Journal of Medicinal and Chemical Sciences 6 (2023) 2300-2309

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Prophylactic Low Dose Intravenous Ketamine Infusion in Prevention of Intraoperative and Postoperative Shivering after Spinal Anesthesia in Adults Scheduled for Abdominal and Lower Limb Surgeries- A Prospective Randomized Controlled Trial

Surya R[1]*, Vaishali A.S[2], Tasneem Fathima Ahmed[2], Prem Chandar L.K[2], Yachendra V.S.G[3], Lakshmi R[4]

[1]*Associate Professor, Department of Anesthesiology, Saveetha Medical College & Hospital, Chennai, Tamilnadu, India*
[2]*Post graduate resident, Department of Anesthesiology, Saveetha Medical College & Hospital, Chennai, Tamilnadu, India*
[3]*Associate Professor, Department of Anesthesiology, Saveetha Medical College & Hospital, Chennai, Tamilnadu, India*
[4]*Professor and Head, Department of Anesthesiology, Saveetha Medical College & Hospital, Chennai, Tamilnadu, India*

ARTICLE INFO

Article history

Receive: 2023-01-13
Received in revised: 2023-03-04
Accepted: 2023-05-02
Manuscript ID: JMCS-2303-1982
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Majid Hajifaraji

DOI:10.26655/JMCHEMSCI.2023.10.5

KEYWORDS

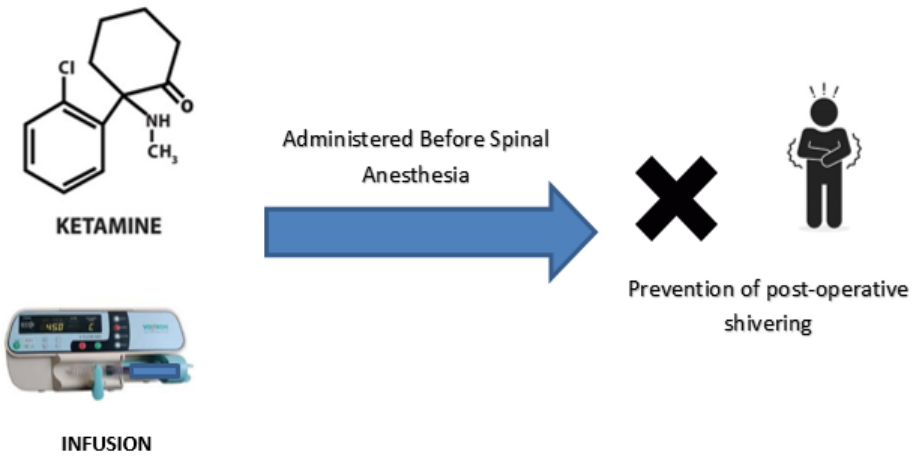
Spinal
Hypothermia
Shivering
Prophylactic
Ketamine

ABSTRACT

Background: Incidence of perioperative shivering following spinal anesthesia (SA) is 40% to 60% based on current literature. Ketamine in doses between 0.2 to 0.75 mg/kg has been used to prevent shivering after SA, but associated with dose dependent side-effects. This study evaluated the efficacy of Ketamine in a lower dose (0.1 mg/ kg) for prevention of intraoperative shivering (IOSH) and postoperative shivering (POSH) following SA.
Methods: Seventy patients who belong to ASA 1 and 2 posted for elective abdominal and lower limb surgeries were randomized among two groups. Adults in Group K were subjected to 0.1 mg/kg of ketamine as intravenous (IV) bolus succeeded by an infusion of 0.1 mg/kg/hr, while adults in Group S received 5 ml saline succeeded by 0.1 ml/kg/hr saline as IV infusion till the end of surgery. 3 ml of hyperbaric bupivacaine 0.5% without additive was used for SA. The incidence of IOSH and POSH was the primary outcome, degree of shivering, sedation scores, side-effects, and hemodynamics among the groups were the secondary outcomes.
Results: Demographic parameters and Hemodynamics were comparable among groups. IOSH incidence was significantly higher in Group S (60%) upon comparison with Group K (20%) ($p<0.001$) and POSH incidence was significantly higher in Group S (22.9%) upon comparison with Group K (2.9%) ($p<0.012$). Grades of shivering were more among Group S when compared with Group K ($p<0.001$). Sedation scores were remarkably higher in Group K ($p < 0.001$) without any other side-effects.
Conclusion: Prophylactic low dose ketamine (0.1 mg/kg) as IV bolus and infusion (0.1 mg/kg/hr) significantly decreased IOSH and POSH following SA with significant sedation and without other side-effects when compared to saline.

