

## COMPARISON OF KETAMINE AND TRAMADOL FOR PREVENTION OF SHIVERING DURING SPINAL ANESTHESIA

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**Abstract:** Shivering is a common side effect after receiving a spinal anesthetic. This research aimed to compare the effectiveness of Ketamine and Tramadol in reducing the occurrence of shivering. One hundred and fifty patients aged 18 to 60 with ASA physical status I or II having different surgical procedures were randomly assigned to receive either Intravenous (IV) normal saline (Group P), IV 0.5mg/kg ketamine (Group K), or IV 0.5kg/mg tramadol (Group T). The frequency of shivering, its impact, and the onset of nausea, vomiting, sweating, and nystagmus were all noted. Patients were similar in demographics, body temperature at baseline, operation type, median sensory blockage, surgery duration, and anesthetic. 23.3% of patients (35/150) experienced shivering episodes. Twenty-two patients in the placebo group, followed by eight in treatment Group T, and five in treatment group K, reported shivering. The study revealed a statistically significant difference ( $p = 0.006$ ) between Group K and P. When comparing Group T to Group K ( $p = 0.871$ ) and Group P ( $p = 0.724$ ), however, no group showed statistical significance. In group K, nystagmus was one of the most commonly reported adverse effects of IV ketamine, affecting 35 patients (70%). Therefore, compared to the placebo group, Ketamine at a dose of 0.5mg/kg reduces the shivering associated with spinal anesthesia. But there was no statistically significant difference between Ketamine and the intravenous 0.5 mg/kg Tramadol group found in our study.

**Keywords:** Spinal anesthesia, shivering, Ketamine, Tramadol

### Introduction

After receiving spinal anesthesia, a patient may experience hypothermia due to vasodilation below the blockade level, a transfer of body heat from the core to the periphery, and a resistance of shivering to the muscle mass above the level of blockade (Qona'ah et al., 2019). The risk exists that perioperative shivering causes physiological stress. This condition may be linked to several issues, including an increase in oxygen consumption caused by sympathetic activation greater than 200 percent, lactic acidosis, and the creation of carbon dioxide (AHMED et al., 2021; Prasad, 2018). Patients with a limited cardiopulmonary reserve may be put at risk because of this. Shivering of the body can also increase the pressure inside the head and eyes, which can be dangerous (Elinder et al., 2018). Shivering during the perioperative period can lead to surgical complications, the displacement of blood clots, and increased postoperative bleeding and pain simply because it stretches surgical incisions (Noaman et al.,

2019). It is also possible to interfere with the ECG, blood pressure measurements, and oxygen saturation. Shivering and thermoregulation have been the subject of investigation in many research projects that have been carried out in recent years (Moghadam et al., 2019; Safavi et al., 2019).

Competitive NMDA receptor antagonist ketamine has lost its favor as a primary anesthetic medication because of unpleasant symptoms, including hallucination and postoperative vomiting. On the other hand, it has been observed that low dosages of Ketamine can help lower the incidence of perioperative and postoperative shivering while undergoing regional anesthesia. At these subanaesthetic levels, Ketamine's adverse effects were mainly negligible (Ameta et al., 2018; Thangavelu et al., 2020).

In addition to its ability to alleviate pain, Tramadol has also been demonstrated to be an effective treatment for the shivering that might occur after

surgery (Edinoff et al., 2021). The researchers Wahid and colleagues observed that administering 0.5 mg/kg of Tramadol intravenously just before the introduction of neuraxial anesthesia resulted in a considerable reduction in the frequency and intensity of shivering (Wahid et al., 2019). Tramadol has a mild agonist action and inhibits the reuptake of neurotransmitters, including noradrenaline and serotonin. Tramadol also has some analgesic properties. The anti-shivering action of Tramadol is caused by the drug's activity along the serotonergic or noradrenergic pathways (Edinoff et al., 2021). There have been reports that low dosages of Tramadol, between 0.25 and 0.5 mg/kg, can help lower the frequency of shivering without causing a significant increase in adverse effects (Gemechu et al., 2022). The objective of the study was to evaluate and contrast the efficacy of intravenous Ketamine and intravenous Tramadol in preventing shivering, which is commonly associated with spinal anesthesia.

