ORIGINAL RESEARCH PAPER

Anesthesiology

# A COMPARATIVE STUDY BETWEEN INTRAVENOUS DEXMEDETOMIDINE AND 50% MAGNESIUM SULFATE IN ATTENUATION OF CARDIOVASCULAR RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION.

**KEY WORDS:** laryngoscopy, dexmedetomidine, magnesium sulphate, hemodynamic changes

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**ABSTRACT**

***INTRODUCTION*:** Hypertension and tachycardia subsequent to tracheal intubation have been well documented. In susceptible patients it can cause increase in perioperative morbidity and mortality. Many agents have been used to attenuate these undesirable hemodynamic responses to laryngoscopy and intubation with varying success. Dexmedetomidine increases the hemodynamic stability by altering the stress induced sympatho-adrenal responses to laryngoscopy and intubation during surgery and emergence from anesthesia. On the other hand, magnesium sulfate can significantly attenuate the release of catecholamines at the time of laryngoscopy and tracheal intubation.

***AIM:*** The present study was aimed to compare Inj, Dexmedetomidine 1μg/kg and Magnesium sulfate 50mg/kg in attenuation of cardiovascular response to laryngoscopy and intubation.

***METHODS:*** A randomized prospective study was conducted in Silchar Medical College and Hospital, Silchar, Assam after obtaining Institutional Ethical Committee clearance and written informed consent from the patients.

***INCLUSION CRITERIA:*** Patients between age 18-60 years, of both sexes, ASA grade I&II and scheduled for elective surgical procedure under general anesthesia

***EXCLUSION CRITERIA:*** Refusal to informed consent, anticipated difficult airway, ASA grade III&IV, history of allergy to study drug, pregnant and lactating mother, any disorders of cardiovascular system, respiratory system, renal system, hepatic and neuromuscular conditions and duration of surgery less than 60mins. 100 patients were randomly allocated to two groups of 50 patients each. Group A received inj. dexmedetomidine (1$\mu$g/kg) and Group B received inj. Magnesium sulfate (50 mg/kg). Hemodynamic parameters of patients (HR, SBP, DBP, and MAP) were recorded immediately before anesthesia induction, just before intubation, just after intubation, at 2min, 5min and 10 minutes for the study purpose. All analyses were done by using two tailed test; p-value<0.05 was considered significant and <0.001 as highly significant.

***RESULTS:*** There was no significant difference between the groups with regard to demographic variables. The mean fall in HR, SBP, DBP and MAP values at 2 and 5 minutes of intubation were statistically highly significant (p=0.000) in group A as compared to group B.

***DISCUSSION:*** The results were compared with various other similar studies which had analyzed the effect of dexmedetomidine and magnesium sulfate for attenuation of cardiovascular response during laryngoscopy and intubation and our results correlated with those studies.

## INTRODUCTION

It is well proven that direct laryngoscopy and intubation are very noxious stimuli and induce stress response in the form of laryngo-sympathetic stimulation and hemodynamic responses. These responses are well tolerated in an otherwise healthy individual, but in patients suffering from hypertension, coronary artery disease, cerebrovascular disease, intracranial aneurysms etc, these transient hemodynamic changes can result in potentially deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral hemorrhage.[1]

These changes are maximum in the first 1 minute and last for 10 minutes after the procedure. To attenuate these deleterious effects various methods and drugs have been tried[2-11].

Dexmedetomidine is a α2 receptor selective and specific adrenergic agonist.[12,13]. These drugs by virtue of their sympatholytic (i.e. antihypertensive and negative chronotropic) action, attenuate the hemodynamic response following laryngoscopy and endotracheal intubation[8].

Magnesium is well known to block the release of catecholamines from both adrenergic nerve terminals and the adrenal gland, and intravenous magnesium sulfate inhibits catecholamine release associated with laryngoscopy. Moreover, magnesium produces vasodilator effect by acting directly on blood vessels, and high-dose magnesium attenuates vasopressin-stimulated vasoconstriction[14,15]

The present study was undertaken to compare the efficacy of magnesium sulphate and dexmeditomidine for attenuation of haemodynamic responses following laryngoscopy and endotracheal intubation.

## METHODS

The study was undertaken after obtaining Institutional Ethical Committee clearance and written informed consent from the patients. A randomized prospective study involving 100 patients of both sexes between 18-60 years, requiring endotracheal intubation and general anaesthesia for various elective surgical procedures belonging to ASA grade I and II were included in the study.

The study population was divided into 2 groups with 50 patients in each group.

Patient with anticipated difficult airway, ASA grade III&IV, History of allergy to study drug, pregnant and lactating mother, patient with any disorders of cardiovascular system, respiratory system, renal system, hepatic and neuromuscular conditions, duration of surgery less than 60mins and refusing consent were excluded from the study.

