Research Article

A comparative study of two doses of magnesium sulphate in attenuating haemodynamic responses to laryngoscopy and intubation

Manish B. Kotwani[1]*, Deepti M. Kotwani[1], Vandana Laheri[2]

[1]Department of Anaesthesiology, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai, India
[2]Department of Anaesthesiology, ESIC and MGM Hospital, Parel, Mumbai, India

*Correspondence:
Dr. Manish B. Kotwani,
E-mail: drmanishkotwani@gmail.com

ABSTRACT

Background: Laryngoscopy and intubation evoke a presser response in the human body by causing catecholamine release due to sympatho-adrenal stimulation. Various drugs have been tried to attenuate haemodynamic response to laryngoscopy and intubation during general endotracheal anaesthesia. In the last few years there has been an explosion of interest in both the physiological and pharmacological properties of magnesium and its clinical use. We planned this comparative, prospective dose response study compare the efficacy of two doses (30 mg/kg and 40 mg/kg) of intravenous magnesium sulphate in attenuating the cardiovascular response to laryngoscopy and intubation.
Methods: Seventy five patients aged 15-50 years, scheduled for elective surgery under general anaesthesia, were randomly assigned to one of the three pre-treatment groups of 25 each, group C- control group, group T ($MgSO_4$ 30 mg/kg) and group F ($MgSO_4$ 40 mg/kg). Study drug was given 90-120 seconds before tracheal intubation. Heart rate, systolic blood pressure and rate pressure product were recorded at different intervals (baseline values, after study drug, after induction, at laryngoscopy, after intubation, 2 and 3 minutes after intubation).
Results: Mean heart rate and systolic blood pressure was significantly high (P <0.0001) after laryngoscopy and intubation, in group C (46.87% and 40.81% from baseline) than in group T (22.78% and 7.25% from baseline) and group F (24.55% and 5.83 from baseline) respectively.
Conclusions: Intravenous $MgSO_4$ successfully attenuates the haemodynamic changes during laryngoscopy and intubation. 30 mg/kg gives adequate cardiovascular control without any complications. Transient tachycardia is more with higher doses.

Keywords: Laryngoscopy, Intubation, Presser response, Magnesium sulphate

INTRODUCTION

The most important development in recent years is, understanding the series of physiological changes (stress response) due to anesthesia and surgery.[1,2] These changes in cardio-vascular and neuro-humoral systems may directly affect the physiology of patients and increase the risk.[3] Tracheal intubation is often mandatory in most surgical patients requiring general anaesthesia and critically ill patients needing mechanical ventilation. Like all interventional procedures, laryngoscopy and tracheal intubation too evoke a stress response in the human body by causing catecholamine release due to the sympathoadrenal stimulation. The magnitude of these responses if smaller, then it is better tolerated in healthy normo-tensive individuals with no systemic illness.[4] But such effects can be detrimental in susceptible individuals, in whom sympatho-adrenal stimulation with sudden rise

in heart rate and blood pressure can lead to left ventricular failure, myocardial ischemia, cerebral hemorrhage, pulmonary edema, increase in intracranial tension and its complication.[5,6]

So far, various techniques like topical and intravenous lignocaine; sympatholytic drugs like phentolamine, narcotic agents like nalbuphine fentanyl and alfentanil beta blockers like intravenous landiolol, labetalol, metoprolol and esmolol; alpha adrenergic blocking drugs like oral and intravenous clonidine; vasodilators like nitrogycerine and hydralazine; calcium channel blockers like diltiazem; deep general anesthesia and various other drugs have been tried.[7-15]

Until recently, the function of magnesium in biological processes was largely ignored to the point where it was described as the "for-gotten ione". However, in the last few years there has been an explosion of interest in both the physiological and pharmacological properties of magnesium. Magnesium sulphate which is an established agent as anti-convulsant in eclampsia have recently been under trial for its utility in reducing cardiovascular effects and attenuating the stress responses associated with laryngoscopy and tracheal intubation, when used in relatively small doses.[16-20]

We therefore, planned this comparative, prospective dose response study to evaluate and compare the efficacy of two doses (30 mg/kg and 40 mg/kg) of intravenous magnesium sulphate in attenuating the cardiovascular response to laryngoscopy and tracheal intubation.