### Methodology

This randomized control study was conducted at the Aziz Bhatti Teaching Hospital in Gujrat from 1st June 2022 to 30th September 2022. The institutional review board and the College of physicians and surgeons(CPSP) both gave their approval to proceed with this study. A total of one hundred fifty patients who were scheduled to undergo elective procedures under spinal anesthesia were randomly assigned to one of three groups using numbers generated by a computer. Patients were given 0.5 mg/kg of Ketamine intravenously (IV), 0.5 mg/kg of Tramadol, and 0.9 percent normal saline as a placebo solution. Ketamine was assigned to Group K, Tramadol to Group T, and the placebo solution was given to Group P. There is the same number of patients in each of the groups. Patients in this study ranged from 18 to 60 years old and belonged to either ASA classification I or II. Patients were not allowed to participate in the trial if they had a history of ischemic heart disease, psychiatric or psychological problems, epilepsy, glaucoma, or an allergy to the study medicines. Patients whose initial body temperature was below 36.5 degrees Celsius, or above 38.0 degrees Celsius were likewise disqualified.

Patients were placed in a seated position before receiving spinal anesthesia, and the procedure was carried out in the midline of the L3-L4 or L4-L5 interspaces with a spinal needle measuring 27 gauges. The process was carried out using an aseptic method. For spinal anesthesia, a combination of 12.5 mg (2.5 ml) of hyperbaric bupivacaine at a concentration of 0.5 % and 25 micrograms (mcg) of fentanyl was employed as the local anesthetic agent. Following the delivery of spinal anesthesia, patients in Group K, Group T, and Group P received intravenous doses of Ketamine 0.5 mg/kg, tramadol 0.5 mg/kg, and normal saline (placebo), respectively. The attending anesthesiologists and the patients had their eyes covered, so they could not see which medications were being tested. Every patient was positioned so they were lying prone and were covered with their robe, a single layer of the cotton blanket, and a surgical drape over the top half of their bodies. During the procedure and the recovery phase, a simple face mask was used to provide supplemental oxygen at a rate of 5 liters per minute. The temperature of all intravenous fluids and irrigation fluids was brought up to 37 degrees Celsius before usage, and an intravenous line warming device was not utilized. The temperature in the operation area was kept between 18 and 20 degrees Celsius at all times.

The intensity of shivering during the operation was monitored at five-minute intervals for one hour. Shivering was evaluated using the following scale: 0 indicated that there was no shivering, 1 stated that there was piloerection or peripheral vasoconstriction but no visible shivering, 2 indicated that there was muscular activity in only one muscle group, 3 stated that there was muscular activity in more than one muscle group but that it was not generalized, and 4 indicated that there was shivering that involved the entire body (Salahat, 2020). Hallucinations, nausea, vomiting, nystagmus, and sweating were some of the adverse effects of the medications that were used in the study. Hallucination was defined as a false sensory experience documented whenever a patient claimed to have seen, heard, smelled, tasted, or felt anything that did not exist. A dose of 10 milligrams of metoclopramide was given intravenously to each patient who had nausea and vomiting. The patients were kept under surveillance in the recovery room for thirty minutes. During that time, the observer,

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who was also blinded to the medicine that was being researched, continued to monitor the parameters that were discussed previously.

The Chi-square test was used to examine the frequency of adverse medication reactions and the incidence of shivering within the first sixty minutes of taking any pharmaceuticals under study. An ANOVA with Bonferroni correction was used to analyze the differences across groups and for repeated measurements. When doing statistical analysis, the SPSS version 21 software was utilized, and a p-value of less than 0.05 was regarded as significant.

**Results**

The trial had 150 patients, including 50 participants in each group. Table 1 displays demographic information.

**Table 1 Demographic parameters**

Variables	Groups		
	Group K	Group T	Group P
Age (Years)	49.5 ± 11.6	52.4 ± 13.5	55.8 ± 14.7
<b>Gender (n, %)</b>			
Male	38 (76)	40 (80)	35 (70)
Female	12 (24)	10 (20)	15 (30)
<b>ASA (n, %)</b>			
Class I	16 (32)	21 (42)	14 (28)
Class II	34 (68)	29 (58)	36 (72)

There were no differences in the three groups regarding age, gender, ASA classification, or type of operation. Figure 1 depicts the distribution of surgical operation types in groups.

