RESEARCH ARTICLE

The Effect Comparison of Two Injections Doses of Magnesium Sulfate on Hemodynamic Changes Caused by Laryngoscopy and Endotracheal Intubation in Caesarean Patients with General Anesthesia

Anahita Hirmanpour[1], Mohammadreza Safavi[1]*, Reihanak Talakoub[1], Azim Honarmand[1], Marjan Ghasri[1], Navid Chitsaz[1]

Background: The aim of this study was to evaluate the effect of two injections doses of magnesium sulfate for controlling and reducing hemodynamic changes caused by laryngoscopy and endotracheal intubation in pregnant women who were candidates for caesarean section with general anesthesia.

Methods: In this controlled randomized double-blind clinical trial, 165 pregnant women who were candidates for caesarean section were allocated into three groups of receiving 40mg/kg of magnesium sulfate (M1 group), 60 mg/kg of magnesium sulfate (M2 group) and placebo (P group) before induction of anesthesia. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean of arterial pressure (MAP), heart rate (HR) and arterial oxygen saturation (SPO2) were measured and recorded at the baseline (before the induction), right before the intubation and 1, 3, 5 and 10 minutes after laryngoscopy and endotracheal intubation. The Apgar score of the neonates was also measured and recorded 1 and 5 minutes after delivery.

Results: The mean of changes in systolic blood pressure and mean of arterial pressure showed a significant difference between the M1 and M2 groups with the placebo group right before the intubation and 1, 3 and 10 minutes after laryngoscopy. The mean of changes in heart rate was specifically significant 1, 5 and 10 minutes after intubation in the M2 group ($p < 0.05$). The Apgar score of neonates had no significant difference 1 and 5 minutes after delivery ($p > 0.05$).

Conclusion: For inducing anesthesia in pregnant women, using 60 mg/kg of magnesium sulfate decreased the hemodynamic changes after laryngoscopy and endotracheal intubation and it had no adverse effect on the Apgar score of the neonates.

Keywords: caesarean section; general anesthesia; laryngoscopy; magnesium sulfate

Laryngoscopy and endotracheal intubation, like any other interventional procedure, would lead to stress response and release of catecholamine to patient's blood flow; this condition is transient and harmless in patients with nor cardiovascular diseases [1]. These effects, including sudden increase in heart rate and systolic blood pressure, could cause left ventricular failure, myocardial ischemia, cerebral hemorrhage, pulmonary edema and increased intracranial pressure in patients with history of blood pressure, ischemic heart diseases, valvular heart disease, cerebral vascular diseases, pheochromocytoma and preeclampsia [2-3]. Different drugs have been studied for reducing these effects including adrenergic receptors blockers [4], narcotics [5-6], sodium channel blockers [7], vasodilators [8-9], gabapentin [10] and other drugs like paracetamol [11] and lidocaine [12].

Magnesium sulfate, which is known as an anticonvulsant drug for preeclampsia, has been studied in different doses for reducing stress response after laryngoscopy and endotracheal intubation among non-pregnant women [13-17] and its effectiveness for reducing hemodynamic changes after laryngoscopy with minimum side effects has been approved [18]; also its effectiveness has been compared to other drugs [6,19-20]. The effect of magnesium sulfate has also been studied on reduction of incidence of intraoperative awareness and increase of blood pressure during caesarean section [21]. The aim of the present study is evaluation of the effect of two intravenous injection doses of magnesium sulfate on hemodynamic changes caused by laryngoscopy and endotracheal intubation in patients undergoing caesarean section with general anesthesia.

Methods

This randomized double-blind clinical trial was conducted in Shahid Beheshti hospital on ASA I & II patients who

From the [1]Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

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*Corresponding author: Mohammadreza Safavi, MD. Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: safavi@med.mui.ac.ir

were candidates for caesarean section with general anesthesia, after being approved by the research committee of the faculty and taking permission from the ethics committee of the university. Patients who had nor types of myopathies, nor head or neck problems and nor cervical tumors, nor history of difficult laryngoscopy, nor diagnosed allergy to magnesium sulfate and have not received magnesium sulfate for any other diseases were selected for the study.

