*Original Article*

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# A Study of Effect of Intravenous Magnesium Sulphate with Lignocaine and Intravenous Clonidine with Lignocaine on Blood Pressure in Response to Laryngoscopy and Tracheal Intubation during General Anaesthesia

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**Abstract**

*Background and Objectives:* Laryngoscopy and tracheal intubation is invariably associated with a reflexsympathetic pressor response resulting in elevated heart rate and blood pressures. Thismay prove detrimental in high risk patients. The main objectives of the present study are:

1. To study the effect of intravenous magnesium sulphate 30 mg/kg with intravenous lignocaine 1.5mg/kg, and intravenous clonidine 3mcg/kg with intravenous lignocaine 1.5mg/kg on changes in the Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial blood pressure (MAP) during laryngoscopy and intubation under general anesthesia. *Methods:* 60 ASA I and II status normotensive patients scheduled for elective surgical Procedures were selected randomly and divided into three groups of 20 each. Allpatients received premedicationwith studydrug. Induction of anesthesia was standardized for all patients who received, thiopentone 5 mg/kg i.v.and preservative free lignoaine 1.5mg i.v and were relaxed with succinylcholine 2mg/kg i.v. and laryngoscopy and intubation is done with appropriate sized endotracheal tube. HR, systolic, diastolic blood pressure were recorded noninvasively before induction, postintubation, 1,3,5, 7 and 10 minutes from the onset of laryngoscopy. ' z' test was used for statistical analysis. *Results:* The basal and pre laryngoscopy mean SBP and standard deviations in CL group were 122.15 +/- 8.12 and 114.50 +/- 7.30 respectively. In ML group basal systolic blood pressure was 117.30 -+-/- 9.78. After giving study drug prelaryngoscopy SBP decreased by 3mm of mm Hg to 114.15 +1-15.26. *Conclusion:* Both study drugs were more effective in attenuation of pressor response to intubation than when lignocaine alone was used

**Keywords**: Attenuation; Pressor Response; Laryngoscopy; Intubation; Lignocaine; Magnesium-sulphate; Clonidines.

## Introduction

Laryngoscopy and endotracheal intubation are associated with significant hypertension, tachycardia and arrhythmias. These hemodynamic responses were first recognised as early as in 1940 by Reid and Bruce et al [1].

In 1950 Burstein et al [2]studied the effects of laryngoscopy and tracheal intubation on ECG changes and suggested the pressor response as consequences of an increase in sympathetic and sympathoadrenal activity. These facts were further confirmed by various investigators[3].

These responses are transitory, variable and unpredictable and are much more pronounced in hypertensive patients than in normotensive individuals [4]. These transient changes can result in potentially deleterious effects like, left ventricular failure, pulmonary edema, Myocardialischaemia, ventricular dysrhythmias and cerebral hemorrhage.

Various attempts [5-9]were made in the past to reduce the pressor response to laryngoscopy and intubation using inhalational anesthetics, á adrenergic drugs, â blockers, calcium channel blockers, vasodilators, low dose opioids, all with one or other adverse effects.

Robert K Stoelting [10] noted that the best way to prevent laryngoscope reaction was to minimize the duration of laryngoscopy and intubation to 15seconds. He also suggested that, Intravenous Lignocaine given in the doses of 1.5 mg/kg 3 minutes before laryngoscopy and intubation sufficiently attenuates

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the laryngoscopic reactions. The advantages of intravenous lignocaine claimed by this author was intravenous lignocaine depressed the autonomic nervous system and in addition had antiarrhythmic properties.

Many studies have shown that magnesium sulphate can attenuate cardiovascular response to endotracheal intubation. Jame MF et al [11] in 1989 showed that pretreatment with magnesium sulphate 60mg/kg body weight attenuates catecholamine mediated responses to tracheal intubation. K Montazeri MD and M Fallah MD [12] in 2005 showed that intravenous magnesium sulphate in the dose of 30mg/kg body weight was equally effective.

In 1991, Wright PMC et al and CarabineUA et al [13] showed that intravenous clonidine sufficiently attenuates pressor response to intubation. Ishiyama T et al [14] in 2006 demonstrated that clonidine produced stable hemodynamic condition during induction sequence.

Hence the main objectives of the present study is to study the effect of intravenous magnesium sulphate 30 mg/kg with intravenous lignocaine 1.5mg/kg, and intravenous clonidine 2mcg/kg with intravenous lignocaine 1.5mg/kg on changes Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial blood pressure (MAP) during laryngoscopy and intubation under general anesthesia.

