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Original Article

Comparative Study between Intravenous Ketamine and Magnesium Sulphate for Prevention of Shivering Post-Intrathecal Anesthesia

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Abstract

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Background: Spinal anesthesia is recognized for its ability to greatly hinder the body's ability to regulate temperature. It does this by suppressing the body's natural vasomotor and shivering reflexes, as well as by moving heat away from the central part of the body to the peripheral tissues.

Aim: This study aimed to contrast the efficiency of intravenous ketamine against Magnesium sulphate added to 100 ml saline to prevent shivering associated with spinal anesthesia.

Methods: This is a prospective, randomized, double blinded controlled work. The present study was performed on 180 patients admitted to Al-Azhar University Hospitals, undergoing different elective procedures utilizing spinal anesthesia. Each participant was ASA physical status I and II.

Results: A statistically significant reduction in the frequency of shivering [grade II or greater] in the two groups, group K [23.3%] and group M [40%] contrasted to the frequency of 51% in the control group. Incidence of shivering was insignificantly different Immediately after spinal anesthesia, 5min, 10min, 15min and 90 min and was substantially lower in group K in contrast to group M and group C and was significantly reduced in group M in contrast to group C [P value<0.05]. These results suggest that both Ketamine and Magnesium sulphate substantially decrease the frequency of shivering contrasted to the control group. And also, both delay the onset of shivering [if it happens] by a considerable amount.

Conclusion: Administering Ketamine at a dosage of 0.5 mg/kg, diluted in 100 ml of normal saline, over a 10minute period as a preventive measure is more effective compared to administering Magnesium sulphate at a dosage of 50 mg/kg, diluted in 100 ml of normal saline, over a period of 10 minutes in managing shivering after spinal anesthesia.

Keywords: Ketamine; Magnesium sulphate; Shivering; Spinal; Anesthesia.



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INTRODUCTION

Spinal anesthesia is a secure anesthesia method employed for both elective and urgent surgical procedures. Shivering is a common occurrence among individuals who undergo surgeries with neuraxial anesthesia, with an incidence rate ranging from 40% to 70% [1]. Post-operative shivering is a frequently occurring complication following regional or general anesthesia [2]. Nevertheless, pharmacological approaches are more convenient to implement and more cost-effective. These methods encompass the utilization of various substances, including opioids, neostigmine, Alpha agonists [Clonidine], magnesium sulphate, and ketamine [3].

Magnesium sulphate [M] has anti shivering effect either given intravenously or intrathecally. It exerts its anti-shivering effect through peripheral vasodilatation, that potentially enhances cutaneous circulation, thus reducing the frequency of shivering [4]. Ketamine [K] is a substance that competes with N-Methyl-d-aspartate [NMDA] receptors and acts as an antagonist. It has a function in regulating body temperature at different levels. These receptors regulate the activity of serotonergic and noradrenergic neurons in the locus ceruleus. Ketamine elevates arterial pressure, HR, and cardiac output by directly stimulating the sympathetic nervous system and inhibiting the absorption of noradrenaline into the postganglionic sympathetic nerve terminals [5]. Therefore, this work aimed to contrast the efficiency of IV ketamine against Magnesium sulphate among individuals having spinal anesthesia for decreasing incidence of shivering.

PATIENTS AND METHODS

A Clinical prospective, randomised, double-blinded controlled work. The study was performed on individuals ASA physical status I and II, aged 21-60 of both genders, undergoing an elective lower abdominal surgery under spinal anesthesia between March 2023 to December 2023. Time of surgeries ranged from 30 min to 120 minutes. Participants had been categorized at random into three groups equally [60 participants for each group]. Patient < 21 years and > 60 years, individuals having a medical history of uncontrolled comorbidities, such as cardiac, pulmonary, hepatic, or renal illness, individuals who had allergies to any drug or contraindications to spinal anesthetic, fever >38 Celsius or less than 36 Celsius, patient with body mass index more than 35 and patient who has history of alcohol intake were excluded. The work is submitted to the research ethical committee of the Faculty of Medicine, Al-Azhar University, Assiut, for approval before starting the study. Following permission of the local medical ethics committee of faculty of medicine [Assiut] at Al Azhar University code [MSc/AZ.AST. /AIP219/10/216/2/2023] and a well-informed written consent taken from 180 patients included in this work.