Patients who ought to have a changed method of anesthesia or the anesthesiologist not being able to intubate them with a Macintosh blade 3 laryngoscope, patients who were not suited for intubation and were mechanically ventilated through another methods, patients who had difficult grade 4 laryngoscopy and those who required more than 2 tries for intubation were excluded from the study.

Indications for general anesthesia in the studied patients were patient's unwillingness or refusal for performing regional anesthesia and decrease in patient's platelet count below 100000 without any associated complications like preeclampsia or HELLP syndrome.

The required sample size for each group in this study, considering a 95% confidence interval, 80% test power and 0.8 as the least meaningful difference between groups, was calculated to be 55. Patients were randomly allocated into three groups of receiving 40 mg/kg of magnesium sulfate, receiving 60 mg/kg of magnesium sulfate and control using randomized block design. Drugs were injected using identical syringes with similar capacities and the nurse who prepared the drugs was different from the one who injected them. After admission, patients were positioned supine with an appropriate wedge under right hip to prevent supine hypotension syndrome and monitored for electrocardiogram, blood pressure and arterial oxygen saturation. The two intervention groups were infused with 40 mg/kg and 60 mg/kg of magnesium sulfate and the control group was infused with normal saline. After prepping and draping the patient and surgeon's preparation and also after 3 minutes of pre-oxygenation with 100% oxygen and administration of 5 mg/kg of sodium thiopental and 1.5 mg/kg of succinylcholine, patient's laryngoscopy was conducted by an anesthesiologist with at least 5 years of experience using Macintosh 3 blade. Intubation was conducted for all the patients with tube no. 7 (with Sellick's maneuver) and patients were connected to anesthesia machine under controlled mechanical ventilation with normocapnia. Systolic blood pressure, diastolic blood pressure, mean of arterial pressure, heart rate and arterial oxygen saturation were measured and recorded for all the patients before the induction of anesthesia, right before endotracheal intubation and 1, 3, 5 and 10 minutes after intubation. The duration of surgery, which was from putting the patient on the operating table until closing up, the duration of extubation, which was stopping the anesthetics until extubation, and the duration of recovery, which was from patient's entrance to recovery until discharge from recovery according to Modified Aldrete score, were measured and recorded. Gathered data were analyzed with SPSS 22 (SPSS Inc., Chicago, IL, USA) using Chi square test, t test and variance analysis with repeated measures.

Results

In this study, 165 patients who were candidates for caesarean section and had the inclusion criteria were evaluated. Demographic characteristics and the time of surgery, anesthesia and recovery of all patients are shown in table 1. All of the above mentioned factors, except for age, had no significant difference between the groups (Table 1).

All of the vital signs of patients were measured and recorded before induction of anesthesia, right before intubation and 1, 3, 5 and 0 minutes after intubation.

Systolic and diastolic blood pressure had significant differences between all the measured times; meaning that the lowest mean of systolic and diastolic blood pressure belonged to the M2 group (receivers of 60 mg/kg of magnesium sulfate) and then the M1 group (receivers of 40 mg/kg of magnesium sulfate). From the third minute after intubation until the 10th minute, the mean of systolic blood pressure was decreased in all three groups; these changes were statistically significant at all times in the M2 group and at the 5th and 10th minutes in the M1 and the control groups.

Table 1- Frequency distribution of demographic characteristics and the mean duration of surgery, extubation and recovery for all the patients

Variable	M1 group	M2 group	Control group	P value
Age (year)	28.25 ± 0.63	29.44 ± 0.65	31.30 ± 0.67	0.005
Weight (kg)	84.47 ± 1.68	81.37 ± 9.19	82.79 ± 1.65	0.559
Height (cm)	161.13 ± 0.89	159.65 ± 0.93	162.24 ± 0.87	0.126
Body mass index (m2/kg)	32.44 ± 0.57	31.98 ± 0.62	31.44 ± 0.567	0.487
Duration of surgery (minutes)	59.35 ± 1.26	59.36 ± 1.15	57.36 ± 2.52	0.149
Duration of extubation (minutes)	6.67 ± 0.22	6.56 ± 0.25	6.84 ± 0.45	0.227
Duration of recovery (minutes)	59.34 ± 1.17	57.27 ± 1.52	56.18 ± 2.15	0.079