METHODS

After obtaining the approvals from the institutional review board, this double blind randomized prospective clinical study was designed. Seventy five ASA-grade I and II patients of either sex in the age group of 15-50 years, posted for elective surgical procedures lasting for an hour or more and requiring general anaesthesia were enrolled for the study. Patients were thoroughly examined during pre-operative visit and patients below 15 years and above 50 years of age, belonging to ASA grade III or more, with anticipated difficult airway, with de-compensated systemic illness or neuromuscular disease were excluded from the study. The selected patients were randomly divided into 3 groups (25 patients each) depending upon the study drug administered. group C-received 20 ml normal saline (control group); group T-received intravenous $MgSO_4$ (30 mg/kg) in 20 ml normal saline; group F-received intravenous $MgSO_4$ (40 mg/kg) in 20 normal saline. Premedication was uniform for all the patients in the form of intravenous glycopyrrolate 0.004 mg/kg, ranitidine 1 mg/kg, metoclopramide 0.2 mg/kg and midazolam 0.03 mg/kg 10 minutes prior to induction. Study drug was given over a period of one minute 3 minute before induction of general anaesthesia. Rest of the general anaesthetic technique was same for all the three groups. After pre-oxygenation with 100%

oxygen. General anaesthesia was induced with intravenous thiopentone sodium (~5 mg/kg) till the disappearance of eye lash reflex, followed by intravenous suxamethonium 2 mg/kg to facilitate tracheal intubation. Patients were ventilated on mask using 100% oxygen until the disappearance of fasciculations. Laryngoscopy was carried out by an experienced anaesthesiologist with McIntosh curved blade laryngoscope and orotracheal intubation was achieved with appropriate sized cuffed endotracheal tube. Study included only those patients in whom intubation was achieved in single attempt within 30 seconds. Surgical stimulation was not allowed until five minute after intubation. Maintenance of general anaesthesia, intraoperative monitoring and reversal of neuro-muscular blockade and/or extubation followed the standard practice. Parameters like heart rate (HR); systolic blood pressure (SBP); diastolic blood pressure (DBP) were recorded at following time intervals. Baseline; after administering the study drug; after induction of general anaesthesia; at laryngoscopy; just after intubation; at 2 minutes and at 5 minutes after intubation. Rate pressure product (RPP) defined as the product of HR and SBP was calculated at baseline and at different time intervals.

As magnesium is known to potentiate the action of both depolarizing and non-depolarizing muscle relaxants, the duration of suxamethonium (intubating dose) and 1st dose of non-depolarizing muscle relaxant was monitored using TOF and was compared to the control group, so as to avoid unnecessary delay in reversal and extubation. Complications of magnesium like hypotension, circulatory collapse, arrhythmias, nausea, flushing, sweating and hot sense etc. were also looked for.

Parametric data (age, HR, SBP and RPP) was reported as mean±SD and was analyzed by unpaired Student's test. Categorical data was reported as number and percent and analysed using the Pearson's chi-square test/Fischer exact test. Percentage change from the baseline values of HR, SBP and RPP at different time intervals were calculated. The data were subjected to statistical analysis using t-test, chi-square, ANNOVA and post hoc tests. P-value of 0.05 was considered as statistically significant.

RESULTS

Patients in all three groups were comparable with respect to age, gender or weight (Table 1). It was observed that the mean baseline parameters (HR, SBP and RPP) in all the three groups were comparable (P > 0.1) (Table 1).

There was significant rise in the HR (P < 0.001) from the baseline values after giving the study drug (magnesium sulphate). Increase in HR was more in group F (22.33%), than in group T (17.96%) HR increased significantly (P <0.001) during laryngoscopy and intubation, (46.87% from the baseline) in group C. HR was persistently high (p <0.001) at 2 minutes (32.20% from baseline) and 5 minutes (26.55 % from baseline) (Table 2).

Table 1: Demographic data and baseline parameters.