Pre-operative evaluation: A detailed clinical examination, together with laboratory tests including a full blood picture, coagulation profile, blood urea, serum creatinine, and fasting blood sugar. Individuals were linked to conventional monitoring equipment, which included an electrocardiogram, a non-invasive arterial blood pressure monitor on the dominant arm, a peripheral pulse oximeter, and a tympanic membrane probe for measuring core temperature.

Surgical anesthesia method: A cannula with a diameter of 18-Gauge was inserted into the non-dominant arm/hand of each subject to establish intravenous access., Each patient received 500 ml Ringer lactate; fluids kept at room temperature, The spinal anesthesia had

been conducted with the participant in the sitting position at L3-4 through a 25 G Quincke's spinal needle, No premedication was given , Supplemental oxygen [4 L/min] delivered via facemask throughout the surgery. Maintenance of intravenous fluid calculated as the following: Basal requirement for the first ten kg body weight [BW] calculated by 4ml/kg/hr, second ten kg BW calculated by 2ml/kg/hr and each remaining kg calculated by 1ml/kg/hr. Losses replaced by lactated Ringer's solution at room temperature. A reduction in the MAP by $\geq 20\%$ from baseline value controlled with IV ephedrine bolus 6mg IV that repeated; if hypotension persists or recurs. Heart rate <60 beats/min treated with 0.4mg IV atropine sulfate. For every patient included in this study the following parameters were measured: patient characteristics, duration of surgery [minutes] and Hemodynamic measurements. Pulse rate assessed by electrocardiogram and Non-invasive measures of arterial blood pressure. Core temperature in celisius measured using tympanic membrane probe by Advisor monitors. Shivering measured at the following time points and grading of shivering done using bedside shivering assessment scale [BSAS]. Frequency of peri-operative vomiting and nausea was noted in the studied patient.

Statistical Analysis: It had been conducted utilizing SPSS v27 [IBM©, Chicago, IL, USA]. Shapiro-Wilks test and histograms had been employed to assess the normality of the data distribution. Quantitative parametric data had been expressed as mean and standard deviation [SD] and had been analyzed employing ANOVA [F] test with post hoc test [Tukey's]. Qualitative parameters had been displayed as frequencies and percentages [%] and had been analyzed employing the Chi-square test. A two tailed P value < 0.05 was considered statistically significant

RESULTS

A total of 204 individuals were evaluated for eligibility to participate in this research. Out of them, 16 individuals did not match the required requirements, and 8 patients declined to take part in the work. The remaining individuals were allocated at random to three groups equally, with 60 participants in each category [Figure 1]. The patients' characteristics and length of operation did not show any significant variations among the three groups, as shown in [Table 1].

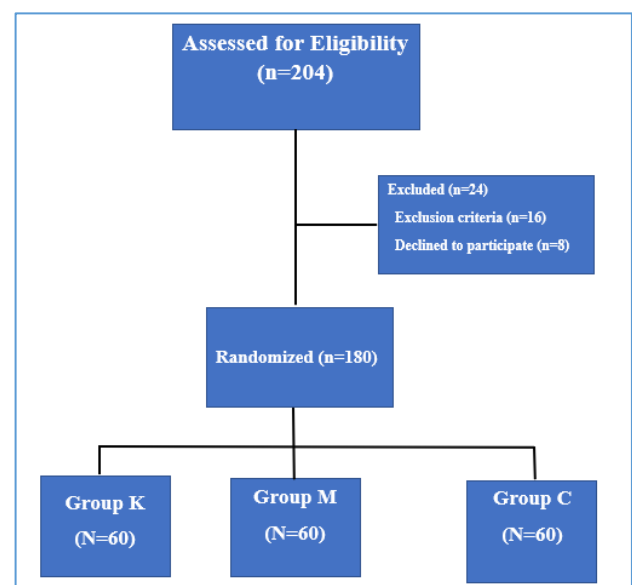


Figure [1]: Flow chart of the studied patients.

