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To Compare The Effect of Magnesium Sulphate And Labetalol In Attenuating Stress Response of Laryngoscopy And Intubation.

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ABSTRACT: Laryngoscopy and tracheal Intubation are invariably associated with certain stress responses due to the sympathoadrenal stimulation. These cardiovascular and neurohumoral alterations may directly affect physiology and increase the risk. So far, various drugs have been tried but none has been considered ideal for blunting this presser response. We, therefore, planned this comparative study to evaluate and compare the efficacy of intravenous magnesium sulfate versus intravenous labetalol in attenuating the presser response to Laryngoscopy and Tracheal Intubation. Sixty patients, aged 18–50 years, scheduled for elective surgery under general anaesthesia, at our tertiary care hospital. During laryngoscopy & intubation, BP rises up to 30-40%, when premedicated with labetalol or magnesium sulphate, BP rises near to baseline levels and came to baseline level in less time. Both the drugs prevent the rise in blood pressure and heart rate during laryngoscopy and intubation but magnesium sulphate is more effective in controlling hemodynamics although it transiently increases the heart rate in the first minute.

KEYWORDS: Laryngoscopy, Intubation, Stress response, Labetalol, Magnesium sulphate

Study Design: A Prospective Clinical Study.

1. INTRODUCTION

In recent years, evaluating stress response during surgery and anesthesia is most important [1,2]. These cardio-vascular changes may directly affect patients'physiology and increase hemodynamic instability [3]. Tracheal intubation is necessary in most surgical patients requiring general anaesthesia and critically ill mechanical ventilated patients. Laryngoscopy and tracheal intubation are noxious stimuli which associated with a transient increase in autonomic response, i.e. increase in heart rate, blood pressure, and could be deleterious and lead to MI, arrhythmia, intracranial hemorrhage in vulnerable patients.[4]. These transitory responses usually produce no consequences in healthy individuals but may be harmful to the patients having reactive airways, hypertension, coronary artery disease, myocardial insufficiency, and cerebrovascular diseases [5].

We, therefore, planned this comparative study to evaluate and compare the efficacy of intravenous magnesium sulphate and intravenous labetalol in attenuating the presser response to laryngoscopy and tracheal Intubation.

AIM - To compare the efficacy of intravenous labetalol and magnesium sulphate in attenuating stress response of laryngoscopy and intubation. The primary objective of this

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study is to measure change in heart rate and blood pressure during tracheal intubation.