## Methodology

60 ASA I and II status normotensive patients scheduled for elective surgicalprocedures were selected randomly and divided into three groups of 20 each. Allpatients received premedication with study drug magnesium sulphate 30mg/kg or clonidine 3µgm / kg or normal saline (as per double blind study protocol) prepared by anaesthesia staff and glyopyrrolate 0.2mg i.v., tramadol 3mg /kg 3min before induction . Induction of anesthesia was standardized for all patients who received, thiopentone 5 mg/kg i.v.and preservative free lignoaine 1.5mg i.v and were relaxed with succinylcholine 2mg/kg i.v. and laryngoscopy and intubation is done with appropriate sized endotracheal tube. HR, systolic, diastolic blood pressure were recorded noninvasively before induction, postintubation, 1, 3, 5, 7 and 10 minutes from the onset of laryngoscopy. 'z' test was used for statistical analysis.

## Results

| SBP | Clonidine with lignocaine (A) | Magnesium sulphate with lignocaine (B) | Lignocaine only (C) | P value * | P value # | | |
|---|---|---|---|---|---|---|---|
| | | | | | A-B | A-C | B-C |
| Baseline | 122.15 +/- 8.12 | 117.30 +/- 9.78 | 117.50 +/- 8.34 | 0.15 | 0.19 | 0.22 | 0.99 |
| Pre laryngeal | 114.50 +/- 7.30 | 114.15 +/- 15.26 | 113.75 +/- 15.07 | 0.98 | 0.99 | 0.98 | 0.99 |
| One min | 138.50 +/- 10.51 | 134.33 +/- 14.16 | 155.80 +/- 13.03 | 0.00 | 0.55 | 0.00 | 0.00 |
| Three min | 127.35 +/- 11..60 | 121.85 +/- 11.63 | 140.65 +/- 15.06 | 0.00 | 0.37 | 0.00 | 0.00 |
| Five min | 119.65 +/- 11.20 | 117.65 +/- 13.83 | 126.65 +/- 12.17 | 0.06 | 0.86 | 0.18 | 0.06 |
| Ten min | 116.20 +/- 9.71 | 119.95 +/- 12.28 | 119.80 +/- 9.57 | 0.06 | 0.40 | 0.52 | 0.05 |

* ANOVA test
# Post-hoc tukey test
All values are in mean +/- sd

Analysis of systolic blood pressure Statistical analysis of changes in systolic blood pressure at basal, prelaryngoscopy ,nost intubation at different (1 ,3, 5, 10, ) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented.

*Group CL (A)*

The basal and pre laryngoscopy mean SBP and standard deviations in this group were 122.15 +/- 8.12 and114.50 +/- 7.30 respectively . After lmin of intubation 16.35 mm Hg (13.38%) increase in mean SBP was observed with mean SBP and standard deviations of 138.50 +/- 10.51. Subsequently a decreasing trend in the SBP was noted starting from 3 minutes to 10 minutes after laryngoscopy. Mean SBP at 3, 5 minutes and 10 minutes were 127.35 +/- 11.60, 119.65 +/- 11.20 and 116.20 +/-9.71. At 10 minutes post laryngoscopy the SBP almost returned to base line with a mean value of 119.95 +1- 12.28.

*Group ML(C)*

In this group basal systolic blood pressure was 117.30 -+-/- 9.78. After giving study drug prelaryngoscopy SBP decreased by 3mm of mm Hg to 114.15 +1- 15.26. Increase in systolic blood pressure Of 17.03 mmHg (14.51%) with a mean of 134.33 +/-

14.16 was observed at 1 minute following laryngoscopy. After 3 min SBP fell by 12mmhg with a mean of 121.85 +/- 11.63, from there on a gradual fall in SBP was observed at 5 minutes mean SBP was 117.65 +/- 13.83. At 10 minutes postlaryngoscopy the SBP almost returned to base line with a mean value of 119.95 +1- 12.28.

*Group NL (C)*

In this group basal systolic blood pressure was 117.50 +/- 8.34. After giving study drug prelaryngoscopy SBP decreased by 4 mm Hg toll 3.75 +/- 15.07. increase in systolic blood pressure Of 38.3 mm Hg(32.59%) with a mean of 155.80 +/- 13.03 was noted at 1 minute following laryngoscopy. After 3 min SBP fell by 23.15 mmHg (19.70%) with a mean of 140.65 +/- 15.06, from there on a gradual fall in SBP was noted. At 5 minutes it was 126.65 +/- 12.17. At 10 minutes post laryngoscopy the systolic blood pressure almost returned to base line with a mean value of 119.80 +1-9.57.

