



Dexmedetomidine Infusion versus Intravenous Low-Dose Ketamine Injection In Preventing Intraoperative Shivering During Spinal Anesthesia: A Comparative Study

Authors

Dr A.Vishnuvardhan Reddy¹, Dr Syed Ali Aasim², Dr K.Kalyan Kumar³, Dr Eshwar Rao Madishetti⁴

¹Associate Professor, Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences
Bommakal Village, Karimnagar District, Telangana State, India

²Professor & HOD, Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences
Bommakal Village, Karimnagar District, Telangana State, India

³Post Graduate, Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences
Bommakal Village, Karimnagar District, Telangana State, India

⁴Assistant Professor, Chalmeda Anand Rao Institute of Medical Sciences, Bommakal Village, Karimnagar District,
Telangana State, India

Correspondence Author

Dr K.Kalyan Kumar

Post Graduate, Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences
Bommakal Village, Karimnagar District, Telangana State, India

Abstract

Background: One of the complication during spinal anesthesia is shivering. It is supposed to increase tissue oxygen demand thereby interfering with patient monitoring.

Aims and Objectives: To compare dexmedetomidine with ketamine in preventing shivering during spinal anesthesia.

Materials and Methods: This prospective randomized controlled study included 80 ASA grade I and II patients of either sex, aged 18–60 years, scheduled for elective lower abdominal and lower limb surgeries, under spinal anesthesia. They were divided randomly into two groups of 40 patients each. Group K received low-dose ketamine (0.25mg/kg) and group D received dexmedetomidine infusion. Along with intraoperative shivering, hemodynamic changes and sedation scores were used as parameters.

Results: Patients in group D had a lower incidence of postspinal anesthesia shivering compared with patients in group K.

Conclusion: Dexmedetomidine infusion was more effective as an anti shivering and sedating agent than low-dose ketamine injection in patients receiving spinal anesthesia.

Keywords: Dexmedetomidine, Ketamine, Shivering, Spinal Anesthesia.

Introduction

Patients undergoing spinal anesthesia report complications like shivering with an incidence about 56.7%.¹⁻³ Shivering is an involuntary oscillatory muscular activity, and is considered a physiological response to core temperature in an attempt to raise the metabolic heat production and is associated with cutaneous vasodilatation.⁴

Shivering increases oxygen consumption and carbon dioxide production, triggers myocardial ischemia, causes arterial hypoxemia, increased intraocular and intracranial pressures, increases wound pain, delayed wound healing, and interferes with pulse rate, blood pressure and electrocardiogram (E.C.G.) monitoring.^{5,6}

Different methods are used to control shivering during anesthesia, broadly grouped as pharmacological or non pharmacological. Clonidine, pethidine, nefopam, tramadol, ketanserin, doxapram, etc are drugs commonly used as pharmacological means to reduce shivering. The advantage of this method is that it is less expensive, simple, and its ease of usage. Whereas non pharmacological methods use equipment to maintain temperature of the body are effective, but expensive and lack practicality.^{6,7}

In recent times, ketamine and dexmedetomidine are used to prevent shivering during anesthesia, with excellent results. Ketamine is a competitive NMDA receptor antagonist and plays a role in thermoregulation at various levels by modulating serotonergic and noradrenergic neurons in the locus ceruleus. Its dosage to control shivering is usually 0.25–0.75mg/kg intravenously, with side effects like drowsiness, delirium, hallucination.⁸ Dexmedetomidine acts as antishivering agent by means it being a α -2-adrenergic receptor agonist with potent effects on the central nervous system.⁹ We carried out this study to compare between an intravenous low dose of ketamine and an intravenous infusion of dexmedetomidine for prevention of intraoperative shivering during spinal anesthesia.

Materials and Methods

Our study included 80 ASA grade I and II patients of either sex, aged 18–60 years, scheduled for elective lower abdominal and lower limb surgeries, under spinal anesthesia. The study was carried out from July 2016 to June 2017. After obtaining institutional ethical committee approval, consent was obtained from all the patients. Initially 87 patients were enrolled in the study. 7 patients were excluded as they did not meet the inclusion criteria (Fig 1). 80 patients were then divided randomly into two groups of thirty each. We followed the methodology used by Houssein MM and Ibrahim IM (2016).

