

A comparison of Prophylactic Intravenous Magnesium Sulphate with Meperidine for Prevention of Shivering during Spinal Anaesthesia.

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Abstract

Background and objective: Shivering increases oxygen consumption, lactic acid and CO₂ production consequence increase in the CO and minute ventilation. Aim of this study is to compare efficacy of Prophylactic Intravenous Magnesium Sulphate With Meperidine For Prevention Of Shivering During Spinal Anaesthesia

Material and Methods: 90 patients between 18 -60 years age, belonging to the ASA grade 1, 2 undergoing surgeries under spinal anesthesia were enrolled into the study. Patients belonging to Group S (control group, n = 30) received saline 10 mL IV, Group MS (magnesium sulphate n = 30) received 30 mg/kg diluted in 10 ml saline IV, whereas those in Group M (Meperidine group, n = 30) received meperidine 0.5 mg/kg diluted in 10 ml saline IV after spinal anesthesia. Incidence and grades of shivering were noted. Data were analyzed using oneway ANOVA test and Chi-square test.

Results : The incidence of shivering in Group MS and Group M was significantly low when compared to Group S. Between group MS and M incidence of shivering was significantly less in Magnesium sulphate group than Meperidine with p=0.015. Axillary Temperature did not influence the outcome of study and is not significant. Haemodynamics like Heart rate was insignificant among groups but pethidine group showed wide fluctuation from baseline. Blood pressure was statistically significant in MS group with p<0.05.

Conclusion: MgSO₄ and Meperidine significantly reduce the incidence of shivering compared to saline when used as prophylaxis in patients under spinal anesthesia. Magnesium sulfate found to be effective way in reducing severity of the shivering.

Key words: Magnesium Sulphate, Meperidine, Shivering, Subarachnoid Block.

Introduction

Perioperative shivering is a common complication in patients undergoing spinal anaesthesia^[1] and has reported incidence of up to 40-60%^[2]. Shivering is one of the frequent, undesirable and unpleasant complications of both general and regional anaesthesia^[2]. Shivering leads to adrenergic activation resulting in increased oxygen consumption, carbon dioxide production, morbid cardiac events, arterial hypoxemia, lactic acidosis, and increase in the intraocular and intracranial pressures^[2]. Also interferes with monitoring. Involuntary contraction of muscles seen with shivering is a protective reflex to increase the core temperature^[1]. Hypothermia is a major risk factor for shivering, but there is no definite linear relationship between body temperature and the

occurrence of shivering. Other methods to reduce shivering are use of warm blankets, warm IV fluids, reducing the OT temperature, warmer and so on. Other major risk factors include age, sensory block level, temperature of the operating room and temperatures of the IV solutions^[3]. The neurotransmitter pathways responsible for shivering are complex, and different receptors such as opioid, α -2 adrenergic, serotonergic, and anti-cholinergic receptors are involved^[3]. MAGNESIUM SULPHATE is gaining popularity in modern anaesthesia and pain medicine^[2]. It is widely used in preeclampsia and eclampsia. It is a N-methyl D-Aspartate receptor antagonist and calcium competitor. It reduces the shivering threshold and is shown to suppress postoperative shivering^[3]. MEPERIDINE HYDROCHLORIDE also

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known as pethidine is a synthetic opiate agonist belonging to the phenylpiperidine class^[4]. Its effective in pain management, postspinal shivering when given intravenously. It has various side effects like itching, respiratory depression, tachycardia, physical dependency hypotension, nausea, vomiting and decreased gastrointestinal (GI) motility. In the present study we compared the efficacy of Prophylactic Intravenous Magnesium Sulphate With Meperidine For Prevention Of Shivering During Spinal Anesthesia. Also the incidence and severity of shivering in both the groups.

Material And Methods

Study was conducted after obtaining Institutional Ethical Committee clearance [IEC recognised by CDSCO vide Regn.No. ECR/952/Inst/KA/2017 and our study details - SIMS/ IEC/ 489/2019-20 on 19/11/2019]and Patients Consent. Sample size - 90; Study design - Prospective Randomised Single Blinded Comparative Clinical Study; Duration of study- November 2019 to April 2020 ; Sample size of 24 in each group was obtained based on the incidence of shivering in previous study by Solhpur Ali et al^[5] and substituting the results in statistical formulae. Taking into consideration of 10% loss of follow up, 30 in each group was recruited in study. Patients aged between 18-60 years, Both genders, Undergoing elective surgeries under spinal anaesthesia, Belonging to ASA grade 1 and 2, Weight = 50-80 kg, Height = > 150 cm were included in the study. ASA physical status 3,4 ; Obesity (BMI > 28 kg/m²); Initial body temperature more than 38°C or less than 36° C ; Contraindications to regional anesthesia; Allergy to the study medication, Thyroid disease, uncontrolled DM. Parkinson's disease, dysautonomia or Raynaud's syndrome, ischemic heart disease, cerebrovascular disease, psychiatry disorders; Requiring blood transfusion during surgery; Receiving vasodilators or medications likely to alter thermoregulation ; Renal or liver disease; Patients with failed spinal anesthesia on the first try were excluded from the study.

