ORIGINAL RESEARCH PAPER

Anaesthesiology

A COMPARATIVE STUDY BETWEEN INTRAVENOUS ESMOLOL AND MAGNESIUM SULPHATE IN ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

KEY WORDS: Esmolol, Magnesium Sulphate, Laryngoscopy, Hemodynamics..

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ABSTRACT

Background and Objectives: Laryngoscopy and endotracheal intubation are noxious stimuli which are associated with stress response like increase in blood pressure and heart rate which occur most commonly from sympathetic discharges in response to laryngotracheal stimulation. It may be well tolerated in the healthy but may be hazardous in patients with hypertension, myocardial infarction etc. Many attempts have been made to attenuate these responses. The present study has been undertaken to compare the effects of intravenous esmolol and magnesium sulphate on attenuation of the stress response to laryngoscopy and intubation. **Methods :** A prospective, Randomized double blinded study was conducted on 100 ASA I/II adult patients undergoing elective surgery. Patients were divided into group E (received Esmolol 1.5mg/kg) and Group M (received Magnesium Sulphate 50mg/kg). Heart rate, systolic, diastolic blood pressure and mean arterial pressure were recorded before induction, just before intubation, just after intubation, 2 minutes, 5 minutes, 10 minutes and 15 minutes after intubation. **Results:** Baseline Parameters were comparable in both the groups. Both Esmolol and MgSO4 attenuated the hemodynamic responses to laryngoscopy and intubation. The attenuation caused by Esmolol was statistically significant than MgSO4. **Conclusion:** Esmolol is a better agent than MgSO4 in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation

INTRODUCTION:

Intubation of trachea is the most secure and life saving interventions performed to establish a secure airway[9]. Hypertension and tachycardia have been reported during intubation since 1940[1]. Laryngoscopy and intubation are associated with tachycardia and increase in blood pressure and possibly dysrhythmias which greatly increase the risk of MI, infarcts and stroke in the elderly[6]. It was shown that there is increase in the nervous system activity in the cervical sympathetic efferent by mechanical stimulation of the respiratory tract. King and Harris[3] confirmed the adverse effects of pressor response. This hemodynamic response is transient and occurs approximately 30 seconds after intubation and lasts for less than 10 minutes[10]. Many attempts have been made to attenuate the pressor response by the use of topical anesthesia or ganglion blockers or deepening anesthesia. Pharmacological agents like morphine, fentanyl, beta blockers like esmolol, calcium channel blockers like diltiazem, vasodilators like nitroglycerine and sodium nitroprusside have also been used[9]. Magnesium Sulphate is a bivalent salt which inhibits catecholamine release from adrenal medulla and adrenergic terminals during intubation[8]. It causes vasodilation and drop in blood pressure by diminishing excitability of muscle cells[10]. It is also used in the treatment of resistant arrhythmias. Esmolol is an ultra-short acting 1adrenergic blocker with a short duration of action and reaches peak effect in 1-2 minutes after bolus[6]. These characteristics makes esmolol a useful drug for preventing or treating adverse systemic blood pressure and heart rate increase which occur intraoperatively in response to noxious stimulation such as laryngoscopy and intubation.

METHODOLOGY:

The present study which was a prospective, randomized, double blinded study was conducted on 100 adults with ASA grade I/II posted for elective cases requiring general anesthesia under the Department of anesthesiology and Critical Care in different operation theatres of Silchar Medical College and Hospital, Silchar. The study was carried out from 01.06.2020 to 31.05.2021.

Inclusion Criteria:

- Patient aged 18-60 years
- Informed consent form
- ASA I/II physical status.

Exclusion Criteria:

- Patient refusal
- Patients suspected to have a difficult airway
- Systemic diseases
- Pregnant and lactating

Sample Size Estimation

According to the study conducted by SA Aasim et al[6], the mean and standard deviation of heart rate at 5 minutes post intubation in Group Esmolol was 80 ± 9.68 and the mean and standard deviation of heart rate at 5 minutes post intubation in Group Magnesium Sulphate was 85.86 ± 10.05. Taking 95% confidence interval with 80% power, the sample size is calculated as

$$N = (Z_{1-\alpha/2} + Z_{1-\beta})^2 * 2 * \sigma^2 / (\mu_1 - \mu_2)^2$$

$Z1\text{-}\alpha/2$ - two tailed probability for 95% confidence interval = 1.96

$Z1\text{-}\beta$ - two tailed probability for 80% power = 0.84

$\mu 1$ - mean of post intubation of heart rate in 5 minutes of Esmolol group = 80

$\mu 2$ - mean of post intubation of heart rate in 5 minutes of magnesium sulphate group = 85.86

σ - average standard deviation of heart rate at 5 minutes post intubation in Group Esmolol and that in Group Magnesium Sulphate = 9.87

N = (1.96 + 0.84) ^2 * 2 * 9.865^2 / (80 - 85.86) ^2

N = 44.49

Thus, the sample size required for each group is 44 and the total sample size is 88. We had conducted the study on 100 patients taking into account the possibility of attrition.