Inclusion Criteria

1. Patients undergoing lower limb surgeries,

2. Patients above 18 years of age and
3. Patients not allergic to the study drugs.

Exclusion Criteria

1. Patients with contraindications for spinal anaesthesia,
2. Patients with thyroid disease, Parkinson's disease, dysautonomia, Raynaud's syndrome, cardiopulmonary disease,
3. patients with a history of allergy to the agents to be used, a known history of alcohol use, use of sedative–hypnotic agents, use of vasodilators.

The patients were divided randomly into two groups of 40 patients each. Group K received low-dose ketamine (0.25mg/kg) and group D received dexmedetomidine infusion. Along with intraoperative shivering, hemodynamic changes and sedation scores were used as parameters.

Operation theatres were maintained a constant humidity of 70% and an ambient temperature of around 23°C. A core temperature below 36°C was considered to indicate hypothermia. Prior to spinal anesthesia, each patient received 10ml/kg of lactated Ringer's solution and standard monitoring of heart rate (HR), non invasive blood pressure, oxygen saturation (SpO₂) and body temperature (axillary) was recorded and then for every 10 minutes. Subarachnoid anesthesia was administered at either the L3/L4 or the L4/L5 interspace with 3 ml of 0.5% hyperbaric bupivacaine using a 25-G Quincke's needle and blockade up to the T9–T10 dermatome was achieved. Motor block was assessed using a modified Bromage scale (0=no motor block, 1=can flex the knee, move the foot, but cannot raise the leg, 2=can move the foot only, 3=cannot move the foot or the knee). Sensory block was assessed by the pinprick test.¹⁰

After administration of spinal anesthesia, group K received a prophylactic low dose of ketamine (0.25mg/kg), whereas group D received a prophylaxis of dexmedetomidine (Precedex). Dexmedetomidine ampoule (200 µg/ml) was diluted to a volume of 50 ml (4µg/ml). Patients received a dose of 1µg/kg dexmedetomidine over

10min by a syringe pump, followed by a continuous infusion of 0.4µg/kg/h during the surgery, which was stopped at the completion of surgery. Supplemental oxygen (2 l/min) was delivered through a nasal cannula during the operation.

Grading of shivering was performed as follows¹¹

- 1) Grade 0: No shivering.
- 2) Grade 1: Peripheral vasoconstriction or piloerection or peripheral cyanosis without visible muscle activity.
- 3) Grade 2: Visible muscle activity confined to one muscle group.
- 4) Grade 3: Visible muscle activity in more than one muscle group.
- 5) Grade 4: Gross muscle activity involving the entire body.

If shivering grade was 3 or greater at 15 minutes after spinal anesthesia, the prophylaxis was considered ineffective and 25 mg pethidine was administered by the intravenous route. Side effects such as nausea, vomiting, bradycardia (<60/min), hypotension (>20% decline below baseline), dizziness, and sedation were recorded.

The degree of sedation was assessed using a five-point scale¹²:

1=fully awake and oriented patient.

2=Drowsy.

3=eyes closed, arousable on command.

4=eyes closed, arousable to physical stimuli.

5=eyes closed, unarousable to physical stimuli.

If the patient's HR decreased below 60 beats/min, 0.5 mg atropine was administered by the intravenous route. If the Mean Arterial Pressure (MAP) decreased more than 20% from baseline, 10mg ephedrine through an intravenous bolus was administered and further intravenous infusion of lactated Ringer's solution was required. If the patients developed nausea and vomiting, 10mg metoclopramide was administered through the intravenous route.

HR, MAP, temperature and oxygen saturation (SpO₂) were recorded as a baseline before the start of spinal anesthesia and then recorded every 10 minutes during the intraoperative period till the end of the operation.

The primary outcome measure noted was the intraoperative shivering score. The secondary outcome measures were hemodynamic parameters (HR, MAP, oxygen saturation, and temperature) measured at baseline and then every 10 minutes, in addition to sedation scores.

Statistical analysis

Sample Size: Sample size calculation was done using online power/sample size calculator (<http://www.stat.ubc.ca>).

