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ORIGINAL ARTICLE

A COMPARATIVE STUDY BETWEEN I.V 50% MAGNESIUM SULPHATE AND DEXMEDETOMIDINE FOR ATTENUATION OF CARDIOVASCULAR STRESS RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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ABSTRACT: BACKGROUND: Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response due to reflex sympathetic stimulation. This response may be hazardous in patients with hypertension, coronary artery disease, myocardial disease, cerebrovascular disease. Numerous agents have therefore been utilized to blunt this response. **OBJECTIVES:** The present study was undertaken in view of above mentioned facts, to compare effectiveness of intravenous Magnesium sulphate and Dexmedetomidine in suppressing the cardiovascular stress response. **METHODS:** 60 Patients were divided in to two groups of 30 patients each. Group-M received 30mg/kg of Magnesium sulphate and Group-D received 1 mic/kg Dexmedetomidine ten minutes before intubation. Both the groups were observed for changes in hemodynamic parameters i.e. heart rate (HR) systolic and diastolic blood pressure at 0, 1, 3, 5, 10 minutes post intubation. **RESULTS:** Statistical analysis was performed using SPSS version 20 (USA). It was observed that both magnesium sulphate and dexmedetomidine attenuated the rise in systolic and diastolic blood pressure, but magnesium failed to attenuate increase in the heart rate which is less than 10 beats/ min. compared to dexmedetomidine which effectively controlled the rise heart rate following intubation. **CONCLUSION:** Our study proves that magnesium sulphate is as effective as dexmedetomidine in attenuating the cardiovascular stress response to laryngoscopy and endotracheal intubation.

KEYWORDS: Stress response, magnesium sulphate, dexmedetomidine, systolic blood pressure, Diastolic blood pressure, heart rate, and laryngoscopy.

INTRODUCTION: Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic simulation. The response is transient occurring 30 seconds after intubation and lasting for less than 10 minutes.[1]

It may be well tolerated in healthy people, but may be hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease, myocardial infarction and thyrotoxicosis.[2]Numerous agents like opioids; calcium channel blockers, beta blockers, alpha 2 agonists, magnesium sulphate, local anesthetics etc. have been used to blunt it.[3, 4]

Several studies have looked at the efficacy of intravenous lignocaine as an agent to blunt the hemodynamic response to laryngoscopy and intubation.[5] Magnesium sulphate blocks the release of catecholamines from adrenergic nerve terminals and from the adrenal gland in vitro.

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Increased serum magnesium levels may also inhibit the release of catecholamines. Dexmedetomidine, an alpha2 receptor agonist produces sympatholysis. The present study was undertaken to compare the effectiveness of intravenous magnesium sulphate and dexmedetomidine for attenuation of stress response to laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS: This prospective randomized double blind study was conducted after obtaining clearance from Institutional Ethical Committee of the institute and written informed consent from all patients. 60 patients of American Society of Anesthesiologists physical status I & II of either sex in the age group of 20-40 years for elective non cardiac surgery were included in the study.

Patients with heart rate <70/mt., systolic blood pressure (SBP) <100mm Hg, mallampatti grading iii and iv, anticipated difficult intubation, h/o of asthma, cardiac disease & presence of heart block were excluded from the study. Preoperatively patients were advised fasting overnight and sedated with tab. alprazolam 0.5mg orally at bed time. Patients were randomly allocated to 2groups of 30 each.

On the day of surgery, in the operation theatre intravenous line was started and pulse oxymeter, noninvasive blood pressure cuff and ECG monitors were connected. Baseline parameters i.e. heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were noted before administration of drugs. After preoxygenation for 3 minutes, group M patients were administered 30mg/kg of 50% magnesium sulphate and group D patients received intravenous dexmedetomidine 1mic/kg 10mintes before intubation.