On the day prior to surgery a thorough clinical examination of the patient was performed. All patients were explained about the anaesthetic technique and written informed consent was taken. Patients were kept NPO for 8 hours prior surgery. All patients were given tablet alprazolam 0.5 mg orally at bed time on the previous night of the surgery.

On arrival of the patient in the operating room, a 20-gauge intravenous cannula was secured and connected to IV fluid

ringer lactate. The baseline systolic, diastolic blood pressure, mean arterial pressure and heart rate was recorded after 5mins of settling in the operative room. All patients were being premedicated with intravenous (IV) glycopyrrolate (0.05mg/kg) midazolam 0.03mg/kg, IV fentanyl (2μg/kg). Patients in group A received inj. Dexmedetomidine 1μg/kg body weight diluted in 10 ml normal saline intravenously over 10 min and patients in group B received inj. Magnesium sulfate 50 mg/kg diluted to 10 ml with normal saline over 10 minutes.

The patients were then pre oxygenated for 3 minutes, anesthesia was induced with propofol (titrated till loss of verbal response). Endotracheal intubation was facilitated with IV Atracurium 0.5mg/kg three minutes prior to laryngoscopy and intubation. If time for laryngoscopy and intubation exceeded 15 seconds, such patients were excluded from the study. Anesthesia was maintained using 60% nitrous oxide and 40% of oxygen with isoflurane and inj.Atracurium.

Hemodynamic parameters of patients including systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP) and heart rate (HR) were recorded immediately before anesthesia induction, just before intubation, just after intubation, 2min, 5min,10min, and every 15 mins after intubation till the operation ended as the hemodynamic changes and intubation mostly occurs in the first minute and last for approximately 10 mins after the procedure. At the end of the surgical procedure patients was reversed with neostigmine 0.05 mg/kg body weight and glycopyrrolate 0.02mg/kg.

## STATISTICAL METHOD EMPLOYED

All data are presented as Mean ± SD (Standard Deviation). All Quantitative data are assessed using Student's t - test to analyse changes over a period of time. Qualitative data are assessed using Fisher exact Test or Chi- square test. P value < 0 .05 is considered significant. The statistical software **GRAPHPAD INSAT-3** was used for the analysis of data.

## RESULTS:

The mean age, weight, height and duration of surgery of both the groups were comparable. There was no significant difference amongst the groups with regard to demographic variables (P value < 0.05).

## CHANGES IN HEART RATE :

**Table 1:- Comparison of mean heart rate between two groups**

| | Heart Rate (beats/min) | | | | P-value |
|---|---|---|---|---|---|
| | Groups A (DEXMED) N=50 | | Groups B (MgSO4) N=50 | | |
| | Mean | SD | Mean | SD | |
| HR T0 (Baseline) | 85.36 | 5.55 | 86.56 | 7.07 | 0.348 |
| HR T (Before Induction) | 84.82 | 5.72 | 85.46 | 6.55 | 0.604 |
| HR T1 (Before Intubation) | 74.68 | 6.45 | 77.52 | 6.95 | 0.037 |
| HR T2 (Just After Intubation) | 83.02 | 5.45 | 96.14 | 4.48 | 0.000 |
| HR T3 (2mins After Intubation) | 77.06 | 5.37 | 90.46 | 3.79 | 0.000 |
| HR T4 (5mins After Intubation) | 73.44 | 5.55 | 84.52 | 3.41 | 0.000 |
| HR T5 (10mins After Intubation) | 84.90 | 5.32 | 85.90 | 8.72 | 0.490 |

The mean HR decrease observed just after intubation, at 2 and 5 minutes after intubation in Group A was statistically highly significant compared to mean HR in group B (p=0.000).

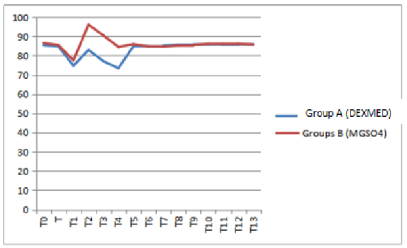


Figure 1 – Line diagram showing comparison of mean heart rate between the two groups.