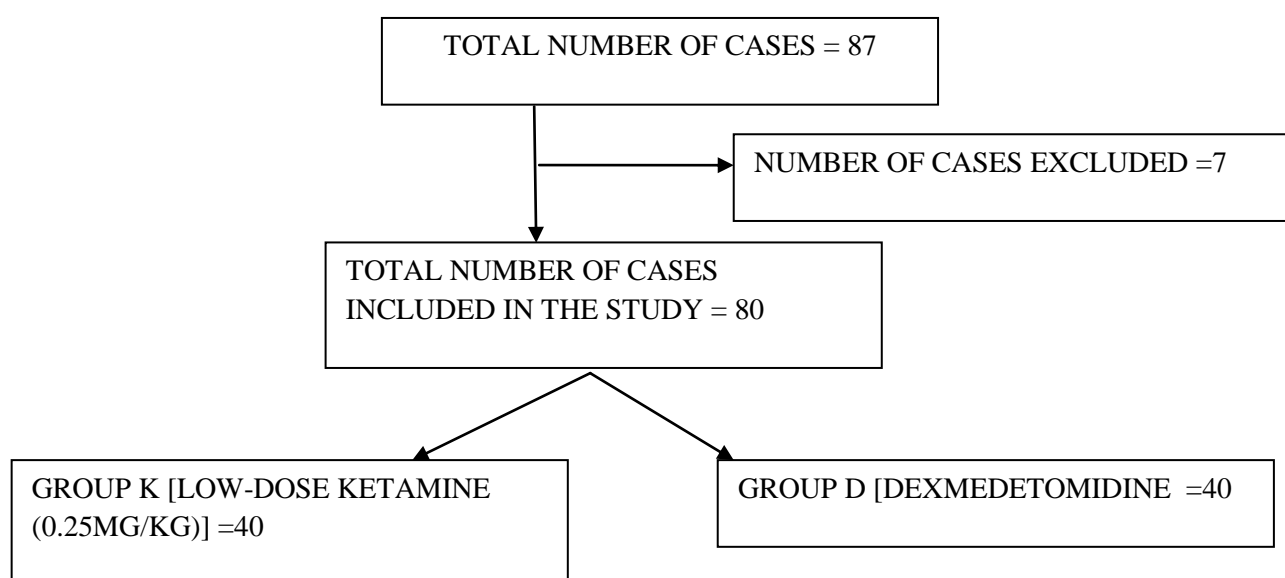


Fig 1: The study flow diagram

Methods of randomization: Randomization of patients was performed using a computerized program (SPSS).

- A. Sealed envelopes were numbered according to the randomization tables.
- B. Packing, sealing, and numbering of the envelopes were performed by a neutral medical personnel (under the supervision of doctors from the Department of Anesthesiology).
- C. The number of cases included in this study was simple allocated randomly to two groups (40 patients in each group).

The obtained data was entered on a microsoft excel sheet and analyzed using the Statistical Program for Social Science (SPSS) version 20 (SPSS Inc., Chicago, IL). Numerical data were presented as mean ± S.D. and categorical data as proportions (%).

The following tests were performed:

- I. A paired-sample t-test of significance was used when comparing between related samples.
- II. The χ^2 -test of significance was used to compare proportions between two qualitative parameters.
- III. Probability (P-value): (a) P-value of 0.05 or less was considered significant. (b) P-value of 0.01 was considered highly significant.

Results

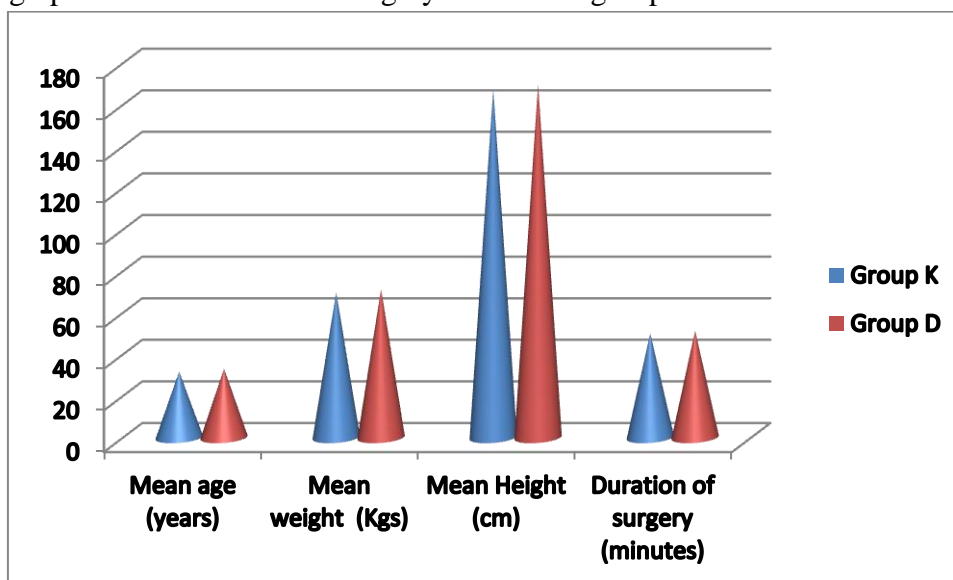
When demographic data was compared, no statistically significant difference was found between the two groups ($P > 0.05$) (Table 1, Graph 1).

