ORIGINAL RESEARCH

Attenuation of pressor response to laryngoscopy and intubation with I.V. Magnesium Sulphate and I.V. Esmolol – A comparative study

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ABSTRACT

Introduction: The larynx, pharynx, and trachea are directly stimulated during a standard laryngoscopy and intubation procedure. These structures are highly innervated by the autonomic nervous system, specifically the parasympathetic innervation via the vagus and glossopharyngeal nerves and the sympathetic innervation via the superior cervical ganglion. **Aim:** The aim of the present study was to compare the effects of magnesium sulphate and esmolol in. reducing the pressor effects to laryngoscopy and intubation based on the basis of heart rate changes from the baseline values. Materials and **Methods:** The present hospital based prospective comparative observational study was conducted in Nil Ratan Sircar Medical college and hospital, Kolkata, West Bengal, India between February 2020 to August 2021. Informed consent of 88 patients of both sexes who were scheduled for elective urosurgical procedures under general anesthesia were included in the study based on the inclusion and exclusion criteria. Software such as SPSS V.24 and Microsoft Excel were used to analyze statistical data. **Results:** The mean age in years and mean BMI in kg/m2 were similar in two Groups. The baseline mean HR was 96.8 +/-18.9 beats/min and 103.1 +/- 20.7 bpm in group A and group B respectively. This showed that the basal heart rate in the two groups was not significantly different from each other. The baselinemean systolic BP in group A and group B were 125.1 +/- 9.3 mmHg and 122.6 +/- 15.3 mmHg respectively. Hence the P value was 0.391 which was statistically insignificant. Mean diastolic blood pressure in mmHg with standard deviation at different time intervals. The baseline DBP were 85.9 +/- 4.0 mmHg in group A and 80.1 +/- 3.9 mmHg in group B which was statistically insignificant. hypotension was found in either of the group but that was comparable, hence as per the study design adverse reaction which was observed intraoperatively and till 1 hr post-operative period was insignificant.

Conclusion: In this study it was concluded that considering the changes of decrease in mean heart it was found that administration of esmolol was better than magnesium sulphate to prevent pressor response following laryngoscopy and tracheal intubation.

Keywords: IV Esmolol, Laryngoscopy, Magnesium Sulphate

Introduction

In their daily work, anesthesiologists often induce general anesthesia and perform intubation to maintain airway patency and prevent aspiration. Thus, the release of catecholamines upon direct stimulation of the larynx and pharynx with a laryngoscope blade and the insertion of an endotracheal tube triggers a sympathetic nervous system reaction.1,2 With a reflex known as the "pressor" response, which consists of a brief rise in heart rate, blood pressure, and the occurrence of dysarrhythmias.This is a brief reaction that happens 30 seconds after intubation and lasts for under ten minutes.3 Anaesthesiologists frequently worry about the hemodynamic response to tracheal intubation and laryngoscopy.4 In healthy individuals,

it might be well tolerated. However, patients who already have systemic hypertension, coronary artery disease, eclampsia, aneurysmal vascular disease, head injury, thyrotoxicosis3, or other conditions where such a change could result in peri-operative myocardial ischemia or infarction, cardiac failure, dysarrhythmias, cerebrovascular accidents, or secondary brain injury may find this to be of significant clinical significance.3

Thus, for many years, a variety of medications have been used to lessen the pressor response to laryngoscopy and intubation, including lignocaine, magnesium sulfate, beta blockers, alpha 2 agonists like clonidine, opioids, calcium channel blockers, nitroglycerin (NTG), and dexmedetomidine.5,6

With this background the present study included effect of esmolol and magnesium sulphate regarding attenuation of pressor response to laryngoscopy and intubation.

Material and Methods

Present hospital based observational comparative study was conducted in Nil Ratan Sircar Medical college and hospital, Kolkata, West Bengal, India between February 2020 to August 2021.

Total 88 patients of both sexes based on inclusion and exclusion criteria scheduled for elective urosurgical operations under general anaesthesia in elective operating room, over a period of 18 months. The Institutional Ethics Committee gave its approval, and patients provided informed written consent in the local tongue.

