



ORIGINAL RESEARCH PAPER

Anaesthesiology

PREVENTION OF POST SPINAL SHIVERING: USING COMBINATION OF KETAMINE PLUS MIDAZOLAM VS TRAMADOL AND PLACEBO.

KEY WORDS: Ketamine, Midazolam, Tramadol, Spinal analgesia.

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ABSTRACT

Shivering is frequently found during post-spinal anaesthesia period in recovery rooms. This is distressing to patients. The objective of this study was to compare the effectiveness of Ketamine plus Midazolam with that of Tramadol, and placebo in the prevention of post-spinal shivering.

Material & Methods: We studied 90 patients between the age group of 30 to 65 years undergoing elective surgery under spinal anaesthesia. Patients were allocated to one of three groups each of 30 patients, group T (n= 30) received 1mg/Kg of Tramadol, group K (n= 30) received Ketamine 0.25 mg/Kg plus Midazolam 40 micro-gm/ kg while group S (n= 30) received saline 0.9% as placebo.

Results: - Significant reduction was observed in the incidence of shivering in group T and group K in comparison to group S. There were no significant differences in hypotension and bradycardia in all groups. There was significant sedation in group K in comparison with groups N and S.

Conclusion: The conclusion of our study drawn was that 1mg/Kg of Tramadol is as effective as Ketamine 0.25 mg/Kg plus Midazolam 40 microgram/ kg in the prophylactic prevention of post spinal shivering. We found sedation in patients in group K in comparison with other two groups.

Introduction

Shivering is found frequently following spinal anaesthesia. It is one of the most common finding of regional anaesthesia. This is defined as an involuntary movement of one or more muscles during early phase of post regional anaesthesia or general anaesthesia [1].

Post spinal shivering causes discomfort to patient and can cause severe complications in patients of cardio-respiratory diseases. These include increased oxygen consumption, hypoxemia, increase in carbon dioxide production and lactic acidosis [2]. There is increase in intra-cerebral and intraocular pressure during shivering. There is also interference with ECG and NIBP monitoring [3-5].

Studies have been done for finding the drugs or methods to prevent and treat shivering. The recommendations have come up to use certain drugs for the control of shivering like Meperidine, Ketamine plus Midazolam, Neostigmine and Ketanserin [6, 7]. Ketamine acts in thermoregulation by different action, it is competitive receptor antagonist of Nmethyl- D-aspartic acid (NMDA) [9]. NMDA receptors modulate noradrenergic and serotonergic neurons in the locus ceruleus. NMDA receptors also modulate ascending nociceptive transmission at dorsal horn of the spinal cord [10].

The shivering is controlled by Ketamine by non-shivering thermogenesis either at the level of hypothalamus or by the B-adrenergic effect of Nor-epinephrine [11]. In a study in mice Benzodiazepines have been reported to reduce repetitive firing response of depolarizing pulses spinal cord neurons [12]. This action can be responsible for suppressing shivering.

Diazepam is reported to be effective in the prevention of post spinal shivering among benzodiazepines [13]. This also causes minimal impairment of thermoregulatory control [14]. It is a non-opioid analgesic drug; it is safe and effective in prevention of shivering after neuraxial anaesthesia and general anaesthesia with little effect on the sweating and vasoconstriction thresholds [15-18].

In present study we have compared anti-shivering effect of Tramadol versus Ketamine plus Midazolam and placebo after

spinal anaesthesia.

Side effect if any of such medications were also studied.

Material and Methods:

After getting approval of Institutional ethical committee and written informed consent from patients were obtained; we studied 90 patients of ASA status I and II, planned to undergo elective surgery under spinal analgesia. . Patients were randomly divided to one of three groups:

Group T: received 1 mg/kg Tramadol (n = 30).

Group K: received 0.25 mg Ketamine plus 40 microgram/Kg of Midazolam (n= 30).

Group S: received same volume of saline 0.9% as placebo (n = 30).

The drugs under study were diluted with normal saline 0.9% 20 ml fixed volume. These diluted drugs administered intravenously 5 min before spinal anaesthesia using a double blind protocol. All the studied drugs were administered to the patients by separate anaesthesiologist, not involved in the study.

Exclusion criteria

Patients with a known allergy to any medication under study , with fever (temperature >37.5 C), with known muscle diseases, Parkinson's disease, impaired hepatic or renal disease, on MAOI or tricyclic antidepressants, alpha 2 agonist or beta receptor blockers as medication treatment were excluded from study. Patients with H/O cardiac arrhythmias or heart failure (NYHA III or IV), those with H/O urinary retention, glaucoma or known alcohol abuse were also excluded. The patients unwilling for regional analgesia were excluded and those patients with failure of effect of spinal analgesia due to any patient factors were not included in study.