2. MATERIALS AND METHODS

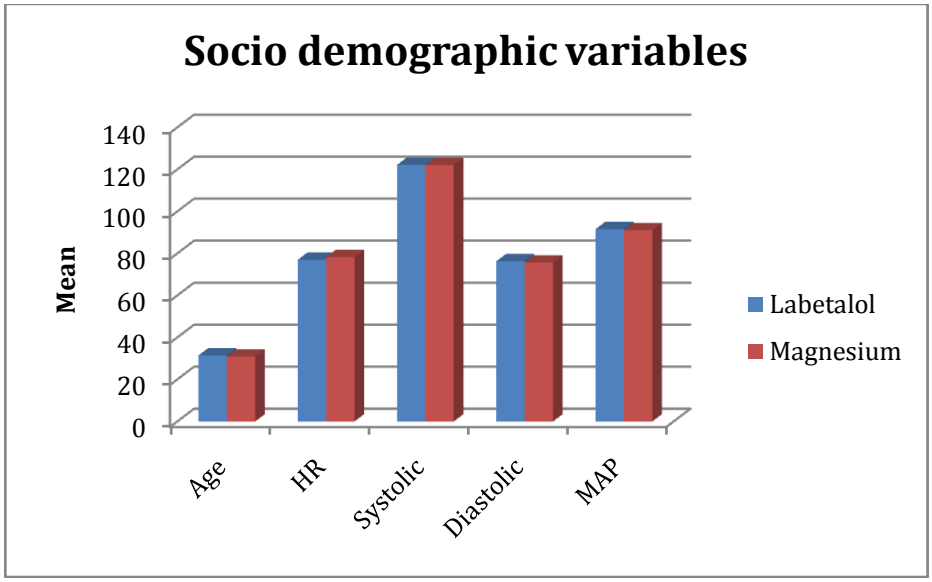
After obtaining the approvals from the institutional review board, a prospective clinical study was designed and conducted in a tertiary care hospital. Sixty Patients (30 in each group) were taken for study who were posted for surgeries under general anaesthesia at our tertiary care centre. Patients were thoroughly examined during the pre-operative visit and patients between 18 years to 50 years of age with ASA GRADE I & II and Mallampatti grade 1 & 2 are included in the study, whereas patients below 18 years and above 50 years with ASA GRADE III & IV and Mallampatti grade 3 &4 were excluded from this study. Monitors were attached and i.v. line was secured. The patients were randomly divided into 2 groups (30 patients each) depending upon the study drug administered. Group A – Patient received intravenous MgSO4 (30 mg/kg) over 90 seconds; Group B –patient received intravenous labetalol (0.14mg/kg). Premedication was uniform for all the patients in the form of intravenous Ondansetron 4mg, Ranitidine 50mg, Glycopyrrolate 0.2mg, Midazolam 0.01 mg/kg, Fentanyl 1mc g/kg. The patient was induced with intravenous propofol 2 mg/kg. intravenous succinylcholine (1.5mg/kg) was given. The study drug was given 3 minutes before the intubation. The rest of the general anaesthetic technique was the same for all the patients. Patients' heart rate and blood pressure were measured and recorded every minute till 3 minutes after intubation.

Statistical analysis -From study published previously, Standard deviation obtained was 6.3 and expected difference between the means was calculated as 3.1. Assuming the power of our study 80% and an alpha error of 0.05, sample size was calculated to be 60. Online software was used for the statistical analysis of the compiled data by applying Chi-square test and the One-Way Analysis of Variance (ANOVA). $P < 0.001$ was considered significant.

3. RESULT

Patients in both groups were comparable with age, weight [Graph 1] Baseline blood pressure and heart rate were comparable among the groups. The difference in heart rate was not statistically significant between groups throughout the study period. SBP and DBP decrease after induction of anaesthesia which increases towards baseline after intubation in both groups.

Graph 1: Initial and basic values of patients based on the medication group:



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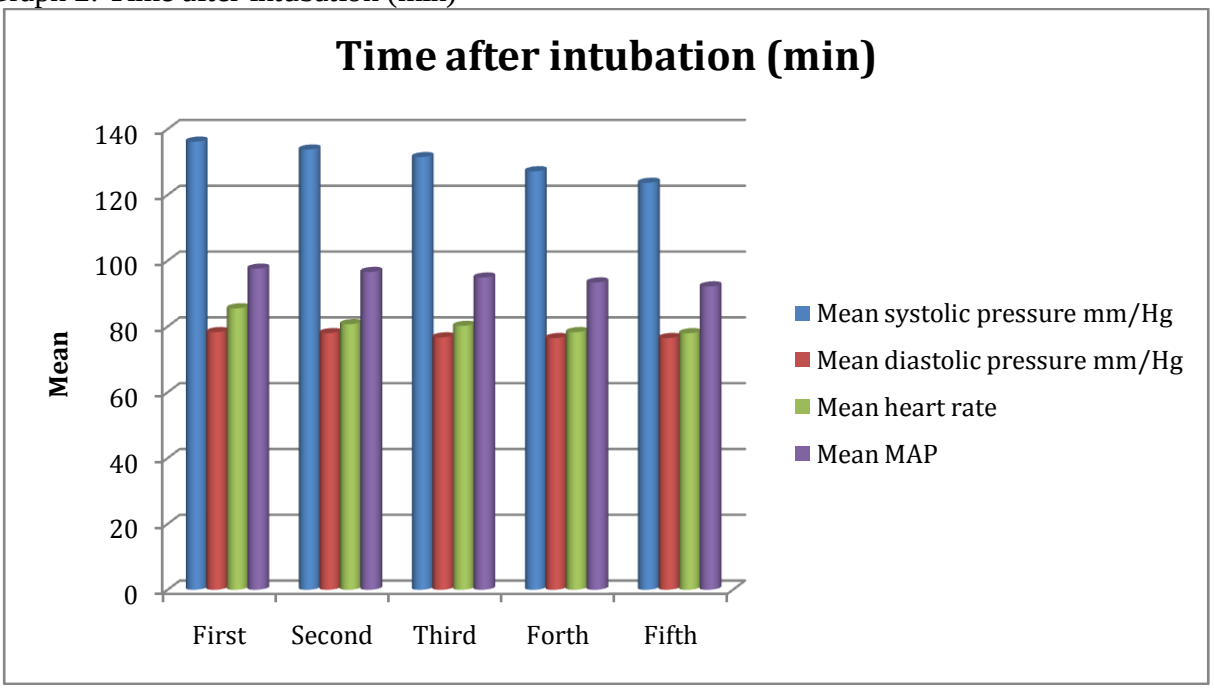
Time after intubation (min)	Mean systolic pressure mm/Hg	P-value	Mean diastolic pressure mm/Hg	P-value	Mean heart rate(per min)	P value	Mean MAP	P-value
Baseline	136.2±10.3	0.001	78.3±7.6	0.076	85.53±5.85	0.001	97.6±5.4	0.001
Laryngoscopy	133.8±13.2	0.001	78±7.3	0.245	80.73±5.73	0.027	96.6±6.8	0.001
First	131.5±20.3	0.049	76.7±7.1	0.856	80.2±4.92	0.68	94.9±8.9	0.138
Second	127.2±14.7	0.161	76.5±6.3	0.926	78.3±7.05	0.519	93.4±5.3	0.259
Third	123.7±13.8	0.582	76.5±5.6	0.928	77.97±6.68	0.579	92.2±5.6	0.187

Table 1- Systolic and diastolic blood pressure changes as well as heart rate and mean MAP changes after intubation compared to the baseline value in the Labetalol group.

Graph 2: Time after intubation (min)



Graph 2 shows changes in mean systolic pressure, mean diastolic pressure, mean heart rate, and mean MAP (mean arterial pressure) with increasing time after intubation.

Table 2- Systolic and diastolic blood pressure changes as well as heart rate and mean MAP changes after intubation compared to the baseline value in the magnesium group.

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Time after intubation (min)	Mean systolic pressure mm/Hg	P-value	Mean diastolic pressure mm/Hg	P-value	Mean Heart rate(/min)	P-value	Mean MAP	P-value
Baseline	126.8±10.7	0.011	80.3±7.4	0.118	85.23±6.31	0.001	93.6±6.3	0.003
Laryngoscopy	126.2±11.3	0.183	79.1±6.9	0.38	84.3±6.73	0.004	93.9±5.4	0.095
First	126.3±8.6	0.189	75.3±7.1	0.54	83.27±5.4	0.004	93.3±5.9	0.141
Second	125.7±8.7	0.238	77.7±6.3	0.67	82.9±8.04	0.037	92.1±5.1	0.254
Third	123.1±13.8	0.679	72.1±7.8	0.74	80.1±8.9	0.225	92±6.6	0.567