* Corresponding author: Surya. R
✉ E-mail: suryaratnasamy@gmail.com

GRAPHICAL ABSTRACT



Introduction

Incidence of perioperative shivering following Spinal anesthesia (SA) is observed from 40 to 60% based on current literature [1]. SA produces vasodilation which facilitates hypothermia by heat redistribution from core to periphery, eventually vasoconstriction, and finally causes shivering rostral to the level of spinal blockade. Shivering secondary to subarachnoid blockade is mediated by numerous factors such as total number of blocked segments of spinal cord, elderly age, higher level of block, and concomitant usage of other additives with SA which can influence the regulatory mechanisms [2]. Many drugs have been proposed to combat perioperative shivering following SA, in which ketamine is one among them [3].

Ketamine competitively antagonizes N-methyl-D-aspartate (NMDA) receptors and causes perioperative sedation, analgesic, and anti-shivering effect [4]. However, it has side-effects like nausea, vomiting, sedation, nystagmus, hyperthermia hallucination, and so forth [5].

Various doses have been tried with ketamine between 0.2 and 0.75 milligram (mg)/ kilogram (kg) for prevention of shivering with dose dependent side-effects [6]. There is less evidence available for the use of ketamine as intravenous (IV) bolus followed infusion for the shivering prevention in intraoperative and postoperative following SA [7]. Thus, a meagre dose of 0.1 mg/kg of ketamine as IV bolus and infusion which has not been evaluated earlier was chosen for the current study.

Thus, this study compared the incidence of intraoperative shivering (IOSH) and postoperative shivering (POSH) following spinal anesthesia between 0.1 mg/kg of IV ketamine administered as bolus succeeded by 0.1 mg/kg/hr infusion and placebo. The Primary outcomes were to compare the incidence of IOSH and POSH after administration of low dose IV ketamine and placebo. The secondary objectives were to compare grades of IOSH and POSH, incidence and severity of Intraoperative Sedation (IOSD) and Postoperative sedation (POSD), side-effects such as hallucination, nausea, headache, vomiting, nystagmus, and haemodynamic profile - oxygen saturation, mean arterial pressure, heart rate, and temperature monitoring of the patient between both groups.

Materials and Methods

After obtaining Institutional Ethical Committee approval (SMC/IEC/2022/09/018) and prospective clinical trial registration (CTRI/2022/12/048466) registered on 26/12/2022, this placebo controlled randomized trial was conducted on 70 patients ASA 1 and 2 of 18 to 50 years aged adults scheduled for abdominal and lower limb surgeries under SA in a tertiary care center between December 2022 and January 2023 for a period of 2 months.

The exclusion criteria was pregnant women, adults with history of allergy to ketamine, history of psychiatric, neurological disorder, thyroid disorders, adults with body mass index >30

kg/m^2, patients with uncontrolled hypertension,

vascular or coronary disease, patients with raised cranial pressure and intraocular pressure, adults who are refusing or non-cooperative for SA, contraindication for SA, and prolonged duration of surgery more than 120 minutes.

After obtaining a well informed and written consent, all patients were administered with tablet Pantoprazole 40 mg and tablet Alprazolam 0.25 mg in the previous night and morning of surgery. After transferring the patient to the OT, ISA standard monitoring was done, and then preloading with 10 ml/kg of Ringer lactate was done. Temperature inside the OT was adjusted between 24 °C and 26 °C.

Patients were recruited using simple random sampling and randomized into two groups - Group S and Group K, using computer generated allocation of random numbers. In Group K (n=35), patients received IV ketamine of 0.1 mg/kg diluted in 5 mL succeeded by an IV infusion of ketamine 0.1 mg/kg/hr from 20 ml study solution and Group S (n=35), patients were administered 5 mL of normal saline as an intravenous bolus succeeded by an intravenous infusion of 0.1 mL/kg/hr of saline from a study solution of 20 mL.

The primary attending anesthesia consultant was blinded to assignment strategy of the study groups and he/she administered the drugs to the patients in two groups. The anesthesiologist administered the initial bolus of study drug before SA. Under sterile aseptic precaution, SA was performed L3-L4 or L4-L5 interspinous spaces with a 25 G Quincke's spinal needle in lateral position and 3 ml of hyperbaric solution of 0.5% bupivacaine was administered. Next, the patients were positioned supine. After the block, the sensory evaluation was done by pinprick until it reached T6 dermatome, every minute. The motor blockade was monitored using modified scale of Bromage. Thereafter, patients were fully covered with blankets. After the achievement of the adequate blockade, infusion of the study drug was initiated and continued during the entire surgical period by the attending anesthesiologist. IV Boluses of 6 mg injecting Ephedrine were administered in the MAP event fall more than 20% from baseline. Axillary temperatures were monitored. Another second blinded anesthesia consultant was recording the parameters such as grades of shivering, hemodynamic parameters (HR, MAP, and SpO_2), temperature monitoring, and degree of sedation, every 5 minutes once for the initial 30 minutes followed by every 15 minutes once up to the finish of the surgery.

