Original Research Article

A Comparative Study to Assess the Efficacy and Safety of Intrathecal Bupivacaine Alone, Intrathecal Bupivacaine Plus Dexmedetomidine and Intrathecal Bupivacaine Plus Magnesium Sulphate for the Prevention of Post-Spinal Anaesthesia Shivering in Transurethral Resection of Prostate (TURP)

Saharan Sunil[1], Maurya Neetu[2], Sukhdev Rao[3], Paliwal Naveen[4*], Tak M.L[5]

[1]Senior Resident, Department of Anaesthesia, Dr. S N Medical College, Jodhpur, Rajasthan, India
[2]Assistant Professor, Department of Anaesthesia, Pacific Medical College and Hospital, Udaipur, Rajasthan, India
[3]Senior Resident, Department of Anaesthesia, Dr. S N Medical College, Jodhpur, Rajasthan, India
[4]Associate Professor, Department of Anaesthesia, Dr. S N Medical College, Jodhpur, Rajasthan, India
[5]Senior Professor, Department of Anaesthesia, Dr. S N Medical College, Jodhpur, Rajasthan, India

Received: 07-10-2021 / Revised: 28-11-2021 / Accepted: 25-12-2021

Abstract

Background: Preventing the post spinal shivering that occurs frequently in patients undergoing TURP would be beneficial. This trial aimed at evaluating the affect of intrathecal Mgso4 and dexmedetomidine in terms of incidence and intensity of shivering. **Methods:** This prospective randomized, double-blinded control study enrolled Seventy five patients randomized in three groups. All patients received standard spinal anaesthesia with 2.5ml of hyperbaric bupivacaine heavy 0.5% (12.5mg). Group A- received 0.5ml of normal saline, Group B- received 5µg dexmedetomidine in 0.5ml saline, and Group C- received 25mg MgSO4 in 0.5ml saline in addition to hyperbaric bupivacaine. The primary objectives of this study were incidence and intensity of shivering, while secondary objective were total dose of Pethidine required to control Shivering, Sedation score and Complications including Hypotension, bradycardia, Nausea, Vomiting. All data were summarized as mean ± SD for continuous variables, numbers and percentages for categorical variables. P <0.05 was accepted as statistically significant. **Results:** incidence of post spinal anaesthesia shivering was statistically significant in group A (56%) as compare to group B (12%) and group C (32%). The shivering grades of the groups A and C were statistically significant (P<0.001) and B was not significant (P>0.05). Nausea, vomiting, bradycardia and hypotension were comparable between the groups. All patients in group A, 22 patients in group B, and 21patients in group C had sedation score of 2. Three patients in group B and four in group C had a sedation score of 3. **Conclusion:** Intrathecal injection of dexmedetomidine and MgSO4 with bupivacaine were effective in reducing the incidence as well as intensity of post-SA shivering.

Keywords: Dexmedetomidine, Magnesium, Spinal, Shivering.

Introduction

The Endoscopic urological procedures are performed under spinal anaesthesia and a large volume of irrigation solution is required. The use of the irrigation solution to wash of the debris and blood during Transurethral resection of prostate (TURP) and Ureteroscopic removal of stone (URS) can cause hypothermia and shivering[1,2].

Shivering is extremely distressing to the patient, surgeon and anaesthesiologist. It can provoke bleeding, cause hemodynamic instability, arrhythmia and delay wound healing[1]. Shivering increases the myocardial oxygen consumption by causing tachycardia, metabolic heat production, carbon dioxide production and lactic acidosis. Factors which affect the severity of hypothermia in spinal anaesthesia are aging, level of sensory block, and temperatures of the local anaesthetic, operating room and IV solutions[3].

Pharmacological therapies such as opioids, tramadol, Physostigmine, clonidine, ketamine, and magnesium sulfate have been used to prevent shivering[4-6]. Meperidine is among opioids, which is extensively studied due to its anti-shivering effect, but they have many side effects and their results have not been conclusive[2].

*Correspondence
Dr. Paliwal Naveen
Associate Professor, Department of Anaesthesia, Dr. S N Medical College, Jodhpur, Rajasthan, India
E-mail: drnaveenpaliwal@yahoo.com

Magnesium sulphate has antishivering and neuroprotective effect, most of the research on the role of MgSO4 in prevention of shivering has focused on i.v. infusion. There are clinical trials which examine the effect of intrathecal MgSO4 on post operative analgesia & sensory blockade without any additional side effects however it may induce respiratory depression[7-9].