Methodology

This study was conducted in patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 18 -60 years, undergoing elective surgery under spinal anaesthesia. All the patients underwent a preanesthetic check-up the day before surgery, and all the routine and specific investigations were noted. The patients were electively kept nil by mouth as per ASA guidelines ; All patients received Tab Alprazolam 0.5 mg at night and a dose of antibiotic I.V, I.V ranitidine 50 mg and metoclopramide 10 mg before the surgery as per the institutional protocol. Before surgery a

written informed consent was taken. On arrival to the operating room, all patients were monitored with noninvasive blood pressure, ECG, pulse oxymeter (SpO₂), and digital thermometer. The temperature of the operating room was maintained in the range of 24-25°C. The baseline values of all vital parameters were noted. All patients were coloaded with 10 ml/kg Ringer lactate solution at room temperature. Using computer generated random number and sealed envelope technique, study population were divided into three groups -Group MS : received 30 mg/kg of Magnesium Sulphate diluted to 10 ml; Group M : received 0.5 mg /kg of meperidine diluted to 10 ml ; Group S : received 10 ml saline. Timing of administration was just after intrathecal injection. Method of administration -Study drug was prepared in a 10 ml syringe which contains either Magnesium sulphate, meperidine or saline. Study drugs prepared was infused according to body weight by anaesthesiologist involved in the study. Magnesium sulphate over 20 minute, Meperidine over 60 -75 seconds and Saline over 1 minute. All patients were monitored for vital signs during the period of observation. The parameters was recorded and tabulated by the anesthesiologist involved in the study. Vital parameters (HR, SPO₂, BP, axillary temperature) were monitored at 0,5,10,15,20,30,45, 60 minutes and post surgery for 20 minutes) : T₀ - Basal reading when the patient is shifted to OT ; T₁ - 5 minutes after study drug ; T₂ -10 minutes after study drug ; T₃ -15 minutes after study drug ; T₄ -20 minutes after study drug ; T₅ - 30 minutes after study drug ; T₆ - 45 minutes after study drug ; T₇ - 60 minutes after study drug ; T₈ -10 minutes after completion of surgery ; T₉ - 20 minutes after completion of surgery. Incidence and Severity of shivering was assessed at 0, 5, 10, 15, 20, 30, 45, 60 minutes and post surgery for 20 minutes) Severity of shivering was assessed using Crossley and Mahajan scale -0 = No shivering; 1 = Cyanosis and piloerection ; 2 = Visible tremors only in one muscle group ; 3 = Visible tremors in more than one muscle group ; 4 = Intense shivering, tremors of the head, arm. Adverse reactions such as nausea or vomiting, hallucinations, Hypotension, bradycardia were recorded. Arterial hypotension was defined as systolic BP <90 mm Hg or <25% of the basal mean arterial blood pressure (MAP) reading, crystalloid Infusion and if needed injection mephentramine 6-12 mg i.v was administered. Injection atropine 0.5 mg i.v was administered if HR <50 bpm. Metaclopramide 10 mg IV was given for the treatment of nausea and vomiting. When patients developed false sensory experience (they saw, heard, smelled, tasted, or felt something that was nonexistent), it was recorded as hallucination. Low saturation was defined as SpO₂

< 94% at any time during surgery or in the recovery room.

Statistics^[6,7,8].

Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data. Post Hoc Bonferroni test was used to determine the intergroup analysis. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and line diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results

Demographic variables: The groups were comparable with respect to demographic variables like age and gender. Outcome measures: Include Incidence and Severity of Shivering, Axillary Temperature, Heart rate (HR), Systolic blood Pressure (SBP), Diastolic blood Pressure (DBP and Mean Arterial Blood Pressure (MAP)

Table 1: Age distribution comparison between three groups

		Age		P value
		Mean	SD	
Group	Magnesium Sulphate	35.23	11.97	0.745
	Pethidine	36.37	13.17	
	Saline	37.73	12.64	