Graph 3

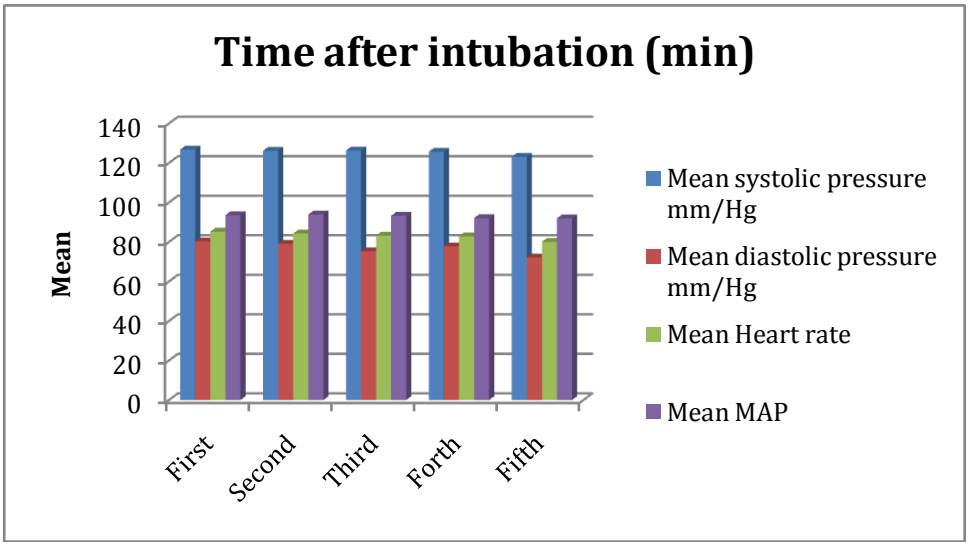

Table 3- Comparison of systolic blood pressure changes in Labetalol and magnesium groups after intubation-

Time after intubation	Systolic blood pressure(mmHg)		P value
	Magnesium group	Labetalol group	
Baseline	126.8±10.7	126.2±10.3	0.001
Laryngoscopy	126.2±11.3	133.8±13.2	0.033
First	126.3±8.6	131.5±20.3	0.207
Second	125.7±8.7	127.2±14.7	0.6
Third	123.7±13.8	123.6±13.9	0.98

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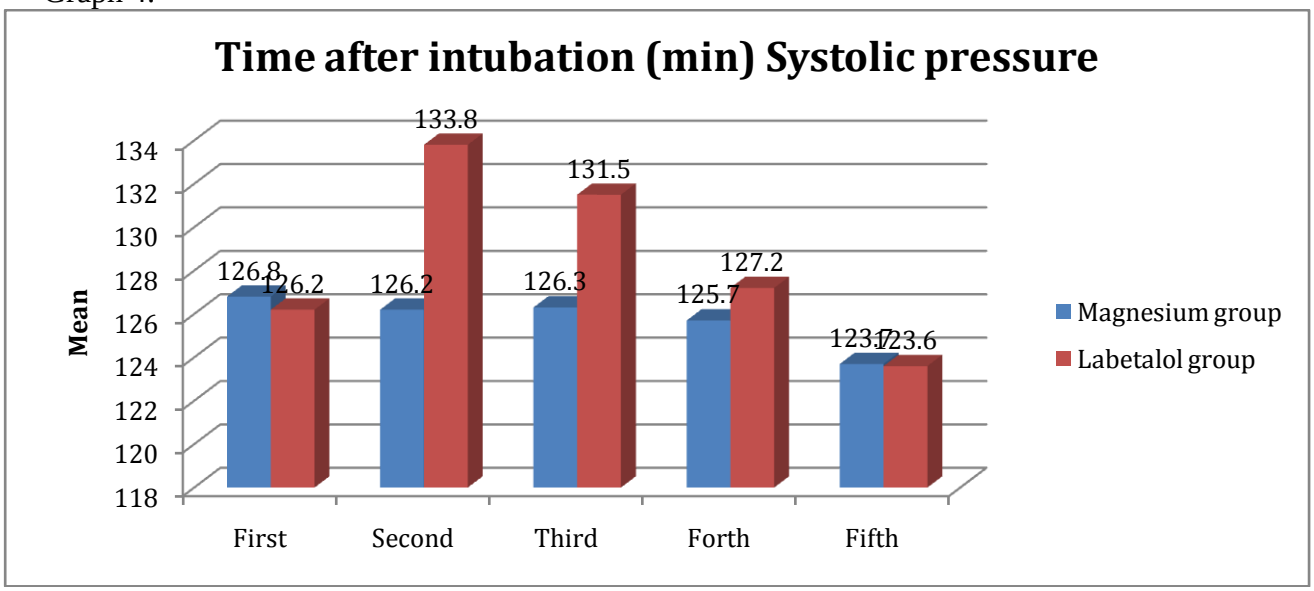
Graph 4:



Graph 4 shows the comparison in systolic pressure after intubation with magnesium vs labetalol; showing magnesium shows lesser variation in comparison to labetalol

Table 4- Comparison of diastolic blood pressure changes in Labetalol and Magnesium groups after intubation.

Time after intubation (min)	Diastolic blood Pressure(mmHg)		P value
	Magnesium group	Labetalol group	
Baseline	80.3±7.4	78.3±7.6	0.551
Laryngoscopy	79.1±6.9	78±7.3	0.511
First	75.3±7.1	76.7±7.1	0.919
Second	77.7±6.3	76.5±6.3	1
Third	72.1±7.8	76.3±7.5	0.821

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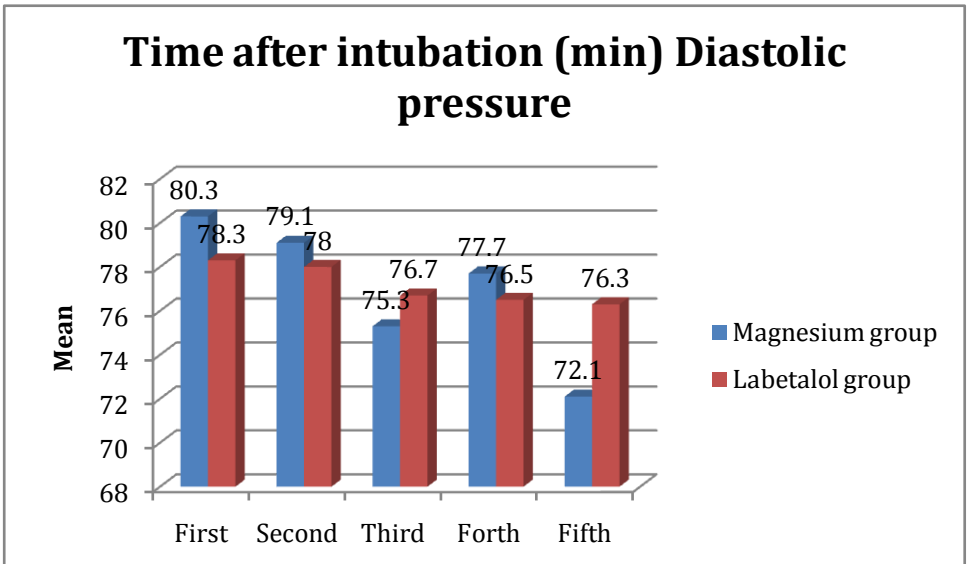

Graph 5

Graph 5 shows the comparison in diastolic pressure after intubation in both groups that is magnesium group and the labetalol group.

Table 5- Comparison of heart rate in magnesium and Labetalol groups after intubation.

Time after intubation (min)	Heart rate (/min)		P value
	Magnesium group	Labetalol group	
Baseline	85.23±6.3	83.53±5.58	0.182
Laryngoscopy	84.3±6.73	80.73±5.73	0.038
First	83.37±5.4	80.2±4.92	0.027
Second	82.9±8.04	78.3±7.05	0.014
Third	80.1±8.92	77.97±6.68	0.343