Shivering was reported in 23.3 percent (35/150) of the patients. As indicated in Table 2, the placebo group (22) had the most patients suffering from shivering within the first 60 minutes of observation, followed by Group T (8), and Group K (5) had the fewest patients experiencing shivering.

**Table 2 Comparison of frequency of shivering**

Shivering	Group K	Group T	Group P	Total (150)
Yes	5 (10)	8 (16)	22 (44)	35 (23.3)
No	45 (90)	42 (84)	28 (56)	115(76.7)

Grades (n, %)				
Grade 4	0 (0)	0 (0)	0 (0)	0 (0)
Grade 3	1(2)	2 (4)	5 (10)	8(5.3)
Grade 2	1 (2)	3 (6)	10 (20)	14(9.3)
Grade 1	3 (6)	3 (6)	7 (14)	13 (8.7)

Subsequent analysis revealed that the difference between Group K and Group P was statistically significant ( $p = 0.006$ ). There was no statistical significance when Group T was compared to Group K ( $p = 0.871$ ) and Group P ( $p = 0.724$ ). Shivering at the Grade 4 level was not noticed in any patients. Nystagmus was statistically significant ( $p < 0.001$ ) in group K, where 35 (70 percent) of patients experienced nystagmus after receiving IV ketamine during the first 15 or 30 minutes. Three patients in Group K also reported hallucinations during surgery, albeit the difference was not statistically significant. In groups K, T, and P, nausea and vomiting were reported in five, four, and one patient. Table 3 shows that none of the results were statistically significant regarding sweat, nausea, and vomiting.

**Table 3 Comparison of side effects**

Side effects	Group K	Group T	Group P	p-value
Nausea/vomiting	5(10)	4 (8)	1 (2)	0.425
Hallucination	3 (6)	1 (2)	0 (0)	0.318
Sweating	2 (4)	1 (2)	0 (0)	0.335
Nystagmus	35 (70)	0 (0)	0 (0)	<0.001

**Discussion**

Shivering is an involuntary, repetitive movement in the skeletal muscles that typically occurs as a thermoregulatory response to hypothermia. Shivering is an activity in the skeletal muscles (Thorstensen et al., 2018). Anesthesia-induced disruption of thermoregulatory regulation, a cool operating room atmosphere, and variables peculiar to surgery that cause excessive heat loss may all contribute to hypothermia. Hypothermia is a medical emergency and should be treated immediately (Paal et al., 2022). Intraoperative hypothermia triggers a thermogenic shivering response in the body as it strives to recover from normothermia. This happens regardless of the etiology of hypothermia.

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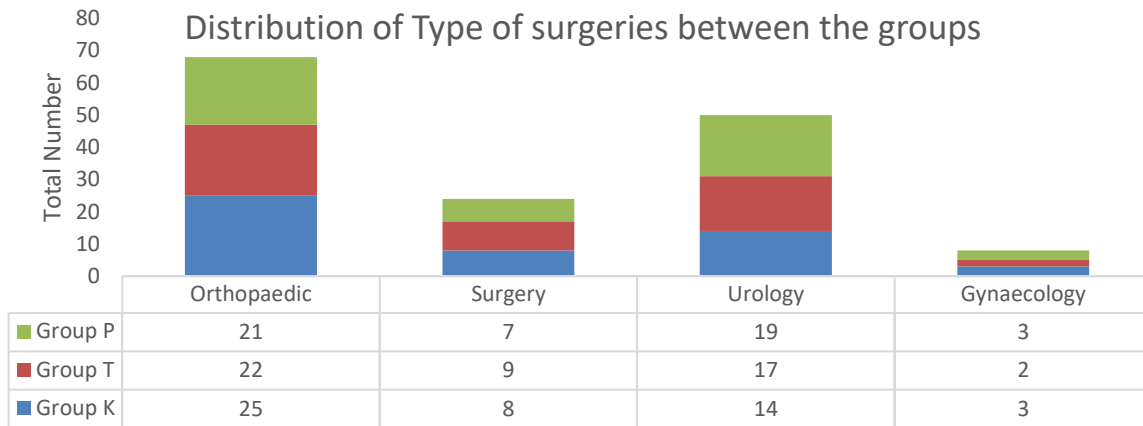


