A Comparison Between Effectiveness of Intravenous Magnesium Sulphate and Dexmedetomidine on Attenuation of Haemodynamic Stress Response to Laryngoscopy and Endotracheal Intubation: A Randomised Control Trail

ABSTRACT

Introduction: Hemodynamic stress responses to laryngoscopy and endotracheal intubation, can pose significant risks, especially in patients with cardiovascular comorbidities. This study aimed to compare the efficacy of magnesium sulphate and dexmedetomidine in attenuating these responses.

Methods: A randomized controlled trial was conducted on 80 patients (40 in each group), aged 18-60 years, undergoing elective surgeries under general anesthesia at Meenakshi Mission Hospital, Madurai. Patients were randomized into two groups: Group M received 30 mg/kg magnesium sulphate, and Group D received 0.75 mcg/kg dexmedetomidine. Hemodynamic parameters (heart rate, systolic, diastolic, and mean arterial pressure) were measured at baseline, after drug administration, and at 1, 3, and 5 minutes post-intubation. Data were analyzed using Student t-tests and chi-square tests, with $p < 0.05$ considered significant.

Results: Dexmedetomidine (Group D) showed significantly lower heart rate and systolic blood pressure at all post-intubation intervals compared to magnesium sulphate (Group M). Specifically, Group D demonstrated lower mean heart rates at 3 minutes post-drug (77.3 ± 15.8 vs 86.5 ± 13.0; p=0.006) and 5 minutes post-intubation (72.1 ± 9.8 vs 77.1 ± 11.5; p=0.04). Systolic blood pressure was also significantly lower in Group D at 1 minute post-intubation (123.7 ± 16.1 vs 136.9 ± 12.6; p=0.001). Complication rates were low in both groups, though hypotension occurred more frequently in Group D (10% vs 2.5%, p=0.166).

Conclusion: Dexmedetomidine was more effective than magnesium sulphate in attenuating the hemodynamic stress response to laryngoscopy and intubation, with a slightly higher incidence of hypotension. Both agents were generally safe and well-tolerated.

Keywords: Laryngoscopy, Endotracheal Intubation, Hemodynamics, Magnesium Sulfate, Dexmedetomidine

1. INTRODUCTION

Both laryngoscopy and endotracheal intubation are common airway management methods used in emergency medical care and surgery [1]. However, they are commonly linked to notable hemodynamic responses that are characterized by sympathetic activation resulting in an elevation of blood pressure, heart rate, and plasma catecholamine levels. This condition, which is also known as the "pressor response," might put patients at serious risk, particularly those who have intracranial diseases, hypertension, or cardiovascular comorbidities [2,3]. Therefore, it is essential to attenuate this hemodynamic stress response to lower perioperative morbidity and death among patients undergoing laryngoscopy and endotracheal intubation.

The primary cause of the laryngoscopic stress response is the activation of mechanoreceptors in the larynx, epiglottis, and pharyngeal wall. These receptors then set off a series of autonomic reflexes through the sympathetic nervous system [4].These reflexes cause an abruptly increase the catecholamine release, which raises heart rate and blood pressure resulting in myocardial ischemia, cerebrovascular accidents, or other harmful cardiovascular effects [5]. Thus, controlling this response has gained attention in contemporary anaesthesiology, and many pharmaceutical treatments have been investigated for their potential to reduce this pressor response [6].

Numerous medications, such as beta-blockers, calcium channel blockers, opioids, and local anaesthetics, have been studied for their potential to lessen this hemodynamic response; yet, the quest for the ideal treatment modality persists. Recent years have seen an increase in interest in two pharmacological drugs namely magnesium sulphate and dexmedetomidine, due to their potential to modify the cardiovascular response during laryngoscopy and intubation [7].

Magnesium sulfate is a divalent cation that has anti-nociceptive, vasodilatory, and anti-arrhythmic effects in addition to acting as a calcium channel blocker. Magnesium sulfate reduces sympathetic outflow by blocking catecholamine release from peripheral nerve endings and the adrenal medulla. This may lessen the tachycardic and hypertensive response that occurs during airway manipulation. Magnesium also functions as an N-methyl-D-aspartate (NMDA) receptor antagonist, which may be part of the reason for its ability to reduce nociception and improve perioperative analgesia. Magnesium sulfate has a broad pharmacological profile, which makes it a promising drug to reduce the hemodynamic stress response [8].

