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Research Article

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A Comparison of Two Different Doses of Magnesium Sulfate on Hemodynamic Stability During Induction and Orotracheal Intubation in Adult Patients with Diabetes

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Abstract

Background: *General anesthesia induction and tracheal intubation are associated with hemodynamic effects, which are issues in patients with diabetes.*

Objective: *This study compared the effect of two doses of magnesium sulfate on hemodynamic stability during induction and orotracheal intubation in adult patients with diabetes.*

Methods: *Fifty male and female patients with diabetes (ASA II, 40–65 years) undergoing elective surgery under general anesthesia were included. Patients received either 30 mg/kg (M30, n=25) or 50 mg/kg (M50, n=25) intravenous magnesium sulfate added to 100 mL of normal saline 15 min before induction of general anesthesia. After induction of general anesthesia, an oral endotracheal tube was inserted.*

Results: *Heart rate in both groups increased after induction of anesthesia and at 1, 5, and 10 min after intubation (heart rate increased more in the M50 group). Systolic and diastolic blood pressure in both groups decreased after induction of anesthesia and at 1, 5, and 10 min after intubation (the M50 group had larger reduction). These differences were not significant.*

Conclusion: *Both doses of IV magnesium sulfate administered 15 min before induction of general anesthesia maintained hemodynamic stability during induction and orotracheal intubation in adult patients with diabetes.*

Keywords: Magnesium Sulfate, Hemodynamic Stability, Diabetes

Introduction

The induction of general anesthesia and tracheal intubation have significant hemodynamic effects; the increase in sympathetic hormones during intubation can lead to complications in high-risk patients, with resultant increase in morbidity and mortality [1,2]. These responses are of concern in patients with diabetes, due to autonomic neuropathy that can alter the hemodynamic response to induction and intubation [3,4].

Magnesium decreases the blood pressure by many mechanisms. It inhibits catecholamine release from the adrenal medulla and peripheral nerve endings, and directly blocks catecholamine receptors, which leads to sympathetic block and indirect dilation of the blood vessels [5]. Furthermore, it can induce endothelium-derived nitric oxide production, which has a vasodilatory effect [6]. It also acts as a vasodilator by increasing prostacyclin synthesis and inhibiting angiotensin-converting enzyme activity by its blocking effects on calcium channels and N-methyl-D-aspartate receptors [7,8].

Puri et al found that magnesium was effective in attenuating the pressor response to endotracheal intubation and results in fewer ST changes in patients with coronary artery disease presenting for coronary artery bypass grafting [9].

The aim of this study was to evaluate the effect of magnesium sulfate on hemodynamic stability during induction of anesthesia and orotracheal intubation in adult patients with diabetes undergoing elective surgeries under general anesthesia.

Patients and Methods

Study Design and Setting.With approval of the ethics committee, the study was registered at www.AZNCTR clinical trial registry, registration number: ACTRN12614001012662. Written informed consent was obtained from 50 male and female patients (ASA II, 40–65 years of age) with controlled type II diabetes mellitus scheduled for elective surgery under general anesthesia requiring orotracheal intubation from November 2015 to November 2016.Patients were excluded from the study if they had history of type I diabetes mellitus, hypertension, cardiac disease, hypomagnesemia or hypermagnesemia; a known allergy to the study drugs; neuromuscular, liver and renal

diseases; suspected difficult intubation (El-Ganzouri multivariate risk index) or history of difficult intubation; prolonged intubation attempt (longer than 30 s); more than one intubation attempt required; and body mass index >30 kg/m2. Patients undergoing cardiac and neurosurgical procedures were also excluded.

Randomization and Concealment

The patients were randomly divided using a closed envelope randomization method into one of two groups. The M30 group (n=25) received IV magnesium sulfate 30 mg/kg added to 100 mL of normal saline over 15 min before induction of general anesthesia. The M50 group (n=25) received IV magnesium sulfate 50 mg/kg added to 100 mL of normal saline over 15 min before induction of general anesthesia.

Study Procedures

Preoperatively, patient history was obtained, and patients underwent physical examination and routine investigations including electrocardiogram (ECG), complete blood count, and liver and kidney functions.

The presence or absence of autonomic neuropathy was investigated by taking the history for symptoms of autonomic neuropathy (resting tachycardia, and noting the cardiovascular response to Valsalva's maneuver, deep breathing, potential hypotension. The tests were conducted in the ward, one day before surgery; a positive response to two of the tests was considered to indicate presence of autonomic neuropathy.