Dexmedetomidine is a highly selective α-2 adrenergic receptors agonist[10]. It has sedative, analgesic, perioperative sympatholytic, anaesthetic sparing, and hemodynamic-stabilizing properties. Intravenous dexmedetomidine has been effectively used for prevention and treatment of shivering following spinal anaesthesia without any major adverse effects.

So we hypothesised that similar to infusion, addition of intrathecal MgSO4 and dexmedetomidine would prevent post spinal shivering. The aim of this study to compared between intrathecal dexmedetomidine and intrathecal magnesium sulphate for the prevention of post-spinal anaesthesia shivering in Transurethral Resection of the Prostate Surgery (TURP).

The primary outcomes were incidence and intensity of shivering, while secondary outcomes were total dose of pethidine required to control shivering, sedation score and Complications including hypotension, bradycardia, nausea, vomiting and allergy.

Materials and methods

This prospective randomized comparative study was conducted in the Department of Anaesthesiology in tertiary care hospital on patients undergoing Transurethral Resection of the Prostate Surgery (TURP) after approval from Institutional Ethics committee (certificate Ref No-SNMC/IEC/2020/Plan/315.) and informed written consent from patients. Study was initiated after obtaining approval for surgery and was carried out under strict CIVID-19 protocol. Seventy-five patients belonging to American Society of Anaesthesiology (ASA) physical status I, II and scheduled for elective Endoscopic Urological surgeries under spinal anaesthesia (from September 2020 to February 2021) were enrolled. Exclusion criteria included were patient refusal, conditions contraindicating spinal anaesthesia, obesity (BMI>28kg/m2), patients with chronic kidney disease and pregnant females.

Preoperative evaluation and preparation were standardized, and patients were explained in detail about the anaesthesia procedure and drug. The randomization was done using computer-generated randomization tables. The allocation was done by using concealed closed opaque envelopes. Patient in all group received standard spinal anaesthesia with 2.5ml of hyperbaric bupivacaine 0.5% (12.5mg) along with it in Group A (n =25) received 0.5ml of normal saline, Group B (n =25) received 5µg dexmedetomidine in 0.5ml saline, and Group C (n =25) received 25mg MgSO4 in 0.5ml saline. Patient's assigned numbers and treatments were concealed in closed opaque envelopes, that was retain by two members on the authors' team who have no interaction with the patients. The specific intrathecal drug solutions were prepared and inject by an anaesthesiologist who was not involve in the study. The anaesthesiologists involved in patient observation and data collection was blinded to the treatment group, as were the patients.

On arrival to the operation room, venous access was prepared with 18-gauge intravenous catheter on forearm and an intravenous infusion was started in all patients with 20ml/kg crystalloid fluid. ASA standard monitoring including electrocardiogram, non-invasive blood pressure measurement, pulse oximetry and temperature probe were applied. Baseline vitals [heart rate (HR), mean arterial pressure (MAP), peripheral oxygen saturation (Spo2) and temperature were recorded.

Spinal anaesthesia was given at L3-4 or L4-5 interspinous space in sitting position via midline approach by using 25-gauge (B BRAUN) Quincke needles. The onset and durations of the motor and sensory blocks were assessed by the Bromage scale and pinprick test, respectively. The level of the block was assessed to ensure that it is between T10-T8; blocks higher than T8 and failed blocks were excluded. A surgical drape was placed over the patient, the room temperature was maintained at 24℃, and all the irrigation and IV fluids were given at room temperature. No warming device was used.

The incidence and intensity of shivering was assessed by a blinded observer immediately after the block was administered, every 5min for the first 15min, and then every 10min for 2 h after the block using the Crossley and Mahajan scale36 (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 generalized shivering, 4=shivering involving the whole body). Twenty-five milligrams of IV pethidine was given when a patient presented grade 3 and high intensity of shivering. The core temperature was monitored using a tympanic probe before the block, immediately after the block and every 5 minutes for first 15 minute and then every 10 minutes for 2 hour after the block. Hypothermia and active warming were considered if the core temperature reached 36℃. The patient's HR, BP and SPO2 were recorded every 5min for the first 15min and then every 10min for 2 h after the block. The sedation level was observed and recorded every 10min for 2 h or until the administration of IV pethidine using the Ramsay sedation scale 37 (1=the patient was anxious, agitated or restless; 2=the patient was cooperative, oriented, and tranquil; 3=the patient only responded to commands; 4=the patient exhibited an immediate response to light glabellar tap or loud auditory stimulus; 5=the patient exhibited a sluggish response to a light glabellar tap or loud auditory stimulus; and 6=the patient exhibited no response). The patients were monitored for complications. Hypotension (20% decrease in the SBP from baseline or SBP<90mm of Hg) was treated with incremental administration of 3mg of ephedrine and 200ml of lactated Ringer's solution, and bradycardia (HR<50) was treated with a bolus of 0.01– 0.02mg/kg of atropine. Nausea and vomiting were treated with 10mg of metoclopramide. Postoperatively, patients were transferred to the post anaesthesia care unit (PACU), monitored and covered with a cotton sheet. The PACU temperature was maintained at 25℃.