## CHANGE IN SYSTOLIC BLOOD PRESURE

**Table 2:- Comparison of mean systolic blood pressure in between two groups**

| | SBP | | | | P-value |
|---|---|---|---|---|---|
| | Groups A (DEXMED) N=50 | | Groups B (MgSO4) N=50 | | |
| | Mean | SD | Mean | SD | |
| SBP(mmHg) T0 (Baseline) | 127.68 | 7.05 | 129.96 | 6.76 | 0.102 |
| SBP(mmHg) T (Before Induction) | 126.62 | 7.58 | 128.64 | 7.72 | 0.190 |
| SBP(mmHg) T1 (Before Intubation) | 103.04 | 7.30 | 105.90 | 5.51 | 0.029 |
| SBP(mmHg) T2 (Just After Intubation) | 116.18 | 7.45 | 136.46 | 8.65 | 0.000 |
| SBP(mmHg) T3 (2mins After Intubation) | 108.28 | 5.73 | 128.38 | 7.08 | 0.000 |
| SBP(mmHg) T4 (5mins After Intubation) | 102.44 | 5.42 | 120.88 | 7.75 | 0.000 |
| SBP(mmHg) T5 (10mins After Intubation) | 126.68 | 7.04 | 127.36 | 8.77 | 0.670 |

The mean fall in SBP in group A just after intubation, at 2 and 5 minutes after intubation was statistically highly significant (p=0.000) compared to group B.

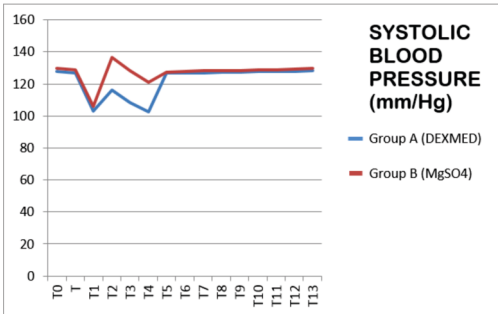


**Figure 2– Line diagram showing comparison of mean systolic blood pressure between two groups.**

## DIASTOLIC BLOOD PRESSURE

**Table 3:- Comparison of mean diastolic blood pressure between the two groups.**

| | DBP | | | | P-value |
|---|---|---|---|---|---|
| | Groups A (DEXMED) N=50 | | Groups B (MgSO4) N=50 | | |
| | Mean | SD | Mean | SD | |
| DBP(mmHg) T0 (Baseline) | 82.02 | 4.22 | 82.36 | 4.29 | 0.690 |
| DBP(mmHg) T (Before Induction) | 81.12 | 4.25 | 81.56 | 4.27 | 0.607 |
| DBP(mmHg) T1 (Before Intubation) | 72.12 | 5.36 | 73.94 | 3.80 | 0.053 |
| DBP(mmHg) T2 (Just After Intubation) | 68.62 | 6.06 | 69.96 | 5.23 | 0.240 |
| DBP(mmHg) T3 (2mins After Intubation) | 69.24 | 3.92 | 79.94 | 3.48 | 0.000 |

| | | | | | |
|---|---|---|---|---|---|
| DBP(mmHg) T4 (5mins After Intubation) | 66.34 | 3.85 | 75.94 | 3.38 | 0.000 |
| DBP(mmHg) T5 (10mins After Intubation) | 81.60 | 3.86 | 82.30 | 5.32 | 0.453 |

The fall in mean DBP values at 2 and, 5 minutes of intubation were statistically highly significant (p=0.000) in group A compared to group B.

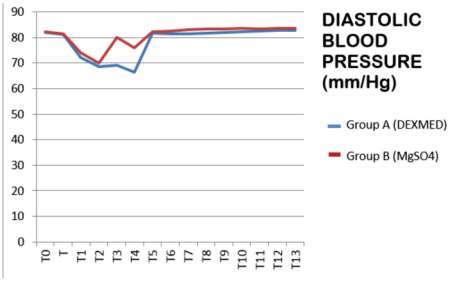


**Figure 3 – Line diagram showing comparison of mean diastolic blood pressure between the two groups.**

**MEAN ARTERIAL PRESSURE**

**Table 4:- Comparison of mean arterial pressure between the two groups.**

| | MAP | | | | P-value |
|---|---|---|---|---|---|
| | Groups A (DEXMED) N=50 | | Groups B (MgSO4) N=50 | | |
| | Mean | SD | Mean | SD | |
| MAP(mmHg) T0 (Baseline) | 96.98 | 4.31 | 97.86 | 3.99 | 0.292 |
| MAP(mmHg) T (Before Induction) | 95.98 | 4.47 | 97.02 | 3.81 | 0.214 |
| MAP(mmHg) T1 (Before Intubation) | 82.38 | 4.96 | 83.94 | 4.56 | 0.105 |
| MAP(mmHg) T2 (Just After Intubation) | 80.02 | 4.88 | 81.88 | 4.60 | 0.053 |
| MAP(mmHg) T3 (2mins After Intubation) | 81.98 | 3.62 | 95.50 | 3.62 | 0.000 |
| MAP(mmHg) T4 (5mins After Intubation) | 77.96 | 3.54 | 90.46 | 3.45 | 0.000 |
| MAP(mmHg) T5 (10mins After Intubation) | 96.04 | 4.25 | 96.84 | 5.48 | 0.417 |

The fall in mean MAP values in group A at 2 and 5 minutes of intubation were statistically highly significant (p=0.000) compared to group B.