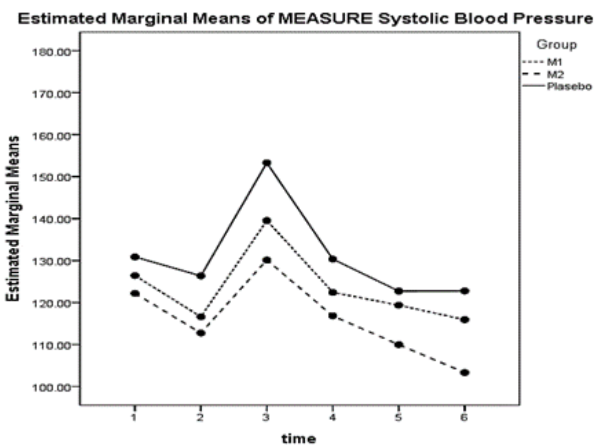
M1: receivers of 40 mg/kg of magnesium sulfate, M2: receivers of 60 mg/kg of magnesium sulfate; level of significant difference: $p < 0.05$.

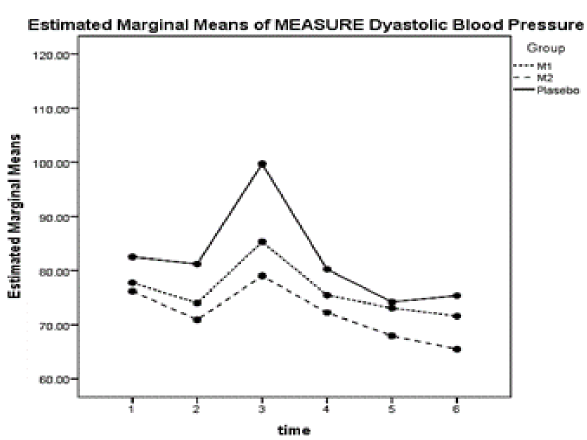
The mean of diastolic blood pressure was decreased right before intubation but this change was not significant in any groups compared to before the induction of anesthesia and it increased 1 minute after intubation and its change was statistically significant in the M1 and the control groups ($p < 0.05$). The highest rate of decrease in the mean of systolic and diastolic pressure compared to previous the induction of anesthesia was observed in the M2 group.

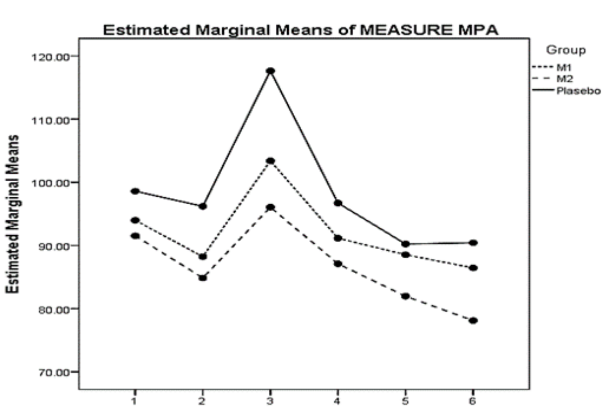
The mean of arterial pressure was significantly decreased right before intubation compared to the previous induction of anesthesia in the M1 and the M2 groups ($p < 0.05$) but in the control group this decrease was not significant ($p > 0.05$). The mean of arterial pressure was increased at the first minute after intubation and this change was significant in all three groups ($p < 0.05$). From the 3rd minute after intubation until the 10th minute, the mean of arterial pressure was decreased in all three groups and the decrease was significant compared to previous induction of anesthesia except for the third minute ($p > 0.05$). The highest rate of decreasing in the mean of arterial pressure compared to previous induction of anesthesia was observed in the M2 group.