Occurrence of shivering was assessed by a scale which was first used by Crossley *et al.* [8] which graded shivering as follows:

Grade "0": Absence of shivering.

Grade "1": Either peripheral vasoconstriction or piloerection, but no visible evidence of shivering.

Grade "2": Muscular activity involving only one group of muscle.

Grade "3": Muscular activity involving more than one group of muscle, but no generalized activity.

Grade "4": Shivering of the entire body.

Depending upon the grades of shivering observed, patients with grade of shivering of 3 or higher were considered to be significant shivering and defined to have "presence of shivering".

20 minutes following SA and prophylactic infusion of study drug solution was commenced, if there was shivering presence, the treatment was declared ineffective and 1 mg/kg of injecting Tramadol was administered as an IV rescue medication. The sedation degree was evaluated by the attending anesthesiologist using Ramsay Sedation Scale [9, 10] which are as follows:

Score "1": Either agitated and anxious or restless or both.

Score "2": Oriented, calm, cooperative, and tranquil.

Score "3": Responsive to only commands.

Score "4": Brisker response to either loud auditory stimulus or light glabellar tap.

Score "5": Sluggish responsiveness to either loud auditory stimulus or light glabellar tap.

Score "6": Absence of response to either loud auditory stimulus or light glabellar tap.

Incidence of IOSH and POSH were the primary trial outcomes and grades of IOSH and POSH, IOSD and POSD scores, hemodynamic profile, and side-effects were the secondary outcomes of this study. Headache, episodes of vomiting, nausea, hallucinations, and nystagmus were also recorded if present. After the finish of surgery, the patients were wheeled to the recovery room

and were monitored up to 2 hours post-procedure.

Statistical evaluation and sample size calculation

Patients' demographics and clinical parameters were recorded. Chi Square test was exercised to compare the difference in incidence of IOSH, POSH, IOSD, and POSD. Mean+/-Standard deviation and median and range were used to report continuous variables. Repeated measures of ANOVA were exercised to analyze hemodynamic parameters over different time intervals. P-value was considered as significant if $p< 0.05$.

According to Thangavelu *et al.* [7], the IOSH incidence in saline group was found to be 58%. Based on a pilot study done with small sample size of 10 patients, it was observed that 15% patients with IV bolus of low dose ketamine bolus of 0.1 mg/kg succeeded by 0.1 mg/kg/hr of infusion was observed to have IOSH following SA. Hence, the IOSH incidence in Ketamine group was presumed to be 15% and sample size was calculated using following formula with an Alpha error 1 and power 90%.

$$N = [Z_{1-\infty}/2 + Z_{1-\beta}] (P_1+P_2) \text{ divided by } D^2$$

Where

$$[Z_{1-\infty}/2 + Z_{1-\beta}] (P_1+P_2)$$

is the numerator and D^2 is the denominator. The sample size estimated to be 33 in each group, hence concerning dropouts, it was decided to take n = 35 in each group (totally 70 patients) in this study.

Results and Discussion

70 patients were enrolled in this study with 35 patients in Group S and 35 patients in Group K. No dropouts were observed and all 70 patients were analyzed in this study. Both the groups were similar with respect to age, gender, weight, height, ASA grades, median level of sensory block, and surgical duration (Table 1).

The IOSH incidence was observed to be 60% among Group S (21/35) and 20.0% (7/35) in Group K. The IOSH incidence was remarkably higher in Group S in comparison with Group K ($p<0.001$) and the IOSH grades were also exponentially higher in Group S (Figure 1) ($p<0.001$).

The POSH incidence was observed to 22.9% (8/35) in Group S and 2.9% (1/35) in Group K. The POSH incidence was significantly higher in Group S upon compared with Group K ($p<0.012$) and the POSH grades were further exponentially higher in Group S (Figure 2) ($p<0.001$).

In Group S, 60.0% of patients (21/35) required Tramadol as rescue medication for the shivering treatment which was significantly higher when compared with Group K where only 20.0% patients (7/35) required the same *($p<0.001$).* None of the patients, who received tramadol as rescue medication for shivering, did not require any further doses of tramadol.

The grades of IOSD and POSD were exponentially more in Group K upon comparison with Group S as depicted in Figure 3 and Figure 4 ($p<0.001$).