All patients were kept nil by mouth overnight or for at least 6-8 hours pre-operatively before the spinal anaesthesia

Patients of all three groups were pre-loaded with lactated Ringer's solution (15 ml/ kg body weight) before spinal analgesia.

On arrival to Operation theatre all Patients were monitored with

ECG and heart rate, pulse oximetry, non-invasive blood pressure measurement and parameters were recorded by anaesthesia resident blind to the patient group.

With full aseptic technique, spinal anaesthesia was given in all cases in the sitting position. Lumbar puncture was performed at L 3–4, with a 25 gauge Quincke spinal needle via midline approach. After successful lumbar puncture 3 ml of 0.5% heavy Bupivacaine was injected through a spinal needle over a period of 15 seconds. The spinal needle was withdrawn and the patients were positioned supine with slight elevation of the head (15–20 deg.) Cotton gowns were given for wearing as O.T. attire to all the patients and they were draped with a single blanket. The patients were covered with sterile surgical drapes, the head and neck area was not covered. No other warming equipment was used for patient in O.T. The surrounding temperature of operating room was kept between 22 and 25 C with constant humidity of approximately 55 to 65%. The level of sensory block was tested by pin-prick method in mid-axillary line as explained to the patients earlier before taking them to O.T. The highest level of sensory block was recorded. Vital parameters NIBP, heart rate, Oxygen saturation (SpO2) & sedation score (0= Alert, 1= awake but drowsy, 2= asleep but can be aroused 3= cannot be aroused) were noted and recorded. All these were recorded as base line and at regular time interval of 5, 10, 15, 20, 25, 30, 40, 50, 60, and 90 min after spinal anaesthesia.

Inj. Ephedrine 5 to 10 mg I.V. was given in case of drop of systolic B.P below 90 mm of Hg. It was repeated if required. The bradycardia (Heart rate below 50 beats /min) was not detected in our patients.

For fluid resuscitation I.V. Ringer Lactated fluid was given and calculated as per following criteria:

First 10 kg of body weight 4ml /kg, second 10 kg of body weight 2ml/kg, remaining body weight 1 ml/kg. 50% of this was infused in First hour and remaining 50% in second hour.

The body temperature was monitored in left axillary pit at beginning and at interval of 20 min.

The shivering severity was assessed at 5 point scale as used by Wrenchet al. [19] as follows:

- 0= no shivering;
- 1 = one or more of the following symptoms,
Pilo-erection,
Peripheral vasoconstriction,
Peripheral cyanosis without other cause,
(But without visible muscular activity)
- 2 = visible muscular activity confined to one muscle group
- 3 = visible muscular activity in more than one muscle Group
- 4 = gross muscular activity including the entire body.

The evaluation of shivering score was done by anesthetist who was not aware of study groups.

After the surgical procedure was over, patients were sent to post operative recovery/SICU

Here continuous monitoring of blood pressure, heart rate and oxygen saturation was done.

Results

Total 90 patients were included in the study, each group having 30 numbers of patients. Unwilling patients for regional analgesia and those with failure of effect of spinal analgesia due to patient factors were also excluded.

Patients in all the groups were similar in demographic distribution. The onset of sensory block to the highest level and maximum level of motor block were similar in all the groups. There were no significant differences in hypotension and bradycardia in all groups. We found significant sedation in group K in comparison with groups T and S.

No patient in group K and T showed any muscular activity (shivering score grade 2–4). While in group S, 04 patients showed visible muscular activity confined to one muscle group, 04 patients showed muscular activity in more than one muscle Group and 04 patients showed gross muscular activity including the entire body. It was found that there was higher incidence of shivering in group S in comparison to other two groups. It was found that more patients in group K were sedated than other two groups

Heart rate and arterial blood pressure showed approximate 10 to 30% decrease after spinal analgesia as compared to base line readings and required no treatment. There was no significant difference in all the three groups.

Table 1 Demographic characteristics, peri-operative data and lowest vital signs.