Using computer generated random numbers, patients satisfying the inclusion criteria were assigned to one of the two groups of 50 persons each. Group E consisted of patients receiving 1.5 mg/kg of intravenous Esmolol while Group M participants received 50mg/kg of intravenous Magnesium Sulphate. All study drugs were diluted upto 10 ml with distilled water and administered over 30 seconds.

History taking, general examination and systemic examinations were conducted and investigations including complete blood count including hemoglobin and KFT, LFT, CXR PA View and ECG were done. Patients were given Tablet Ranitidine 150 mg and tablet Alprazolam 0.5 mg on the previous night of surgery.

In the operating room, intravenous cannula was secured and infusion with 500 ml Ringers Lactate premedicated with 100 mg of Injection Ranitidine and 4mg of injection ondansetron was started. The patient was then connected to a multiparameter monitor which recorded heart rate, SpO2, non-invasive measurements of SBP, DBP, MAP, EtCO2 and continuous ECG monitoring. The baseline heart rate, systolic, diastolic blood pressure, and mean arterial pressure was recorded after 5 minutes of settling in the operating room. The cardiac rate and rhythm were monitored from a continuous visual display of electrocardiogram from lead II.

After recording the baseline parameters, patients were premedicated with intravenous glycopyrrolate (0.004mg/Kg) and IV tramadol (1mg/Kg body weight), given 10 minutes prior to induction of anesthesia. The study drugs were administered intravenously over 30 seconds, prior to induction and laryngoscopy. The study drugs were administered by an independent post-graduate student who did not participate in observation or collection of data.

Patients were pre oxygenated for 4 vital capacity breaths and anesthesia was induced with injection propofol, which was titrated to loss of verbal response. Endotracheal intubation was facilitated with injection succinylcholine (1.5mg/kg) given intravenously. Laryngoscopy and oral intubation were performed using appropriately sized Macintosh blade and after confirmation of bilateral equal air entry, the endotracheal tube was fixed. If laryngoscopy and intubation required more than 15 seconds, that patient was excluded from the study. Manual ventilation was started at the rate of 14-18 breaths/min using circle absorption system and later connected to mechanical ventilator (Mindray A5) once the initial dose of muscle relaxant (Inj. Vecuronuim) was given. Anesthesia was maintained using 60% nitrous oxide and 40% Oxygen and Inj Vecuronium (0.1 mg/kg) and supplemented if necessary. Before the beginning of the surgery, injection paracetamol 1gram was given intravenously and inhalational anesthetic in the form of isoflurane was added. Hemodynamic parameters of patients including heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded before induction, just before intubation, just after intubation, 2, 5, 10 and 15 minutes after intubation. At the end of surgery, residual paralysis was antagonized with injection Neostigmine (0.05mg/kg) and Glucopyrrolate (0.01mg/kg), given intravenously .

RESULTS:

Statistical Analysis:

Data was presented as mean ±standard deviation. Student t-test was used for comparison of data which are quantitative. Qualitative data was assessed using Fischer exact test or Chi-square test. Results were considered statistically significant $p<0.05$, highly significant if $p<0.001$ and extremely significant if $p<0.0001$ and not significant if $p>0.05$.

All 100 patients were comparable in age, sex and weight.

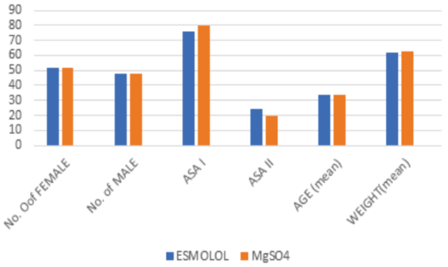

Fig.:1- Demographic Data of Patients in Group ESMOLOL and Group MgSO4

Study Period	Heart Rate (beats/min)				P-value
	Group E (ESMOLOL) N=50		Group M (MgSO4) N=50		
	Mean	SD	Mean	SD	
HR T0 (Baseline)	84.92	5.341	84.14	6.273	0.5048
HR T (Before Induction)	84.42	5.606	85.46	6.550	0.8529
HR T1 (Before Intubation)	74.68	6.447	77.52	6.952	0.0367
HR T2 (Just After Intubation)	82.24	5.702	96.14	4.481	<0.0001
HR T3 (2mins After Intubation)	76.2	4.785	90.48	3.792	<0.0001
HR T4 (5mins After Intubation)	72.76	5.200	84.52	3.406	<0.0001
HR T5 (10mins After Intubation)	82.94	4.950	85.90	8.718	0.0394
HR T6 (15mins After Intubation)	84.68	5.141	84.8	8.640	0.9329

Table :1. Comparison of mean heart rate between Group E and Group M

Mean heart rate (HR) decrease was observed in both Group E and Group M. The fall in HR after administration of the drugs, that is, before intubation (T1) was significant (p-value=0.0367) when comparing both the groups. It became extremely significant (p-value≤0.0001) just after intubation (T2) and at 2 (T3) and 5 minutes (T4) after intubation. The fall in HR was significant at 10 minutes after intubation (T5) as well (p-value=0.0394).