The hemodynamic profile such as SpO_2, MAP, HR, and axillary temperatures which were noted at different point of time in both the groups were comparable with each other in intraoperative and postoperative period.

Table 1: Demographic parameters are similar among the groups

Parameters	Group S	Group K	P-value
Age (years)	30.8 ± 6.8	31.9± 6.8	0.487
Weight (Kg)	67.4 ± 7.9	68.9 ± 9.6	0.463
Height (cm)	163.3 ± 6.8	160 ± 9.3	0.295
Gender (M/F)	21/14 (60%/40%)	25/10 (71.4%/28.6%)	0.314
ASA (I/II)	26/9 (74.3%/25.7%)	20/15 (57.1%/47.9%)	0.131
Median Level of sensory block	T6	T6	-
Duration of Surgery (min)	113 ± 38	112 ± 43	0.656

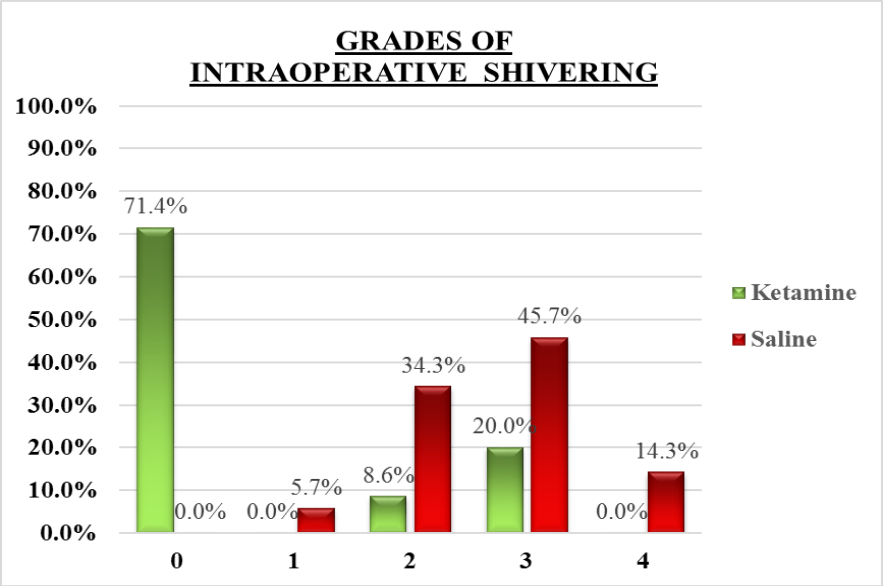


Figure 1: Grades of Intraoperative shivering (IOSH) in Group S and Group K

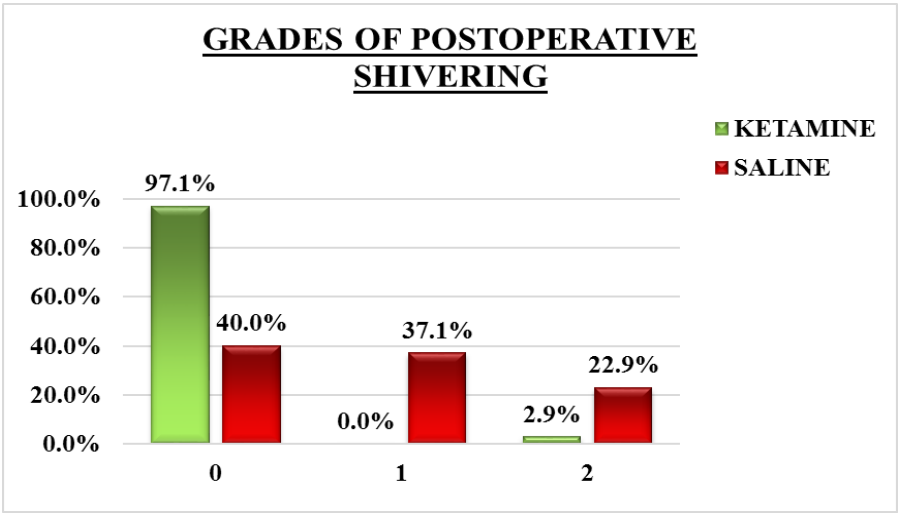


Figure 2: Grades of Postoperative shivering (POSH) in Group S and Group K

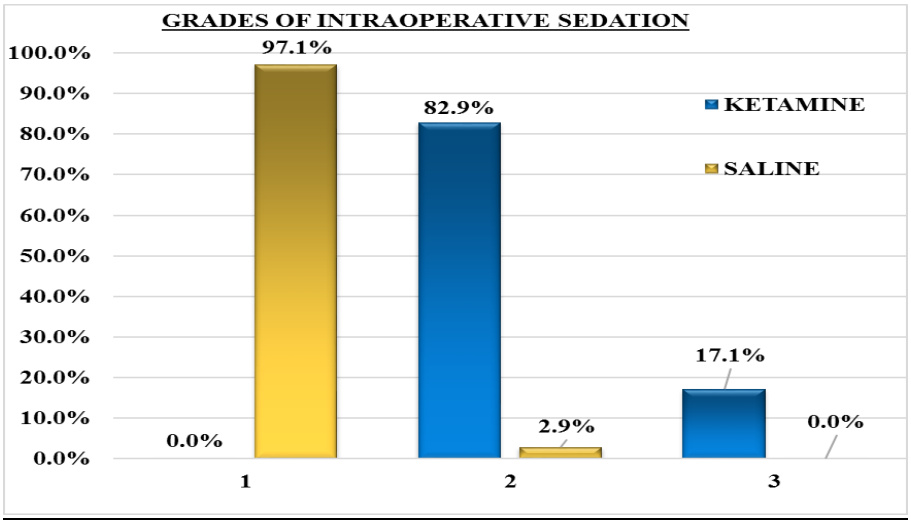


Figure 3: Grades of Intraoperative sedation (IOSD) in Group K and Group S

None of the patients in either of the groups had incidence of hypotension requiring vasopressors, nausea, vomiting, headache, nystagmus, and hallucinations at any point of time in the intraoperative and postoperative period.

Shivering is a repetitive involuntary spontaneous muscular movement. Although it is a compensatory mechanism in response to hypothermia to preserve heat, it places the body under physiological stress such as increased oxygen consumption, carbondioxide production, lactic acidosis, and increased metabolic rate to 400% [11]. One among of the commonest undesirable side effect of regional anesthesia is perioperative shivering [12]. The shivering mechanisms in succeeding SA is still vague, but hypothermia secondary to redistribution of heat produced by vasodilation below the level of spinal segmental block is the widely accepted theory [13, 14]. Many pharmacological and non-pharmacological methods have been tested to find the most efficacious method to combat post anesthesia shivering and the journey is indeed, unfortunately, continuing [15].

Ketamine, a phencyclidine derivative, a dissociative anesthetic and a non-competitive NMDA antagonist is known to have anti-shivering action due to its thermoregulatory action at multiple stages (modulation of noradrenergic and serotenergic neurons at locus coeruleus and hypothalamus) at subanaesthetic doses [4]. Although ketamine is known for its anti-shivering