The linear graph for the changes of systolic and diastolic blood pressure and the mean of arterial pressure at the studied time intervals are shown in (Figures 1-3).

Figure 1-3- The linear graph for the changes of the mean of systolic, diastolic and mean arterial blood pressure in all three groups, 1-before the induction of anesthesia, 2-right after intubation, 3- at the first, 4- the third, 5- the fifth and 6- the tenth minutes after the intubation

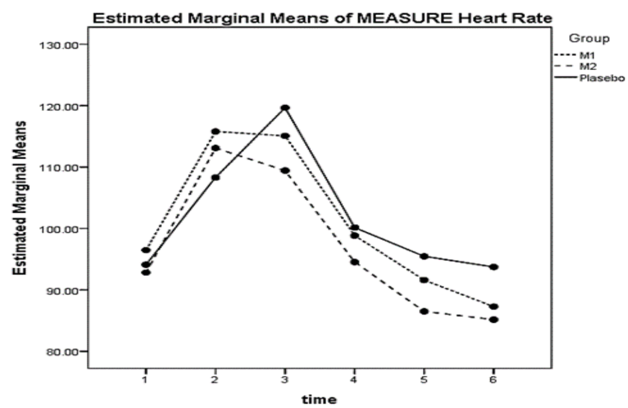






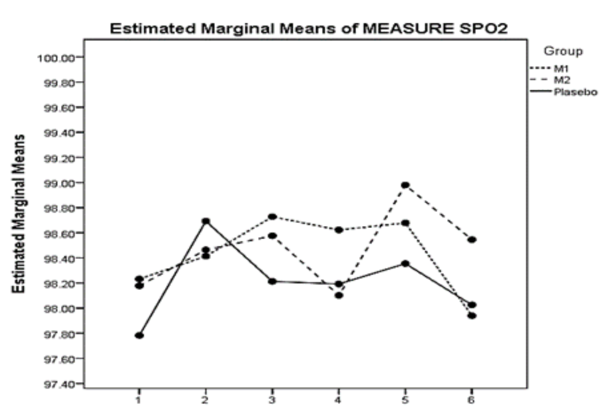
The mean of heart rate 1, 5 and 10 minutes after intubation, by controlling the effect of the variable of age, had a significant difference between all three studied groups ($p< 0.05$). In all the three groups, right before intubation and 1 minute after intubation the mean of heart rate was significantly increased ($p< 0.05$). The decrease in the mean of heart rate of the M1 and M2 groups was significant 3 and 5 minutes after intubation and it was also significant compared to the control group 3, 5 and 10 minutes after intubation; these changes are shown in (Figure 4).

Figure 4- The linear graph for the changes of the mean of heart rate in all three groups, 1-before the induction of anesthesia, 2-right after intubation, 3- at the first, 4- the third, 5- the fifth and 6- the tenth minutes after the intubation



As comparison of oxygen mean saturation at the studied time intervals showed that 1, 5 and 10 minutes after intubation, by controlling the effect of the variable of age, the meaning of oxygen saturation had a significant difference between all three groups ($p< 0.05$). The changes in the mean of arterial oxygen saturation in all three groups were not significantly different between all the studied time intervals ($p> 0.05$). Although it must be noted that the mean of arterial oxygen saturation of the M2 group had a significant increase 5 minutes after intubation compared to before the induction of anesthesia ($p< 0.05$). (Figure 5)

Figure 5- The linear graph for the changes of the mean of arterial oxygen saturation in all three groups, 1-before the induction of anesthesia, 2-right after intubation, 3- at the first, 4- the third, 5- the fifth and 6- the tenth minutes after the intubation.



The mean of Apgar score of neonates 1 and 5 minutes after delivery had no significant difference between the groups (Table 2).