An alpha-2 adrenergic receptor agonist with a unique mode of action is dexmedetomidine. By lowering sympathetic tone and preventing the release of norepinephrine from pre- and post-synaptic alpha-2 receptors in the central nervous system, it causes drowsiness, analgesia, and anxiolysis. Apart from its central actions, dexmedetomidine also causes peripheral vasodilation, which helps lessen the pressure response to intubation and laryngoscopy [6]. The drug's benefits for anaesthesia include steady hemodynamics, a decreased need for anaesthetic, and a sedative profile without respiratory depression. As a result, dexmedetomidine has become more widely used in perioperative care, particularly for its ability to reduce the hemodynamic response to airway instrumentation [9]. Only very few research

works are available from India, that has compared the use of these drugs in attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation, Thus, we decided to take up this study.

Aim:
To evaluate the effectiveness and complications of magnesium sulphate and dexmedetomidine in attenuating hemodynamic stress response to laryngoscopy and intubation.

2. MATERIAL AND METHODS

2.1 Study design and setting:
We conducted a randomized control trail among patients aged 18 to 60 years, with inclusion criteria of i) Undergoing Elective Surgeries Under General Anaesthesia ii) Mallampati Class I and II iii) Belonging to ASA Grade I and II admitted in Meenakshi mission hospital and research centre, Madurai over a period of 2 years [August 2019 – October 2020]. We excluded the following patients: i) Had anticipated difficult airway ii) Laryngoscopy time exceeded 15 seconds iii) History of hiatus hernia or full stomach or GERD (gastroesophageal reflux disease) iv) Physically dependent on narcotics, drugs or alcohol abuse v) Pregnant women and vi) Patient on beta blockers

2.2 Sample size:
The sample size was calculated based on the previous study done by Krishna Chaithanya et al[10]assuming power at 80% and confidence interval at 95% with Group 1 and 2 mean [SD] to be 80.5 (13.8) & 89.4 (13.5), using the formula:

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2 / \kappa)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_2 = \frac{(\kappa * \sigma_1^2 + \sigma_2^2)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

The final sample size was arrived at 40 in each group [80 in total]
Randomisation and Allocation concealment:
Patients who fulfilled the inclusion and exclusion criteria and were willing to participate in the study were allotted to either of the 2 groups based on computer-generated randomization. The random numbers were generated using the statistical software STATA version14 (Texas, USA) and allocated into:
Group M received Magnesium sulphate 30mg/kg diluted to 50 ml with normal saline
Group D received Dexmedetomidine 0.75mcg/kg diluted to 50 ml with normal saline
Allocation concealment was ensured using the SNOSE [Sequentially numbered opaque sealed envelopes]

2.3 Study procedure:
After obtaining institutional ethical committee approval (IEC), 80 patients belonging to ASA grade I and II aged between 18-60 years of either gender, who fulfilled the inclusion and exclusion criteria posted for elective surgeries under general

anaesthesia were assigned to the study. Demographic data were recorded. All patients were evaluated for anaesthesia fitness and surgical procedures on the day before surgery. A thorough history was obtained and a clinical examination was performed.

On the day of surgery, the patient was identified and all vital parameters, NPO status, consent for anaesthesia and consent for study were checked. The procedure was done under the guidance of a senior consultant anesthesiologist. The patient was shifted to operating room and intravenous (IV) access was secured, standard monitoring including ECG, NIBP, and pulse oximeter were connected and the baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were noted. All patients received injection of glycopyrolate 0.2mg intravenously as premedication half an hour before induction.Patients were divided into two groups by computer-based randomisation.After completing either magnesium sulphate or dexmedetomidine infusion, before inducing the patient, heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were noted. The patient was pre-oxygenated for 3 minutes with 100% oxygen and induced with IV fentanyl 1.5mcg/kg, and IV propofol 1.5mg/kg. After checking for the ease of bag-mask ventilation, the patient was paralyzed with IV rocuronium 1mg/kg and bag-mask ventilation was done for 1 minute with 100% oxygen and patient's heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were noted.

After 1 minute of assisted mask ventilation, laryngoscopy and endotracheal intubation was done. The duration of laryngoscopy and intubation was limited to the minimum possible time and was less than 15 seconds for all patients. Proper placement of the endotracheal tube and ventilation was checked by auscultation of breath sounds and capnography. Then the patient was connected to a mechanical ventilator and ventilated using volume-controlled ventilation mode. Anaesthesia was maintained with O_2 and N_2O in the ratio of 50% each and isoflurane 1vol%. Hemodynamic parameters were measured before magnesium sulphate/dexmedetomidine infusion (baseline), 3 minutes after the study drug (before induction), 1 minute after induction, 1 minute, 3 minutes and 5 minutes after intubation. At the end of surgery, patients were reversed with neostigmine 0.05mcg/kg and glycopyrrolate 0.01mcg/kg.