Patients were induced with intravenous injection of thiopentone sodium 5mg/kg followed by intravenous succinylcholine 1.5mg/kg and inj. fentanyl 2mics/kg to facilitate intubation. Total duration of laryngoscopy was noted. Patients whose total duration of laryngoscopy was more than 30 seconds were excluded from the study. Heart rate, systolic blood pressure and diastolic blood pressure were noted at 0, 1, 3, 5 and 10 minutes after intubation. Anesthesia was maintained with O2, N2O, isoflurane and inj. vecuronium. At the end of the surgery patients were reversed with neostigmine 0.05mg/kg and glycopyrollate 0.01mg/kg.

Statistical Analysis: Statistical analysis was performed using SPSS version 20 (USA). Categorical variables were expressed as actual numbers and percentages. Continuous variables were expressed as mean and standard deviations. Between groups analysis was done using unpaired T-test. A two tailed probability of less than 0.005 was considered statistically significant.

RESULTS: There was no statistically significant difference in the demographic and clinical characteristics among the two groups (Table 1). Both Magnesium sulphate and dexmedetomidine controlled the systolic and diastolic blood pressure to laryngoscopy and endotracheal intubation effectively. There was no statistically significant difference between both the drugs at 0, 1, 3, 5, and 10 minutes for systolic and diastolic blood pressures ($p > 0.005$) (table 2) (Fig. 1 and Fig. 2).

But the decrease in heart rate was more with dexmedetomidine compared to magnesium sulphate. Heart rate values are statistically significant in dexmedetomidine group compared to magnesium sulphate group ($p<0.005$) (Table 3) (Fig. 3). At preinduction, the mean value for heart rate (HR) in group M is 89.27 and in group D is 85.93. At 0 minute that is immediately after intubation, mean heart rate in group M is 98.27 and in group D is 85.13. At 1 minute, HR in group M is

92.13 and in group D is 82.17.At 3 minutes, HR in group M is 91.13 and in group D is 80.47. At 5 minutes, HR in group M is 89.37 and in group D is 80.00. At 10 minutes, HR in group M is 85.37 and in group D is 75.17.

Though the p value for HR is statistically significant, the mean values for heart rate in magnesium sulphate group did not change more than 10 beats/minute. And HR returned to normal with-in 5 minutes. This shows that magnesium sulphate is also effective in abolishing the cardiovascular stress response compared to dexmedetomidine.

DISCUSSION: Laryngoscopy and endotracheal intubation are considered as the most critical events in conducting general anesthesia. They provoke a transient but marked sympathoadrenal response. Beta blockers, alpha 2 agonists, magnesium sulphate, lignocaine attenuate these potentially harmful cardiovascular reactions during intubation. In this study we compared Magnesium sulphate and Dexmedetomidine for attenuating stress response to laryngoscopy and tracheal intubation.

Magnesium has been described as the physiological calcium antagonist[6] because it competes with calcium for membrane channels and can modify many calcium-mediated responses. The ability of magnesium ions to inhibit the release of catecholamine's from both the adrenal gland and peripheral adrenergic nerve terminals has been known for over 25 years[7] and is now well established.

However, until recently, no clinical use has been made of this potentially valuable phenomenon. The use of magnesium in conditions where catecholamine excess is prevalent, such as in tetanus [8] and phaeochromocytoma,[9] has recently been described and the ability of magnesium infusions to lower catecholamine levels in a patient with tetanus has been demonstrated.[10]

The present study shows that magnesium can significantly attenuate the release of catecholamines at the time of tracheal intubation and thus reduce the severity of cardiovascular disturbances. Magnesium acts by slowing the atrial rate by inhibiting the calcium mediated depolarizing current in pacemaker tissue[11,12] and, therefore, the overall effect is the mild increase in heart rate.

Magnesium is a highly effective arteriolar vasodilator but with minimal dilatory effects on the venous circulation, resulting in maintained cardiac filling and enhanced cardiac output.[13] The vasodilator effects of magnesium[11] are characterized by a mild and transient decrease in blood pressure associated with peripheral vasodilatation and a consistent increase in cardiac index.