Sample Size

Sample size was calculated at alpha error 0.05 and study power 80%, assuming proportion of patients who developed shivering in the two groups to be 60% and 14.3% respectively.

Sample size was calculated to be a minimum of 21 subjects. Considering 10% attrition rate, Sample size was increased and rounded off to 25 subjects in each group. In this study all statistical analyses were performed by using SPSS 22.0 software package (SPSS Inc., Chicago, IL, USA). Yates continuity correction test (Chi square test), Fisher's exact test and Fisher---Freeman---Halton test were used for comparison of qualitative data.

Results

This study was conducted in 75 adult patients divided into three groups of 25 each (figure 1) from age 18 to 60 years, belonging to ASA I and II, BMI <28 Kg/m² COVID-19 Negative who were scheduled for elective endoscopic urological surgeries namely Transurethral resection of Prostate (TURP) suitable for administration of regional anaesthesia**.** The demographic profile (age, height and BMI), ASA grade was comparable between groups (table1).

Table 1: Demographic data

	Group A	Group B	Group C	P value
Age (yr)	54.8±6.2	55.7±3.2	56.3±2.7	0.499
Weight (kg)	65.5±5.1	64.0±5.2	63.8±5.5	0.450
Height (mt)	166.6±4.9	163.7±4.6	166.0±5.6	0.103
ASA I	52%	44%	48%	0.852
ASA II	48%	56%	52%	

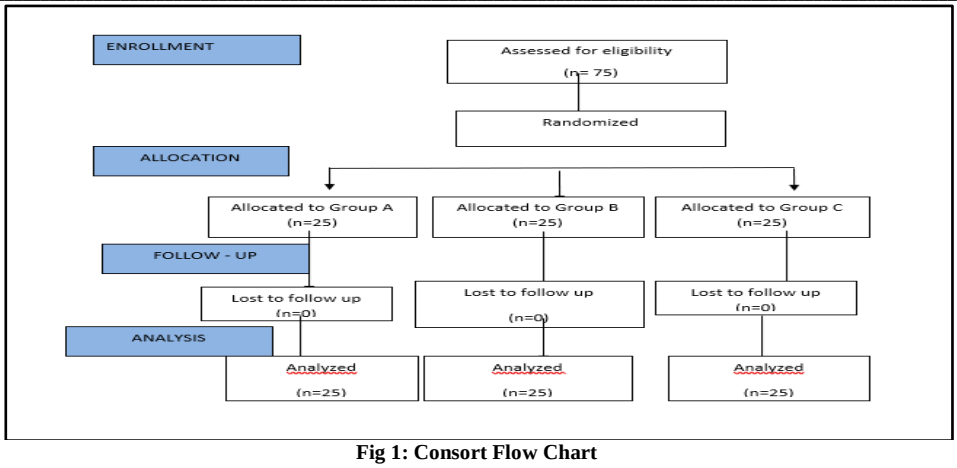

Fig 1: Consort Flow Chart

At 15, 25 and 115 minutes, the HR differed significantly between the groups (P<0.05) and at other minutes Heart rate (HR) showed no significant difference between the groups (figure 2).