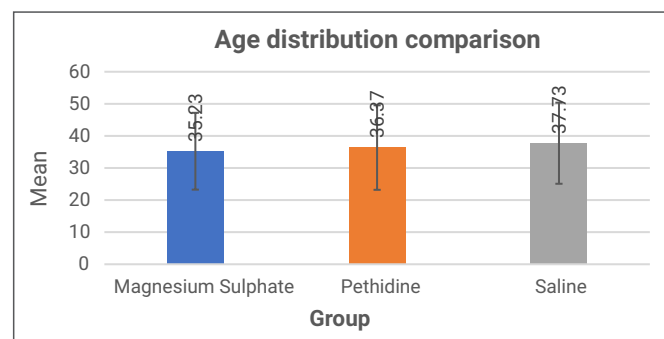


Figure 1: Bar diagram showing Age distribution comparison between three groups

Table 2: Sex distribution comparison between three groups

		Group					
		Magnesium Sulphate		Pethidine		Saline	
		Count	%	Count	%	Count	%
Sex	Female	7	23.3%	11	36.7%	6	20.0%
	Male	23	76.7%	19	63.3%	24	80.0%

• $\chi^2 = 2.386, df = 2, p = 0.303$

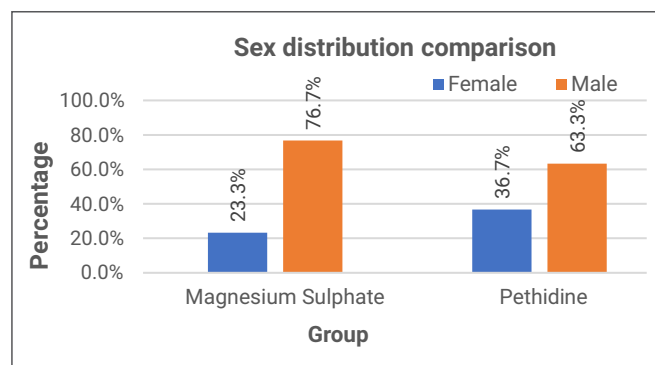


Figure 2: Bar diagram showing Sex distribution comparison between three groups

Table 3: Weight distribution comparison between three groups

		Weight		P value
		Mean	SD	
Group	Magnesium Sulphate	64.80	10.68	0.008*
	Pethidine	57.07	6.09	
	Saline	60.60	10.59	

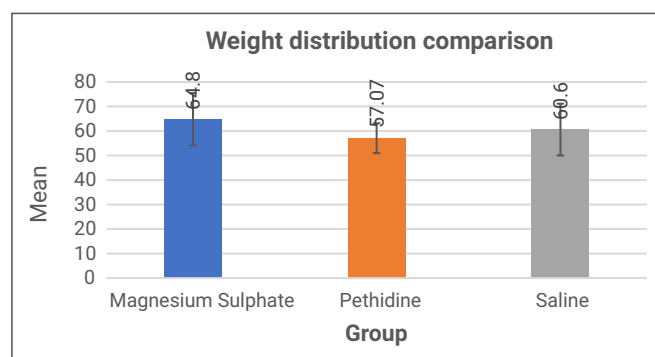


Figure 3: Bar diagram showing Weight distribution comparison between three groups

Table 4: Incidence and Severity of shivering distribution comparison between three groups at various intervals

Incidence and Severity of Shivering		Group						P value
		Magnesium Sulphate		Pethidine		Saline		
		Count	%	Count	%	Count	%	
T0	No	30	100.0%	30	100.0%	30	100.0%	-
T1	No	30	100.0%	28	93.3%	26	86.7%	0.015*
	Yes and Grade 2	0	0.0%	2	6.7%	0	0.0%	
	Yes and Grade 3	0	0.0%	0	0.0%	4	13.3%	
T2	No	30	100.0%	28	93.3%	22	73.3%	0.002*
	Yes and Grade 1	0	0.0%	0	0.0%	2	6.7%	
	Yes and Grade 2	0	0.0%	2	6.7%	0	0.0%	
	Yes and Grade 3	0	0.0%	0	0.0%	6	20.0%	
T3	No	30	100.0%	30	100.0%	22	73.3%	0.002*
	Yes and grade 2	0	0.0%	0	0.0%	2	6.7%	
	Yes and Grade 3	0	0.0%	0	0.0%	6	20.0%	
T4	No	30	100.0%	30	100.0%	20	66.7%	<0.001*
	Yes and Grade 2	0	0.0%	0	0.0%	4	13.3%	
	Yes and Grade 3	0	0.0%	0	0.0%	6	20.0%	
T5	No	30	100.0%	30	100.0%	20	66.7%	<0.001*
	Yes and Grade 2	0	0.0%	0	0.0%	6	20.0%	
	Yes and Grade 3	0	0.0%	0	0.0%	4	13.3%	
T6	No	30	100.0%	30	100.0%	20	66.7%	0.001*
	Yes and Grade 1	0	0.0%	0	0.0%	2	6.7%	
	Yes and Grade 2	0	0.0%	0	0.0%	4	13.3%	
	Yes and Grade 3	0	0.0%	0	0.0%	4	13.3%	
T7	No	25	83.3%	28	93.3%	20	66.7%	0.124
	Yes and Grade 1	2	6.7%	0	0.0%	4	13.3%	
	Yes and Grade 2	3	10.0%	2	6.7%	4	13.3%	
	Yes and Grade 3	0	0.0%	0	0.0%	2	6.7%	
T8	No	23	76.7%	26	86.7%	16	53.3%	0.002*
	Yes and Grade 1	0	0.0%	2	6.7%	4	13.3%	
	Yes and Grade 2	0	0.0%	0	0.0%	6	20.0%	
	Yes and Grade 3	7	23.3%	2	6.7%	4	13.3%	
T9	No	19	63.3%	22	73.3%	16	53.3%	<0.001*
	Yes and Grade 1	0	0.0%	0	0.0%	4	13.3%	
	Yes and Grade 2	0	0.0%	8	26.7%	6	20.0%	
	Yes and Grade 3	11	36.7%	0	0.0%	4	13.3%	