Table 1: Demographics and duration of surgery in both the groups

Parameter	Group K	Group D	P value
Mean age (years)	31.75±11.86	33.14±9.08	0.5579
Mean weight (Kgs)	69.89±17.68	71.48±11.96	0.6389
Mean Height (cm)	167.81±11.83	169.96±14.53	0.4702
Duration of surgery (minutes)	50.13±10.10	51.48±9.85	0.5468

$P > 0.05$ was considered statistically nonsignificant

Graph 1: Demographics and Duration of Surgery in both the groups



We found a statistically significant difference between the two groups in HR, MAP, and temperature (Tables 2, 3, and 4). HR and MAP were lower in group D in comparison with group

K. Body temperature was lower in group K than group D. There was no statistically significant difference between the two groups in oxygen saturation (SpO_2) (Table 5).

Table 2 Heart rate changes

Duration	Group K	Group D	P value
Baseline	68.4±6.9	68.1±8.8	0.8657
After 10 minutes	76.1±9.1	72.1±12.9	0.1131
After 20 minutes	77.2±10.2	71.4±12.3	0.0244*
After 30 minutes	80.1±9.1	70.8±12.2	0.0002*
After 40 minutes	82±8.1	68.1±5.3	<0.0001*
After 50 minutes	83.9±7.1	67±6.2	<0.0001*
After 60 minutes	83.1±6.1	65.8±9.6	<0.0001*

P<0.05 was considered statistically significant.

P<0.001 was considered statistically highly significant.

Table 3 Mean arterial blood pressure changes

Duration	Group K	Group D	P value
Baseline	89.5±8.1	89.3±7.8	0.9107
After 10 minutes	94.2±22.5	84.6±13.4	<0.0001*
After 20 minutes	96.8±19.8	80.4±15.3	<0.0001*
After 30 minutes	100.8±9.2	75.5±17.2	<0.0001*
After 40 minutes	104.1±14.4	73.3±16.9	<0.0001*
After 50 minutes	103.9±16.5	68.9±15.5	<0.0001*
After 60 minutes	106.5±14.2	66.8±14.2	<0.0001*

P<0.05 was considered statistically significant.

P<0.001 was considered statistically highly significant.

Table 4 Temperature changes

Duration	Group K	Group D	P value
Baseline	36.6±0.2	36.6±0.14	1.0000
After 10 minutes	36.7±0.15	36.8±0.06	<0.0002
After 20 minutes	36.6±0.1	36.75±0.05	<0.0001*
After 30 minutes	36.6±0.09	36.7±0.03	<0.0001*
After 40 minutes	36.8±0.11	36.75±0.05	0.0106
After 50 minutes	36.7±0.08	36.5±0.06	<0.0001*
After 60 minutes	36.6±0.12	38±0.04	<0.0001*

P<0.05 was considered statistically significant.

P<0.001 was considered statistically highly significant.

Table 5: SpO₂ changes

Duration	Group K	Group D	P value
Baseline	96.4±2.7	96.12±2.58	0.6367
After 10 minutes	95.8±2.5	95.75±1.1	0.9081
After 20 minutes	97.8±3.0	94.1±2.2	<0.0001*
After 30 minutes	96.4±1.8	97.4±0.3	0.0009*
After 40 minutes	98.2±0.9	98.2±1.4	1.0000
After 50 minutes	97.9±3.2	97.8±2.1	0.8692
After 60 minutes	96.8±2.4	96.78±2.3	0.9697

P<0.05 was considered statistically significant.

P<0.001 was considered statistically highly significant.