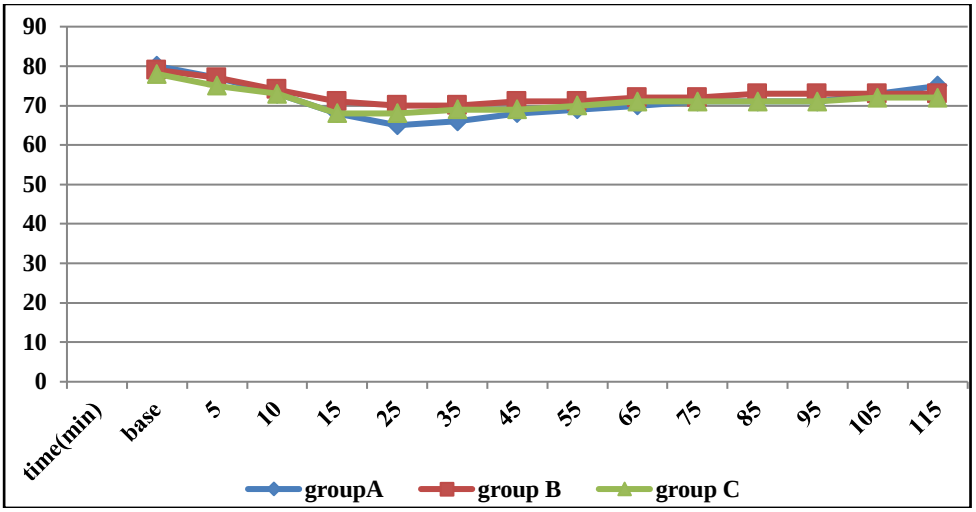

Fig 2: Comparison of HR between the three group (Group-A=1. Group-B=2, Group- C=3)

The figure 3 compares the mean BP between the three groups. At 10, 15 and 85 minutes, mean BP of the groups were significantly differed (P<0.05). At other minutes, the three groups were not statistically significantly differed (P>0.05).

The (Table 2) compares the incidence of shivering between three groups.

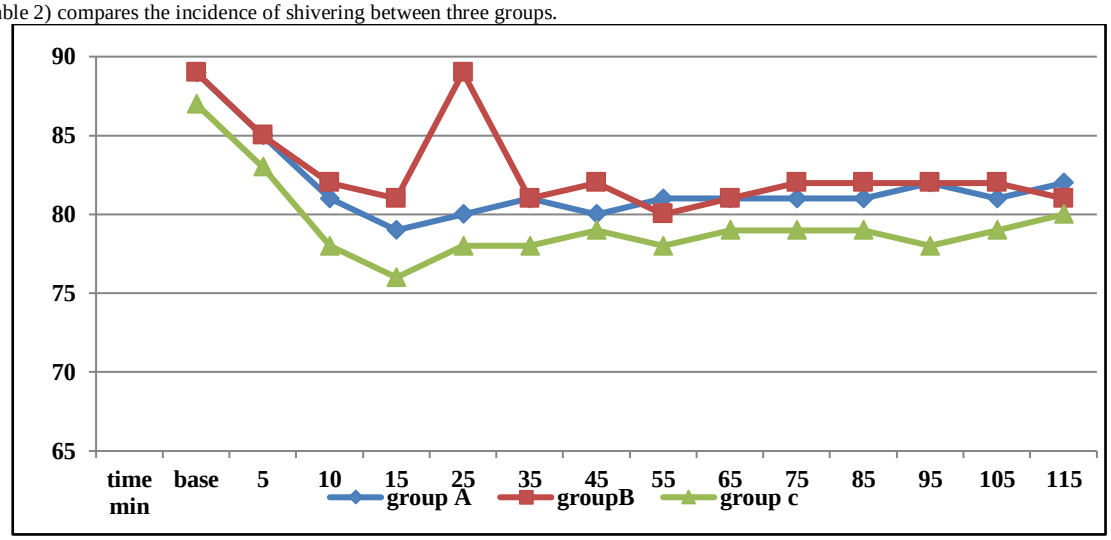

Fig 3: Comparison of mean BP between the three groups: (Group-A=1. Group-B=2, Group- C=3)

Table 2: Shivering incidence and grades

Grading	Group A	Group B	Group C	p	P1	P2	P3
No shivering	44%	88%	68%	<0.05	<0.01	>0.05	>0.05
1	0	0	0	Nil	Nil	Nil	Nil
2	4	4	8	>0.05	1.00	>0.05	>0.05
3	0	0	8	Nil	Nil	Nil	Nil
4	52	8	16	<0.001	<0.0001	<0.001	>0.05

The difference was found statistically significant or not as follows. No Shivering: The 3 groups were statistically significantly differed (P<0.05). The groups A&B were statistically significant (P<0.01). The groups A&C was not statistically significant, and Band C was not statistically significant. Grade-2 Shivering: The 3 groups were not statistically significantly differed (P>0.05) and all combinations were also not statistically significant (P>0.05). Grade-4 Shivering: The 3 groups were statistically significantly differed (P<0.001). The groups A&B and A&C were statistically significant between them P<0.001). The groups B&C was not statistically significant (P>0.05). Incidence of Nausea, vomiting bradycardia, hypotension and allergy were compared among the groups (table 3).