property, it is also known for its dose dependent side-effect profile [5, 6]. Various doses of ketamine have been tried from 0.2 mg/kg to 0.75 mg/kg only as an IV bolus with or without infusion following spinal anesthesia to exercise only its anti-shivering property with minimal side-effects [6]. Thus, this current study was conducted with a further reduced meagre IV dose of 0.1 mg/kg of ketamine as a bolus and 0.1 mg/hr infusion to prevent IOSH and POSH following SA in patients undergoing elective infraumblical surgeries.

In this study, the presence of shivering was defined as a grade of more than or equal to 3 according to the grades of shivering originally used by Crossley *et al.* [8]. It was observed that incidence of IOSH was 60% in Group S and 20% in Group K *(p<0.001)*. Thangavelu *et al.* [7] also observed a remarkable reduction in incidence of IOSH in ketamine group with a dose slightly more than the current study (0.2 mg/kg bolus succeeded by 0.1 mg/kg/hr of IV infusion until the finish of surgery). They found that the IOSH incidence was remarkably lesser in ketamine group (13.79%) when compared with its placebo (58.06%) in patients undergoing elective abdominal and lower limb surgeries under spinal anaesthesia (p<0.001). Seyam *et al.* [16] and Zoengmawia *et al.* [17] compared ketamine as a single IV bolus at a dose of 0.2 mg/kg compared with tramadol and ketamine in two different doses (0.25 mg/kg and 0.5 mg/kg), respectively, with placebo and concluded that the incidence of IOSH was much lesser in ketamine after SA (p<0.05). All these three studies were consistent with the results of this study and proved that the dose of 0.1 mg/kg of ketamine is also effective to control IOSH when compared with higher doses of ketamine as used in these studies.

It was found that individual grades of IOSH was remarkably lesser in Group K upon comparison with Group S in the current study (p<0.001). It was observed in the current study that only 20% of the patients had shivering of Grade 3 and none had shivering of Grade 4 in Group K in comparison with Group S where 45 % of patients had Grade 3 and 14.3 % had Grade 4 of shivering. The finding was similar to Seyam *et al.* [16] and Zoengmawia *et al.* [17] where only 14% of the patients had IOSH more than Grade 3 in ketamine group and none among the patients had IOSH more than Grade 3 in ketamine group respectively in either of the studies.