On arrival to the operating theatre, an 18 G intravenous cannula was inserted and intravenous (IV) crystalloid fluids were infused. Patients were attached to ECG, noninvasive arterial blood pressure, and pulse oximetry monitors. Patients were preoxygenated for 3–5 min with 100% oxygen 5 L/min by facemask, then anesthesia was induced with IV propofol (2 mg/kg slowly), fentanyl (2 µg/kg), and atracurium (0.5 mg/kg). Patients were ventilated manually with sevoflurane 2%, and oxygen 100% 5 L/min via a face mask for 3 min; then, an oral cuffed polyvinyl chloride endotracheal tube was inserted by an expert anesthesiologist. Muscle relaxation was monitored by a nerve stimulator (Life-Tech EZstim II).

Hypotension (decreased blood pressure more than 20% of the baseline) was treated with volume replacement and ephedrine as indicated. Persistent hypertension (increased blood pressure more than 20% of baseline) was treated with deepening of anaesthesia , propofol or IV nitroglycerin. Tachycardia (HR more than 120 B/min) was treated with IV boluses of isoptine at dose of 0.2 to 0.3 mg/kg slowly IV. Bradycardia (HR less than 50 B/min) was treated with 0.5 mg atropine IV.

At the end of surgery, neuromuscular blockade was reversed with IV neostigmine 0.04 mg/kg and atropine 0.02 mg/kg. The trachea was extubated when the patient responded to commands; all patients were transferred to the post-anesthesia care unit.

The following parameters were evaluated and recorded by the senior anesthesiologist who was blinded to the study protocol:

1. Demographic data: age, sex, weight, height;
2. The expired fraction of sevoflurane at the time of tracheal intubation; and
3. The systolic, diastolic, and mean arterial blood pressure, as well as heart rate:

-before the administration of the study drug at baseline;
-after induction of anesthesia; and
-at 1, 5, and 10 min following tracheal intubation and before skin incision.

Statistical Methods

Data are presented as mean ± standard deviation (SD), median (range), or numbers as appropriate. Student's t test was used for comparison between means of two groups, and the Mann–Whitney U test was used to analyze nonparametric data. P values <0.05 was considered statistically significant. Statistical Package for Social Science (SPSS) software version 17 was used.

Sample size calculation was conducted after a pilot study in five patients using the comparison of systolic blood pressure at 1 min after intubation between M30 and M50 groups. In the M30 group, mean ± SD systolic blood pressure at 1 min after intubation was approximately 136.2 ± 5.4 mmHg, while in the M50 group, it was approximately 116 ± 17.2 mmHg. Accordingly, we calculated that the minimum acceptable sample size to be able to detect a real difference of 20 mmHg with 95% power at $\alpha = 0.05$ level using Student's t test for independent samples would be 22 participants in each group. We increased the number to 25 patients in each group to compensate in case of exclusion of any case. Sample size calculation was conducted using Stats Direct statistical software version 2.7.2 for MS Windows, Stats Direct Ltd., Cheshire, United Kingdom.

Results

Two patients were excluded from the M30 group and one patient from the M50 group because intubation required a second attempt due to unsuspected difficult intubation (Figure 1). There were no significant differences in demographic data between the two groups (Table 1).

Table 1: Demographic data and presence of autonomic neuropathy

Variables	M 30 group (n = 23)	M 50 group (n =24)	p-value
Age (years)	48.96±5.48	49.6±7.34	0.72
Weight (Kg)	82.04±6.85	81.76±8.62	0.89
Height (cm)	160.4±4.98	161.92±5.48	0.31
Sex (male/female)	12/11	10/14	
autonomic neuropathy n (%)	4 (17%)	5 (20%)	

M 30 group : magnesium sulfate 30 mg/kg
M 50 group : magnesium sulfate 50 mg/kg
No statistically significant difference between the study groups. P value> 0.05

The mean expired fraction of sevoflurane at the time of tracheal intubation was 1.1 in the M30 group and 1.2 in the M50 group (the difference was not significant).

Mean heart rate in the two groups increased after induction of anesthesia and at 1, 5, and 10 min after intubation; the increase was higher in the M50 group than in the M30 group, but the difference was not statistically significant at any time point. In the M30 group,

heart rate was statistically significantly higher after induction of anesthesia and at 1 min after intubation compared with baseline. In the M50 group, heart rate was significantly higher after induction of anesthesia and at 1, 5, and 10 min after intubation compared with baseline (Table 2).

Systolic arterial blood pressure in the two groups decreased after induction of anesthesia and at 1, 5, and 10 min after intubation; it was lower in the M50 group than in the M30 group, but the difference was not significant. However, systolic arterial blood pressure was significantly lower in both groups compared with the baseline reading (Table 2).

Table 2: Heart Rate (Bpm), systolic, diastolic and Mean arterial blood pressure (mmHg), between study groups. Data are presented asmean ± SD.