Parameter	Group C (n=25)	Group T (n=25)	Group F (n=25)	P-value
Age in years (mean±SD)	31.7±9.620	30.4±9.896	30.1±11.661	0.856
Weight in kg (mean±SD)	55.8±9.120	54.3±10.575	53.5±9.435	0.705
Sex (M:F)	12:13	9:16	8:17	0.481
Baseline HR (mean±SD)	83.88±11.875	84.32±9.673	89.92±11.76	0.110
Baseline SBP (mean±SD)	118.72±14.673	117.60±9.292	122.40±9.018	0.297
Baseline RPP (mean±SD)	9928.88±1688.024	9936.48±1532.868	10921.92±1832.951	0.064

HR: Heart rate; SBP: Systolic blood pressure; RPP: Rate pressure product

Table 2: Percent change in heart rate (HR) from baseline.

Study group	Mean±SD	% Change	P-value
Group C			
Baseline	83.88±11.875	-	
After study drug	85.92±12.589	2.92	0.282
After induction	84.72±12.648	1.19	0.566
At laryngoscopy	101.04±16.247	21.11	0.000*
Just after intubation	121.60±12.583	46.87	0.000*
At 2 minutes	109.80±16.442	32.20	0.000*
At 5 minutes	104.64±13.385	26.55	0.000*
Group T			
Baseline	84.32±9.673	-	
After study drug	99.08±10.606	17.96	0.000*
After induction	100.08±10.512	19.09	0.000*
At laryngoscopy	101.04±10.490	20.22	0.000*
Just after intubation	103.52±14.734	22.78	0.000*
At 2 minutes	102.76±14.263	21.98	0.000*
At 5 minutes	95.76±12.614	13.75	0.000*
Group F			
Baseline	89.92±11.768	--	
After study drug	109.76±14.356	22.33	0.000*
After induction	109.12±12.937	21.85	0.000*
At laryngoscopy	108.48±12.978	21.56	0.000*
Just after intubation	111.12±14.225	24.55	0.000*
At 2 minutes	107.52±1.391	20.82	0.000*
At 5 minutes	100.24±13.208	12.48	0.001*

SD = standard Deviation, * P<0.001 is highly significant

Table 3: Inter-group comparison of %change in HR.

Point of time	P-value		
	Group C Vs T	Group C Vs F	Group T Vs F
Baseline	0.889	0.059	0.080
After study drug	0.000*	0.000*	0.004
After induction	0.000*	0.000*	0.010
At laryngoscopy	1.000	0.054	0.054
After intubation	0.000*	0.009	0.057
At 2 minutes	0.084	0.572	0.239
At 5 minutes	0.019	0.238	0.230

* P<0.001 is highly significant

Mean HR values were significantly high from the baseline, in all the groups after laryngoscopy and intubation and at 2 and 5 minutes thereafter. On intergroup comparison (Table 3) it was observed that HR was significantly high in group C than group T and group F.

There was fall in SBP after giving magnesium sulphate in group T (-6.02% from baseline) and group F (-7.69% from baseline). There was significant (P=0.000) rise in SBP during laryngoscopy (12.47%) and intubation (40.81%) in group C. Mean SBP was significantly high (P=0.000) at 2 min and 5 min after intubation (Table 4). On intergroup comparison it was observed that mean SBP was significantly lower (P=0.000) after laryngoscopy and intubation in group T and group F when compared with group C. There was no significant difference in mean SBP at all intervals after laryngoscopy between group T and group F (Table 5).

RPP was increased by 10.75% and 14.36% from the baseline values after giving magnesium in group T and group F respectively. We observed significant increase in RPP at laryngoscopy and intubation and later at 2 and 3 minutes in all the groups (Table 6). However on intergroup comparison it was seen that the rise in RPP was more significant in group C (106.95% above baseline) after intubation than in group T (31.68% above baseline) and group F (33.27% from baseline) (P=0.000). However, there was no significant difference in the mean RPP between group T and group F at all intervals (Table 7).

Table 4: Percent change in systolic blood pressure from baseline.