The POSH incidence was noted to be much lesser in Group K (2.9%) upon comparison with Group S (22.9%) in the current study (p<0.012). Thangavelu *et al.* [7] who had used a dose of 0.2 mg/kg of ketamine (slightly more than the dose used in current study) as IV bolus succeeded by an IV infusion of 0.1 mg/kg/hr of ketamine noted that POSH incidence was exponentially lower in ketamine group (0%) upon comparison with placebo (30.7%). In a trial done by Hussain *et al.* [18] where either ketamine (0.25 mg/kg) or ondonsetron (4 mg) was only administered as an intravenous bolus immediately after SA and no IV

infusion was administered, it was found that POSH incidence was noted to be exponentially lesser in patients who received ketamine (18.2%) when compared with patients receiving ondonsetron (81%) ($p<0.003$). Both of these studies are observed to be consistent with our current study. Thus, choosing an IV bolus dose with IV infusion of ketamine in the intraoperative period has probably maintained a steady state of plasma concentration of ketamine (although not measured) even in the postoperative period after cessation of infusion at the finish of surgery and has produced the desirable clinical effect of anti-shivering in the postoperative period.

Among the study subjects who had POSH in this study, it was found that the individual grades of POSH were remarkably lesser in Group K upon comparison with Group S ($p<0.001$). Kose *et al.* [19] administered a single IV bolus of either Meperidine 25 mg or Ketamine in two different doses (0.25 mg/kg and 0.5 mg/kg) following General anesthesia in the recovery room were compared and observed for the incidence and grades of POSH. It was found out that shivering grades were remarkably lesser in ketamine groups upon comparison with meperidine group ($p<0.05$). This observation is in concordance with the current study in terms of POSH grades.

In addition to its anti-shivering property of Ketamine, it is also known to produce procedural sedation, relieves anxiety, and prevents perioperative awareness [20]. In the current study, it was observed that the Ramsey Scores of Sedation in the intraoperative and postoperative period were exponentially higher in Group K upon comparison with Group S ($p<0.001$). In Group K, About 82.9% had IOSD of 2 and 17.1% had IOSD of 3 and 74.2% had POSD of 1 and 25.7% had POSD of 2. Thangavelu *et al.* [7] had used a different scale of sedation which is similar to Ramsey sedation scale where score 3 of both the score were similar to each other and the patients responded to verbal commands only. Thangavelu *et al.* [7] observed that there was significantly higher IOSD (100%) and POSD (20.69%) when compared to placebo group ($p<0.05$). Kose *et al.* [19] studied a single IV bolus dose of ketamine administered as 0.5 mg/kg and 0.75 mg/kg compared with meperidine 25 mg in the recovery room after general anesthesia in the postoperative period. It was observed there was a significantly increase in sedation score in patients receiving ketamine compared to meperidine and when compared between two doses of ketamine, there were significantly higher incidence of sedation scores in patients who were administered 0.75 mg/kg compared with patients who got 0.5 mg/kg. Hence, there is a dose dependent rise in sedation score in patients subjected to ketamine. Both of these studies were consistent with the present study in terms of sedation.