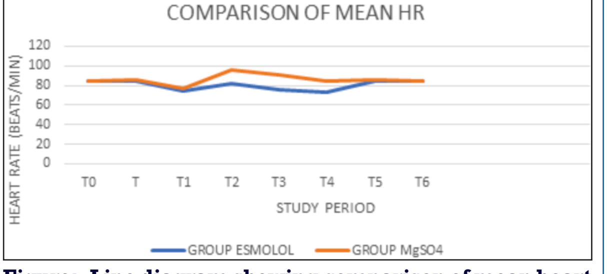

Figure:- Line diagram showing comparison of mean heart rate between Group ESMOLOL and Group MgSO4

Table:4:- Comparison of mean arterial blood pressure between Group E and Group M

Study Period	Mean Arterial Blood Pressure (mmHg)				P-Value
	GROUP E (ESMOLOL)		GROUP M (MgSO4)		
	Mean	SD	Mean	SD	
T0 (Baseline)	95.82	4.667	96.54	5.600	0.4866
T (Before Induction)	95.50	4.147	96.28	5.650	0.4332
T1(Before Intubation)	90.70	4.505	93.60	5.942	0.0071
T2(just after intubation)	94.32	4.744	98.88	5.001	<0.0001
T3 (2 min after intubation)	93.54	4.381	98.20	4.823	<0.0001
T4 (5 min after intubation)	94.46	4.263	97.72	4.422	0.0003
T5 (10 min after intubation	95.10	3.940	97.34	3.685	0.0041
T6 (15 min after intubation)	95.58	4.686	96.97	3.597	0.0992

The fall in mean arterial pressure (MAP) was seen in both the groups. The fall was significant after the administration of study drug that is just before intubation (T1) (p-value=0.0071). Extremely significant fall in MAP between Group E and Group M was obtained just after intubation (T2) and at 2 minutes after intubation (T3) (P-Value≤0.0001). The fall in MAP at 5 minutes after intubation (T4) was highly significant (P-Value=0.0003) and significant at 10 minutes after intubation (T5) (p-value=0.0041).

DISCUSSION:

Laryngoscopy and endotracheal intubation have become a routine procedure in anesthesiology ever since it was introduced in the 19th century by Rowbotham and Magill. The hemodynamic response to laryngoscopy and endotracheal intubation is associated with increase in heart rate, blood pressure. It can even cause cardiac dysrhythmia as shown in the study by Prys Roberts et al[5]

Tomori and Widdicombe[2] showed that mechanical stimulation of the respiratory tract or chemical irritation of the nasal mucosa caused activation of irritant reflexes and brought about hypertension. The above-mentioned changes during laryngoscopy and intubation brought about transient tachycardia and hypertension which is tolerated well by healthy adults. Although these changes are short-lived, in susceptible individuals, they can cause myocardial infarction and even an increase in intracranial pressure.

Magnesium Sulphate is a physiological calcium antagonist[4] which competes with calcium for membrane channels. It also inhibits release of catecholamine both from the adrenergic nerve terminals and the adrenal medulla. Esmolol is a cardio-selective β1 blocker and ultra-short duration of action. Thus the effects of esmolol may be rapidly discontinued in clinical situations when necessary. In our study, we have used Esmolol at a dose of 1.5 mg/kg body weight as a bolus dose to be administered to participants in Group E and 50 mg/kg Magnesium sulphate was administered to Group M participants. Bolus dose was preferred to infusion due to the practicality and ease of administration.

Authors studied 100 patients of both sexes aged between18 and 60 years with ASA I/II physical status The mean age, weight, height of patients in Group E and Group M were comparable and statistically not significant.

Heart Rate

The mean baseline heart rate of both the groups were comparable. Just before intubation (T1), that is after the study drug was administered, there was a fall in mean HR in both the groups. The mean HR in Group E was 74.68±6.447 and that in Group M was 77.52±6.952. The fall in HR was statistically significant with p-value=0.0367. Just after intubation, (T2), on comparing the mean HR between the 2 groups, it was found to be statistically extremely significant (p-value≤0.0001). At 2 minutes and 5 minutes after intubation, (T3 and T4), it was found to be statistically extremely significant(p-value≤0.0001). At 10 minutes after intubation (T5), the mean HR increased in both Group E and M and there was a significant difference between the two groups (p-value0.0394). From 15 minutes after intubation the mean HR difference between both the groups were not significant and also, the heart rates stabilized at near the baseline value.