The sample size was estimated using the change of mean HR from the baseline as the primary outcome from a previous study and with a 95% confidence limit predicting 80% power, a sample size of 40 was obtained in each group by taking 5.397 as pooled standard deviation and 3.38 as the mean difference. With 10% drop -out the final sample size of 40+4=44 was taken in each study group.

Inclusion criteria:

- Patients with physical status with ASA grade I and grade II
- Age between 18-45yrs, belonging to both sexes
- Body weight 45-60 kgs
- Patients with Mallampati score I
- Patients requiring general anaesthesia

Exclusion criteria:

- known hypertensive
- unstable blood pressure SBP<70mmHg and >150 mmHg
- Heart rate<60beats/minute, heart block, heart failure
- h/o asthma, chronic obstructive pulmonary disease
- diabetics
- difficult airways, Mallampati score II, III, IV
- ASA grade III and IV
- emergency surgeries
- impaired renal function and electrolyte imbalance
- patients allergic to any drugs
- morbidly obese
- regularly taking drugs like narcotics, hypnotics, antihypertensive
- major organ dysfunction

A few days prior to the procedure, a pre-anaesthetic checkup was performed, and laboratory results were carefully examined to rule out any systemic illnesses. Eighty-eight patients who met the inclusion and exclusion criteria described above were chosen for the study and provided their informed written consent Then those selected patients who received the stipulated study drugs respectively were observed and data were collected and analysed accordingly.

GROUP A- 44 patients receiving i.v. magnesium sulphate 20mg/kg through infusion 10 min before induction.

GROUP B- 44 patients receiving i.v. esmolol 0.3 mg/kg bolus 3min prior induction.
Patients were advised for overnight fasting normally after 10 p.m. with premedication of Tab. pantoprazole 40 mg, Tab alprazolam 0.5 mg orally at the night before the surgery.

Anaesthesia Technique:

A standard technique of anaesthesia was followed in all patients. On arrival in the operation theatre pulse, blood pressure was recorded as baseline (i.e. HR0, SBP0, DBP0) and monitoring was started with the help of ECG

In group A: patients received iv. Magnesium suphate20mg/kg diluted in 15ml NS over 10 minutes and 10 minutes before induction. Every patient received 100% O2 for 3 mins. If glycopyrrolate 200mcg, iv. ondansetron 4mg, iv. Fentanyl 2mcg/kg were given to every patients as premedication. Induction was done with iv. Propofol 2mg/kg and then succinyl choline 1.5 mg/kg was given facilitate intubation. But before intubation the values of the vitals (HR, SBP, DBP) were taken as the pre -intubation values of the parameters i.e.HR (PI), SBP(PI), DBP(PI).

In group B: Every patient received 100% O2 for 3mins for preoxygenation. Iv. glycopyrrolate
200mcg, iv.ondansetron 4mg,iv.fentanyl 2mcg/kg were given to every patients as premedication. Iv. esmolol 0.3mg/kg as bolus was administered 3 min prior to induction.

Then the induction was done with iv. Propofol 2mg/kg succinylcholine 1.5mg/kg was given to facilitate tracheal intubation. At this time the values of the vitals were taken as the PRE-INTUBATION values i.e. HR(PI), SBP(PI), DBP(PI).

Method of Data Analysis Plan: They all are compared in both groups. χ^2 (Chi Square) test was used to analyze the data and p value <0.05 was considered as statistically significant

Ethical considerations- Study was initiated after obtaining the informed consents from the participants and ethical clearance from the institutional ethical committee.

Results

The data was tabulated in Microsoft Excel software and analyzed with SPSS V.24 software. The groups were compared using the independent t test. A p-value of less than 0.05 was deemed statistically significant.

Table 1. Comparison of demographic variables between the groups

Variables	GROUP	N	Mean	Std. Deviation	Mean difference	P value
Age (yrs)	A	44	36.6	6.0	1.6	0.196
	B	44	38.2	4.4		
Ht.(cm)	A	44	155.7	3.9	4.4	0.000*
	B	44	160.1	2.6		
Wt.(kg)	A	44	54.0	4.1	2.9	0.000*
	B	44	56.9	1.9		
BMI	A	44	22.5	.6	0.2	0.762
	B	44	22.3	.5		

*Statistically significant difference exists between the groups (p<0.05)

The mean age in years and mean BMI in kg/m2 were similar in twoGroups. (Table 1)

Table 2. Comparison of Gender and ASA between the groups

Variables	GROUP	Group A	Group B	P value
Gender	Male	47%	44%	0.221
	Female	53%	56%	
ASA	I	48%	46%	0.538
	II	52%	54%	

Table 2 showed comparison of gender and ASA grade between the two groups which were comparable (not significant) periods.