The hemodynamic parameters monitored included:**i)** Heart rate **ii)** Systolic blood pressure **iii)** Diastolic blood pressure **iv)** Mean arterial pressure

These parameters were measured at the following intervals:

i) baseline (before study drug),
ii) 3 minutes after the study drug (before induction),
iii) 1 minute after induction,
iv) 1 minute after intubation,
v) 3 minutes after intubation,
vi) 5 minutes after intubation.

Complications like hypotension, bradycardia and desaturation were noted with the definition:

1. Hypotension – systolic blood pressure less than 30% of patient's baseline value or systolic blood pressure less than 90 mmHg whichever is lower and can be managed with intravenous fluids and Ephedrine 6mg IV bolusand further doses titrated according to response

2. Bradycardia - heart rate less than 20% of patient's baseline value or heart rate less than 50 beats per minute whichever is lower. If heart rate less than 50 beats per min, that was treated with injection atropine 0.6 mg
3. Desaturation - oxygen saturation less than 90%. And if the patient desaturates, supplemented with 15L O_2 through non rebreathing face mask with nasopharyngeal airway if there is upper airway obstruction

2.4 Statistical analysis:

All necessary information was collected and entered into a Microsoft Excel worksheet. Data analysis was done with the help of a computer using SPSS Statistics 26.0 software (SPSS Inc. Bangalore India). The chi-square test and Fisher's exact test were used to find out the association between the categorical variables. Independent's 'T-test was used to find the significance of the difference between groups. A 'p' valve less than 0.05 was considered statistically significant. The performed the analysis based on per protocol analysis

3. RESULTS

We finally recruited around 80 patients [40 in each group] who fulfilled the inclusion criteria [0% non-response rate]. The comparison of sociodemographic and baseline hemodynamic parameters across the study groups is explained in **Table 1.** The mean age in group M was 44.3 ± 8.6 years and in group D was 42.4 ± 11.0 years, and mean weight in group M was 59.0 ± 8.1 kgand in group D was 62.2 ± 9.1 kg. In group M 21 (52.5%) were male patients and 19 (47.5%) were female patients. In group D 25 (62.5%) were male patients and 15 (37.5%) were female patients. The percentage of patients belonging to ASA I and II in group M was 16 (40%) and 24 (60%) respectively. The percentage of patients belonging to ASA I and II in group D was 20 (50%) and 20 (50%) respectively. There was no statistically significant difference in the sociodemographic variables in the two groups (>p=0.05) and they were comparable.

Table 1: Comparison of sociodemographic and baseline hemodynamic parameters across the study groups, N=80

Parameter	Group M	Group D	Students T test (t value)	p-value
	Mean ± SD	Mean ± SD		
Age (years)	44.3 ± 8.6	42.4 ± 11.0	-0.8837	0.38
Weight (kg)	59.0 ± 8.1	62.2 ± 9.1	1.7084	0.09
Baseline hemodynamic parameters				

HR (beats/min)	83.5 ± 13.4	88.8 ± 14.9	1.6707	0.09
SBP (mm of Hg)	138.7 ± 11.8	136.6 ± 12.9	-0.7680	0.44
DBP(mm of Hg)	82.2 ± 9.1	83.5 ± 9.0	0.6575	0.51
MAP(mm of Hg)	99.6 ± 8.4	99.2 ± 7.9	-0.2052	0.82
Parameter	**N (%)**	**N (%)**	**Chi square ()**	**p-value**
Gender				
Male	21 (52.5)	25 (62.5)	0.8184	0.36
Female	19 (47.5)	15 (37.5)		
ASA status				
I	16 (40.0)	20 (50.0)	0.8081	0.36
II	24 (60.0)	20 (50.0)		

Table 2: Comparison of hemodynamic parameters [Heart rate, systolic & diastolic blood pressure, and mean arterial pressure during the time intervals across the study groups, N=80

