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Original Research Article

Efficacy of esmolol and magnesium sulphate in attenuation of haemodynamic response during laryngoscopy and intubation: a clinical comparative study

Arbind K. Ray, Babita Lahkar, Trina Sen, Hrishikesh Bharali*

Department of Anaesthesiology and Critical Care, Gauhati Medical College and Hospital, Guwahati, Assam, India

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***Correspondence:**
Dr. Hrishikesh Bharali,
E-mail: hrishi46@gmail.com

ABSTRACT

Background: Hypertension and tachycardia accompanying laryngoscopy and tracheal intubation are deleterious, especially in patients with cardiovascular or intracranial diseases. The aim of the present study was to compare and evaluate the efficacy of magnesium sulphate and esmolol in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation.
Methods: A prospective study was conducted with ninety patients undergoing elective surgery under general anaesthesia who were randomized into three groups of thirty patients each. Group I received 10 ml of 0.9% normal saline, group II received magnesium sulphate 50mg/kg body weight and group III received esmolol 2mg/kg body weight. The study drugs were administered intravenously over 30 seconds, 3 minutes prior to laryngoscopy. Induction was done with sodium thiopentone and endotracheal intubation was performed after one minute of administration of succinylcholine 1.5mg/kg. Heart rate and blood pressure were recorded from preinduction up till 10 minutes after intubation.
Results: There was a significant rise in heart rate and blood pressure in group II as compared to group I.
Conclusions: Esmolol is a better agent than magnesium sulphate to attenuate hemodynamic response to laryngoscopy and intubation.

Keywords: Attenuating hemodynamic response, Esmolol, Laryngoscopy and intubation, Magnesium sulphate

INTRODUCTION

The advent of endotracheal intubation was seen as a boon by the anaesthesiologist. Intubation of the trachea is the most secure and lifesaving intervention that is performed to establish and maintain a secure airway. Hypertension and tachycardia have been reported since 1950 during intubation under general anaesthesia. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased plasma norepinephrine concentration.[1] These changes cause significant adverse effects especially in patients with heart diseases and pulmonary disorders.[2,3] King and Harris confirmed the adverse effects of pressor response. Many attempts have been made to attenuate the pressure response, e.g. deep anaesthesia, topical anaesthesia, use of ganglionic blockers, beta blockers, antihypertensive agents like phentolamine, nitroglycerine, etc.[4] In recent years, magnesium sulphate have been used to control hypertensive response. Magnesium sulphate has a fairly good control over blood pressure. Besides it is also known that magnesium sulphate is useful in treating various arrhythmias which are otherwise

resistant. Magnesium sulphate blocks the release of catecholamines from the adrenergic nerve terminals and adrenal glands in vitro. Magnesium has been shown to inhibit catecholamine release during tracheal intubation.[5] Increased serum magnesium level may also inhibit the release of catecholamine in humans in whom catecholamine excess is present. Calcium exerts major role in the release of catecholamines in response to sympathetic stimulation. Magnesium has been described as physiological calcium antagonist.[6] It has been used to control hypertension in obstetric patients of pre eclamptic toxaemia to attenuate the pressor response. Increased serum magnesium level may also inhibit the release of catecholamine in humans in whom catecholamine excess is present. At the moderate blood level magnesium has relatively minor cardiovascular side effects and its only respiratory depressant effect is related to its well known ability to potentiate the action of nondepolarizing neuromuscular blocking agents. It also has bronchodilator properties. Esmolol is a cardio selective beta1 adrenergic receptor antagonist, which has short onset and a short duration of action. These characteristics make esmolol a useful drug for preventing or treating adverse systemic blood pressure and heart rate increases that occur intraoperatively in response to noxious stimulus such as during laryngoscopy and intubation.

METHODS

The present study used a prospective, randomise, patient and observer blinded, placebo controlled design. After approval from the institutional ethical committee, the clinical study was conducted on ninety (90) patients requiring endotracheal intubation for maintenance of anaesthesia under the Department of Anaesthesiology and Critical Care in different operation theatres of Gauhati Medical College and Hospital, Guwahati.

Inclusion criteria

- American Society of Anaesthesiologists physical status class (ASA) I or II,
- Mallampati score I and II,
- Age between 18 to 60 years,
- Belonging to any gender,
- Elective, non-cardiac surgery.

