Original Article

A Dose – Response Study of Magnesium Sulfate in Suppressing Cardiovascular Responses to Laryngoscopy & Endotracheal Intubation

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ABSTRACT

Background: The effects of pretreatment with magnesium on cardiovascular responses associated with intubation have been studied previously**.** In this study we wanted to find optimal dose of magnesium that causes decreased cardiovascular responses after laryngoscopy & endotracheal intubation.

Methods: In a double-blind , randomized, clinical trial ,120 ASA-1 patients with ages between 15-50 years old , who were candidates for elective surgery, were selected and classified in 6 groups (20 patients in each). The pulse rate and arterial blood pressure were measured and recorded at 5 minutes before taking any drug then, according to different groups, patients took magnesium sulfate (10, 20, 30, 40, 50mg/kg) and lidocaine (1.5 mg/kg).
The induction of anesthesia was same in all groups and the pulse rate and arterial blood pressure were measured and recorded just before intubation and also at 1, 3 , and 5 minutes after intubation (before surgical incision) .
Statistical analysis was performed by use of ANOVA, Post Hoc test (Duncan), Pearson correlation, and Chi square test.

Results: there were no statistically significant differences in blood pressure, pulse rate, Train Of Four (TOF), and complications between groups who received magnesium but the significant differences in these parameters were seen between magnesium and lidocaine groups.

Conclusion: We concluded that pretreatment with different doses of magnesium sulfate have a safe decreasing effect on cardiovascular responses that is more effective than pretreatment with lidocaine.

Keywords: magnesium sulfate, cardiovascular responses, lidocaine.

Until recently, the function of magnesium in biological processes was largely ignored to the point where it was described as the "forgotten ione". However, in the last few years there has been an expolsion of interest in both the physiological and pharmacological properties of essential substances. Magnesium is the forth most abundant cation in the body and the second most abundant intracellular cation. It activates many of the enzyme systems[1].

It is also involved in several processes; like, control of vasomotor tone, cardiac excitability, and neurotransmitter release. In many of its actions, it is likened to a physiological calcium antagonist[2].

It is well known that laryngoscopy and tracheal intubation result in marked increase in pulse rate and blood pressure due to the release of catecholamines in large amounts. There are various techniques which attenuate the stress response by reducing the input of stimuli or blockade of adrenergic responses after intubation. All of these techniques which are suggested have same disadvantages related to either cardiovascular or respiratory depression, but none of them directly inhibits the release of catecholamines. Magnesium sulfate blocks the release of catecholamines from the adrenergic nerve terminals and adrenal glands invitro. Increased serum magnesium level may also inhibit the release of catecholamines in humans in whom catecholamine excess is present [4].

At the moderate blood level, $Mg2^{+}$ has relatively minor cardiovascular side effects and its only

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respiratory depressant effect is related to its well known ability to potentiate the action of nondepolarizing neuromuscular blocking agents [4].

Laryngoscopy and endotracheal intubation may produce adverse hemodynamic effects. Magnesium has direct vasodilating properties on coronary arteries and inhibits catecholamine release, thus attenuates the hemodynamic responses during endotracheal intubation [5].

G.D puri and his coworkers studied about the effect of magnesium sulfate to attenuate the hemodynamic response after endotracheal intubation in coronary artery disease. They showed that administration of magnesium before endotracheal intubation can attenuate hemodynamic responses better than lidocaine. In all of the mentioned studies, different doses (40-50-60 mg/Kg) of magnesium sulphat were administered to patients. None of them reported any side effect due to & depend on effective doses [3,4,5,11,12,13].

When MgSO4 is administered IV, the onset of action is immediate and the duration of action is about 30 minutes. So, in this study, unexpected effects of MgSO4 in patients were noted until the patients discharged from post anesthetic care unit (PACU) [14].

Symptoms and electrocardiographic changes of hypermagnesemia correspond to serum level; depressed cardiac conduction, widened QRS complexes, prolonged P-Q intervals, and nausea appear between 5 and 10 mg/dl; Sedation, hypoventilation, loss of deep tendon reflex, and muscle weakness appear at levels between 20 and 34 mg/dl; hypotention , bradycardia , and diffuse vasodilation occurring at levels of 24 to 48 mg/dl, and areflexia , coma , and respiratory paralysis occur at 48 to 72 mg/dl . For these reasons, all patients being treated with magnesium must be clinically observed for magnesium intoxication [6].