Study group	Mean±SD	% Change	P-value
Group C			
Baseline	118.72±14.673		
After study drug	117.20±14.877	-0.59	0.615
After induction	112.32±14.568	-4.44	0.083
At laryngoscopy	132.40±16.381	12.47	0.001
Just after intubation	165.36±17.017	40.81	0.000*
At 2 minutes	150.64±14.897	28.44	0.000*
At 5 minutes	139.76±12.101	19.56	0.000*
Group T			
Baseline	117.60±9.292		
After study drug	110.24±6.790	-6.02	0.000*
After induction	108.08±7.884	-7.69	0.000*
At laryngoscopy	116.32±11.101	-0.89	0.524
Just after intubation	125.84±12.123	7.25	0.001
At 2 minutes	126.48±13.245	7.72	0.001
At 5 minutes	118.72±10.212	1.211	0.568
Group F			
Baseline	122.40±9.018		
After study drug	112.80±9.592	-7.69	0.000*
After induction	114.24±16.816	-6.54	0.017
T laryngoscopy	116.80±10.033	-4.48	0.001
Just after intubation	129.28±10.163	5.83	0.001
At 2 minutes	120.16±8.204	-1.52	0.238
At 5 minutes	112.96±6.611	-7.32	0.000*

SD = standard Deviation, * P<0.001 is highly significant

Table 5: Inter-group comparison of % change in SBP.

	P-value		
Point of time	Group C Vs T	Group C Vs F	Group T Vs F
Baseline	0.727	0.253	0.137
After study drug	0.028	0.160	0.411
After induction	0.275	0.620	0.114
At laryngoscopy	0.000*	0.000*	0.895
After intubation	0.000*	0.000*	0.368
At 2 minutes	0.000*	0.000*	0.077
At 5 minutes	0.000*	0.000*	0.043

* P<0.001 is highly significant

None of our patients had any complications of magnesium, like flushing and sense of warmth, arrhythmias, nausea, sweating, etc, after intravenous administration. We did not observe any prolongation in duration of action of neuro-muscular blocking agents, with the doses (30 mg/kg and 40 mg/kg) included in our study.

Table 6: Percent change in rate pressure product from baseline.

Study group	Mean±SD	% Change	P-value
Group C			
Baseline	9928.88±1688.02		
After study drug	10102.72±2140.76	2.57	0647
After induction	9570.56±2163.21	-3.21	0.297
At laryngoscopy	13471.60±3251.68	36.65	0.000*
Just after intubation	20167.12±3330.83	106.95	0.000*
At 2 minutes	16634.32±3473.23	69.60	0.000*
At 5 minutes	14661.20±2461.81	51.07	0.000*
Group T			
Baseline	9936.48±1532.86		
After study drug	10916.08±1302.91	10.75	0.000*
After induction	10830.08±1480.74	9.78	0.000*
At laryngoscopy	11766.88±1731.79	19.08	0.000*
Just after intubation	13047.52±2317.33	31.68	0.000*
At 2 minutes	13066.16±2696.42	31.37	0.000*
At 5 minutes	11454.08±1807.25	15.21	0.000*
Group F			
Baseline	10921.92±1832.95		
After study drug	12406.72±2123.39	14.36	0.000*
After induction	12519.04±2713.49	15.33	0.001
At laryngoscopy	12693.12±2078.08	17.65	0.000*
Just after intubation	14413.28±2436.52	33.27	0.000*
At 2 minutes	12926.40±1671.86	20.72	0.000*
At 5 minutes	11346.72±1807.25	5.74	0.342

SD = standard Deviation, * $P<0.001$ is highly significant

Table 7: Inter-group comparison %change in RPP.

	P – value		
Point of time	Group C Vs T	Group C Vs F	Group T Vs F
Baseline	0.987	0.041	0.043
After study drug	0.134	0.000*	0.007
After induction	0.045	0.000*	0.008
At laryngoscopy	0.015	0.263	0.184
After intubation	0.000*	0.000*	0.081
At 2 minutes	0.000*	0.000*	0.856
At 5 minutes	0.000*	0.000*	0.865

* $P<0.001$ is highly significant

DISCUSSION

Laryngoscopy and intubation, like any other procedure, can evoke sympathetic response in the body.[4] This is well established and there have been number of ways to control or reduce the stress response evoked by such stimuli.[21] Magnesium is already studied and has been proved to attenuate the sympathetic outburst during stress. We planned this study, to compare two different doses 30 mg and 40 mg/kg of magnesium in attenuating the cardiovascular effects of the stress response during laryngoscopy and intubation.