HR measurements were insignificantly different at baseline, 3min, 6min, 9min, 70min, 80min and 90min and were significant different at 12 min, 15min, 20min, 30min, 40min, 50min and 60min [P value <0.001]. HR measurements were significantly elevated in group K in contrast to group M and group C and had been significantly decreased in group M in contrast to group C at 20min, 30min, 40min, 50min and 60min [P value <0.05] [Table 2]. Mean arterial blood pressure [MAP] measurements were insignificantly different at baseline, 3min, 6min, 9min, 70min, 80min and 90min and were significant different at 12min, 20min, 30min, 40min, 50min and 60min [P value <0.001]. MAP measurements were significantly elevated in group K in contrast to group M and group C and were significantly decreased in group M in contrast to group C at 9min,

12min, 20min, 30min, 40min, 50min and 60min [P value <0.05] [Table 3]. Temperature measurements were insignificantly different at baseline and 90min and were significant different at immediately after the spinal anesthesia, 30min and 60min [P value <0.001]. Temperature measurements were significantly decreased in group M in contrast to group K and group C and were significantly decreased in group M in contrast to group C at immediately after the spinal anesthesia, 30min and 60min [P value <0.05] [Table 4]. Frequency of shivering was insignificantly different Immediately after spinal anesthesia, 5min, 10min, 15min and 90min and was significantly lower in group K than group M and group C and was significantly decreased in group M than group C [P value <0.05] [Table 5]. Complications were insignificantly distinct between all groups [Table 6].

Table [1]: Patients' characteristics and duration of surgery of the groups under the study

		Group K [n=60]	Group M [n=60]	Group C [n=60]	P value
Age [years]	Mean ± SD; [Min. – Max.]	40.8 ± 0.53; 22-58	39.5 ± 11.3; 21-59	42.9 ± 9.53; 24-58	0.215
Gender	Male	40 [66.67%]	34 [56.67%]	36 [60%]	0.520
	Female	20 [33.33%]	26 [43.33%]	24 [40%]	
Weight [kg]	Mean ± SD; [Min. – Max.]	71.4±8.28; 58-90	69.9 ± 11.14; 53-89	70.3 ± 9.12; 55-88	0.680
Height [m]	Mean ± SD; [Min. – Max.]	1.65 ± 0.08; 1.53-1.77	1.68 ± 0.08; 1.55-1.8	1.67 ± 0.07; 1.56-1.78	0.113
BMI [kg/m ²]	Mean ± SD; [Min. – Max.]	26.4 ± 3.9; 19.9-33.9	24.9 ± 4.04; 17.6-32	25.3 ± 3.64; 17.4-31.6	0.097
Surgery Duration [min]	Mean ± SD; [Min. – Max.]	80.1 ± 7.16; 70-90	77.9 ± 8.94; 65-90	78.3 ± 7.35; 70-90	0.279