Magnesium also reduces the responsiveness of vascular smooth muscle to norepinephrine stimulation.[14]

Neurophysiologic studies have demonstrated that magnesium is a physiological and pharmacological blocker of N-methyl-D-aspartate (NMDA) receptors in neuronal tissue. This observation raised a variety of possibilities for the use of magnesium as a neuroprotective agent in a number of forms of neurological injury[15] and for neuronal protection of the premature fetus. As the role of the NMDA receptor in pain perception has become apparent, there has been increasing use of magnesium for the management of both acute and chronic pain.[16]

There have been several recent reports of improved postoperative pain control from the addition of magnesium to epidural or spinal infusions during surgery. Magnesium has no primary analgesic activity but may have value as a secondary analgesic, enhancing the actions of more established pain medication.

Several recent reports have described the efficacy of magnesium infusions in moderate dosage both during surgery and in the postoperative period for decreasing postoperative morphine requirements.[17]

Dexmedetomidine (Dex), a highly selective α_2-adrenoreceptor agonist which offers an unique pharmacological profile with sedation, sympatholysis, analgesia, cardiovascular stability and with great advantage to avoid respiratory depression. It is used for sedation in various clinical settings and shows an anesthetic-sparing effect.[18-22]

Dexmedetomidine increases the hemodynamic stability by altering the stress induced sympatho-adrenal responses to intubation during surgery and emergence from anesthesia. Dex by activating pre and post -synaptic α2-receptors of sympathetic system produces vasodilatation; also by acting on post-synaptic α2-receptors of vascular smooth muscle cells it produces vasoconstriction. It there by shows a biphasic, dose dependent response on blood pressure and heart rate, characterized by an initial short-term increase in BP followed by a longer lasting reduction in BP and HR.[23-26]

$\alpha_{2\text{-}A}$ receptors mediate sedation, analgesia and sympatholysis whereas $\alpha_{2\text{-}B}$ receptors mediate vasoconstriction. Dexmedetomidine produces sedation by inhibiting the pontine locus ceruleus which has highest densities of α2 receptors.[27] It produces sympatholysis by stimulating α2 adrenergic inhibitory neurons in medullary vasomotor center which is manifested as peripheral vasodilatation and decrease in systolic blood pressure, heart rate and cardiac output. Atipamezole is a specific and selective α_2 receptor antagonist that rapidly and effectively reverses the sedative and cardiovascular effects of i.v dexmedetomidine.[28]

In our study we compared Magnesium sulphate with Dexmedetomidine to attenuate the stress response to laryngoscopy and endotracheal intubation. Both the drugs were effective in controlling the blood pressure but dexmedetomidine was more effective in controlling the heart rate. But the increase in heart rate in magnesium sulphate was not more than 10 beats/min. and also the heart rate returned to baseline within 5minutes.

When compared to dexmedetomidine which reduces the heart rate, magnesium sulphate does not reduce but maintains the heart rate at patient's baseline level. Patients in both the groups were hemodynamically stable throughout the perioperative period. Both the drugs reduced the requirements of opioids, muscle relaxants and volatile anesthetics. Recovery in both the groups was uneventful.

CONCLUSION: Many studies proved dexmedetomidine as an effective drug to reduce the stress response to laryngoscopy and intubation. But magnesium sulphate has been used very rarely for this purpose. Our study proves that magnesium sulphate is also an effective agent to attenuate the stress response. Magnesium sulphate also reduces the requirement of anesthetic agents in the intraoperative period.

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	Magnesium sulphate N=30	**Dexmedetomidine N=30**
Age (yr.)	33.67±8.79	32.52±8.84
Gender (M/F)	8/22	6/24

Table 1

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GROUP	N		Mean	Std. Deviation	P VALUE
SBP preinduction	Dex	30	127.90	15.712	.047
	MgSo4	30	120.47	12.475	
SBP0	Dex	30	126.47	18.686	.344
	MgSo4	30	131.93	25.196	
SBP1	Dex	30	123.83	14.511	.920
	MgSo4	30	124.27	18.655	
SBP3	Dex	30	116.23	12.280	.342
	MgSo4	30	120.07	18.145	
SBP5	Dex	30	113.03	14.924	.761
	MgSo4	30	114.30	17.104	
SBP10	Dex	30	108.80	13.798	.639
	MgSo4	30	110.50	14.142	
DBP preinduction	Dex	30	77.37	8.479	.148
	MgSo4	30	73.97	9.438	
DBP0	Dex	30	79.30	14.339	.092
	MgSo4	30	86.37	17.431	
DBP1	Dex	30	76.97	9.964	.795
	MgSo4	30	77.73	12.673	
DBP3	Dex	30	72.10	8.519	.393
	MgSo4	30	74.47	12.428	
DBP5	Dex	30	68.37	10.156	.231
	MgSo4	30	71.60	10.546	
DBP10	Dex	30	67.50	10.471	.825
	MgSo4	30	68.07	9.255	