Table 3. Comparison of heart rate at different times between the groups

	GROU P	N	Mean	Std. Deviation	Mean difference	P value
HR0	A	44	96.8	18.9	6.3	0.161
	B	44	103.1	20.7		
HR(PI)	A	44	85.3	14.7	13.7	0.000*
	B	44	71.6	13.6		
HR(DI)	A	44	102.1	12.4	27.2	0.000*
	B	44	74.9	14.1		
HR1	A	44	104.7	12.7	26.5	0.000*
	B	44	78.2	14.0		
HR3	A	44	97.9	13.5	15.9	0.000*
	B	44	82.0	16.0		
HR5	A	44	87.1	12.5	3.8	0.228
	B	44	83.3	14.9		
HR10	A	44	83.3	12.0	1.8	0.557
	B	44	81.5	15.4		

*Statistically significant difference exists between the groups (p<0.05)

Table 3 showed mean heart rate with standard deviation at different time.

The baseline mean HR was 96.8 +/-18.9 beats/min and 103.1 +/- 20.7 bpm in group A and group B respectively. This showed that the basal heart rate in the two groups was not significantly different from each other (P value 0.161). Induction of anaesthesia resulted in decrease in HR of the order of approximately 10 bpm from baseline (85.3 +/- 14.7 bpm) in group A and decrease of 30 bpm (71.6 +/- 13.6 bpm) in group B. Hence there was significant decrease in HR after induction with propofol and administration of iv. Magnesium sulphate/iv. Esmolol. Therefore, decrease in HR(PI) was statistically significant (P value 0.000). During intubation the HR [i.e. HR(DI)] was 102.1 +/- 12.4 bpm in group A and 74.9 +/- 14.1 bpm in group B which was statistically significant (P value 0.000). The heart rate touched a peak of 104.7 +/- 12.7 bpm 1min after intubation in group A (magnesium sulphate) while it rose upto 78.2

+/- 14.0 bpm in the group B (esmolol); so HR1 between two groups was also statistically significant (P value 0.000).

The HR remained persistently elevated above the baseline after intubation and returned to baseline (97.9 +/- 13.5 bpm) 3 min after intubation in group A. After that the HR fell below the baseline. On the contrary, in group B, HR which decreased rapidly after induction, remained below the baseline even immediately after tracheal intubation and thereafter throughout the whole observation-period i.e. upto 10 min after intubation. Therefore, at 3 min after intubation HR (HR3) in group A (97.9+/-13.5 bpm) and group B (82.0 +/- 16.0 bpm) resulted into a P value of 0.000 which was statistically significant. At 5 min after intubation HR (HR5) in group A was 87.1 +/- 12.5 bpm; HR in group B was 83.3 +/- 14.9 bpm and the P value was 0.228 which was not statistically significant.

At 10 min after intubatin the HR (HR10) in group A was 83.3 +/- 12.0 bpm and in group B was 81.5 +/- 15.4 bpm which resulted in a P value of 0.557. So it was not statistically significant.

Table 4. Comparison of systolic blood pressure at different times between the groups

	GROU P	N	Mean	Std. Deviation	Mean difference	P value
SBP0	A	44	125.1	9.3	2.5	0.391
	B	44	122.6	15.3		
SBP (PI)	A	44	107.0	5.0	4.7	0.05*
	B	44	102.3	14.2		
SBP (DI)	A	44	115.5	6.7	23.2	0.000*
	B	44	92.3	15.0		
SBP1	A	44	118.9	3.6	13.6	0.000*
	B	44	105.3	15.2		
SBP3	A	44	114.7	10.5	20.4	0.000*
	B	44	94.3	24.3		
SBP5	A	44	116.7	14.5	13.4	0.003*
	B	44	103.3	23.0		
SBP10	A	44	124.7	15.9	26.1	0.000*
	B	44	98.6	11.1		