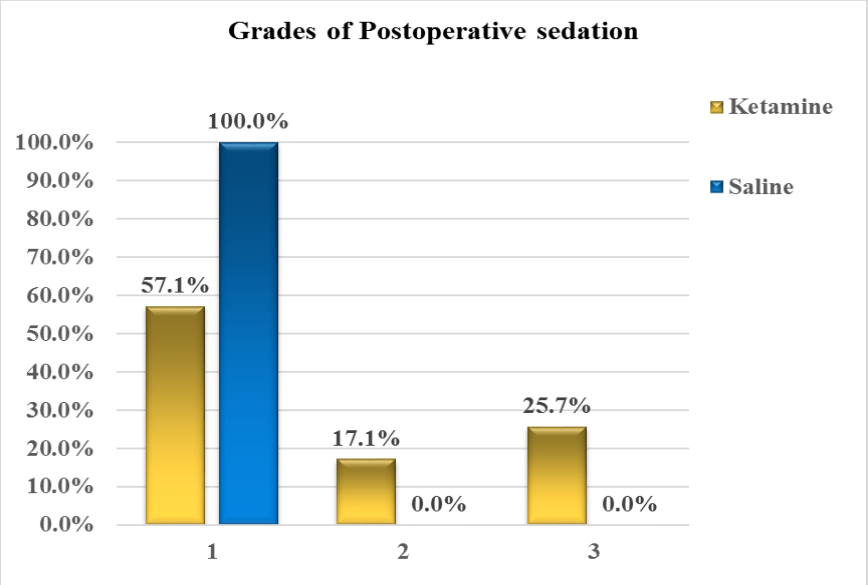


Figure 4: Grades of Postoperative sedation (POSD) in Group K and Group S

Peripheral temperature measured in the axillary region was comparable among the groups in the current study. Thangavelu *et al.* [7] measured Nasopharyngeal temperature and Seyam *et al.* [16] measured Nasopharyngeal and Tympanic membrane temperature for temperature monitoring in the intraoperative and postoperative period. Both of the studies concluded that there were no differences in the temperature measurements among ketamine groups with their respective comparators at any point of time during the study. Both these studies were in concordance with the present study in terms of temperatures in intraoperative and postoperative period.

In the current study, a ketamine dose of 0.1 mg/kg as an IV bolus and infusion in the intraoperative period was used and at this dose, there were no incidence of side effects like psychomimetic behavior, hallucinations, hypotension requiring vasopressors, nausea, vomiting, headache, and nystagmus at any point of time in the intraoperative and postoperative period. This observation is in concordance with Thangavelu *et al.* [7] and Seyam *et al.* [16]. Only studies which had used ketamine at a higher doses (>0.5 mg/kg) had reported increased incidence of hallucinations and nystagmus [6]. This explains the decreased incidence of undesirable side effects with the ultra-low dose of 0.1 mg/kg of ketamine used in this study.

This study is not devoid of limitations. Firstly, plasma concentrations of ketamine were not analyzed at any point of time during the study period. Secondly, although recordings of grades of shivering lesser than 3 were done, shivering of grade 3 or more only were considered as significant, and were treated as described in study by Thangavelu *et al.* Thirdly, axillary temperature monitoring which is not a reliable source of peripheral temperature monitoring was used because of logistical issues.

Conclusion

Prophylactic low dose ketamine (0.1 mg/kg), as intravenous bolus and infusion (0.1 mg/kg/hr) in the intraoperative period, decreased IOSH and POSH significantly in adults undergoing abdominal and lower limb surgery after SA with significant sedation and without other side-effects when compared to saline. More studies with adequate population should be done with further reduced doses of ketamine and with significant reduction in sedation.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

ORCID

Surya R
https://orcid.org/0000-0003-1021-5833
Vaishali A.S.
https://orcid.org/0000-0001-7340-6325
Tasneem Fathima Ahmed
https://orcid.org/0000-0001-6397-285X
Prem Chandar L.K.
https://orcid.org/0000-0002-8294-9302
Yachendra V.S.G.
https://orcid.org/0000-0002-0218-8284
Lakshmi R
https://orcid.org/0000-0003-4984-4688

References

[1]. Crowley L.J., Buggy D.J., Shivering and neuraxial anesthesia, *Regional Anesthesia & Pain Medicine*, 2008, **33**:241 [Crossref], [Google Scholar], [Publisher]

[2]. Ferede Y.A., Aytolign H.A., Mersha A.T., The magnitude and associated factors of intraoperative shivering after cesarean section delivery under Spinal anesthesia: A cross sectional study, *Annals of Medicine and Surgery*, 2021, **72**:103022 [Crossref], [Google Scholar], [Publisher]

[3]. Esmat I.M., Mohamed M.M., Abdelaal W.A., El-Hariri H.M., Ashoor T.M., Postspinal anesthesia

shivering in lower abdominal and lower limb surgeries: a randomized controlled comparison between paracetamol and dexamethasone, *BMC Anesthesiology*, 2021, **21**:262 [Google Scholar], [Publisher]

[4]. Samimi Sadeh S., Hashemi E., Aminnejad R., Bastanhagh E., The Impact of Optimal Dose of Ketamine on Shivering Following Elective Abdominal Hysterectomy: A Randomised Comparative Study, *Anesthesiology and Pain Medicine*, 2020, **10**:e106220 [Crossref], [Google Scholar], [Publisher]

[5]. Imani F., Varrassi G., Ketamine as Adjuvant for Acute Pain Management, *Anesthesiology and Pain Medicine*, 2019, **9**:e100178 [Crossref], [Google Scholar], [Publisher]

[6]. Zhou Y., Mannan A., Han Y., Liu H., Guan H.L., Gao X., Dai M.S., Cao J.L., Efficacy and safety of prophylactic use of ketamine for prevention of postanesthetic shivering: a systematic review and meta analysis, *BMC Anesthesiology*, 2019, **19**:245 [Crossref], [Google Scholar], [Publisher]