Exclusion criteria

- Unwilling patients
- Emergency surgery
- Psychologically ill patients
- H/O allergy to the study drugs
- Patients taking sedatives and hypnotics regularly
- Significant cardiac, respiratory, hepatic, renal, and neurological disorders
- Pregnancy or lactating
- Patients on α- or β- adrenergic agonists or antagonists
- Patients on calcium channel blockers
- Uncontrolled hypertension
- Anticipated difficult intubation
- Patients in whom laryngoscopy and intubation required > 1 attempt and/or lasted >30 second.

Using block randomisation, 90 patients satisfying the inclusion criteria were randomly assigned to one of the three groups of 30 patients each, after informed and written consent from the patients. Group I received 10ml of 0.9% normal saline (control), group II received magnesium sulphate 50mg/kg body weight and group III received esmolol 2mg/kg body weight. All studied drugs were prepared in a 10ml volume solution using distilled water. All patients were administered oral alprazolam 0.25mg on the night before surgery.

In the operation theatre, intravenous infusion line was secured and standard monitoring devices measuring non-invasive blood pressure (NIBP), pulse rate (PR), percentage oxygen saturation (SPO_2) and continuous electrocardiograph (ECG) were attached and baseline values were recorded. In all three groups, anaesthesia procedures were standardised according to departmental protocol. All patients were premedicated with injection glycopyrrolate (0.004mg/kg body weight) and injection tramadol (1mg/kg body weight) which were given intravenously 10 minutes prior to induction of anaesthesia. The study drugs were administered intravenously over 30 seconds, 3 minutes prior to laryngoscopy. The study drugs were administered by an independent post-graduate student in a double-blind fashion who did not participate in observation or collection of data. The study drugs were code numbered and were decoded only after completion of the whole trial.

Anaesthesia was induced with injection thiopentone titrated to loss of eyelash reflex and injected over a period of 15sec after preoxygenation for 3 minutes. Hemodynamic variables were recorded again following which endotracheal intubation was performed facilitated by injection succinylcholine (1.5mg/kg) given intravenously. The laryngoscopy and intubation time were noted. During laryngoscopy PR, SPO_2, SBP, DBP were noted; and then recorded at 1^{st}, 3^{rd}, 5^{th}, 7^{th} and 10^{th} minutes of laryngoscopy. Any changes in the ECG were also noted. Manual ventilation was started at the rate of 14-18breaths/min using circle absorption system. Anaesthesia was maintained with 67% of N_2O and 33% of O_2 during the study period. Injection vecuronium (0.1mg/kg) was given for relaxation and was supplemented when needed. At the end of the study period, positioning of the patient and surgery was permitted. After completion of the study period but before the beginning of surgery injection ketorolac (0.5mg/kg) and injection ondansetron (4mg) were given intravenously and inhalational anaesthetic in the form of halothane was added. At the end of surgery, residual neuromuscular paralysis was antagonised with injection

neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg) given intravenously. Oropharyngeal suctioning was done and when adequate spontaneous ventilation was established, patients were extubated. Subsequently, patients were shifted to their respective wards.

Postoperatively, injection tramadol or ketorolac was given 6-8 hourly by deep intramuscular and/or intravenous route. Any incidence of adverse effects like nausea, vomiting, headache or dizziness were recorded in all three groups during the first 24 hours postoperatively and were treated accordingly if present.

Outcome

In this study, authors evaluated the efficacy of $MgSO_4$ and esmolol in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

Secondary outcomes were to evaluate the incidence and severity of adverse effects of MgSO4 and esmolol and to evaluate any other significant observation if they arise.

Statistical analysis

Data were presented as mean ±standard deviation. Students t-test was used for comparison of the data. Results were considered statistically significant if $p<0.05$, highly significant if $p<0.001$ and not significant if $p>0.05$.

RESULTS

Data are present as mean ±standard deviation, unless otherwise denoted. All the 90 patients who were included in the study were comparable in age, sex and weight (Figure 1).

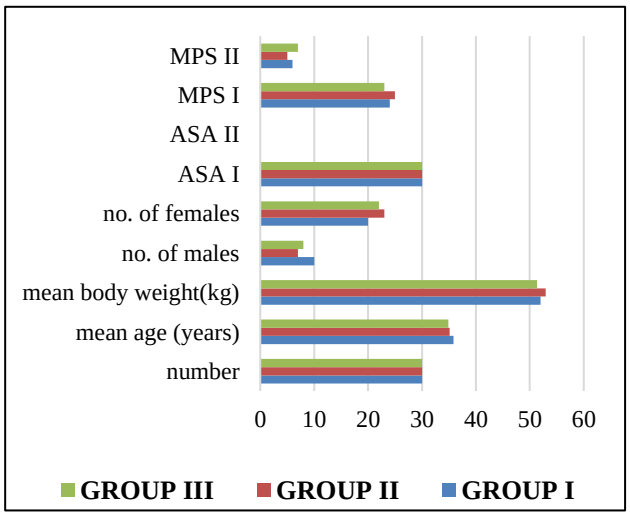

Figure 1: Demographic data of patients.