The incidence and severity of shivering was statistically significantly less in Magnesium Sulphate compared to Pethidine and Saline group at all intervals of time except at 60 minutes after drug administration. Postoperative incidence and severity of shivering was more in Group MS than Group M.

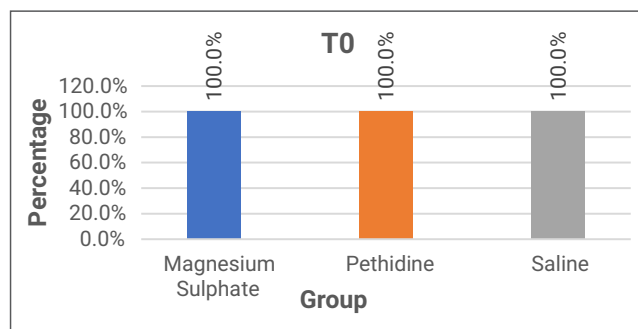


Figure 4: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

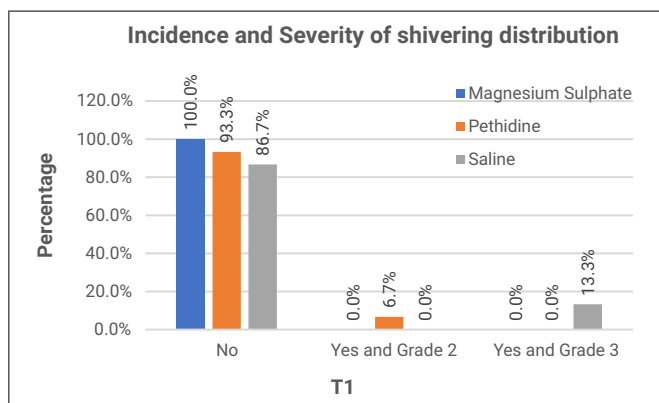


Figure 5: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

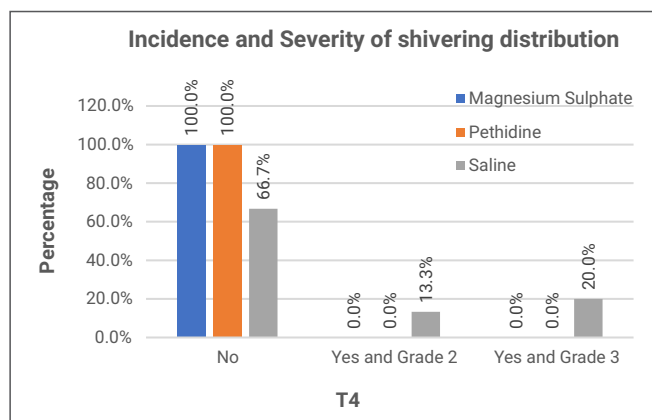


Figure 8: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

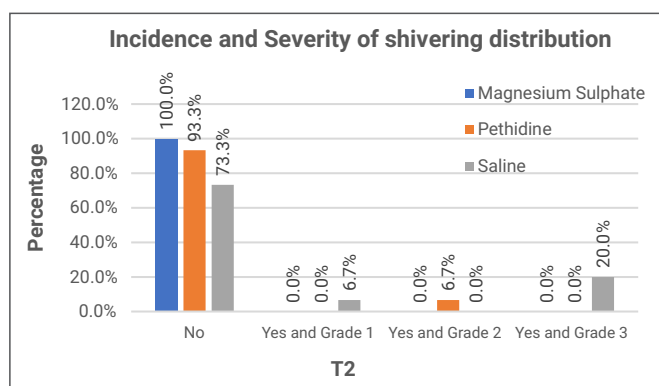


Figure 6: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

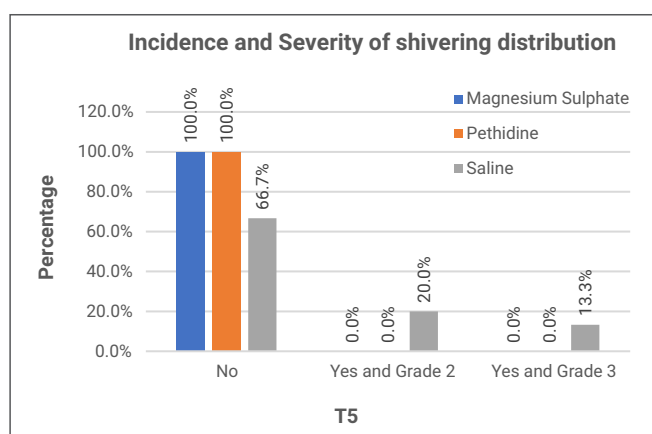


Figure 9: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

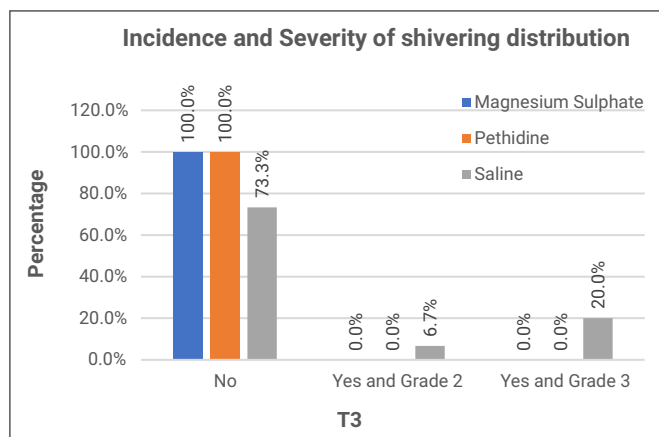


Figure 7: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

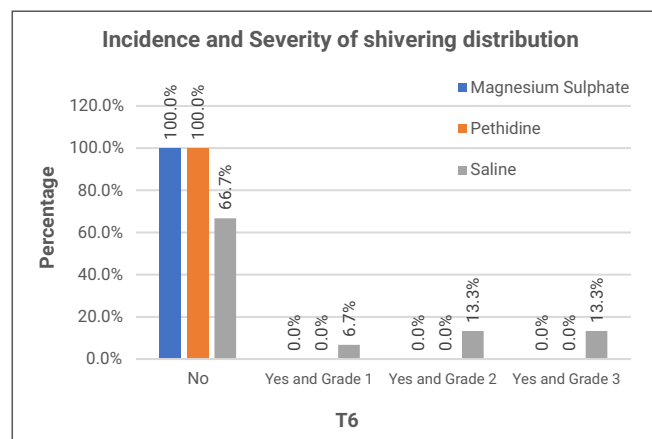


Figure 10: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

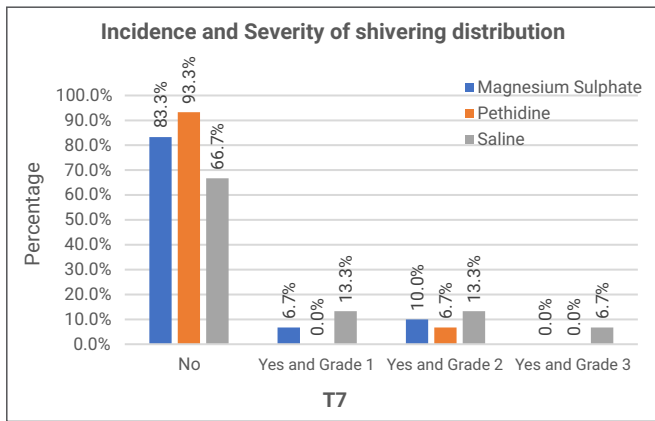