Parameter	Follow up time	Group M	Group D	Students T test (t value)	P-value
		Mean ± SD	Mean ± SD		
Heart Rate (beats per minute)	**Base line**	83.5 ± 13.4	88.8 ± 14.9	1.6707	.099 NS
	3 min after study drug	86.5 ± 13.0	77.3 ± 15.8	-2.8534	**.006 Sig**
	1 min after induction	79.4 ± 12.5	72.2 ± 11.7	-2.6690	**.009 Sig**
	1min after intubation	90.1 ± 11.7	78.4 ± 9.3	-4.9552	**.001 Sig**
	3 min after intubation	81.0 ± 10.4	74.4 ± 9.4	-2.9833	**.004 Sig**
	5 min after intubation	77.1 ± 11.5	72.1 ± 9.8	-1.9197	**.040. Sig**
Systolic blood	**Base line**	138.7 ± 11.8	136.6 ± 12.9	-0.7680	.449 NS

pressure (mm Hg)	**3 min after study drug**	131.6 ± 9.6	123.4 ± 11.7	-3.4314	**.001 Sig**
	1 min after induction	117.9 ± 13.0	110.9 ± 14.1	-2.3204	**.023 Sig**
	1 min after intubation	136.9 ± 12.6	123.7 ± 16.1	-4.0929	**.001 Sig**
	3 min after intubation	124.7 ± 19.6	108.2 ± 14.6	-4.2447	**.001 Sig**
	5 min after intubation	116.3 ± 14.9	100.3 ± 13.5	-5.0290	**.001 Sig**
Diastolic blood pressure (mm Hg)	**Base line**	82.2 ± 9.1	83.5 ± 9.0	0.6575	.513 NS
	3 min after study drug	79.0 ± 8.9	78.9 ± 8.6	-0.0896	.929 NS
	1 min after induction	71.7 ± 10.9	71.4 ± 10.8	-0.1235	.902 NS
	1 min after intubation	89.5 ± 13.0	80.9 ± 14.0	-2.8522	**.006 Sig**
	3 min after intubation	79.1 ± 14.9	68.2 ± 12.3	-3.5578	**.001 Sig**
	5 min after intubation	72.4 ± 13.0	62.2 ±10.7	-3.8326	**.001 Sig**
Mean arterial pressure (mm Hg)	**Base line**	99.6 ± 8.4	99.2 ± 7.9	-0.2052	.826 NS
	3 min after study drug	95.8 ± 7.8	92.2 ± 7.5	-2.1082	**.038 Sig**
	1 min after induction	86.1 ± 9.7	83.5 ± 11	-1.1487	.254 NS
	1 min after intubation	104 ± 10.7	94.0 ± 14.5	-3.6401	**.001 Sig**
	3 min after intubation	93.0 ± 14.4	81.4 ± 12.0	-3.9221	**.001 Sig**
	5 min after intubation	86.0 ± 12.3	74.1 ± 10.8	-4.5819	**.001 Sig**

NS – not significant, Sig - Significant

The comparison of hemodynamic parameters [Heart rate, systolic & diastolic blood pressure, and mean arterial pressure during the time intervals across the study groups are explained in **table 2**. In our study, group D (dexmedetomidine 0.75mcg/kg) had lower mean heart rate than group M (magnesium sulphate 30mg/kg) at all time intervals and was statistically significant at 3 minutes after study drug, 1 minute after induction, 1 minute, 3 minutes and 5 minutes after intubation ($p<0.05$). Study group D (dexmedetomidine 0.75mcg/kg) had a statistically lower mean systolic blood pressure compared to group M (magnesium sulphate 30mg/kg) at all post-infusion points, while the diastolic blood pressure in Group D remained significantly lower across the time points 1, 3 and 5 minutes after induction compared to Group M. (p value <0.05)

Table 3: Comparison of complications across the study groups, N=80

Complications	Group M	Group D	P-Value
Hypotension			
Yes	1(2.5%)	4(10%)	.166 NS
No	39 (97.5)	36 (90%)	
Bradycardia	0(0%)	0(0%)	Not applicable
Desaturation	0(0%)	0(0%)	

Table 3 explains the incidence of complications across the study groups. We noted that Group M reported complications (hypotension) in only 1 patient (2.5%) whereas Group D reported in 4 (10%) patients. None reported bradycardia and desaturation. **Fig 1** explains the change in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure, compared to baseline and the time point of measurement. We noted that Group M showed a significant change when compared to the baseline for all time points across all parameters, when compared to Group D [Data showed only in figures