[7]. Thangavelu R., George S.K., Kandasamy R., Prophylactic low dose ketamine infusion for prevention of shivering during spinal anesthesia: A randomized double blind clinical trial, *Clinical Pharmacology*, 2020, **36**:506 [Crossref], [Google Scholar], [Publisher]

[8]. Usta B., Gozdemir M., Demircioglu R.I., Muslu B., Sert H., Yaldiz A., Dexmedetomidine for the prevention of shivering during spinal anesthesia, *Clinics*, 2011, **66**:1187 [Crossref], [Google Scholar], [Publisher]

[9]. Singariya G., Malhotra N., Kamal M., Jaju R., Aggarwal S., Bihani P., Comparison of nebulized dexmedetomidine and ketamine for premedication in pediatric patients undergoing hernia repair surgery: a randomized comparative trial, *Anesthesia and Pain Medicine*, 2022, **17**:173 [Google Scholar], [Publisher]

[10]. Rasheed A.M., Amirah M.F., Abdallah M., P. J. P, Issa M., Alharthy A., Ramsay Sedation Scale and Richmond Agitation Sedation Scale: A Cross-sectional Study, *Dimensions of Critical Care Nursing*, 2019, **38**:90 [Crossref], [Google Scholar], [Publisher]

[11]. De Witte J., Sessler D.I., Perioperative Shivering: Physiology and Pharmacology, *Anesthesiology*, 2002, **96**:467 [Crossref], [Google Scholar], [Publisher]

[12]. Kanchan S., Shah A.M., Shah A., Sameen Z., Arya A., Riaz S., Post spinal anaesthesia shivering-incidence and associated risk factors in patients undergoing lower limb and abdominal surgeries, *International Journal of Research in Medical Sciences*, 2022, **10**:2285 [Crossref], [Publisher]

[13]. Bhattacharya P.K., Bhattacharya L., Jain R.K., Agarwal R.C., Post anaesthesia shivering (PAS): A Review Article, *Indian Journal of Anaesthesia,* 2003, **47**:88 [Google Scholar], [Publisher]

[14]. Lopez M.B., Postanaesthetic shivering – from pathophysiology to prevention, *Romanian journal of anaesthesia and intensive care,* 2018, **25**:73 [Crossref], [Google Scholar], [Publisher]

[15]. Amsalu H., Zemedkun A., Regasa T., Adamu Y., Evidence-Based Guideline on Prevention and Management of Shivering After Spinal Anesthesia in Resource-Limited Settings: Review Article, *International Journal of General Medicine*, 2022, **15**:6985 [Crossref], [Google Scholar], [Publisher]

[16]. Seyam S.H., Prevention of post-spinal anesthesia shivering: Low dose ketamine vs tramadol, *Al-Azhar International Medical Journal*, 2020, **1**:108 [Crossref], [Google Scholar], [Publisher]

[17]. Sailo L., Control of Shivering with Prophylactic Ketamine During Subarachnoid Block: A Placebo-Controlled Randomised Double-Blind Study, *International journal of Contemporary medical research*, 2019, **6**:K6 [Google Scholar], [Publisher]

[18]. Hussain T., Afridi K.K., Mir A.A., Ondansetron versus Ketamine to control intra-op and post-op shivering caused by subarachnoid block: A comparative phase study, *Medicine Science | International Medical Journal*, 2018, **7**:35 [Google Scholar], [Publisher]

[19]. Kose E.A., Dal D., Akinci S.B., Saricaoglu F., Aypar U., The efficacy of ketamine for the treatment of postoperative shivering, *Anesthesia & Analgesia*, 2008, **106**:120 [Crossref], [Google Scholar], [Publisher]

[20]. Eydi M., Golzari S.E., Aghamohammadi D., Kolahdouzan K., Safari S., Ostadi Z., Postoperative Management of Shivering: A Comparison of Pethidine vs. Ketamine, *Anesthesiology and pain*

medicine, 2014, **4**:e15499 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Surya.R, Vaishali.A.S.,Tasneem Fathima Ahmed, Prem Chandar.L.K., V.S.G.Yachendra, Lakshmi.R. Prophylactic Low Dose Intravenous Ketamine Infusion in Prevention of Intraoperative and Postoperative Shivering after Spinal Anesthesia in Adults Scheduled for Abdominal and Lower Limb Surgeries- A Prospective Randomized Controlled Trial. *J. Med. Chem. Sci*., 2023, 6(10) 2300-2309
DOI: https://doi.org/10.26655/JMCHEMSCI.2023.10.5
URL: http://www.jmchemsci.com/article_171040.html