No significant variations were noted in all groups in SBP at basal and after giving study drug. The increase of systolic blood pressure at one and three minutes after intubation was significantly less in ML group and CL group compared to NL group, But there was no significant reduction in increase of SBP at five and ten minutes of recording. there was no significant changes in attenuation of SBP response between ML group and CL group at any time of recording.

**Table 2:** Comparison of DBP (mmHg) between three groups

| DBP | Clonidine with lignocaine (A) | Magnesium sulphate with lignocaine (B) | Lignocaine only (C) | P value * | P value # | | |
|---|---|---|---|---|---|---|---|
| | | | | | A-B | A-C | B-C |
| Baseline | 87.90 +/- 5.55 | 78.95 +/- 7.60 | 77.35 +/- 7.48 | 0.11 | 0.37 | 0.10 | 0.74 |
| Pre laryngeal | 77.15 +/- 9.04 | 77.50 +/- 13.87 | 117.30 +/- 18.72 | 0.39 | 1.00 | 0.45 | 0.46 |
| One min | 90.60 +/- 7.68 | 90.25 +/- 13.75 | 101.75 +/- 8.14 | 0.00 | 0.99 | 0.00 | 0.00 |
| Three min | 84.65 +/- 7.80 | 79.90 +/- 11.93 | 92.85 +/- 11.73 | 0.00 | 0.34 | 0.04 | 0.00 |
| Five min | 80.35 +/- 10.27 | 79.60 +/- 15.73 | 82.55 +/- 13.49 | 0.76 | 0.98 | 0.86 | 0.76 |
| Ten min | 76.10 +/- 7.65 | 72.40 +/- 13.78 | 77.15 +/- 9.80 | 0.34 | 0.52 | 0.94 | 0.34 |

* ANOVA test
# Post-hoc tukey test
All values are in mean +/- sd

Analysis of diastolic blood pressure Statistical analysis of changes in systolic blood pressure at basal, prelaryngoscopy ,post intubation at different (1 ,3, 5, 10, ) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented .

***Group CL (A):*** In this group pre-induction diastolic blood pressure was83.90 +1- 5.55 . After giving study drug prelaryngoscopy DBP decreased by 11 mm Hg to mean of 77.15 +/- 9.04 . Increase in diastolic blood pressure Of 6.70mmHg (7.9%) with a mean of 90.60 +7-7.68 was noted at 1 minute following laryngoscopy. After 3 min DBP fell by 6 mmhg(6.8%) with a mean of 84.65 +/- 7.80 , from there on a gradual fall in DBP was noted. At 5 minutes it was 80.35 +/- 10.27. At 10 minutes post laryngoscopy the DBP decreased to less than base line with a mean value of 76.10 +/- 7.65.

***Group ML (B):*** In this group pre-induction diastolic blood pressure was 79.95 +/- 7.60. After giving study drug prelaryngoscopy DBP decreased by 1 mm Hg to mean of 77.50 +/- 13.87. Increase in diastolic blood pressure Of 10.30 mm Hg(12.8%) with a mean of 90.25 +/- 13.75 was noted at 1 minute following laryngoscopy. After 3 min DBP was 79.90 +/- 11.93, from there on a gradual fall in DBP was noted. At 5 minutes it was 79.60 +/- 15.7,. At 10 minutes post laryngoscopy the DBP decreased to less than base line with a mean value of 72.40 +/- 13.78.

***Group NL (C):*** In this group pre-induction diastolic blood pressure was77.35 +/- 7.48. After giving study drug prelaryngoscopy DBP decreased to mean of 75 .30 +1..18.72. Increase in diastolic blood pressure Of 24.40 mm Hg(31.54%) with a mean of 101.75 +/- 8.14 was noted at 1 minute following laryngoscopy. After 3 min DBP fell by 15.5 mmHg (20.0%) with a mean of 92.85 +/- 11.7, from there on a gradual fall in DBP was noted at 5 minutes it was 82.55 +/- 13.49. At 10 minutes post laryngoscopy the DBP decreased to less than base line with a mean value of 77.15 +/- 9.80. No significant variations were noted in all groups in diastolic blood pressure at basal and after giving study drug. There was significant attenuation of DBP response at one minute and three minutes after intubation in CL group and ML group compared to NL group however there was no significant difference in attenuation of DBP at five and ten minutes of recording. There was no significant difference in attenuation of DBP response between ML group and CL group at any time of recording.