Table 2

	Group	N	Mean	Std. Deviation	p value
HR0	Dex	30	85.13	13.338	.000
	MgSo4	30	98.27	13.963	
HR1	Dex	30	82.17	13.522	.002
	MgSo4	30	92.13	10.692	
HR3	Dex	30	80.47	12.851	.001
	MgSo4	30	91.13	11.892	
HR5	Dex	30	80.00	13.861	.010
	MgSo4	30	89.37	13.553	
HR10	Dex	30	75.17	12.900	.003
	MgSo4	30	85.37	12.478	

Table 3

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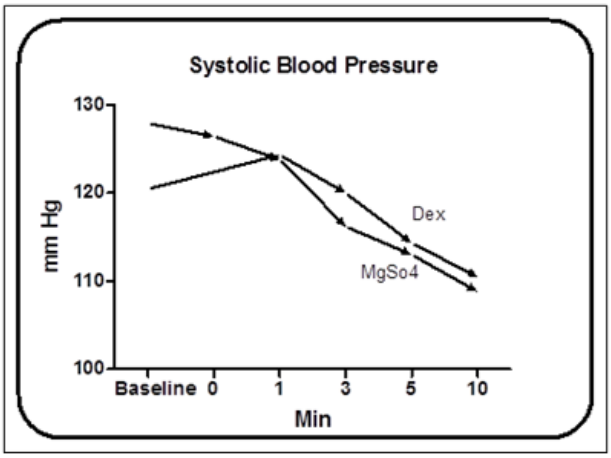

Fig. 1

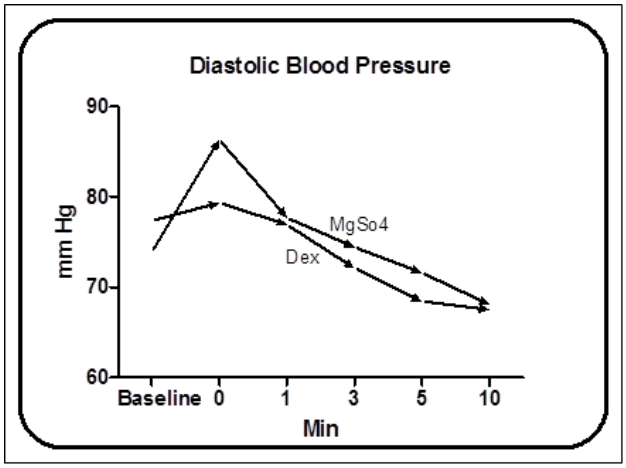

Fig. 2

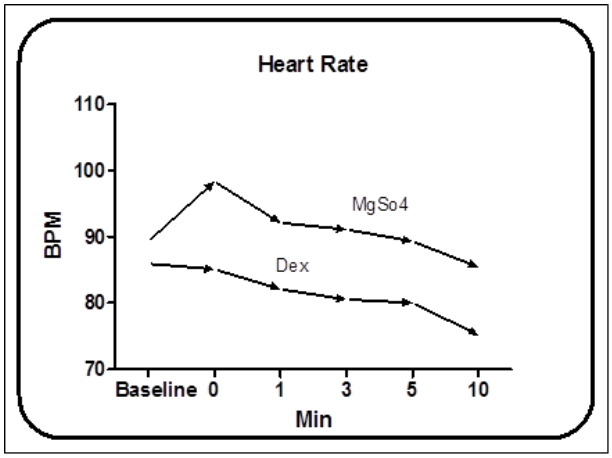

Fig. 3

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