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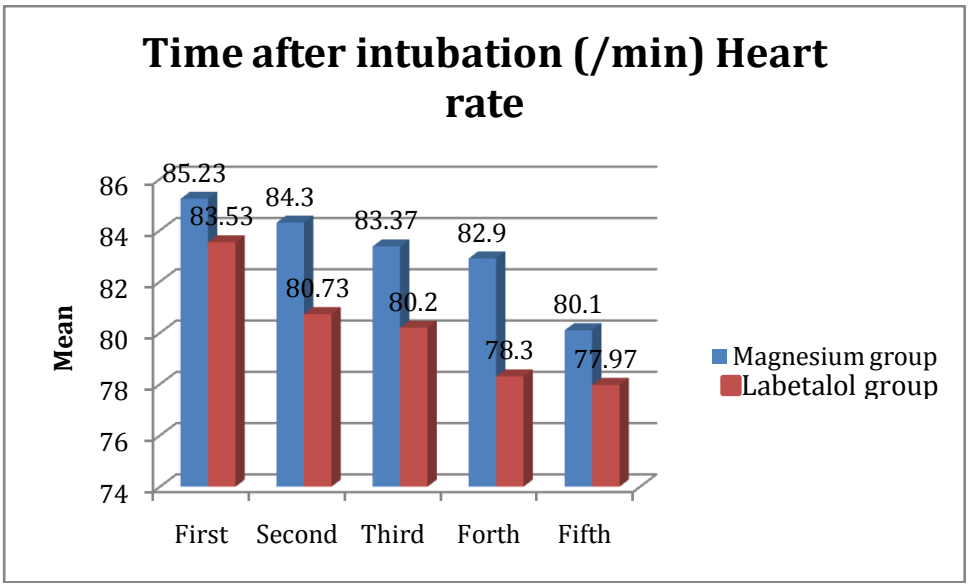
Graph 6:



Time after intubation (min)	Mean MAP(mmHg)		PV
	Magnesium group	Labetalol group	
Baseline	93.6±6.3	97.6±5.4	0.012
Laryngoscopy	93.4±5.4	96.6±6.8	0.04
First	93.3±5.9	94.9±8.9	0.414
Second	92.9±5.1	93.4±5.3	0.654
Third	92±6.1	92.2±5.6	0.821

Table 6- Comparison of mean MAP in magnesium and Labetalol groups after intubation

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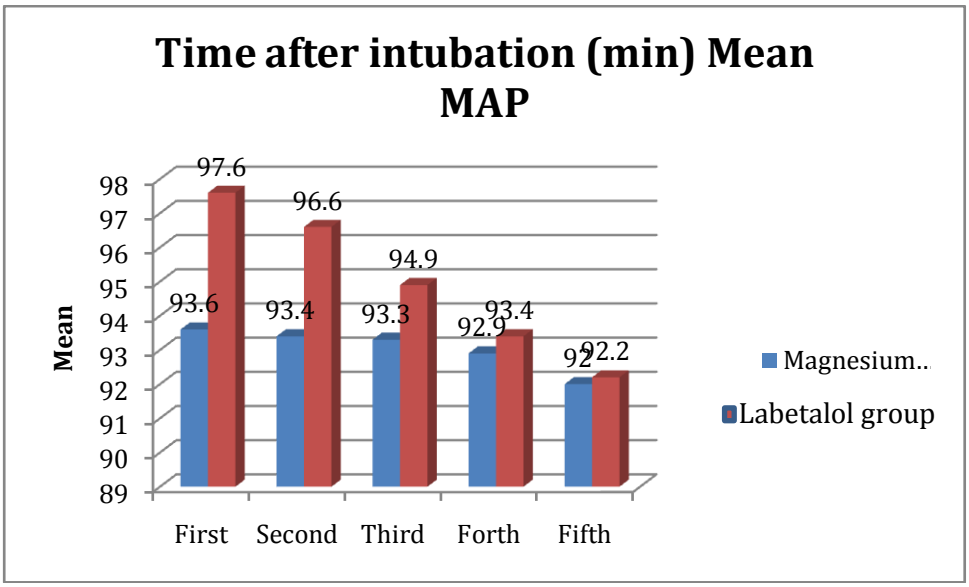
Graph 7:



Graph 7 shows changes in mean MAP (mean arterial pressure) in the magnesium group compared to the labetalol group.