Figure 11: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

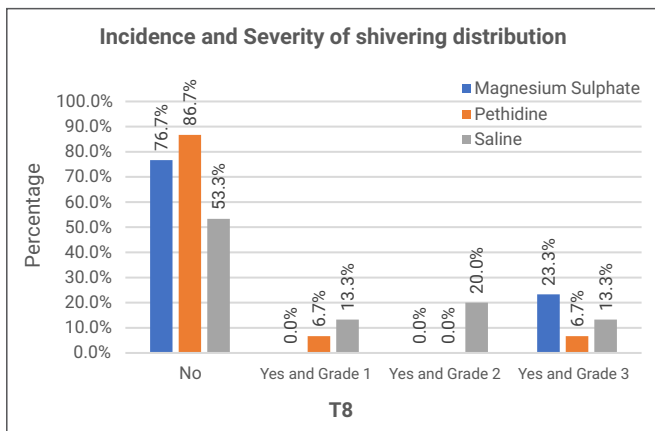


Figure 12: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

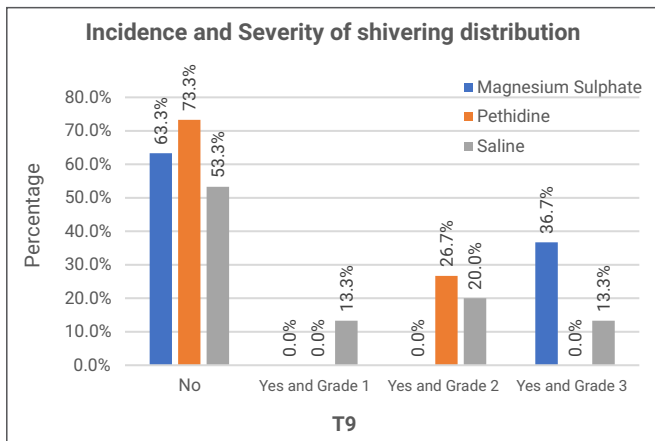


Figure 13: Bar diagram showing Incidence and Severity of shivering distribution comparison between three groups at various intervals

Table 5: Heart rate distribution comparison between three groups at various intervals

HR	Group						P value
	Magnesium Sulphate		Pethidine		Saline		
	Mean	SD	Mean	SD	Mean	SD	
T0	89.10	18.44	88.47	18.64	86.33	16.67	0.823
T1	82.80	17.68	76.27	13.01	85.80	13.37	0.044*
T2	80.10	18.81	70.87	12.33	84.47	16.06	0.005
T3	78.70	16.32	69.53	12.13	84.33	15.11	0.001*
T4	77.53	16.95	68.67	10.42	80.27	15.11	0.007*
T5	74.47	15.85	69.47	12.52	78.93	15.27	0.048*
T6	74.83	14.23	67.60	9.90	79.27	14.01	0.003*
T7	76.33	15.30	69.27	13.27	77.00	14.48	0.075
T8	74.10	13.22	78.20	14.59	75.87	14.17	0.526
T9	76.60	13.95	80.87	15.76	76.47	14.50	0.425

Magnesium sulphate maintained the stable heart rate around basal value throughout the study period without wide fluctuations as seen with pethidine.