Heart rate

Our results and observations, pertaining to heart rate were comparable to James MFM et al in their double blind study.[22,23] They assessed the effects of pre-treatment with intravenous magnesium sulphate 60 mg/kg on cardiovascular responses and the release of catecholamines associated with tracheal intubation in otherwise normal subjects compared to normal saline pre-treated controls. They found that induction of anesthesia produced no changes in HR in either Group, but magnesium pre-treatment produced initial increase in HR by 13±3.9 beats/minute. HR increased by 30.9 beats/minute in the control Group 2 minutes after intubation, whereas in the magnesium group, HR remained virtually unchanged from the post-magnesium values. Puri GD et al studied 36 patients with coronary artery disease to evaluate the hemodynamic effects of magnesium and its efficacy in attenuating the response to intubation.[24] Magnesium group received 50 mg/kg magnesium sulphate and the control group received normal saline solution before the induction of anesthesia. They found that there was initial insignificant (P >0.05) rise in the HR from 65.2±12.7 to 70.5±15.6 after administering the study drug and no further significant rise in HR in the magnesium group after intubation. But in control group though there was no initial rise in HR after the study drug, HR increased significantly

(P <0.001) from 64.2±8.8 to 72.9±8.8 after intubation. This study also supports our findings.

The changes in the heart rate observed in our study as well as the studies quoted above are particularly interesting. It might be expected that magnesium would slow the HR by inhibiting the calcium mediated depolarizing current in the pacemaker tissue, the effect that has been demonstrated in the isolated animal hearts. However, in the intact animal the ability of magnesium to inhibit the release of acetylcholine from the vagus nerve predominates and, therefore, the overall effect is mild increase in the heart rate as seen in this study.

Blood pressure

James MFM et al who studied effects of pre-treatment with intravenous magnesium sulphate 60 mg/kg body weight compared to normal saline on cardiovascular responses and the release of catecholamines associated with tracheal intubation.[22,23] They reported significant increase in SBP (from 106.4±3.1 to 145.1±5.6 mmHg) after intubation in control group but not significantly (P >0.05) in magnesium group (from 106.8±3.1 to 110.0±4.4 mmHg). Puri GD et al, also reported similar observation with the changes in mean arterial pressure (MAP).[24] MAP decreased significantly (P <0.001) from 91.7±14.5 to 76.2±15.6 mmHg after administering the study drug in the magnesium group as compared to control group (from 92.6±8.7 to 91.5±7.8 mmHg). Though MAP increased after intubation in both the Groups, it was significantly (P <0.001) higher than the base line in control Group (92.6±8.7 mmHg to 109.7±19.6 mmHg) immediately after intubation and (92.6±8.7 mmHg to 104.8±16.6 mmHg) at 3 minutes after intubation as compared to magnesium group where the levels were just near baseline (91.7±14.5 mmHg to 92.2±16.5 mmHg) after intubation.

The changes in blood pressure observed in our study as well as the studies quoted above can be attributed to direct vasodilating property of magnesium as well as by its action on sympathetic nervous system and inhibition of catecholamine release. Magnesium also reduces responsiveness of vascular smooth muscles, to nor epinephrine. Parentral magnesium administration results in rapid but transient decrease in systemic vascular resistance (SVR) therefore arterial pressure did not show any appreciable increase after endotracheal intubation in magnesium pre-treated patients compared to those in control group.[24,25] It might be argued that magnesium is producing its effects by a central sedative mechanism, but this is unlikely as magnesium crosses the blood-brain barrier with difficulty and has little or even no central sedative effect even at much higher doses than those used in our study.[24,28]

Rate pressure product

Since RPP is the index of myocardial oxygen demand, rise in RPP, however transient, may be deleterious in patients with compromised medical status.

Our results of changes in RPP could be compared to the study of Vanden Berg AA. et al who conducted a study in 100 middle-aged to elderly patients (52 healthy and 48 suffering from systemic diseases).[9] They observed that magnesium sulphate (40 mg/kg) did attenuate the responses to laryngoscopy and tracheal intubation, but were associated with increase in RPP. Their observations were similar to this study.