*Statistically significant difference exists between the groups ($p<0.05$)

Table 4. showed the mean systolic blood pressure in mm of Hg in both the groups.The baseline means systolic BP in group A and group B were 125.1 +/- 9.3 mmHg and 122.6 +/- 15.3 mmHg respectively. Hence the P value was 0.391 which was statistically insignificant (P value 0.391). Induction of anaesthesia resulted in a decrease of SBP to 107.0 +/- 5.0 mmHg and 102.3 +/- 14.2 mmHg in both group A and B respectively which was a decrease of almost 20mmHg of pressure from the baseline. So there was a significant decrease of SBP in both the groups with administration of iv magnesium sulphate and iv. Esmolol before induction and the decrease [i.e. SBP(PI)] was statistically significant (P value 0.05) between the two groups.

During intubation SBP increased to 115.5 +/- 6.7 mmHg from 107.0 +/- 5mmHg in group A whereas it decreased to 92.3 +/- 15.0 mmHg from 102.3 +/- 14.2 mmHg in group B. So the SBP(DI) between the two groups was statistically significant (P value 0.000). At 1 min after intubation SBP (SBP1) in both the groups rose to 118.9 +/- 3.6 mmHg and 105.3 +/- 15.2 mmHg which was also statistically significant (P value 0.000). At 3 min after intubation SBP (SBP3) decreased to 114.7 +/- 10.5 mmHg and 94.3 +/- 24.3 mmHg in both groups which was statistically

Significant (P value 0.000). At 5 min after intubation SBP (SBP5) increased to 116.7 +/- 14.5 mmHg and 103.3 +/- 23.0 mmHg in both groups; this was also statistically significant (P value 0.003). At10 min after intubation SBP (SBP10) increased to 124.7 +/- 15.9 mmHg in group A whereas it decreased to 98.6 +/- 11.1 mmHg in group B; the P value was 0.000 and it was statistically significant.

Therefore, it was seen that the SBP in group A increased from its pre-intubation value during and after intubation but this increase was below its baseline value upto 10mins after intubation. After that it returns to its baseline.

But in group B the SBP came down below baseline after induction and remained so throughout the whole time period of observation and didn't touch the baseline even 10min after intubation.

Table 5. Comparison of diastolic blood pressure at different times between the groups

	GRO UP	N	Mean	Std. Deviation	Mean difference	P value
DBP0	A	44	85.9	4.0	5.8	0.461
	B	44	80.1	3.9		
DBP (PI)	A	44	72.3	6.0	3.5	0.003*
	B	44	68.8	3.3		
DBP(D I)	A	44	82.9	10.6	18.4	0.000*
	B	44	64.5	3.3		
DBP1	A	44	78.3	5.8	9.2	0.000*
	B	44	69.1	4.1		
DBP3	A	44	75.4	4.7	12.9	0.000*
	B	44	62.5	3.6		
DBP5	A	44	79.4	9.4	8.6	0.000*
	B	44	70.8	3.4		
DBP10	A	44	85.6	11.0	12.3	0.000*
	B	44	73.3	3.3		

*Statistically significant difference exists between the groups ($p<0.05$)

Table5. showed the mean diastolic blood pressure in mmHg with standard deviation at different time intervals. The baseline DBP were 85.9 +/- 4.0 mmHg in group A and 80.1 +/- 3.9 mmHg in group B which was statistically insignificant (P value 0.461). As a result of induction of anaesthesia with propofol DBP decreased to 72.3 +/- 6.0 mmHg in group A and 68.8 +/- 3.3 mmHg in group B and this was statistically significant (P value 0.003). Endotracheal intubation resulted in a rise of in DBP to 82.9 +/- 10.6 mmHg from 72.3 +/- 6.0 mmHg in group A but in group B DBP didn't rise as it became 64.5 +/- 3.3 mmHg from 68.8 +/- 3.3 mmHg.So that was statistically significant (P value 0.000). At 1min after intubation DBP (DBP1) decreased to 78.3 +/- 5.8 mmHg in group a but increased to 69.1 +/- 4.1 mmHg in group B; the P value was 0.000 and it was statistically significant. At 3 min after intubation DBP (DBP3) came down to 75.4 +/- 4.7mmHg and 62.5 +/- 3.6 mmHg in both the groups; P value was 0.000 which was statistically significant. At 5 min after intubation the DBP (DBP5) increased to 79.4 +/- 9.4 mmHg and 70.8 +/- 3.4 mmHg in both the groups which showed statistical significance (P value 0.000).