Figure 1 Distribution of Type of surgeries

Ketamine, classified as a dissociative anesthetic, is a non-competitive antagonist of the N-methyl D-aspartate (NMDA) receptor. It has a role in thermoregulation when administered in dosages below that required for anesthesia. Ketamine can stop shivering through a process known as non-shivering thermogenesis. This can happen either through the action of Ketamine on the hypothalamus or norepinephrine. The NMDA receptor is also responsible for modulating the activity of noradrenergic and serotonergic neurons in the locus coeruleus, which may play a role in controlling body temperature (Dincer et al., 2021). Most of the research done on Ketamine has been carried out with doses of less than 0.5 mg/kg. For both the prevention and treatment of shivering, research has demonstrated that a dosage of Ketamine ranging from 0.5 to 0.75 mg/kg is more effective than a dosage of pethidine (25 mg) (Seyam, 2020). However, the potential for adverse effects prevents widespread use. Therefore, in the current investigation, we noticed a significant incidence of nystagmus, hallucination, nausea, vomiting, and sweating. These findings are comparable to those found in previous studies (Lee et al., 2020; Liang et al., 2022; Zangouei et al., 2019). In the trial that MB Rabi'u et al. carried out, none of the patients in the ketamine group was shivering, which is in contrast to the data that we obtained (10 %) (Rabi'u et al., 2019).

This may be because of the more significant dose employed in their trial. In a study with the same subject population, F Sarshivi et al. found that 8 percent of participants experienced shivering after receiving 0.5 mg/kg of Ketamine (Sarshivi et al., 2020). Maybe a larger dose of Ketamine and the intrathecal administration of fentanyl are to blame for this because administering fentanyl intrathecally lessens the shivering by 30%. Therefore, it is

possible that the shivering that occurred in 10 percent of participants in this study is equivalent to the data obtained by the previous investigators. Tramadol is an opioid produced in a lab that can control the temperature on various levels. The reuptake of serotonin and norepinephrine in the spinal cord is inhibited as a result of this, which in turn, makes it easier for serotonin to be released. Its activity produces anti-shivering effects at kappa, opioid, and alpha-2 adrenoceptors, respectively (Baldo and Rose, 2020). It has been discovered that doses of Tramadol ranging from 0.5 to 3 milligrams per kilogram of body weight can effectively reduce postoperative shivering, with an efficacy that is comparable to that of pethidine at 0.5 mg/kg but with almost no adverse effects (Karbord et al.; Wadud et al., 2022). In the current study, prophylaxis with 0.5 mg/kg of Tramadol decreased the incidence of shivering compared to the patients who received normal saline (NS), and the incidence of shivering was only 16 %, which is comparable to the findings that earlier investigators concluded. Previous research has found that the incidence of shivering while taking tramadol ranges from 8.8 to 16 % of the time (Beck et al., 2020). Compared to Ketamine, Toradol had fewer adverse effects, although it was less effective in preventing perioperative shivering (10 percent Vs. 16 percent respectively). However, statistical analysis revealed that the difference was not significant.

In the placebo arm of our trial, we found that 44% of patients experienced an episode of shivering at some point. The incidence of shivering in the control group was reported to be 55 percent in one study by Sagir et al. and 57 percent in another survey by Bilotta et al. when no premedication was given to the

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patients in either of these trials (Bilotta et al., 2002; Sagir et al., 2007). The fact that we did not monitor the core temperature was one of the shortcomings of our research. However, the temperature of the axilla can sometimes be used as a substitute for the core's temperature, except when the core temperature fluctuates considerably (Javaherforoosh et al., 2009).

### Conclusion

The 0.5mg/kg ketamine effectively reduces shivering associated with spinal anesthesia compared to the placebo group. But when we compared it with IV 0.5mg/kg Tramadol, we did not find a statistically significant difference.

### Conflict of interest

The authors declare no conflict of interest.

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