a unique code. An anesthesiologist who was blinded to the patients' identities kept on the frequency and degree of shivering in each one. For the first group, ketamine and tramadol were both given at a dose of 0.25 mg/kg; for the second group, tramadol was given at a dose of 0.5 mg/kg.

There are two ways to measure onset of shivering (TS-TO): time from spinal anaesthesia to onset of shivering (TS). Rescue medication, in the form of 25 mg of intravenous pethidine, was used to treat shivering that was worse than Grade 2. There was also a 0–3 scale for nausea and vomiting, with zero indicating no vomiting. Students in grades 1–3 were considered at risk of vomiting.

Shivering, nausea/vomiting, hypotension, and bradycardia were seen in patients for up to two hours following intrathecal injection. We used SPSS 19.0 version to analyze complete data.

## RESULTS

In group I mean age of the patients was 33.9±9.76 years and mean age in group II was 31.5±3.23 years. Mean BMI in group I was 29.5±6.41 kg/m$^2$ and in group II mean BMI was 28.9±4.32 kg/m$^2$. Mean time of surgery in group I was 50.2±5.21 minutes and in group II mean time was 49.6±7.61 minutes. There were 55 (64.7%) males and 30 (35.3%) females in group I while in group II 65 (70.6%) were males and 30 (29.4%) females. 50 (58.2%) patients in group I had ASA class II and in group II 54 (63.2%) had ASA class II. (table 1)

Table 1: Enrolled cases with baseline details

| Variables | Group A | Group B |
|---|---|---|
| Mean age (years) | 33.9±9.76 | 31.5±3.23 |
| Mean BMI (kg/m$^2$) | 29.5±6.41 | 28.9±4.32 |
| Mean Time of surgery | 50.2±5.21 | 49.6±7.61 |
| Gender | | |
| Male | 55 (64.7%) | 65 (70.6%) |
| Female | 30 (35.3%) | 30 (29.4%) |
| ASA | | |
| I | 35 (41.2%) | 31 (36.8%) |
| II | 50 (58.2%) | 54 (63.2%) |

Hypertension and diabetes mellitus were the most common comorbidities were found among all patients.(fig 1)

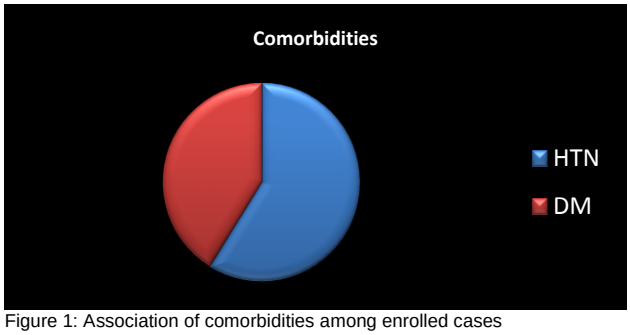


Figure 1: Association of comorbidities among enrolled cases

We found that low dose ketamine to tramadol was effective in reduction of shivering in 33 (38.9%) as compared to tramadol alone shivering found in 41 (48.2%) cases. Mean onset time to shivering in group I 31.13±11.31 minutes and in group II was 24.4±9.52 minutes.(table 2)

Table 2: Post-operative comparison of shivering among both groups

| Variables | Group A | Group B |
|---|---|---|
| Mean time to shivering (min) | 31.13±11.31 | 24.4±9.52 |
| Shivering | | |
| Yes | 33 (38.9%) | 41 (48.2%) |
| No | 52 (61.1%) | 44 (51.8%) |

We found that complications in group I was lower found in 5 (5.9%) as compared to group II in 8 (9.4%) patients.(table 3)

Table 3: Comparison of complications among both groups

| Variables | Group A | Group B |
|---|---|---|
| Complications | | |
| Hypotension | 3 (3.5%) | 5 (5.9%) |
| Nausea & vomiting | 2 (2.4%) | 3 (3.5%) |
| Total | 5 (5.9%) | 8 (9.4%) |

## DISCUSSION

Several theories have been put out to explain the shaking that occurs during and following subarachnoid anaesthesia. Shivering is caused by intraoperative and postoperative hypothermia, which suppresses subarachnoid anaesthesia. This is because hypothermia produces perioperative shivering. Shivering can occur even in the absence of hypothermia, implying that mechanisms other than heat loss are involved in shivering. Some of the processes that may play a part here include postoperative agony, adrenal suppression, sympathetic excessive activity, unrepressed spinal reflexes, and the consequent respiratory alkalosis. Shivering during recovery might make it difficult for the patient to fully recover. Stretching the surgical incision might worsen postoperative pain as a result of shivering. [11]

With doses below those needed to induce sleep, the noncompetitive antagonistic action of ketamine on the N-methyl-D-aspartate receptor plays an important role in the control of body temperature. There are two mechanisms through which norepinephrine, the -adrenergic action of ketamine, or its influence on the hypothalamus work to prevent shivering. Noradrenergic and serotoninergic neurons in the locus coeruleus are modulated by NMDA receptors in thermoregulation. [12]

In current study 170 patients were presented for surgery of inguinal hernia. These were equally divided in two groups. Group A had 85 patients and received low dose ketamine 0.25 mg/kg (K) into tramadol and group B had 85 patients and received tramadol 0.5 mg/kg (T) alone. In group I mean age of the patients was 33.9±9.76 years and mean age in group II was 31.5±3.23 years. Mean BMI in group I was 29.5±6.41 kg/m$^2$ and in group II mean BMI was 28.9±4.32 kg/m$^2$. There were 55 (64.7%) males and 30 (35.3%) females in group I while in group II 65 (70.6%) were males and 30 (29.4%) females. These results were comparable to the studies conducted in past.[13,14] HTN and diabetes mellitus were the most common comorbidities were found among both groups. Mean time of surgery in group I was 50.2±5.21 minutes and in group II mean time was 49.6±7.61 minutes.[15]