At 10 min after intubation the DBP (DBP10) increased to 85.6 +/- 11.0 mmHg and 73.3 +/- 3.3 mmHg; P value was 0.000 and was statistically significant. Therefore, DBP in the group A remained below the baseline values even after intubation until 10min after intubation and then it returned to its baseline values. But in group B DBP remained below the baseline throughout the whole period of observation.

Table 6. Comparison of adverse reactions between two groups

Adverse reaction	GROUP A	GROUP B
BRADYCARDIA	NIL	NIL
HYPOTENSION	2 cases	3 cases
RESPIRATORY DEPRESSION	NIL	NIL
POOR REFLEXES	NIL	NIL

As per the table 6 hypotension was found in either of the group but that was comparable, hence as per the study design adverse reaction which was observed intraoperatively and till 1 hr post-operative period was insignificant.

Discussion

This was a study which was undertaken to evaluate and compare two important drugs frequently used in anaesthetic practice and magnesium sulphate being the newer addition to alleviate laryngeal surge at the time of direct laryngoscopy and tracheal intubation and it was considered in this study against a more traditionally used drug esmolol.

In this study when compared demographically the data were found to be almost comparable in both the groups. (table1, table 2)

In the present study it was further found that the changes of mean heart rate were decreased in both groups from the baseline following administration of the study drugs for intubation with subsequent increase following tracheal intubation in the magnesium sulphate groupwhich gradually reached the baseline value at around 10th min of observation though similar changes found in esmolol group without the values returning to the baseline. (table-3)

Findings of this study were contradictory to the previous studies7,8 where they had shown increase in heart rate above baseline at immediate post intubation period following administration of both of this concerned study drugs. Although he doses of the study drugs chosen in this study were lower Than the previous studies the study design and timing of administration of the drugs for intubation might be the key reasons of these different findings.

There were few other studies9 where changes of heart rate following esmolol administration remained low and increased following laryngoscopic surge which almost corroborated with this study but sometimes these increased HR went passed the baseline values unlike this present study.

Considering the systolic blood pressure as one of the important findings in the present study it was found that the change of mean SBP values following administration of study drugs came down well below the baseline with more fall in the esmolol group and subsequent increase following laryngoscopic surge but did not reach the baseline values in either group (table 4).These finding were very much similar to one of the previous studies7 where it showed the same kind of observation regarding changes of mean values of SBP pre and post tracheal intubation.

Most of the previous studies had used higher doses (as for example 50mg/kg of magnesium sulphate and 1.5 -2 mg/kg of esmolol)7,8 of the study drugs than this present study. However lower dosefor both these study drugs (20mg/kg of magnesium sulphate and 0.3mg/kg of esmolol) were considered in this studydue to clinical perception of lower BMI and to avoid unneccesary overdosing of the drugs resulting adverse effects like bradycardia, hypotension, respiratory depression.
In this study the findings were different from many of the previous studies7 which showed adverse effect already mentioned as per the study design. These could be the result of low study drug doses considered here in this study.
Although diastolic BP also noted and changes of mean DBP noted and analysed and were found to be of lesser importance considering other studies.
So it was a study which could establish a fact that the changes of decrease in mean HR following laryngoscopy and intubation were significantly different in esmolol group from the magnesium sulphate.

Limitations of the study:
Duration of laryngoscopy was not considered. A larger sample size could have been a better option for the study. Estimation of serum noradrenaline and cortisol were not measured due to logistic reasons. Invasive blood pressure monitoring could have given a better estimation of BP monitoring. The study design was such that the delayed respiratory depression and hypotension could not have been monitored and noted in this study.

Conclusions
In this study it was concluded that considering the changes of decrease in mean heart rate as the primary outcome it was found administration of bolus esmolol 0.3mg/kg administered 3min before induction was significantly better thanmagnesium sulphate infusion 20mg/kg administered 10 min before induction to prevent sympathetic surge following laryngoscopy and tracheal intubation in adult patients with no clinical adverse effect

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