Table [2]: Heart rate measurements of the studied groups

	Group K [n=60]	Group M [n=60]	Group C [n=60]	P value	Post hoc
Baseline	83.07±10.42	84.75±8.3	81.65±11.66	0.253	
3min	81.28±10.57	83.3±8.35	80.17±11.6	0.240	
6min	79.97±10.76	82.22±8.26	79.72±11.75	0.349	
9min	78.35±10.57	79.72±8.54	76.78±11.74	0.303	
12min	87.4±10.95	81.63±9.39	76.03±11.24	<0.001*	P1=0.009*; P2<0.001*; P3=0.011*
15min	85.4±10.95	79.27±9.21	74.75±9.98	<0.001*	P1=0.003*; P2<0.001*; P3=0.040*
20min	82.08±11	68.93±6.96	75.5±10.15	<0.001*	P1<0.001*; P2<0.001*; P3<0.001*
30min	84.08±10.52	71.13±7.18	77.03±10.73	<0.001*	P1<0.001*; P2<0.001*; P3=0.003*
40min	79.2±10.34	68.75±6.93	74.45±10.2	<0.001*	P1<0.001*; P2=0.016*; P3=0.003*
50min	80.27±10.85	70.17±6.49	74.52±9.66	<0.001*	P1<0.001*; P2=0.002*; P3=0.028*
60min	76.78±10.91	67.92±5.66	72.13±9.16	<0.001*	P1<0.001*; P2=0.012*; P3=0.026*
70min	72.07±9.51	69.2±6.48	71.15±8.68	0.195	
80min	72.63±9.65	70.17±6.86	72.2±8.15	0.477	
90min	71.69±9.77	71.93±6.88	74.33±8.34	0.737	

Table [3]: Mean arterial blood pressure measurements of the studied groups

	Group K [n=60]	Group M [n=60]	Group C [n=60]	P value	Post hoc
Baseline	94.83±14.49	91.58±11.11	95.67±12.55	0.184	
3min	93.75±14.68	90.45±11.38	94.27±12.58	0.219	
6min	93.75±15	89.53±11.52	93.78±12.53	0.127	
9min	92.8±15.96	87.15±11.82	90.65±12.56	0.073	
12min	91.67±15.6	80.38±11.72	85.62±12.52	<0.001*	P1<0.001*; P2=0.020*; P3=0.019*
15min	91.02±15.49	80.4±11.83	85.13±12.52	<0.001*	P1<0.001*; P2=0.023*; P3=0.035*
20min	93.02±15.07	79.03±12.05	85.43±12.44	<0.001*	P1<0.001*; P2=0.006*; P3=0.024*
30min	93.4±15.23	81.2±12.28	87.37±12.84	<0.001*	P1=0.003*; P2=0.041*; P3=0.035*
40min	91±15.45	78.3±12.73	84.48±13.23	<0.001*	P1=0.001*; P2=0.029*; P3=0.041*
50min	90.62±15.43	76.97±12.84	84.43±12.93	<0.001*	P1<0.001*; P2=0.040*; P3=0.010*
60min	87.78±15.35	75.5±11.99	81.58±12.73	<0.001*	P1<0.001*; P2=0.033*; P3=0.037*
70min	84.63±14.41	80.19±12.05	80.1±12.3	0.101	
80min	83.34±11.38	78.23±11.92	81.3±12.26	0.225	
90min	86±11.05	84.64±11.49	82±14.78	0.752	

Table [4]: Temperature measurements of the studied groups

	Group K [n=60]	Group M [n=60]	Group C [n=60]	P value	Post hoc
Baseline	37.1±0.44	37.06±0.28	37.19±0.28	0.099	
Immediately after anesthesia	37.05±0.45	36.66±0.26	36.82±0.38	<0.001*	P1<0.001*; P2=0.003*; P3=0.048*
30min	36.87±0.42	36.46±0.29	36.65±0.29	<0.001*	P1<0.001*; P2=0.001*; P3=0.010*
60min	36.7±0.45	36.28±0.31	36.51±0.27	<0.001*	P1<0.001*; P2=0.013*; P3<0.001*
90min	36.72±0.47	36.54±0.48	36.62±0.35	0.586	