Table 2- The comparison and mean of Apgar score of neonates 1 and 5 minutes after delivery in each group

	M1 group	M2 group	Control group	P value
Apgar score at the first minute	8.92 ± 0.26	8.91 ± 0.29	8.82 ± 0.38	0.168
Apgar score at the fifth minute	10 ± 0.00	9.98 ± 0.13	9.93 ± 0.26	0.071

M1: receivers of 40 mg/kg of magnesium sulfate, M2: receivers of 60 mg/kg of magnesium sulfate; Statistically significant differences: $p < 0.05$

Two side effects of bradycardia and hypotension did not occur for any of the study groups at any of the time intervals. The occurrence of hypertension was observed in the control group (5.45% right after intubation and 23.6% one minute after intubation) and the M1 group (1.8% one minute after intubation), but none of the patients required the injection of Labetalol for reducing their blood pressure. Before the induction of anesthesia, the frequency of occurrence of tachycardia had no significant difference between the three groups ($p > 0.05$) and, over time, from the second of intubation the frequency of tachycardia was significantly decreased in all three groups ($p < 0.05$).

Overall, the present study showed that the participants of the M2 group (receivers of 60 mg/kg of magnesium sulfate) in comparison to the two other groups had less increase in their systolic and diastolic blood pressure and mean of arterial pressure after intubation. Also, the average reduction of the above mentioned hemodynamic indexes compared to previous the induction of anesthesia, in this group in comparison to the two other groups, was higher during the studied time intervals. After that, the M1 group (receivers of 40 mg/kg of magnesium sulfate) had a better condition regarding the above mentioned indexes in comparison to the control group. The mean of heart rate of the M2 group from the first minute after intubation was lower than the two other groups and it was closer to the normal range; then the M1 group had a lower heart rate compared to the control group.

Discussion

Direct laryngoscopy and endotracheal intubation would increase the blood pressure and heart rate in patients [1] and this has a great importance in pregnant women who do not receive fast-acting analgesic drugs during the induction of anesthesia which could lead to more complications [22-23].

All of the previous studies about the effect of magnesium sulfate on laryngoscopy and endotracheal intubation were either conducted on the normal population [8-9,12,15] or pregnant women with hypertension [16,24].

The present study, which was conducted on ASAI&II pregnant women who were candidates for caesarean section with general anesthesia, was unique in its kind. Calcium has an important role in releasing catecholamines from adrenocortical and adrenergic nerve endings in responding to the stimulation of the sympathetic nervous system. Magnesium would release calcium for connecting to membrane channels. In other words magnesium would act as the antagonist of calcium and could decrease the response caused by calcium. Magnesium sulfate would also block the release of catecholamines reserves and decrease the adrenergic respond [25]. In conditions with increased release of catecholamine such as tetanus [26] and pheochromocytoma [27], magnesium sulfate would also be used.

Also by reducing the tone of vascular smooth muscles, it is effective in reducing the hypertension caused by pregnancy [28]. In studies by Honarmand [13], Puri [14], Panda [17] and Kadam [18] the effectiveness of magnesium sulfate in reducing the hemodynamic response to laryngoscopy and endotracheal intubation, especially during the first 5 minutes after laryngoscopy, has been proved. In the present study, the desirable effect of intravenous magnesium sulfate was observed until the 10th minute after laryngoscopy; this effect could be explained by the mechanism of magnesium sulfate on reducing circulating catecholamine [29] and decreasing the side effects of laryngoscopy. On the other hand, by prescribing these two doses of magnesium sulfate no adverse effect was observed on the Apgar score of the neonates1 and 5 minutes after delivery; while another study which evaluated the effect of prescribing magnesium sulfate for pregnancy-induced hypertension on neonates reported lower Apgar score in neonates 1 and 5 minutes after delivery. It must be noted that higher doses of magnesium sulfate were used in that study [30]. One of the limitations of this study was not measuring the serum levels of magnesium sulfate which could be considered in further studies. However no clinical symptoms of being poisoned with sulfate were observed among patients and even between the extubation and recovery time of groups was no significant difference.

So, it could be concluded that prescribing 60 mg/kg of magnesium sulfate before the induction of anesthesia could have desirable effects in reducing systolic, diastolic and especially the heart rate of pregnant women undergoing caesarean section under general anesthesia; it also has no adverse effects on the Apgar score of the neonates 1 and 5 minutes after delivery.

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