Shivering was considered significant when the patient reaches at least grades 3 and 4 after 10 minutes of spinal anesthesia (Table 6). After 10 minutes, 4 patients (10.00%) of the ketamine group had grade 3 shivering, whereas only one patient (2.50%) of the dexmedetomidine group had grade 3 shivering. After 20 minutes, 3

patients (7.50%) in the ketamine group had grade 3 shivering, whereas only one patient (2.50%) of the dexmedetomidine group had grade 3 shivering. Grade 4 shivering was not noted in any patient in either group.

Table 6: Shivering score

Duration	Group K	Group D	P value
After 10 minutes			0.04
Score 0	20 (50%)	31	
Score 1	12	6	
Score 2	4	2	
Score 3	4	1	
After 20 minutes			0.03
Score 0	21	32	
Score 1	10	6	
Score 2	6	1	
Score 3	3	1	
After 30 minutes			0.81
Score 0	25	29	
Score 1	6	8	
Score 2	5	2	
Score 3	4	1	
After 40 minutes			0.48
Score 0	28	31	
Score 1	6	5	
Score 2	4	2	
Score 3	2	2	
After 50 minutes			0.57
Score 0	27	30	
Score 1	8	6	
Score 2	3	4	
Score 3	2	0	
After 60 minutes			0.9
Score 0	25	29	
Score 1	8	8	
Score 2	4	2	
Score 3	3	1	

P<0.05 was considered statistically significant.

P<0.001 was considered statistically highly significant.

Discussion

Human core temperature normally ranges from 36.5 to 37.5°C. The anterior hypothalamus is a center for thermoregulation, by comparing the peripheral inputs with a threshold value or the set point. Thermoregulation is brought by certain reflexes which either warm or cool the body if the temperature is found to be lower or higher than the threshold/set point respectively. During regional anesthesia, both cooling and warming responses are reduced as it affects central, rather than peripheral control.^{13, 14}

We found that a loading dose of dexmedetomidine of 1µg/kg, followed by a continuous administration at an infusion rate of 0.4µg/kg/h showed antishivering effect with adequate level of sedation. Nevertheless, side effects such as hypotension and bradycardia were found compared with low-dose ketamine.

Dexmedetomidine, an α -2-adrenoceptor agonist, causes sedation by reducing the activity of noradrenergic neurons in the locus ceruleus in the brain stem, thereby increasing the activity of inhibitory gamma-aminobutyric acid neurons in the ventrolateral preoptic nucleus. It also causes a reduction in the release of norepinephrine with inhibition of sympathetic activity, thus decreasing HR and blood pressure. It also has analgesic effects at the spinal cord level and other supraspinal sites.^{15, 16}

Shivering center (posterior hypothalamus) gets activated when it receives impulses from the cold receptors. It sends bilateral impulses to anterior horn cells in the spinal cord, resulting in an increase in the tone of the skeletal muscles over the entire body. Shivering is observed when muscle tone is increased above a certain level. But

the etiology of postspinal shivering is poorly understood.¹⁷

Meperidine (pethidine), is generally suggested for treating postoperative shivering by binding to both κ -opioid and μ -receptors.¹⁸

Reports have shown that shivering can complicate both general and neuroaxial anesthesia. It increases physiological stress, which results in increased oxygen consumption and carbondioxide production and increased cardiacwork. Hence, prevention shivering should be given more importance than its management.¹⁹

The findings of our study are in accordance with Elvan *et al* who found that shivering was prevented when dexmedetomidine infusion was given in patients undergoing an elective abdominal hysterectomy.²⁰

Coskuner *et al* also did not found shivering with the same dose used in our study.²¹ Whereas Bicer *et al* found shivering in 15% of patients with dexmedetomidine following general anesthesia, whereas it was reported in 55% patients who were given placebo.²²

Several studies were carried out to find out the effect of ketamine anesthesia related shivering. Dal et al and Sagir et al reported that ketamine 0.5mg/kg prevented effectively postanesthetic shivering in patients receiving general anesthesia and spinal anesthesia respectively.^{23, 24} Whereas we used 0.25mg/kg of ketamine in our study.

Conclusion

We conclude that dexmedetomidine infusion was more effective as an anti shivering and sedating agent than low-dose ketamine injection in patients receiving spinal anesthesia.

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