Table [5]: Incidence of shivering of the groups under the study

	Group K [n=60]	Group M [n=60]	Group C [n=60]	P value		
Immediately after anesthesia	None[0]	56 [93.33%]	50 [83.33%]	48 [80%]	0.082	
	Mild[1]	3 [5%]	5 [8.33%]	10 [16.67%]		
	Moderate[2]	1 [1.67%]	5 [8.33%]	2 [3.33%]		
	Severe[3]	0 [0%]	0 [0%]	0 [0%]		
5min	None[0]	52 [86.67%]	48 [80%]	46 [76.67%]	0.472	
	Mild[1]	5 [8.33%]	4 [6.67%]	9 [15%]		
	Moderate[2]	3 [5%]	7 [11.67%]	4 [6.67%]		
	Severe[3]	0 [0%]	1 [1.67%]	1 [1.67%]		
10min	None[0]	50 [83.33%]	47 [78.33%]	42 [70%]	0.502	
	Mild[1]	6 [10%]	4 [6.67%]	9 [15%]		
	Moderate[2]	3 [5%]	6 [10%]	7 [11.67%]		
	Severe[3]	1 [1.67%]	3 [5%]	2 [3.33%]		
15min	None[0]	49 [81.67%]	44 [73.33%]	41 [68.33%]	0.307	
	Mild[1]	8 [13.33%]	7 [11.67%]	7 [11.67%]		
	Moderate[2]	3 [5%]	7 [11.67%]	8 [13.33%]		
	Severe[3]	0 [0%]	2 [3.33%]	4 [6.67%]		
20min	None[0]	52 [86.67%]	46 [76.67%]	38 [63.33%]	0.049*	
	Mild[1]	7 [11.67%]	8 [13.33%]	10 [16.67%]		
	Moderate[2]	1 [1.67%]	5 [8.33%]	9 [15%]		
	Severe[3]	0 [0%]	1 [1.67%]	3 [5%]		
30min	None[0]	52 [86.67%]	42 [70%]	36 [60%]	0.030*	
	Mild[1]	3 [5%]	6 [10%]	13 [21.67%]		
	Moderate[2]	5 [8.33%]	10 [16.67%]	9 [15%]		
	Severe[3]	0 [0%]	2 [3.33%]	2 [3.33%]		
40min	None[0]	53 [88.33%]	42 [70%]	38 [63.33%]	0.034*	
	Mild[1]	5 [8.33%]	11 [18.33%]	9 [15%]		
	Moderate[2]	2 [3.33%]	6 [10%]	12 [20%]		
	Severe[3]	0 [0%]	1 [1.67%]	1 [1.67%]		
50min	None[0]	51 [85%]	42 [70%]	34 [56.67%]	0.014*	
	Mild[1]	5 [8.33%]	9 [15%]	7 [11.67%]		
	Moderate[2]	3 [5%]	7 [11.67%]	16 [26.67%]		
	Severe[3]	1 [1.67%]	2 [3.33%]	3 [5%]		
60min	None[0]	48 [80%]	41 [68.33%]	37 [61.67%]	0.018*	
	Mild[1]	6 [10%]	9 [15%]	3 [5%]		
	Moderate[2]	5 [8.33%]	7 [11.67%]	18 [30%]		
	Severe[3]	1 [1.67%]	3 [5%]	2 [3.33%]		
90min	None[0]	11 [84.62%]	8 [57.14%]	5 [55.56%]	0.704	
	Mild[1]	2 [15.38%]	3 [21.43%]	2 [22.22%]		
	Moderate[2]	0 [0%]	3 [21.43%]	2 [22.22%]		
	Severe[3]	0 [0%]	0 [0%]	0 [0%]		
Overall		14 [23.3%]	24 [40%]	31 [51.7%]	<0.001*	P1=0.049*; P2<0.001; P3=0.021

Table [6]: Complications of the studied groups

		Group K [n=60]	Group M [n=60]	Group C [n=60]	P value
Bradycardia	Yes	2 [3.33%]	7 [11.67%]	5 [8.33%]	0.230
	No	58 [96.67%]	53 [88.33%]	55 [91.67%]	
Hypotension	Yes	5 [8.33%]	30 [50%]	24 [40%]	<0.001*
	No	55 [91.67%]	30 [50%]	36 [60%]	
PONV	Yes	6 [10%]	11 [18.33%]	15 [25%]	0.098
	No	54 [90%]	49 [81.67%]	45 [75%]	

DISCUSSION

Postoperative shivering is a frequently seen consequence following regional and general anesthesia. It is an uncomfortable and distressing experience for patients that may worsen postoperative pain [2].