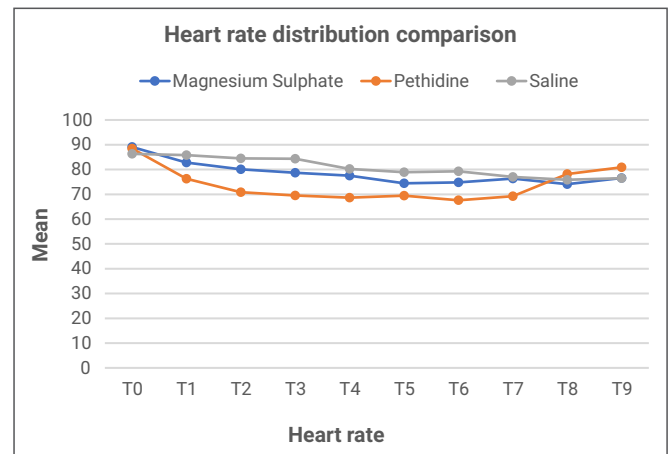


Figure 14: Line diagram showing Heart rate distribution comparison between three groups at various intervals

Table 6: SBP distribution comparison between three groups at various intervals

SBP	Group						P value
	Magnesium Sulphate		Pethidine		Saline		
	Mean	SD	Mean	SD	Mean	SD	
T0	135.37	12.68	127.47	12.19	134.67	11.48	0.024*
T1	120.43	14.06	110.87	13.98	123.40	11.05	0.001*
T2	114.77	13.94	111.47	11.95	119.13	14.97	0.099
T3	115.80	12.75	107.47	11.18	116.53	14.78	0.014*
T4	111.43	13.60	107.60	11.08	116.47	16.18	0.049*
T5	113.57	11.29	107.67	9.32	117.87	18.90	0.019*
T6	116.53	13.57	110.47	9.06	117.20	12.16	0.055
T7	119.90	11.09	108.53	9.34	115.60	13.89	0.001*
T8	116.33	11.87	114.33	11.73	123.40	11.20	0.008*
T9	120.57	10.42	115.47	11.44	117.87	12.32	0.229

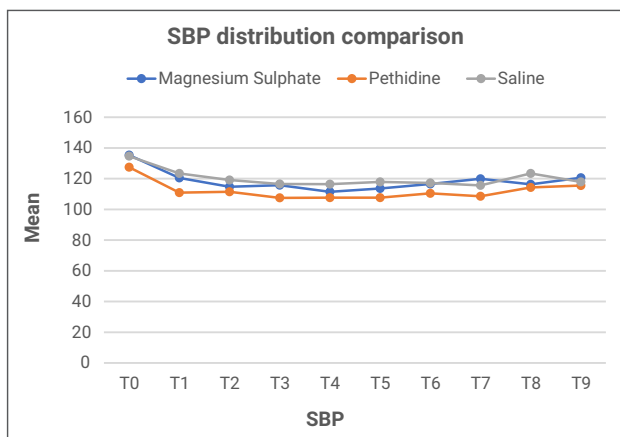


Figure 15: Line diagram showing SBP distribution comparison between three groups at various intervals
Magnesium sulphate maintained stable SBP throughout study period without fluctuations same as heart rate.