4. DISCUSSION

Laryngoscopy can produce a sympathetic response during tracheal intubation [6]. Among the drugs used in suppressing the hormonal stress response to tracheal intubation. Magnesium sulphate is superior as it has direct vasodilator properties as well as suppresses the release of catecholamine. Its alpha antagonistic property leads to a decrease in blood pressure, however, it does not produce significant hypotension due to a concomitant increase in cardiac output. Labetalol has alpha and beta-blocking properties, its alpha-blocking property is 1/7 times that of beta-blocking, it also attenuates stress response but less effectively than magnesium sulphate.

Heart Rate-

Our results and observations, pertaining to heart rate were comparable to James MFM et al in their double-blind study. [7,8] The double-blinded study conducted by James MFM et al assessed the effects of intravenous magnesium sulphate 60 mg/kg on cardiovascular responses and the release of catecholamines associated with tracheal intubation in normal subjects compared to normal saline as controls. They found that induction of anesthesia produced no changes in HR in either Group, but magnesium pre-treatment produced an 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.

A study conducted byPuri et al for evaluating the hemodynamic effects of magnesium and its efficacy in attenuating the response to intubation in 36 patients with coronary artery disease [9]. A group received 50 mg/kg magnesium sulphate and the control group received normal saline solution before the induction of anesthesia. The study showed that there was an 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 the 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 a. It might be expected that magnesium

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would slow the HR by inhibiting the calcium-mediated depolarizing current in the pacemaker tissue, the ability of magnesium to inhibit the release of acetylcholine from the vagus nerve predominates, and therefore, the overall effect is a mild increase in the heart rate as seen in this study.

Blood pressure –

James MFM et al who studied the 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.[7,8] They reported a significant increase in SBP (from 106.4±3.1 to 145.1±5.6 mmHg) after intubation in the control group but not significantly (P >0.05) in the magnesium group (from 106.8±3.1 to 110.0±4.4 mmHg).

Puri et al also reported similar observations with the changes in mean arterial pressure (MAP).[9] They reported that MAP decreased significantly ($p<0.001$) from after administering the study drug in the magnesium group as compared to the control group though MAP increased after intubation in both the Groups, it was significantly ($p<0.001$) higher than the baseline in the control group as compared to magnesium group where the levels were just near baseline after intubation.

From the above discussion, it is clear that both magnesium and labetalol administration leads to tachycardia and hypotension, but by itself, this effect is transient and can be attributed to the reflex tachycardia caused by the vasodilator effect. At the doses (magnesium 30 mg/kg and i.v. labetalol (0.14mg/kg), definitely attenuates the effect on SBP in response to laryngoscopy and intubation. When Group A was compared to Group B, it was seen that under their mechanism of action, both the drugs cause relative hypotension which is comparable in both the groups, thereby blunting the presser effect of laryngoscopy and intubation.

Limitations of our study-

The present study was done in a small sample size. All patients were belonging to ASA I and II. Comorbid patients with diseases i.e. coronary artery disease, hypertension, diabetes, etc. were excluded from the study. In addition, patients' age has effect on pressor response to laryngoscopy and intubation. The role of preoperative antihypertensive medications were not evaluated in our study. Also, we did not compare our results with the control group to know the extent to which the presser response to intubation is attenuated with magnesium and labetalol.

5. CONCLUSION

During laryngoscopy & intubation, BP rises up to 30-40%, when premedicated with Intravenous Magnesium or intravenous labetalol. These drugs may lead to a rise in HR but it is transient and dose-dependent. However, both the drugs can significantly control the hypertensive response after laryngoscopy and intubation, and the effect on SBP and Rate pressure product is comparable. Both the drugs prevent the rise in blood pressure and heart rate during laryngoscopy and intubation but magnesium sulphate is more effective in controlling hemodynamics although it transiently increases the heart rate in the first minute. Safety of magnesium and labetalol pre-treatment in comorbid patients with IHD or hypertension or decompensated systemic illness needs further investigation.

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