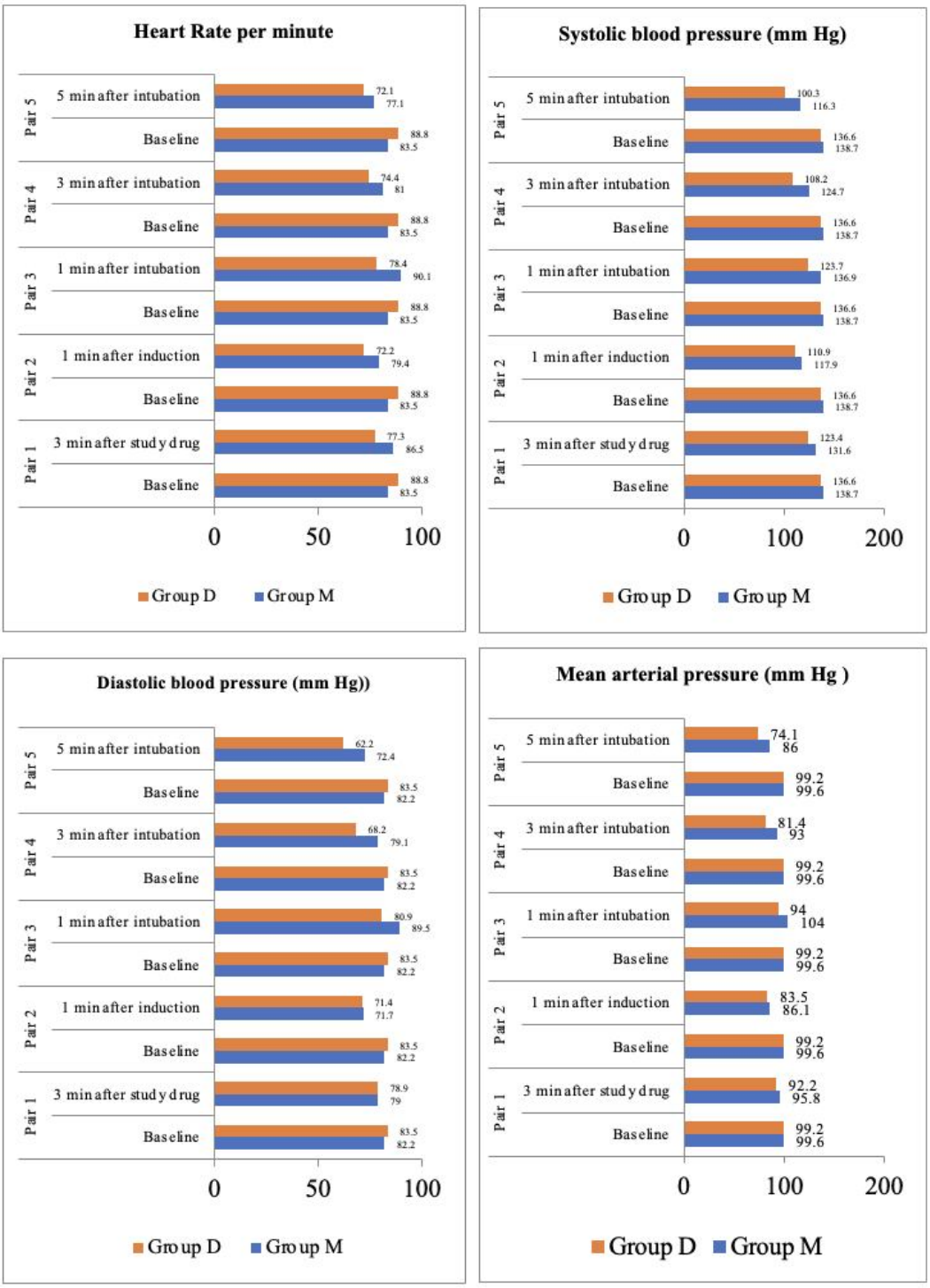

Fig 1: Comparison of hemodynamic parameters [Heart rate, systolic & diastolic blood pressure, and mean arterial pressure during the time intervals within the study groups, N=80

4. Discussion:

We conducted a randomized control trial to evaluate the effectiveness and complications of magnesium sulfate and dexmedetomidine in attenuating the hemodynamic stress response during intubation among adult patients undergoing Elective Surgeries Under General Anaesthesia at a tertiary care institute.