We found that low dose ketamine to tramadol was effective in reduction of shivering in 33 (38.9%) as compared to tramadol alone shivering found in 41 (48.2%) cases. Mean onset time to shivering in group I 31.13±11.31 minutes and in group II was 24.4±9.52 minutes. Yang Zhou et al. found similar patterns in a meta-analysis. For lower limb and abdominal procedures under spinal anaesthesia, [16]Thangavelu and colleagues employed intravenous ketamine bolus dosages followed by infusion. Our study found that only 13.9 percent of the ketamine group reported shivering, compared to 54 percent of the saline group. [17] Ketamine was shown to be more effective than tramadol for reducing postoperative shivering in a study by Akram et al. [18]

We found that complications in group I were minimum in 5 (5.9%) as compared to group II in 8 (9.4%) patients in which nausea/vomiting and hypotension was the most common fund. A review of randomized control trials for post-spinal hypotension found that tramadol was responsible for 2.2% of the hypotension. [19] The preventive use of intravenous low dosage ketamine and tramadol for the prevention of shivering was shown to be superior to the use of tramadol alone in spinal anaesthesia. With ketamine and tramadol, the incidence of nausea, vomiting, hypotension and bradycardia is also lower than when tramadol is used alone.

## CONCLUSION

We concluded in this study that low dose ketamine into tramadol under spinal anesthesia is an effective and useful in terms of reduction in shivering as compared to tramadol alone in patients undergoing surgery. Except this complication were found lower in ketamine+tramadol group.

## REFERENCES


1. Crowley LJ, Buggy DJ. Shivering and neuraxial anesthesia. Reg Anesth Pain Med. 2008;33(3):241–252
2. Yimer HT, Hailekiros AG, Tadesse YD. Magnitude and associated factors of postanaesthesia shivering among patients who operated under general and regional anesthesia, Northwest Ethiopia: a cross sectional study. J Anesth Clin Res. 2015;2015
3. Talakoub R, Meshkat SN. Tramadol versus meperidine in the treatment of shivering during spinal anesthesia in cesarean section. J Res Med Sci. 2006;11(3):151–155
4. De Witte J, Sessler DI. Perioperative shivering: physiology and pharmacology. J ASA. 2002;96(2):467–484
5. Dhiman AA, Patel MG, and Swadia V. Tramadol for control of shivering (comparison with pethidine). Indian J Anaesth. 2007;51(1):28–31
6. Han JW, Kang HS, Choi SK, Park SJ, Park HJ, and Lim TH. Comparison of the effects of intrathecal fentanyl and meperidine on shivering after cesarean delivery under spinal anesthesia. Korean J Anesthesiol. 2007;52(6):657–662
7. Al Maruf A, Islam MS, and Hoq N. Effect of tramadol and pethidine on shivering during cesarean section under spinal anesthesia. J Armed Forces Med Coll Bangladesh. 2015;10(2):27–32.
8. Honarmand A and Safavi M. Comparison of prophylactic use of midazolam, ketamine, and ketamine plus midazolam for prevention of shivering during regional anesthesia: a randomized double-blind placebo-controlled trial. Br J Anaesth. 2008;101(4):557–562
9. Abdelrahman RS. Prevention of shivering during regional anaesthesia: Comparison of midazolam, midazolam plus ketamine, tramadol, and tramadol plus ketamine. Life Sci J. 2012;9(2):132-9
10. Nallam SR, Cherukuru K, Sateesh G. Efficacy of intravenous Ondansetron for prevention of Postspinal shivering during lower segment cesarean section: a double-blinded randomized trial. Anesth Essays Res. 2017;11:508–13
11. Shukla U, Malhotra K, and Prabhakar T. A comparative study of the effect of clonidine and tramadol on post spinal anesthesia shivering. Indian J Anaesth 2011;55:242 6.
12. Kose EA, Dal D, Akinci SB, Saricaoglu F, and Aypar U. The efficacy of ketamine for the treatment of postoperative shivering. Anesth Analg. 2008;106(1):120-2.
13. seyam, S. Prevention of post-spinal anesthesia shivering: Low dose ketamine vs tramadol. Al-Azhar International Medical Journal, 2020; 1(4): 108-115.
14. Zhou, Y., Mannan, A., Han, Y. et al. Efficacy and safety of prophylactic use of ketamine for prevention of postanesthetic shivering: a systematic review and meta analysis. BMC Anesthesiol 19, 245 (2019).
15. 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: a double-blinded, randomized control trial. Int J Womens Health. 2017;9:681-688. Published 2017 Sep 26.
16. Zhou Y, Mannan A, Han Y, Liu H, Guan HL, Gao X, et al. Efficacy and safety of prophylactic use of ketamine for prevention of postanesthetic shivering: a systematic review and meta analysis. BMC Anesthesiol. 2019 Dec;19(1):245
17. Thangavelu R, George SK, Kandasamy R. Prophylactic low dose ketamine infusion for prevention of shivering during spinal anesthesia: A randomized double blind clinical trial. J Anaesthesiol Clin Pharmacol. 2020 Oct;36(4):506-510
18. Shakya S, Chaturvedi A, Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. J Anaesthesiol Clin Pharmacol. 2010;26(4):465-469.
19. Wang J, Wang Z, Liu J, Wang N. Intravenous dexmedetomidine versus tramadol for treatment of shivering after spinal anesthesia: a meta-analysis of randomized controlled trials. BMC Anesthesiol. 2020 Dec;20(1):140