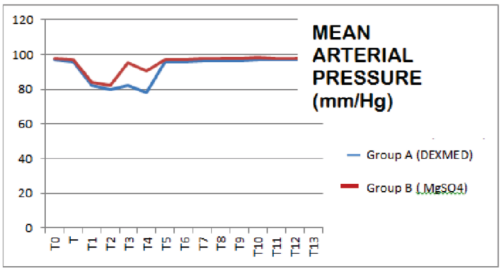


**Figure 4 – Line diagram showing comparison of MAP between two groups.**

In our study, we noticed 6% incidence of PONV and bradycardia and 4% incidence of hypotension in group A. The incidence of hypotension and bradycardia was less with MgSO4 but the difference between the two groups was non-significant. Tachycardia was seen in Group B which were not significant when compared with group A. These side effects didn't require any intervention.

**DISCUSSION.**

Laryngoscopy and intubation is a routine practice in anesthesiology. King et al., (1951)[16] have described the circulatory responses to laryngeal and tracheal stimulation following laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation. Many agents have been used to attenuate undesirable haemodynamic responses to laryngoscopy and intubation with varying success. These include intravenous opioids, vasodilators, calcium channel blockers, intravenous and topical lignocaine and adrenoceptor blocking drugs alone or in combination with other drugs[2-11].

The present study aimed at comparing intravenous dexmedetomidine and 50% Magnesium sulfate for the hemodynamic attenuation during laryngoscopy and endotracheal intubation.

The study population consisted of 100 patients divided equally in two groups. Patients in group A received inj. Dexmedetomidine 1μg/kg body weight diluted in 10 ml normal saline intravenously over 10 min and patients in group B received inj. Magnesium sulfate 50 mg/kg diluted to 10 ml with normal saline over 10 minutes. Attempts have been made to suppress the circulatory response using various pharmacological agents aimed at afferent, efferent or both limbs of response.

Dexmedetomidine, a highly selective α2-adrenoreceptors agonist, increases the hemodynamic stability by altering the stress induced sympatho-adrenal responses to laryngoscopy and intubation during surgery and emergence from anesthesia. Dexmedetomidine 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[17,18,19,20].

Magnesium sulfate, on the other hand, has been described as the physiological calcium antagonist[21] 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[22] and is now well established. So, magnesium sulfate can significantly attenuate the release of catecholamines at the time of laryngoscopy and 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[23,24] and, therefore, the overall effect is the mild increase in heart rate.

In our study we have compared dexmedetomidine with Magnesium sulfate to attenuate the stress response to laryngoscopy and endotracheal intubation. The mean fall in HR and SBP observed just after intubation, at 2 and 5 minutes after intubation in Group A was statistically highly significant compared to mean HR in B group(p=0.000).

The fall in mean DBP and mean MAP values at 2 and 5 minutes of intubation were statistically highly significant (p=0.000) in group A compared to group B.

In conclusion both dexmedetomidine and magnesium sulfate attenuated the cardiovascular response to laryngoscopy and intubation. Inj dexmedetomindine 1μg/kg was more efficient than inj. MgSO4 50mg/kg for attenuation of the cardiovascular response to laryngoscopy and intubation. Dexmedetomdine was associated with greater decrease in heart rate as compared to magnesium sulfate where a mild increase in HR could also be seen in some cases.

Similar findings were also found on several studies which corroborate the finding of the hemodynamic attenuation by the drugs. Chhaya Joshi et al[25], Krishna Chaithanya et al[26], Ismail M.A Ahmed et al[27], Vinit K. Srivastava et al[28], Lakshmi Mahajan et al[29], Kumkum Gupta et al[30], Nabin Pokhrel et al[31].

## CONCLUSION

From this study it was observed that Inj. Dexmedetomidine 1µg/kg caused better attenuation of cardiovascular response to laryngoscopy and intubation as compared to magnesium sulfate. It provided more stable HR, SBP, DBP and MAP during the stressful period following larygoscopy and intubation. There were minimal side effects with no significant difference in both the groups.

On the basis of our present clinical comparative study, we can come to conclusion that

1. Both dexmedetomidine and magnesium sulfate attenuated the cardiovascular response to laryngoscopy and intubation.
2. Inj dexmedetomindine 1µg/kg was more efficient than inj. MgSO4 50mg/kg for attenuation of the cardiovascular response to laryngoscopy and intubation.
3. Dexmedetomdine was associated with greater decrease in heart rate as compared to magnesium sulfate where a mild increase in HR could also be seen in some cases.

1. Conflict of Interest- none
2. Sourse of Support - none

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