Concurrent use of parenteral magnesium sulfate may result in severe and unpredictable potentiation of neuromuscular blockade [14, 15, 16].

Hot sense during receving MgSO4 is depending on the amount of drug that receving in time unit.This unexpected effect can be attenuated with injecting in longer time [18].

The dose dependency of these side effects has been suggested in small open label studies but no randomized double blind trial has been performed to evaluate this relationship [3, 4, 5, 11, 12, 13].

In this study we aimed to determine an optimal dose of magnesium sulfate to have a better efficacy on cardiovascular responses (pulse rate and blood pressure), a lower incidence of side effects after laryngoscopy & endotracheal intubation, and a lower incidence of side effects in comparison with lidocaine.

Subjects and Methods

After approval of ethics committee of isfahan university , in a double blind , randomized , clinical trial , 120 patients of both sexes with the ages between 15- 50 years old , ASA-1 who were candidates for elective surgery ,without any history of drug consumption, and needed tracheal intubation were studied . Every patient whose duration of endotracheal intubation was more than 15 seconds, any problem occured for saving his or her life , or received any drugs (other than drugs of study), was excluded from study.

Patients were randomly allocated to six groups (20 patients in each group). groups A,B,C,D and E received 50 , 40 , 30, 20 , and 10 mg/kg of magnesium sulfate respectively and group F received 1.5mg/kg of lidocaine . Both drugs were given over 1 minute just before induction of anesthesia.

All of the solutions were diluted similarly and labeled .For each 10 kg of body weight, 1 ml of labeled soulution was injected .The induction of anesthesia was similar in all groups by using fentanyl (1 µg/kg), atracurium (0.5 mg/kg) and sodium thiopanthal (5 mg/kg) after preoxygenation.

Two minutes after injection of Atracurium, the intubation was done by one anesthetist in all groups. The anesthesia was maintained by using O2/N2O 50/50 & 1 MAC of halotane to ensure normocapnia and normal O2 saturation.

Pulse rate and arterial blood pressure were measured at 5 minute before giving any drug **(**as basal rest status**)** and just before laryngoscopy and 1, 3, and 5 minutes after intubation. Surgical incision was allowed after the last measurement. (5, 12) Train of four (TOF) was measured 45 min after induction of anesthesia by a nerve stimulator. Monitoring of patients were included routine EKG, capnography, pulse oximetry, and blood pressure which was monitored noninvasively by using an automatic oscillotonometric device that measured and recorded the blood pressure and pulse rate at specific intervals.

In this study, unexpected effects of $MgSO_4$ in patients were noted until the patients discharged from post anesthetic care unit (PACU)[14].
Statistical analysis was performed, using ANOVA, Post Hoc test (Duncan), Pearson corelation, and Chi square tests.

Results

We studied 20 patients in each groups (120 patients). The groups were well matched for demographic data and no statistically significant differences were found between groups in age (Table 1), weight (Table 1), sex (Figure 1), and surgical position.

One patient after injection of 30 mg/kg of magnesium sulfate and before laryngoscopy had multiple PACs, and, after intubation, he had many PVCs. He was treated with 60 mg of lidocaine, IV.The patient was excluded from analysis.

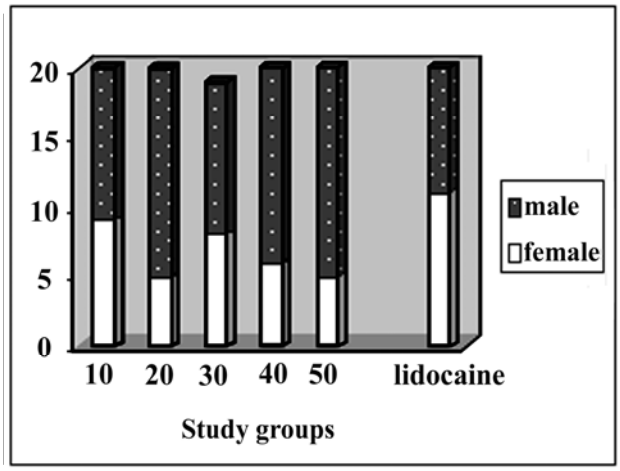

Figure 1. Numbers of patients in each group according to sex (p>0.05). study groups: Mgso4 10,20,30,40,50,mg/kg & lidocaine 1.5 mg/kg

After laryngoscopy and intubation, statistically significant differences as percent base values were found between magnesium groups and lidocaine (P<0.05), but There was not significant difference between magnesium groups (P>0.05) (Figure 2).