From the above discussion it is clear that although magnesium administration leads to tachycardia and hypotension, but by itself this effect is transient. At different doses (30 mg/kg and 40 mg/kg), magnesium definitely attenuates the effect on HR in response to laryngoscopy and intubation (P <0.001 at all the points after laryngoscopy) as compared to control group. Both the doses (30 mg/kg and 40 mg/kg), by themselves cause significant (p<0.001) rise in HR after I.V. administration, as compared to control group. When group T was compared to group F, it was seen that after administering magnesium, rise in HR was more (p <0.001) with 40mg/kg (22.33% from baseline) than with 30 mg/kg (17.96% from baseline).

Similarly, when effects on SBP were compared, it was clear that magnesium in both the doses (30 mg/kg and 40 mg/kg) significantly prevented the rise in SBP in response to laryngoscopy and intubation (p <0.001 at all the points after laryngoscopy) when compared to control Group. There was no difference (p >0.05) in the % change in the SBP between group T and group F when both the groups were compared to each other.

The observations for the two doses of magnesium were comparable to the study done by Falah M. et al using five doses of magnesium (10, 20, 30, 40, 50 mg/kg).[25] In their dose-response study they wanted to find out optimal dose of magnesium that decreased the responses after laryngoscopy and intubation. In their double blind, randomized clinical trial, they observed that after laryngoscopy and intubation there was significant difference in HR and SBP between magnesium groups versus lidocaine group (p<0.05) but percent changes from baseline values between inter-magnesium groups were not significant (p>0.05). In group C (30 mg/kg MgSO$_4$) changes in heart rate and mean blood pressure in relation to baseline values were lower as compared to all other Groups (10, 20, 40 and 50 mg/kg). From our study too, it is evident that magnesium sulphate in 30 mg/kg dose was a better alternative as compared to 40 mg/kg. More tachycardia and hypotension was seen with 40 mg/kg soon after injection as compared to 30 mg/kg. This may be deleterious in co morbid patients with compensated heart disease and other system disorders.

We also looked for complications of magnesium, like flushing and sense of warmth, arrhythmias, nausea, sweating, etc, after intravenous administration. The study did not observe such effects in the dose range of magnesium sulphate. Although magnesium is known to prolong the action of neuro-muscular blocking agents, this was not seen with the doses (30 mg/kg and 40 mg/kg) included in our study.[29] Differences in train of four (TOF) values at 45 minutes after induction of anesthesia in all the groups using magnesium sulphate (10, 20, 30, 40, 50 mg/kg) and lidocaine (1.5 mg/kg) in a study by Montazeri K et al. were also statistically not significant (p >0.05).[28]

According to literature, the actions of magnesium in protecting against the potentially harmful cardiovascular effects of tracheal intubation are not superior to the actions of the potent short acting opiate agents like fentanyl and alfentanil. Alfentanil in particular shows considerable promise in this regard. However, the use of opiates has been associated with muscle rigidity, bradycardia, hypotension, and respiratory depression. In circumstances where these complications may be undesirable, magnesium could be a useful alternative. Magnesium has also been shown to reduce fasciculation and potassium release after succinylcholine and these actions combined with the cardiovascular control that can be achieved by the use of magnesium can be of value.[28,29] A thoughtful use of magnesium sulphate in the dose range of 30 mg/kg may be a useful tool in attenuation of stress responses to laryngoscopy and intubation in selected cases where narcotics are contraindicated, especially so in pregnancy with PIH.