	M 30 group (n = 23)	M 50 group (n =24)	p-value
Heart Rate Preoperative	80.56±7.48	78.96±6.71	0.4
After induction of Anesthesia	85.12±7.48*	86.88±8.23*	0.43
1 minute After ETT	86.76±6.02*	87.28±6.75*	0.77
5 min After ETT	82.72±13.44	84.32±4.75*	0.57
10 min After ETT	81.84±12.24	83.92±4.68*	0.43
Systolic arterial blood pressure			
Preoperative	134.44±10.42	137.52±12.10	0.33
After induction of Anesthesia	125.32±5.04*	124.08±7.63*	0.50
1 minute After ETT	129.2±12.52*	126.56±17.95*	0.54
5 min After ETT	120.64±11.75*	116.04±15.58*	0.24
10 min After ETT	121.44±12.51*	118.52±10.52*	0.37
diastolic arterial blood pressure			
Preoperative	83.04±9.04	81.36±12.30	0.58
After induction of Anesthesia	70.92±8.15*	69.56±5.62*	0.49
1 minute After ETT	79.56±9.92	77.84±10.13	0.54
5 min After ETT	73.6±10.43*	70.44±8.89*	0.25
10 min After ETT	74.32±9.24*	71±8.15	0.18
Mean arterial blood pressure			
Preoperative	94.16±11.58	96.84±11.34	0.41
After induction of Anesthesia	88.4±11.15	82.88±13.57*	0.12
1 minute After ETT	89.44±11.46	85.68±10.63*	0.23
5 min After ETT	87.24±11.01*	84.56±9.55*	0.36
10min After ETT	86.16±10.29*	83.44±9.12*	0.32

M 30 group: magnesium sulfate 30 mg/kg
M 50 group: magnesium sulfate 50 mg/kg

Bpm=beat per minute
*Statistically significant compared to the base line within the same group, p value < 0.05

No statistically significant difference between the study groups. P value> 0.05.

Diastolic arterial blood pressure in the two groups decreased after induction of anesthesia and at 1, 5, and 10 min after intubation; it was lower in the M50 group than in the M30 group, but the difference was not statistically significant. However, diastolic arterial blood pressure was statistically significantly lower in both groups at 5 and 10 min after intubation compared with the baseline reading (Table 2).

Mean arterial blood pressure in the two groups decreased after induction of anesthesia and at 1, 5, and 10 min after intubation; it was lower in the M50 group than in the M30 group, but the difference was not statistically significant. Mean arterial blood pressure was statistically significantly lower in both groups at 5 and 10 min after intubation compared with the baseline reading; in the M30 group, it was statistically significantly lower at 1 and 5 min after intubation compared with base line, and in the M50 group, it was statistically significantly lower after induction of anesthesia and at 1, 5, and 10 min after intubation compared with base line (Table 2).

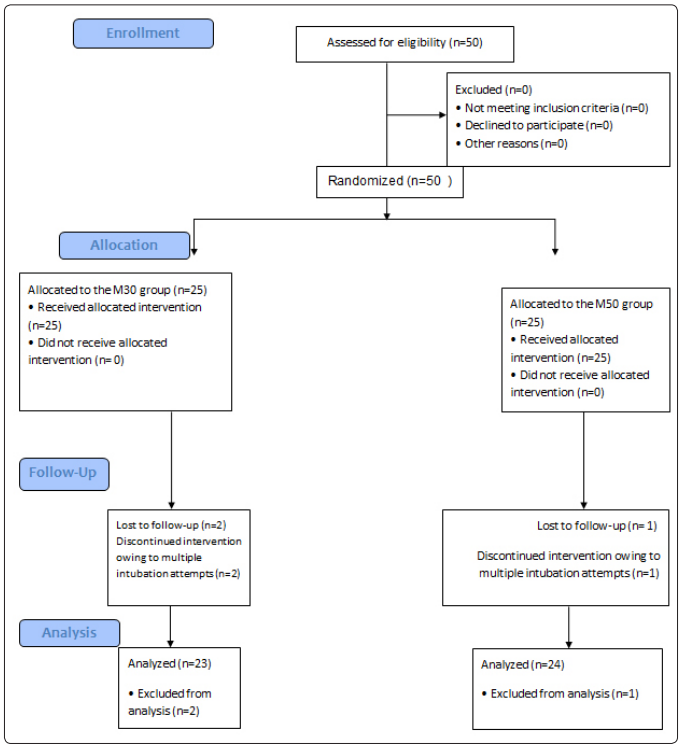
The percent change in the heart rate, as well as systolic, diastolic, and mean arterial blood pressures are shown in Table 3.