Like mean blood pressure , no significant differences as percent base values of mean heart were found between magnesium groups (P>0.05), but between magnesium groups and lidocaine group, the differences were significant (P<0.05) (Figure 3).
In group C (30 mg/kg of mgso4) changes in heart rate and mean blood pressure was less than other groups. TOF at minute 45 after induction of anesthesia in all groups had no statistically significant differences (P>0.05) (Figure 4).

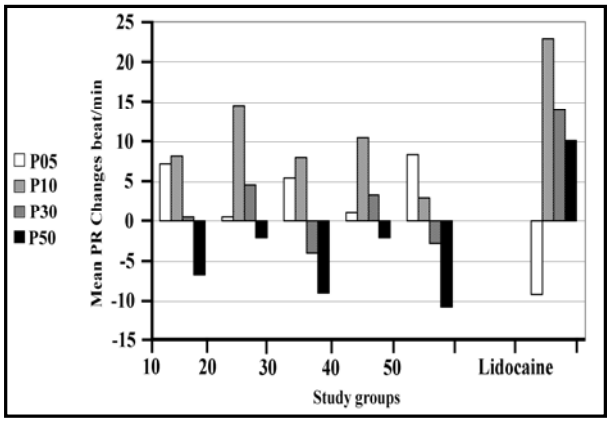

Figure 2. Mean pulse rate changes just before and at 1, 3, and 5 minutes after laryngocopy and intubation as % baseline values that took 5 minutes befor start of study.
Study groups: MgSO4 10, 20, 30, 40, and 50 mg/kg and lidocaine 1.5 mg/kg.
P05: mean pulse rate changes just before larygocopy (P <0.05), p10: mean pulse rate changes at time 1 after laryngocopy (P <0.05), p30: mean pulse rate changes at time 3 after laryngocopy (P <0.05), p50: mean pulse rate changes at time 5 after laryngocopy (P<0.05).

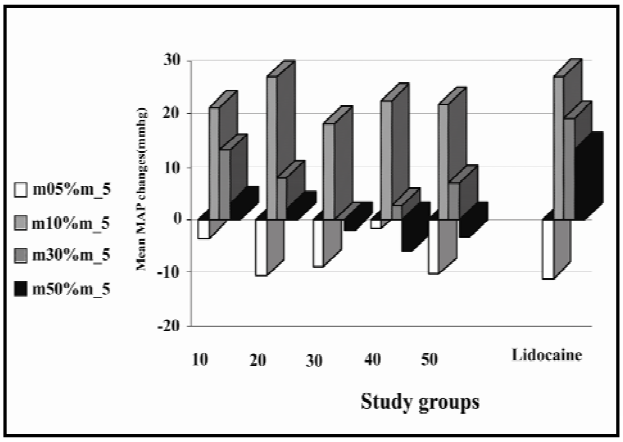

Figure 3. Average Mean Arterial Pressure (MAP) changes just before and at min 1, 3, 5 after laryngocopy and intubartion as % baseline value that took 5 minutes before start of study.
Study groups: MgSO4 10, 20, 30, 40, and 50 mg/kg and lidocaine 1.5 mg/kg.
m05: mean MAP changes just before larygocopy (P<0.05), m10: mean MAP changes at time 1 after laryngocopy (P<0.05), m30: mean MAP at time 3 after laryngocopy (P<0.05), m50: mean MAP changes at time 5 after laryngocopy (P<0.05).

The incidence of complications of magnesium, like hypotension, arrhythmia, nausea, sweating, flashing, and hot sense had no significant differences between all groups (P>0.05) (Figure 5).

Table 1. patients charectristics.

	10 mg	20 mg	30 mg	40 mg	50 mg	lidocaine	P-Value
NO.	20	20	19	20	20	20	
Age (yr)	31.3 (10.3)	26.4 (9.5)	26.5 (9.9)	27.3 (8.4)	31.1 (8.4)	32.6 (11)	0.163
Waite (kg)	69.0 (9.4)	68.0 (9.0)	71.0 (11.0)	71.2 (9.4)	74.2 (14.9)	70.0 (10.2)	0.554

Study groups: MgSO4 10, 20, 30, 40, and 50 mg/kg and lidocaine 1.5 mg/kg.