The mean duration of laryngoscopy and intubation in all the study groups was nearly the same (group I 15.43±2.09 seconds, group II 15.26±2.61 seconds, group III 15.8±2.25 seconds), and also statistically not significant ($p>0.05$).

Figure 1 represents the demographic data of the patients. All the 90 patients who were included in the study were comparable in age, sex, weight, ASA physical status and Mallampati scoring.

Table 1: Comparison of mean heart rate at various intervals among three groups.

Heart rate	Group I	Group II	Group III
Before premedication	75.6±6.69	75.9±5.02	75.26±4.578
P value	I and II	II and III	I and III
	>0.05	>0.05	>0.05
After drug administration	74.9±5.89	78.8±4.61	74.9±4.37
P value	**I and II**	**II and III**	**I and III**
	<0.05	<0.01	>0.05
At induction	75.67±5.29	78.76±4.73	74.7±4.02
P value	**I and II**	**II and III**	**I and III**
	<0.05	<0.01	>0.05
At laryngoscopy	99.3±4.42	89.7±4.23	86.56±3.32
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.05	<0.0001
1 Min after L & I	103.4±4.69	93.1±4.56	90.6±3.47
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.05	<0.0001
3 Min After L & I	97.4±4.06	90.2±5.00	80±4.48
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.0001	<0.0001
5 min after L & I	86.7±3.88	83.06±3.45	75.3±3.82
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.0001	<0.0001
7 min after L & I	75.23±4.80	77.33±3.86	75.16±3.39
P value	**I and II**	**II and III**	**I and III**
	>0.05	<0.05	>0.05
10Min after L & I	74.33±6.25	74.3±4.99	75.3±2.96
P value	**I and II**	**II and III**	**I and III**
	>0.05	>0.05	>0.05

Table 1 shows that patients in group II ($p<0.0001$) and III ($p<0.0001$) had significantly lower mean heart rates during laryngoscopy when compared to group I. It was also noted that group III had a lower mean heart rate during laryngoscopy when compared to group II ($p<0.050$). This pattern persisted at 1, 3 and 5 minutes after intubation. The difference in mean heart rates of group II and III at 7 and 10 minutes after intubation, was not significant ($p>0.05$) when compared to group I.

Intergroup comparison of mean systolic blood pressure at various time intervals is shown in Figure 2. The mean systolic blood pressure increased in all three groups during laryngoscopy which peaked at 1 minute after laryngoscopy and intubation, followed by a gradual

decline upto the end of the study. The increase of mean systolic blood pressure during laryngoscopy and intubation were highly significant (p <0.001) in group II and III when compared with group I, as well as in group II when compared with group III. Similarly, mean diastolic blood pressure (Figure 3) also increased proportionally in all three groups during intubation, peaking at 1 minute after laryngoscopy and intubation, followed by a gradual decline up to the end of the study period.

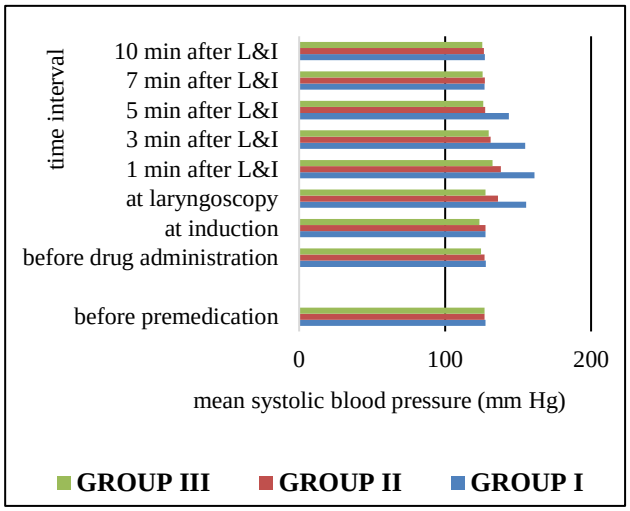

Figure 2: Mean systolic blood pressure at different time points.