Table 3: The % Change in the heart rate, systolic, diastolic and mean arterial blood pressure

	M 30 group (n=23)	M 50 group (n=24)
Heart Rate		
After induction of Anesthesia	4.56(5.7%)	7.92(10.0%)
1 minute After ETT	6.2(7.7%)	8.32(10.5%)
5 min After ETT	2.16(2.7%)	5.36(6.8%)
10min After ETT	1.28(1.6%)	4.96(6.3%)
Systolic arterial blood pressure		
After induction of Anesthesia	-9.12(-6.8%)	-13.44(-9.8%)
1 minute After ETT	-5.24(-3.9%)	-10.96(-8.0%)
5 min After ETT	-13.8(-10.3%)	-21.48(-15.6%)
10 min After ETT	-13(-9.7%)	-19(-13.8%)
Diastolic arterial blood pressure		
After induction of Anesthesia	-12.12(-14.6%)	-11.8(-14.5%)
1 minute After ETT	-3.48(-4.2%)	-3.52(-4.3%)
5 min After ETT	-9.44(-11.4%)	-10.92(-13.4%)
10 min After ETT	-8.72(-10.5%)	-10.36(-12.7%)
Mean arterial blood pressure		
After induction of Anesthesia	-5.76(-6.1%)	-13.96(-14.4%)
1 minute After ETT	-4.72(-5.0%)	-11.16(-11.5%)
5 min After ETT	-6.92(-7.3%)	-12.28(-12.7%)
10min After ETT	-8(-8.5%)	-13.4(-13.8%)

M30 group: magnesium sulfate 30 mg/kg; M50 group: magnesium sulfate 50 mg/kg; ETT: endotracheal tube

Figure 1: Flow Diagram



Discussion

The results of the present study showed that administration of intravenous magnesium sulfate 30 mg/kg and 50 mg/kg before induction of general anesthesia maintained hemodynamic stability during induction and orotracheal intubation in adult patients with diabetes. Systolic, diastolic, and mean arterial blood pressures in the two groups decreased after induction of anesthesia and at 1, 5, and 10 min after intubation, and were lower in the M50 group than in the M30 group.

Direct laryngoscopy and intubation are the most stressful periods during induction of anesthesia [10]. Endotracheal intubation is associated with hemodynamic changes; it causes sympathetic stimulation that results in hypertension and tachycardia that can last for 5–10 min [11,12].

Many drugs have been used to control hemodynamic responses during induction of anesthesia and intubation [13]. Magnesium is a vasodilator with minimal myocardial depression [14]. It has direct vasodilating effect on coronary arteries and inhibits catecholamine release, thus attenuating the hemodynamic responses during intubation [15]. During intubation, magnesium pretreatment (30–50 mg/kg IV) is associated with a good control of the adrenergic response [16]. The preventive effect of magnesium sulfate on hemodynamic stability has been studied [17].

Different doses of magnesium sulfate have been used by different authors to attenuate the hemodynamic response to endotracheal intubation [18-20]. *Puri et al* [9], in their study on patients with coronary artery disease scheduled for elective coronary artery bypass grafting receiving magnesium sulfate (50 mg/kg) before induction of anesthesia, observed a rise in the heart rate and a significant reduction in mean arterial blood pressure compared with patients administered lidocaine [9].

Nooraei et al, in their study of patients who received 60 mg/kg magnesium sulfate or lidocaine before intubation, showed that systolic blood pressure increased compared with the baseline value in the two groups [21]. The increase in diastolic blood pressure was not significant; however, mean arterial pressure increased in the magnesium sulfate group by 1 min after intubation, versus 2 min in the lidocaine group, which was significantly different. The heart rate showed no significant difference after intubation between the two groups.

Autonomic neuropathy occurring in patients with diabetes [4] may cause hemodynamic instability during induction of anesthesia [22]. ***Khan and Khan*** compared the hemodynamic response to induction of anesthetic and intubation in patients with diabetes and patients without diabetes [4]. They reported that systolic blood pressure dropped by 9% after induction and raised by 16% after intubation in patients without diabetes compared with a 12% drop after induction and a 10% rise after intubation in patients with diabetes. Diastolic blood pressure showed no difference; it increased by 27% in patients without diabetes compared with 22% in patients with diabetes. The heart rate increased by 27% in patients without diabetes compared with 17% in patients with diabetes after intubation. A study by *Parish et al* comparing hemodynamic responses to endotracheal intubation in patients with and without diabetes reported no significant differences [22]. They concluded that hemodynamic stability is maintained during induction and intubation in patients with diabetes, and that the presence of autonomic neuropathy did not result in hemodynamic instability.

Conclusion

Either dose of IV magnesium sulfate (30 mg/kg and 50 mg/kg) before induction of general anesthesia maintained hemodynamic stability during induction and orotracheal intubation in adult patients with diabetes.

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