Table 3: Comparison of complications between the three groups A, B & C

Complications	Group A	Group B	Group C	Significance
Nausea	12%	8%	8%	0.854
Vomiting	0	0	0	Nil
Bradycardia	12%	8%	8%	0.869
Hypotension	16%	12%	12%	0.891
Allergy	0	0	0	Nil
Pethidine requires	p	P1	P2	P3
	<0.001	0.0001	0.04	0.126

Discussion

SA has an additional advantage in uroscopic surgeries, especially procedures that require intraluminal fluid irrigation such as TURP, as it allows the early detection of complications such as TURP syndrome in conscious patients. However, SA is not a complication-free technique; shivering is a common complication of SA, with an incidence of 40–60% in patients who undergo SA. Though shivering is a protective mechanism to preserve body heat, it causes patient discomfort and pain and may be dangerous in patients with impaired cardiovascular reserves or limited respiratory capacity, as shivering increases the circulating catecholamine, HR, cardiac output, minute ventilation, oxygen consumption, metabolic CO2 production and lactic acid level. It also increases intraocular and intracranial pressure and postoperative pain due to surgical incision stretching. Shivering may also interfere with the monitoring of patients by causing artefacts on the ECG or disrupting BP and pulse oximetry readings. Hypothermia is a major risk for shivering, but there is no definite linear relationship between body temperature and the occurrence of shivering. Other major risk factors include age, sensory block level, temperature of the operating room and temperatures of the iv solutions. The exact mechanisms to explain the occurrence of shivering during SA have not yet been elucidated. The possible mechanisms include central thermoregulation disturbance, internal body heat redistribution, and body heat loss to the environment. Regional and general anaesthesia are known to impair the efficiency of the hypothalamic thermoregulatory centre, causing different grades of hypothermia. Under regional anaesthesia, vasodilatation and redistribution of the core temperature are restricted to the lower body below the block, while vasoconstriction and shivering are restricted to the upper body, as they are inhibited below the level of the block due to sympathetic and somatic nerve blocks. The results of our study show that there were minimal variations in baseline hemodynamic parameters through 115 minutes post SA mean heart rate, systolic, diastolic, mean arterial blood pressure and oxygen saturation in all three groups, which were statistically insignificant(P value>0.05) .At 10,15 and 85 minutes post SA, mean BP of the groups were significantly differed (P<0.05) (Figure 3) at 15, 25 and 115 minutes post SA, HR differed significantly between the groups (P<0.05) (Figure 2).Our results were in agreement with studies conducted by Omar H et al[11] and most of the previous similar studies.

Incidence

56% of patients in Group A had post spinal anaesthesia shivering which was statistically significant as compared to 12% in group B and 32% in group C (Table-2).

In our study the shivering grade of the three groups at baseline through 115 minutes post SA compared, the shivering grades of the groups A and C were statistically significant (P<0.001) and B was not significant (P>0.05) (Table 2). Our results were in agreement with study conducted by Omar H et al[11]**.**In our study in group A 44%(11) showed no shivering,4%(1) showed grade 2 and 52% (13)showed grade 4 shivering, **i**n group B 88%(22)showed no shivering, 4%(1) showed grade 2 and 8%(2) showed grade 4 shivering, and in group C 68%(17) showed no shivering, 8%(2) showed grade 2, 8%(2) showed grade 3 and 16%(4) showed grade 4 shivering, which was in concordance with Omar H et al[11]**.** Reason for similar results can be explained by similar intrathecal dosage administered for drugs used for SAB in both studies.Our study results show that complications (nausea, vomiting, bradycardia, hypotension, allergy) were not statistically significant within the A, B and C groups (P>0.05) (Table- 3). Our results were in agreement with study conducted by Omar H et al[11] and other studies.

Limitations of the study

The limitations to our study were that we did not estimate the mean volumes of the irrigating fluids in each group. We recommend conducting further studies on both drugs with increased sample sizes and different doses. This study was conducted in a single centre service hospital. Results cannot be generalized to the population of other countries.

Strength of the study: In our study the anaesthesiologist involved in patient observation and data collection, blinded to the treatment group as were the patients to reduce bias in study.

Conclusion

Considering the results of statistical analysis of our study, it can be concluded that intrathecal injection of both dexmedetomidine and MgSO4 with bupivacaine were effective in reducing the incidence of post-SA shivering. Addition of dexmedetomidine intrathecally with hyperbaric bupivacaine reduced the incidence of shivering as compared with addition of MgSO4.

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Conflict of Interest: Nil
Source of support: Nil