No significant differences as regard characteristics of participants and duration of surgery, operative vital signs and medical history. Regarding HR and MAP measurements were insignificantly different.

Seyam [6] investigated the role of a sub-anesthetic dosage of ketamine [K] on the occurrence of hypotension among women having cesarean sections with spinal anesthesia. The K group had a substantially decreased total ephedrine dosage. The incidence of mild hypotension and severe hypotension was much lower in the K group in contrast to the control group. Participants in the control group had mild hypotension, while 55% of this group experienced severe hypotension.

Contrary to the present investigation, **Bhiwal et al.** [8] examined the impact of a sub-anesthetic bolus dosage of an IV ketamine on postoperative pain after a cesarean section. A sample size of 108 individuals was split into three groups. Group C got a 2 ml dose of 0.9% normal saline. Group Ka received a dose of 0.15 mg/kg of ketamine [2 ml], whereas Group Kb received a dose of 0.3 mg/kg of ketamine [2 ml]. There was no notable disparity in the average MAP and HR during surgery at various time intervals among all groups. The occurrence of low blood pressure and the need for ephedrine were not shown to have a statistically meaningful impact. This may be attributed to the reduced dosage of ketamine administered.

Temperature measurements were insignificantly different at baseline and 90min and were significant different at immediately after the spinal anesthesia, 30min and 60min. Temperature measurements were significantly elevated in group K in contrast to group M and group C and were significantly decreased in group M in contrast to group C at immediately after the spinal anesthesia, 30min and 60min.

Contrary to the present investigation **Lema et al.** [9] conducted a research that comprised 123 participants classified as ASA I and II, aging from 18 to 39 years, who had cesarean delivery. Participants were assigned at random to one of three groups: group S [n=41; control group] got saline, group K [n=41] was given ketamine 0.2 mg/kg, and group T [n=41] was tramadol 0.5 mg/kg.

A significant reduction in tympanic temperature had existed in all groups following the administration of anesthesia compared to the initial measurements. The temperature fluctuations over time within each group exhibited statistical significance; yet there were no notable variations seen across the groups.

Ketamine showed more effect than magnesium sulphate in decreasing the incidence and delaying the onset of shivering. In addition, the work by **Ameta et al.** [10] contrasting Ketamine, dexmedetomidine and tramadol in control of post-spinal shivering on individuals undergone lower limb and abdomen surgeries showed contrasting results as the frequency of shivering in the K group was 46% in contrast to 50% in the T group, 24% in the D group and 42% in the control group. This result is despite using the same dose and method of administration of K [0.5 mg/kg diluted in 100 ml and received over 10 minutes]. The only notable difference is the type of surgery.

In agreement, the work conducted by **Sachidananda et al.** [11] showed a statistically significant decrease in the frequency of shivering among individuals who was given a Magnesium dosage of 30mg/kg, with a rate of 39%, in contrast to the control group who was given normal saline and had a rate of 67.5%.

The frequency of vomiting as well as nausea did not vary significantly across the three groups. In a work conducted by **Modir et al.** [13] revealed that the ketamine group had a reduced occurrence of vomiting and nausea contrasted to the placebo group.

In addition, **Seyam** [6] found no significant variation in the frequency of vomiting and nausea among the ketamine group and the placebo control group [22% vs 28%]. The regulation of room temperature and the IV fluids temperature was not precise. The study is not multicentre.

Conclusion:

Administering Ketamine at a dosage of 0.5 mg/kg, diluted in 100 ml of normal saline, over a 10minute period as a preventive measure is more effective compared to administering Magnesium sulphate at a dosage of 50 mg/kg, diluted in 100 ml of normal saline, over a period of 10 minutes in managing shivering after spinal anesthesia.

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