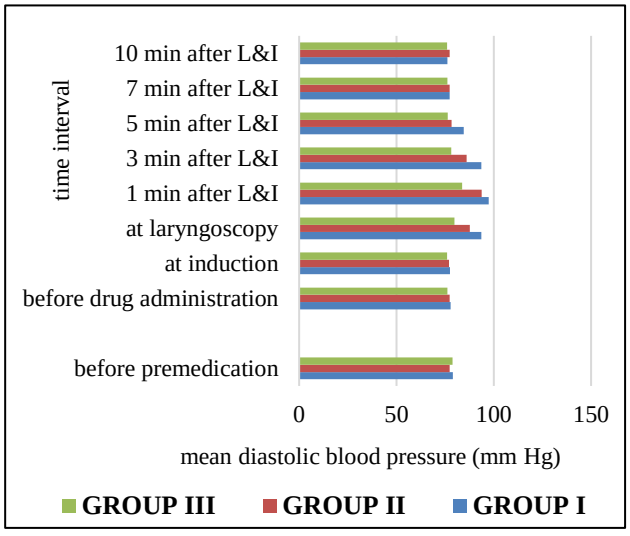

Figure 3: Mean diastolic blood pressure at different time points.

Table 2 shows a comparison of mean arterial pressure at various intervals among all three groups. It was seen that patients in group II (p <0.0001) and III (p <0.0001) had significantly lower mean arterial pressures during laryngoscopy when compared to group I. It was also noted that group III had a significantly lower mean arterial pressure during laryngoscopy when compared to group II (p <0.0001). This pattern persisted at 1, 3 and 5 minutes after intubation. The difference in mean arterial pressure of group II and III at 7 and 10 minutes after intubation, was not significant (p >0.05) when compared to group I.

Table 2: Comparison of mean arterial pressure at various intervals among three groups.

MEAN arterial pressure	Group I	Group II	Group III
Before premedication	95.18±3.83	93.94±3.60	94.85±3.56
P value	**I and II**	**II and III**	**I and III**
	>0.05	>0.05	>0.05
After study drug administration	94.53±2.99	93.86±3.93	92.34±3.39
P value	**I and II**	**II and III**	**I and III**
	>0.05	>0.05	<0.01
At induction	94.2±4.06	93.91±2.94	91.86±2.98
P value	**I and II**	**II and III**	**I and III**
	>0.05	<0.01	<0.05
At laryngoscopy	114.27±4.253	103.90±3.29	95.74±2.21
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.0001	<0.0001
1 min after L & I	118.65±4.50	110.31±3.09	99.97±3.41
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.0001	<0.0001
3 min after L & I	114.04±3.58	101.17±3.58	95.40±3.39
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.0001	<0.0001
5 min after L & I	104.25±3.11	94.73±3.08	92.95±2.09
P value	**I and II**	**II and III**	**I and III**
	<0.0001	<0.05	<0.0001
7 min after L & I	93.95±3.11	93.96±2.34	92.63±2.26
P value	**I and II**	**II and III**	**I and III**
	>0.05	>0.05	>0.05
10 min after L & I	93.22±3.00	93.72±2.67	92.54±2.50
P value	**I and II**	**II and III**	**I and III**
	>0.05	>0.05	>0.05

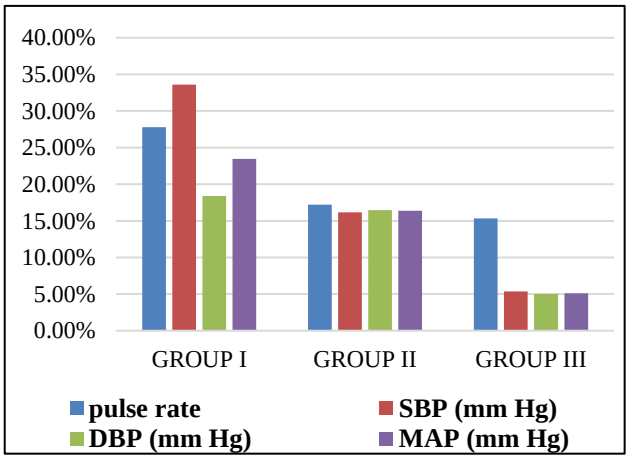

Figure 4: Means of maximum increase of different parameters.

Maximum rise of mean heart rate in group I, II and III were 36.7%, 22.6% and 20.4% respectively. Maximum increase of MAP was 23.47%, 16.37% and 5.12% in group I, II and III respectively at one minute after intubation (Figure 4).