ACKNOWLEDGEMENTS

REFERENCES

1. Singh M. Stress response and anaesthesia altering the peri and postoperative management. Indian J Anaesth. 2003;47(6):427-34.
2. Derbyshire DR, Smith G. Sympathoadrenal responses to anaesthesia and surgery. Br J Anaesth. 1984;56(7):725-39.
3. Bruder N, Granthil C, Ortega D. Consequences and prevention methods of hemodynamic changes during laryngoscopy and intubation. Ann Fr Anaesth Reanim. 1992;11(1):57-71.
4. T Randell. Haemodynamic responses to intubation: what more do we have to know? Acta Anaesthesiologica Scandinavica. 2004;48(4):393.
5. Velickovic I, Yan J, Jaffrey A. Modifying the neuroendocrine stress response seminars in anaesthesia. Perioperative Med Pain. 2002;21(1):16-25.
6. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anesthesiology. 1977;47(6):524-5.
7. Mitra S. Blunting of haemodynamic responses to laryngoscopy and intubation: a review of methods. Indian J Anaesth. 1998;42:14-9.
8. Takita K, Morimoto Y, Kemmotsu O. Tracheal lidocaine attenuates the cardiovascular response to endotracheal intubation. Can J Anaesth. 2001;48:732-6.
9. Vanden BAA, Halliday EM, Soomro NA, Rasheed A, Baloch M. Reducing cardiovascular responses to laryngoscopy and tracheal intubation: a comparison of equipotent doses of tramadol, nalbuphine and pethidine, with placebo. Middle East J Anaesthesiol. 2004;17:1023-36.
10. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J Clinic Anesthesia. 1996;8(1):63-79.
11. Kay B, Healy TE, Bolder PM. Blocking the circulatory responses to tracheal intubation. A comparison of fentanyl and nalbuphine. Anaesthesia. 1985;40(10):960-3.
12. Sugiura S, Seki S, Hidaka K, Masuoka M, Tsuchida H. The hemodynamic effects of landiolol, an ultra-short-acting β1-selectiveblocker, on endotracheal intubationin patients with and without hypertension. Anesth Analg. 2007;104:124-9.
13. Coleman AJ, Jordan C. Cardiovascular responses to anaesthesia; influence of beta-adrenoreceptor blockade with metoprolol. Anaesthesia. 1980;35(10):972-8.
14. Davies MJ, Cronin KD, Cowie RW. The prevention of hypertension at intubation a controlled study of intravenous hydrallazine on patients undergoing intracranial surgery. Anaesthesia. 1981;36(2):147-51.
15. Hasegawa J, Mitsuhata H, Matsumoto S, Enzan K. Attenuation of cardiovascular response to laryngoscopy and tracheal intubation with bolus injection of diltiazem. Masui. 1992;41:356-62.
16. Montazeril K, Falah M. Dose-response study: MgSO$_4$ in cardiovascular responses after laryngoscopy and endotracheal intubation. Canad J Anesthesia. 2005;52:80.
17. Delhumeau A, Granry JC, Monrigal JP, Costerousse F. Therapeutic use of magnesium in anaesthesia and intensive care (French). Ann Fr Anesth Reanim. 1995;14:406-16.
18. Sanders GT, Huijgen HJ, Sanders R. Magnesium in disease: a review with special emphasis on the

serum ionized magnesium. Clin Chem Lab Med. 1999;37:1011-33.

19. Crowther C. Magnesium sulphate versus diazepam in the management of eclampsia: a randomized controlled trial. Br J Obstet Gynaecol. 1990;97:110-7.

20. Reinhart RA. Clinical correlates of the molecular and cellular actions of magnesium on the cardiovascular system. Am Heart J. 1991;121:1513-21.

21. Vigorito C, Giordano A, Ferraro P. Hemodynamic effects of magnesium sulfate on the normal human heart. Am J Cardiol. 1991;67:1435-7.

22. James MFM, Beer RE, Esser JD. Intravenous magnesium sulfate inhibits catecholamine release associated with tracheal intubation. Anesth Analg. 1989;68:772-6.

23. Ashton WB, James MFM, Janicki P, Uys PC. Attenuation of the pressor response to tracheal intubation by magnesium sulphate with and without alfentanil in hypertensive proteinuric patients undergoing caesarean section. Br J Anaesth. 1991;67:741-7.

24. Puri GD, Marudhachalam KS, Chari P, Suri RK. The effect of magnesium sulphate on hemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with coronary artery disease. Anesth Analg. 1998;87:808-11.

25. MontazeriI K, M Falah. Dose-response study: MgSO₄ in cardiovascular responses after laryngoscopy and endotracheal intubation. Canadian J Anesthesia. 2005;52:80.

26. John L, Atlee M, Dhamee S, Olund TL, George V. Use of esmolol, nicardipine, or their combination to blunt hemodyanamic changes after laryngoscopy and tracheal intubation. Anesth Analg. 2000;90:280.

27. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. Anesth Analg. 1979;58(2):116-9.

28. Krendel DA. Hypermagnesemia and neuromuscular transmission. Semin Neurol. 1990;10:42-5.

29. Ghoneim MM, Long JP. The interaction between magnesium and other neuromuscular blocking agents. Anesthesiology. 1970;32:23-7.