Pethidine also maintained the blood pressure stable without fluctuations as seen in heart rate indicating its influence only on heart rate.

Table 7: DBP distribution comparison between three groups at various intervals

DBP	Group						P value
	Magnesium Sulphate		Pethidine		Saline		
	Mean	SD	Mean	SD	Mean	SD	
T0	82.80	12.35	77.60	14.72	81.93	7.79	0.203
T1	71.50	13.22	66.40	12.85	77.47	9.58	0.003*
T2	68.20	10.11	66.73	11.39	72.87	10.80	0.076
T3	72.83	11.87	64.13	11.88	72.20	11.73	0.008*
T4	68.73	13.91	64.40	10.12	72.20	11.57	0.046*
T5	70.57	9.90	64.60	10.28	72.67	11.65	0.012*
T6	70.17	12.79	65.73	10.20	72.40	8.70	0.054
T7	73.57	8.42	64.73	11.21	70.80	11.38	0.005*
T8	73.23	10.96	69.13	10.22	77.07	11.63	0.023*
T9	76.77	15.22	75.60	9.67	74.60	10.34	0.783

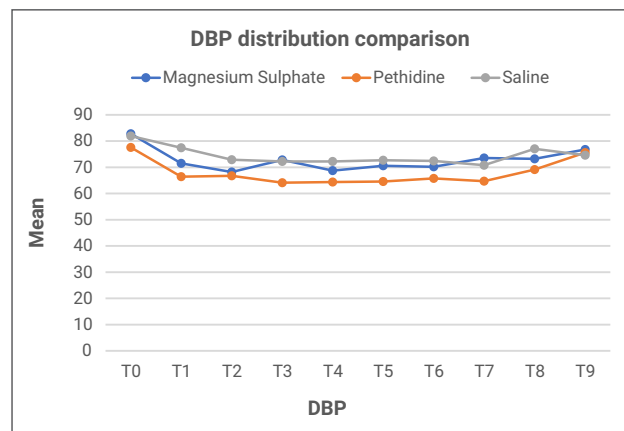


Figure 16: Line diagram showing DBP distribution comparison between three groups at various intervals

Similar response in DBP was observed as seen with SBP among both magnesium sulphate and pethidine.

Table 8: MAP distribution comparison between three groups at various intervals

MAP	Group						P value
	Magnesium Sulphate		Pethidine		Saline		
	Mean	SD	Mean	SD	Mean	SD	
T0	100.67	10.28	95.07	10.10	99.47	8.39	0.066
T1	88.73	13.66	83.13	13.02	92.13	10.32	0.021*
T2	83.37	13.71	83.40	9.24	87.20	10.33	0.321
T3	87.82	12.31	79.20	9.32	86.20	11.02	0.007*
T4	82.00	16.27	79.00	9.89	87.87	11.90	0.031*
T5	85.68	12.46	79.07	9.21	88.13	12.64	0.009*
T6	88.07	12.88	81.73	9.78	87.53	10.56	0.056
T7	91.23	8.83	80.07	11.08	84.53	12.18	0.001*
T8	85.53	15.22	85.20	10.24	90.80	9.21	0.128
T9	90.46	15.67	88.93	8.93	89.60	11.39	0.891

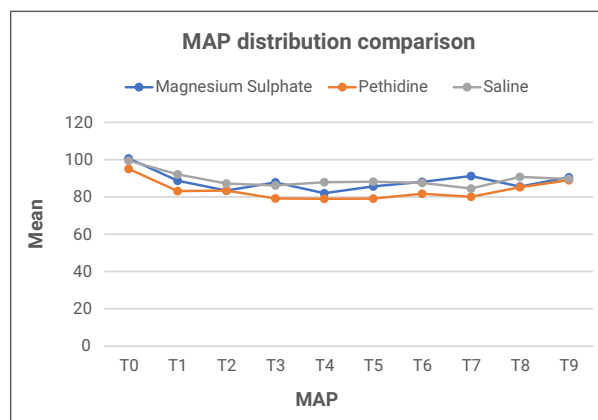


Figure 17: Line diagram showing MAP distribution comparison between three groups at various intervals