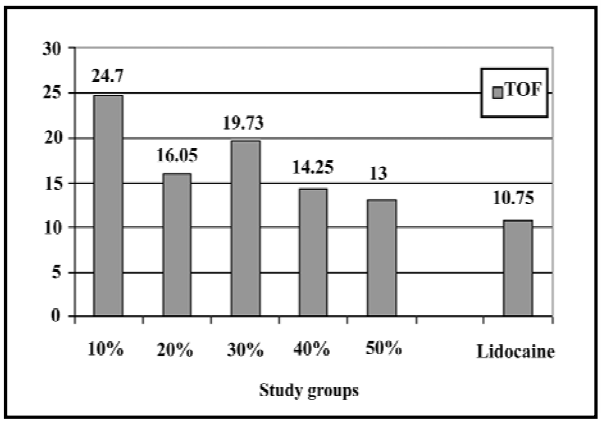

Figure 4. Train of four (TOF) at min 45 after induction of anesthesia.
Study groups: MgSO4 10, 20, 30, 40, and 50 mg/kg and lidocaine 1.5 mg/kg (P>0.05).

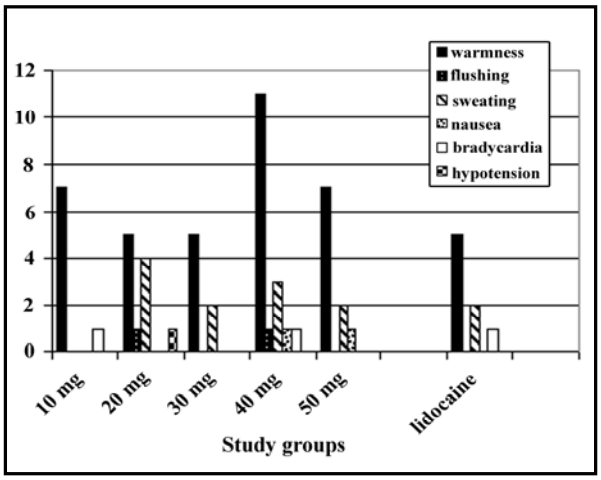

Figure 5. Complications frequency (P>0.05) one patient might have more than one.
Study groups: MgSO4 10, 20, 30, 40, and 50 mg/kg and lidocaine 1.5 mg/kg (P>0.05).

Discussion

Calcium exerts a major role in stimulus-response relationship, including the release of catecolamines from the adrenal gland and adrenergic nerves terminals in response to sympathetic stimulation [7].

Because Magnesium competes with calcium for membrane channels, it has been described as the physiological calcium antagonist [8] and can modify many calcium – mediated responses. The ability of magnesium ions to inhibit the release of catecolamines from both the adrenal glands and peripheral adrenergic nerves terminals has been known for many years [9]. It also produces vasodilation, directly [5].

Many studies have showed that MgSO4 can attenuate cardiovascular responses to endotracheal intubation [2, 3, 4, 5, 11], but dose dependency of it's inhibitory effects on cardiovascular responses were unknown [3, 4, 5, 11, 12, 13].

In this dose response study we used different doses of magnesium to find out the optimal dose which attenuates cardiovascular responses with the least complications.

As it has been showed previously, the present study shows that different doses of magnesium are significantly better than IV lidocaine in attenuating the cardiovascular responses to induction and endotracheal intubation, with favorable hemodynamics [3, 4, 5, 11, 12, 13].

Among all magnesium groups, the group who received 30 mg/kg of magnesium before intubation had less cardiovascular response, but this difference was not statistically meaningful among all groups.

Therefore the improved control of blood pressure in the magnesium group was, probably, due to a combination of vasodilatory effects of the ion and inhibition of catecholamine release.

The enhancing effect of magnesium on neuromuscular block was not seen in our study; as the TOF at minute 45 after induction of anesthesia, didn't show any significant difference between all magnesium groups; and it was not the same as previous studies [15, 17]. We have not any statistically significant complication after use of magnesium .In conclusion, administration of different doses of magnesium at ministration of different doses of magnesium at the time of the induction of anesthesia improves hemodynamic responses to endotracheal intubation, that the dose of 30mg/Kg of magnesium was the most effective with the less unexpected effects. Retry this study with more cases may be better.

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