Mean Arterial Pressure

The Baseline MAP of Group E and Group M were comparable, the difference between them was not significant(p-value=0.4866).Before intubation(T1), that is after the administration of study drugs, there was fall in MAP. In Group E it was 90.70±4.505 and that in Group M was 93.60±5.942. on comparison, this difference was significant (p-value 0.0071). Just after intubation (T2), the difference between the MAP in both the groups were extremely significant (p-value ≤0.0001). At 2 minutes after intubation also the difference between the two groups was statistically extremely significant. On comparing the MAP in both the groups, at 5 minutes after intubation (T4), the difference was statistically highly significant (p-value =0.0003). At 10 minutes after intubation (T5), the difference between the two groups was significant. From 15 minutes after, the MAP was stabilized near the baseline values and there was no significant difference in MAP between the two groups.

SA Aasim et al[6] compared esmolol hydrochloride 1.5mg/kg and magnesium sulphate 50 mg/kg for hemodynamic attenuation during laryngoscopy and intubation. Their study showed that there was a fall in heart rate in group E at 2 minutes and 5 minutes after intubation and there was a rise in heart rate after intubation in Group M at the same intervals. There was a fall in mean arterial pressure in both groups, however, there was no statistical significant difference in mean arterial pressures. They concluded that Esmolol was a better agent to attenuate intubation response than Magnesium Sulphate as it attenuates the rise in both heart rate and blood pressure. Our result was comparable to their study in attenuation of hemodynamic response to laryngoscopy and intubation by Esmolol and Magnesium Sulphate and that Esmolol was more efficient than Magnesium Sulphate for hemodynamic attenuation.

Arbind Ray et al[9] conducted a prospective study in which 90 patients were divided into group I (normal saline 0.9%), group II ($MgSO_4$ 50mg/kg) and Group III (Esmolol 2mg/kg). In their study, it was found that after the drug was given, there was a significant fall in HR in group Esmolol compared to Magnesium Sulphate. Also, the fall in MAP was found to be significant between group Esmolol and $MgSO_4$. They concluded that Esmolol was better drug in attenuating hemodynamic response to laryngoscopy and intubation.

In our study, we found that after the study drugs were given, there was a decrease in HR from the baseline values in both group E and group M and the difference between the two groups was statistically significant. There was a fall in heart rate in both the groups post intubation, but the difference between the two groups was statistically extremely significant just after intubation, at 2 minutes and 5 minutes after intubation. The HR reached baseline values towards the end of study period. In our study, when compared between Group E and Group M, the fall in SBP, DBP and MAP was also found to be significant especially at 2 minutes and 5 minutes post intubation.

Shanti Kumari et al[10] conducted a study among 120 patients divided into Group N (normal saline), Group E (esmolol 2mg/kg) and Group M (magnesium sulphate 50mg/kg). The baseline HR, SBP, DBP and MAP were comparable and statistically nonsignificant. After the administration of study drug, there was fall in HR, SBP DBP and MAP in group E and M which was statistically significant. Although there was an increase in these vital parameters immediately post intubation, there was a fall in these vital parameters which were recorded upto 10 minutes post intubation and on comparing the recorded values between group E and M, it was statistically significant. After about 10 minutes, the values were stabilized around baseline in all the vital parameters recorded. They concluded that intravenous Esmolol 2mg/kg as a bolus proved to be more effective than magnesium sulphate 50mg/kg in attenuating hemodynamic stress response following laryngoscopy and intubation.

Our result was comparable to their study. We saw that the baseline vital parameters were comparable and statistically nonsignificant. In our study, on comparing the values of HR, SBP, DBP and MAP in both the groups, the fall was significant after administration of study drug, just after intubation, 2 minutes after intubation and highly significant at 5 minutes after intubation, significant at 10 minutes after intubation. The values stabilized around baseline towards the end of study period.

Side Effects

In our study, we noted bradycardia in subjects belonging to Group E. and tachycardia in Group M which was nonsignificant. PONV was seen in both the groups. There was no incidence of hypotension in either of the groups. These side effects were transient and did not require any intervention.

CONCLUSION

In conclusion, Esmolol is a better agent to attenuate hemodynamic responses to laryngoscopy and intubation when compared with Magnesium Sulphate as it attenuates both rise in heart rate and blood pressure.

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Conflict of interest: None declared

Ethical Approval:

the study was approved by the institutional ethical committee.

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