Discussion

Spinal anaesthesia significantly decreases the threshold for shivering. During spinal anaesthesia, vasodilatation and redistribution of core temperature are restricted to the lower body below the level of the block, while vasoconstriction and shivering are restricted to the upper body^[1]. Many drugs like meperidine, fentanyl, clonidine, ketamine, and tramadol have resulted in different degrees of efficacy and many associated side effects, such as haemodynamic instability, respiratory depression, nausea and vomiting^[3]. Magnesium (Mg) is a naturally occurring non-competitive antagonist of N-methyl-D aspartate (NMDA) receptors with a good safety profile. Anti-shivering effect of MgSO is by both central and peripheral mechanisms. Centrally by reducing the shivering threshold, blocks NMDA receptors and decreases norepinephrine and 5-HT. peripherally acts by mild muscle relaxation effect that

may reduce the intensity of shivering and also cause peripheral vasodilation, which increases cutaneous circulation, leading to a decrease in the incidence of shivering^[3]. Higher dose of magnesium is associated with peripheral vasodilatation with consequent hypotension, bradycardia, and hypothermia^[2]. Therefore, we limited the dose of magnesium sulfate in our study to 30 mg/kg. Meperidine, which binds to both μ and kappa-opioid receptors, is frequently recommended for the treatment of postspinal shivering. Although the mechanism of action is not fully elucidated, special anti-shivering effect is mediated by its kappa-receptor activity^[9]. The IV administration of 25-50 mg of meperidine suppresses postspinal shivering within 2-15 min in 55%-95% of patients. Minimal effective dose of meperidine for treating postspinal shivering is approximately 0.35 mg/kg^[9]. In our study, a dose of 0.5 mg/kg meperidine was used, which was slightly larger than the suggested minimal effective dose. In the present study, none of the patients developed shivering intraoperatively in Magnesium sulphate group while 2 patients in Meperidine group of severity of Grade 2 and 10 patients in Control (Saline) group of severity grade 2 and 3 developed shivering. Postoperatively 10 patients in Magnesium sulphate group, 8 patients in Meperidine group and 15 patients in Saline group developed shivering. Heart rate was maintained towards the baseline throughout the study period in Magnesium sulphate group compared to Meperidine group. Blood pressure changes were comparable among groups. There was no significant change in the mean temperature among the three groups in our study. We did not find any correlation between incidence of shivering and temperature change in our study. Uninhibited spinal reflexes, decreased sympathetic activity, pyrogen release, and adrenal suppression have been implicated for postoperative shivering^[2]. Adverse effect like hypotension was reported in all groups and treated accordingly. Nausea was reported only in Meperidine group. In a study conducted by Elsonbaty et al^[10] where they administered single intravenous bolus dose of Meperidine (M) 0.5 mg/kg (n=25) for one group and the other group received (n = 25) intravenous (IV) MgSO in a dose of 50 mg/kg over 20 min followed by 0.5 mg/kg/min both. Shivering occurred in 68% of patients in group (M) when compared to group (Mg) where only 28% suffered from shivering which is concurrence with our study. Regarding the complications, local allergy significantly occurred in group (M) in five patients when compare to one patient in group (Mg). Solphour ali et al^[5] study the effect of saline (placebo, group C), meperidine 0.4mg/kg (group Me), ketamine 0.25mg/

kg plus midazolam 37.5 μ g/kg (group KMi), and meperidine 0.2mg/kg plus dexamethasone 0.1mg/kg (group MeD) as an intravenous bolus immediately after intrathecal injection for postspinal shivering and concluded that : Prophylactic use of meperidine 0.2mg/kg plus dexamethasone 0.1mg/kg was more effective than other groups in preventing shivering resulting from spinal anesthesia. Sachidananda R et al^[2] conducted a study to compare the efficacy of tramadol 0.5 mg/kg in 100 mL isotonic saline i.v and magnesium sulfate group 30 mg/kg in 100 ml saline over 20 minutes for postspinal shivering and concluded that Magnesium sulphate was more effective in reducing severity which is in concurrence with our study. S kizilimak et al^[11] administered Magnesium sulfate 30 mg/kg i.v bolus and pethidine 0.5 mg/kg bolus for postanesthesia shivering following general anesthesia. The study concluded that Magnesium sulfate is as effective as pethidine in the treatment of postanesthesia shivering which is in concurrence with our study.

Limitations

Incidence and severity of shivering in our study could have been reduced further with an additional infusion of magnesium sulfate. Present study included only patients with ASA physical status I and II. Magnesium sulphate may be useful in high risk cardiac patients.

Conclusion

Prophylactic administration of Magnesium Sulphate is an effective alternative to Meperidine in reducing the incidence and severity of postspinal shivering without remarkable complications and better haemodynamics.

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