DISCUSSION

Transient, self-limiting increases in heart rate and blood pressure are common sequelae of direct laryngoscopy and intubation and are innocuous in healthy individuals but may be hazardous in patients with or at a risk of hypertension, coronary insufficiency or cerebrovascular disease as it may lead to intraoperative myocardial infarction, acute ventricular decompensation, dysrhythmias and intracranial bleed.[7]

Various methods have been tried to attenuate the hemodynamic response to laryngoscopy and intubation. In this study, authors have compared the efficacy of a single preintubation intravenous bolus dose of esmolol in attenuating these cardiovascular responses to that of a similarly administered dose of magnesium sulphate which has previously been reported to blunt these responses.

Magnesium sulphate inhibits catecholamine release both from the adrenergic nerve terminals and the adrenal medulla in vitro. Esmolol is an attractive option because of its cardioselectivity and ultra short duration of action. Both these drugs have been studied in attenuating the response to intubation and have shown promising result. There have been no studies comparing the efficacy of attenuation of hemodynamic responses of these two drugs in our set up and these drugs are cheap and easily available, so they have been chosen for the study.

Authors studied 90 patients of both sexes aged between 18 and 60 years with ASA-I and ASA-II physical status, MPS-I and MPS-II, requiring endotracheal intubation for maintenance of anaesthesia schedule to undergo various types of elective, non-cardiac surgery. Patients with cardiovascular disorders that might affect the interpretability of data or drugs which alter cardiovascular system function were excluded from the study.

All the ninety (90) patients were anesthetized using the same anesthetic technique and there was no difference between the groups with respect to the premedication and the anesthetic agents used. With conscious efforts, hypoxia and hypercarbia were avoided in all the cases. The hemodynamics were comparable in the respective groups preoperatively with respect to both heart rate and blood pressure ($p > 0.05$).

Puri GD observed that magnesium sulphate in the dose of 50mg/kg body weight could effectively attenuate the pressor responses following laryngoscopy and intubation.[8] Gupta S et al, observed that esmolol in the dose of 2mg/kg body weight was effective in attenuating the hemodynamic responses to laryngoscopy and intubation.[9]

In our study we found that after the trial drug was given, there was a significant increase in heart rate from the basal values in the group magnesium sulphate ($p < 0.05$) whereas no change was observed in the esmolol group; and the difference in increase in heart rate between the two groups were significant ($p < 0.01$). The heart rate increased further in magnesium group after intubation and did not reach baseline values till 7 minutes after intubation. The maximum increase was seen one minute after intubation which was 22.6% from its baseline value. Whereas, in esmolol group heart rate was increased by 20.38% after 1 minute of L and I, showing significant difference between these groups ($p < 0.05$). Heart rate returned to baseline value in magnesium sulphate and esmolol group after 7^{th} and at 5^{th} minute following L and I respectively. Also, it was noted that although the increase in mean heart rate after intubation is significantly low with esmolol and magnesium sulphate when compared to placebo, the effect was more pronounced with esmolol.

The baseline systolic blood pressure values in both the groups were comparable ($p > 0.05$). After the trial drug there was no significant drop in the SBP in both groups. The maximum rise of SBP at the first minute after L and I, in magnesium sulphate and esmolol group were 12.71% and 4.22% respectively and the difference was highly significant ($p < 0.0001$). The increase in SBP normalized to its baseline values after 5 minutes of intubation in both groups. Similarly, the baseline DBP and MAP in both the groups were comparable. They decreased significantly from baseline after the trial drug in esmolol group and increased following L and I. DBP and MAP returned to baseline values 3 minute after L and I in esmolol group. In group magnesium sulphate, there was no change in DBP from baseline after the trial drug, it increased significantly from baseline after intubation and normalized to its basal values after 5 minute of intubation. MAP and DBP were increased by 6.34% and 5.39% one minute after intubation in esmolol group, whereas in magnesium group the values were 21.29% and 17.42%, respectively.

These findings are consistent with the findings of Juhi S et al, who concluded that esmolol is effective in controlling both rise in BP and pulse rate.[10] But in that same study they also found that magnesium sulphate provides fairly good and sustained control over rise in blood pressure during tracheal intubation although rise in pulse rate was not significantly mitigated.

No ECG abnormalities, hypotension, bronchospasm or bradycardia which are known side effects of the study drugs, were observed in either group.

CONCLUSION

In conclusion, esmolol is a better agent to attenuate intubation response than magnesium sulphate as it attenuates the rise in both heart rate and blood pressure.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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