Our study concluded that dexmedetomidine was superior to magnesium sulfate in regulating heart rate. Group D (dexmedetomidine 0.75 mcg/kg) demonstrated consistently lower mean heart rates compared to Group M (magnesium sulfate 30 mg/kg) at key time points: 3 minutes post-drug administration and 1, 3, and 5 minutes post-intubation. These results align with the findings of Joshi et al.[11] and Chaithanya et al.[10], both of whom reported significant reductions in heart rate with dexmedetomidine following intubation compared to magnesium sulfate. Dexmedetomidine's superior sympatholytic effects likely explain its more rapid and sustained control of the hemodynamic response during intubation.

Dexmedetomidine also outperformed magnesium sulfate in controlling systolic blood pressure post-intubation. Group D exhibited significantly lower mean systolic blood pressure at all measured intervals. This outcome is consistent with Borah et al.[12] and Joshi et al.[11], both of whom demonstrated that dexmedetomidine improved systolic pressure regulation compared to magnesium sulfate. However, studies by Khan and Ghodki[13,14] did not observe significant differences between the two drugs, possibly due to variations in dosage and infusion rates. The smaller dexmedetomidine dose in our study might have optimized systolic pressure control without causing severe hypotension, an outcome supported by our findings.

Similarly, dexmedetomidine was more effective at controlling diastolic blood pressure. Our study showed a statistically significant decrease in diastolic blood pressure at 1, 3, and 5 minutes post-intubation in Group D. These findings corroborate previous research by Borah et al.[12] and Joshi et al.[11], which also demonstrated superior diastolic blood pressure control with dexmedetomidine. However, other studies, such as those by Khan and Chaithanya[10], found both drugs to be equally effective in this regard. Differences in patient populations, dosages, and infusion techniques may account for these discrepancies. Nonetheless, the overall trend points to dexmedetomidine as a more reliable option for controlling diastolic blood pressure during intubation.[15-17]

Regarding complications, both magnesium sulfate and dexmedetomidine exhibited low incidence rates. Hypotension occurred in 10% of patients in the dexmedetomidine group and 2.5% in the magnesium group, but all cases were managed effectively with fluid administration, without requiring further therapeutic interventions. No bradycardia or desaturation was observed in either group, likely due to appropriate dosing and premedication with glycopyrrolate. These findings are consistent with those of Joshi et al.[11], who reported similar rates of hypotension without significant adverse events. The safety profiles of both drugs have also been confirmed by studies conducted by Ghodki, Borah, and Mahajan et al.[12,14,18]. While dexmedetomidine appears to provide more effective attenuation of the

hemodynamic stress response, it carries a slightly higher, though manageable, risk of hypotension.[19,20] Based on our findings, we recommend the use of dexmedetomidine for attenuating the stress response to intubation. Further studies should investigate other anesthetic parameters, such as depth of anesthesia and the attenuation of the extubation response, in patients receiving dexmedetomidine and magnesium sulfate.

Our study's primary strength is that it is one of the few conducted in a South Indian setting to compare magnesium sulfate and dexmedetomidine in attenuating the hemodynamic stress response during intubation. The randomization employed in our study adds to the robustness of our findings. However, several limitations must be acknowledged. First, we did not measure plasma catecholamine levels, which could have provided additional insights into the sympathetic response. Additionally, we only included patients with ASA physical status I and II, limiting the generalizability of our findings to cardiac or higher-risk patients, who may also benefit from dexmedetomidine and magnesium sulfate. Finally, our study did not examine the effects of these drugs on intraoperative and postoperative hemodynamic parameters, which warrants further investigation.

5. Conclusion:

From our study, we conclude that dexmedetomidine in a dose of 0.75 mcg/kg significantly attenuates the haemodynamic stress response to laryngoscopy and endotracheal intubation when compared to magnesium sulphate in a dose of 30 mg/kg. Dexmedetomidine consistently showed superior hemodynamic stability, particularly in the reduction of systolic and diastolic blood pressure, which aligns with findings from previous studies. Although both agents were effective, dexmedetomidine's ability to maintain lower blood pressure and heart rate throughout the procedure suggests its greater potency in mitigating the cardiovascular stress response during airway manipulation. We also found that both drugs are devoid of any significant adverse effects like hypotension, bradycardia and desaturation.

ETHICAL APPROVAL AND CONSENT

The patient and attendees were explained about the procedure and the expected complications. They were informed about the present study and their eligibility for participating in the study. Only patients who were willing to participate were included and informed consent was obtained. The study was approved by the Institutional Ethical Committee [NBE/CNC/CET/41159]

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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