Data	Ketamine + Midazolam (Group K)	Tramadol (Group T)	Saline (Group S)
ASA grade	25 05	23 07	25 05
Age (in years)	45 ±10	43 ±12	44 ±14
Sex: M/F	20/10	18/12	22/08
Weight (kg)	59±17	62 ±15	60 ±12
Height (cm)	160±10	165±10	160±9
Duration of surgery (min)	91±13	93 ±16	87 ±15
Duration of analgesia (min)	132±53	141±40	135±52
Baseline Axillary temp (°C)	36.2±0.5	36.1±0.6	36.2±0.6
Time to reach highest block (min)	14.9±5.2	15.2±6.0	17.1±10.1
Lowest HR (beats/min)	60.8±11.2	62.3±12.3	60.5±12.5
Average Highest (dermatome) Blocked	T6	T 7	T6
Lowest SAP (mm Hg)	110.5±14.2	106.2±13.6	109.5±16.6
Time in recovery room (min)	92±21	93 ±26	91 ± 26

Data as mean± SD or median (range)

Table 2 Sedation Score in Groups

Sedation Score	Ketamine + Midazolam (Group K)	Tramadol (Group T)	Saline (Group S)
0	15	25	30
1	10	05	0
2	05	0	0
3	0	0	0

Sedation score (0= Alert, 1= awake but drowsy, 2= asleep but can be aroused 3= cannot be aroused)

Table 3 Shivering in different groups

Shivering severity	Ketamine + Midazolam (Group K)	Tramadol (Group T)	Saline (Group S)
0	25(83.33%)	26(86.66%)	10(33.33)
1	05(16.66%)	04(13.33%)	08(26.66%)
2	0	0	04(13.33%)
3	0	0	04(13.33%)
4	0	0	04(13.33%)

The Scale of Shivering severity

- 0= no shivering
- 1 = one or more of the following symptoms,
piloerection,
peripheral vasoconstriction,
peripheral cyanosis without other cause,
(But without visible muscular activity)
- 2 = visible muscular activity confined to one muscle group
- 3 = visible muscular activity in more than one muscle Group
- 4 = gross muscular activity including the entire body.

Discussion

The shivering is found most commonly in peri-operative period.

This is distressing for the patient and clinician finds hard to deal with the situation. The incidence of shivering can be up to 60%. The causes are redistribution of heat from core body to periphery, depressed thermoregulatory blood vessel constriction in block area. This causes increased heat loss.[21,22]. The decrease in thermoregulatory vasoconstriction threshold is considered to be the additional reason of shivering [23]. The end result is adverse effects like increased oxygen consumption, lactic acidosis, and rise in Carbon di oxide production [24 25]. This worsens the results in moribund patients. Hence the prevention is necessary.

In present study the effect of Inj. Tramadol with Ketamine and Midazolam in prevention of shivering was compared in conjunction with placebo saline.

Tramadol is used as non steroidal analgesic in post operative period frequently [26, 27]

In present study there was no significant difference in axillary temperature in all the groups.

The standard of treatment and prevention of shivering is not defined [25]. Ketamine increases blood pressure, heart rate and cardiac output by sympathetic stimulation. Use of Ketamine has advantage in patients who are at risk of hypothermia due to these factors [30].

In the study done by Sagir et al Ketamine 0.5 mg/Kg I.V. was found to be effective in prevention of post spinal shivering. The chances of development of side effects of hallucinations, nausea or vomiting in the patients are there.[31]

In present study the use of Midazolam plus Ketamine together prevented hallucinations in post operative period. Goold and Colleagues [32] had done study on patients undergoing therapy for cervical cancer. They noted the faster regain of core temperature and no post operative shivering. These results are similar to our study.

There was reduction in heat production after administration of Midazolam in comparison to heat production after induction of anaesthesia with clinical doses of volatile anaesthetics, Propofol and Opioids in a study by Kurz and colleagues [14]

Similarly infusion of low dose Ketamine has resulted in prevention of decrease in body temperature during spinal anaesthesia as found by Kinoshita T, Suzuki M, Shimada Y, Ogawa R. [33]. This finding is also similar in our study.

The use of Ketamine or Midazolam in preventing post spinal shivering was less effective than the prophylactic use of I.V. Ketamine or Midazolam in prevention of shivering, as found in the study by Honarmand and Safayi [9]

Conclusion

We conclude that Inj. Ketamine 0.25 mg/Kg plus Midazolam 40 microgram/Kg significantly reduces the incidence of post operative shivering which is comparable to Tramadol, and both regimes are better in comparison to placebo.

The sedative effects of Ketamine plus Midazolam is more that of Tramadol when used in prevention of post spinal shivering

Further studies are needed to confirm this result.

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