**Table 3:** Comparison of MAP (mmHg) between three groups

| Heart rate | Clonidine with lignocaine (A) | Magnesium sulphate with lignocaine (B) | Lignocaine only (C) | P value * | P value # | | |
|---|---|---|---|---|---|---|---|
| | | | | | A-B | A-C | B-C |
| Baseline | 94.55 +/- 7.01 | 91.45 +/- 8.58 | 134.55 +/- 20.07 | 0.43 | 0.99 | 0.52 | 0.47 |
| Pre laryngeal | 87.50 +/- 6.49 | 87.50 +/- 11.90 | 88.35 +/- 13.08 | 0.96 | 1.00 | 0.96 | 0.96 |
| One min | 107.30 +/- 13.01 | 103.35 +/- 13.22 | 116.80 +/- 10.66 | 0.00 | 0.57 | 0.04 | 0.00 |
| Three min | 97.25 +/- 8.61 | 95.35 +/- 11.16 | 107.75 +/- 14.36 | 0.00 | 0.86 | 0.01 | 0.04 |
| Five min | 93.25 +/- 10.31 | 91.70 +/- 15.00 | 97.25 +/- 12.25 | 0.36 | 0.92 | 0.58 | 0.35 |
| Ten min | 90.25 +/- 7.55 | 84.70 +/- 11.64 | 95.65 +/- 13.61 | 0.37 | 1.00 | 0.44 | 0.44 |

* ANOVA test
# Post-hoc tukey test
All values are in mean +/- sd

Analysis of MAPStatistical analysis of changes in MAP at basal.prelaryngoscopy ,post intubation at different (1, 3, 5, 10, ) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented .

***Group CL (A):*** In this group basal MAP was 94.55 +/- 7.01 . After giving study drug prelaryngoscopy MAP decreased by 7.06 mm Hg to mean of 87.50 +/- 6.49. Increase in MAP of 10.30 mm Hg(11.13%) with a mean of 107.30 +1- 13.01 was noted at 1 minute following laryngoscopy. After 3 minutes mean MAP was 97.25 +/- 8.61, from there on a gradual fall in MAP was noted. At 5 minutes it was 9325 +/- 10.31. At 10 minutes post laryngoscopy the MAP almost returned to base line with a mean value of 90.25 +/- 7.55.

***Group ML (B):*** In this group pre-induction MAP was 91.45 +/- 8.58. After giving study drug prelaryngoscopy MAP decreased by 4mm hg to mean of 87.50 +/- 11.90. Increase in MAP Of 11.9(13.01%) mm hg with a mean Of 103.35 +/- 13.22 was noted at 1 minute following laryngoscopy. After 3 min mean MAP was 95.35 +/- 11.16, from there on a gradual fall in MAP was noted as at 5 minutes it was 91.70 +/- 15.00. At 10 minutes post laryngoscopy the DBP almost returned to base line with a mean value of 84.70 +/- 11.64.

***Group NL (C):*** In this group pre-induction MAP was 94.55 +/- 20.07. After giving study drug prelaryngoscopy MAP decreased by 6 mm Hg to mean of 88.35 +/- 13.08. Increase in MAP Of 22.2.5 mm Hg (24.35%) with a mean of 116.80 +1- 10.66 was noted at 1 minute following laryngoscopy. After 3 min mean MAP was107.75 +/- 14.36 , from there on a gradual fall in MAP was noted. At 5 minutes it was of 97.70 +/- 12.25. At 10 minutes post laryngoscopy the systolic blood pressure almost returned to base line with a mean value of 95.65 +/- 1.3.61. No significant variations were noted in all groups in mean arterial pressure at basal and after giving study drug. There was significant reduction of increase in MAP at one minute and three minutes after intubation in CL group and ML group compared to NL group, however there was no significant difference in attenuation of MAP between CL group and ML group at any time of recording.

## Discussions

Many factors influence the cardiovascular changes associated with laryngoscopyand intubation. Age, drugs, type and duration of procedures, depth of anesthesia,hypoxia, hypercarbia etc., influence the pressor responseVariations of heart rate changes decrease with increasing age. Young patientsshow more extreme changes [18]. Marked fluctuations in hemodynamic responses areoften seen in geriatric patients[15,16].

In our study we selected the optimal age range of 18 to 50 years. Patients on antihypertensive drugs may exhibit a decrease in pressor response. Weexcluded the patients on antihypertensive medications from our study Thiopentone was selected for induction since it still continues to be the mostpopular agent for induction. In normovolemic patients thiopentone 5mg/kg i.v cantransiently decrease 10-20mm Hg of blood pressure and increase the heart rate by 15-20 beats/min. There is increase in catecholamine levels, both noradernaline andadrenaline [17].

Succinyl choline has negative inotropic and chronotrpic effect. It acts on themuscarinic receptors of SA node. A marked noradrenergic response was noted whenintubation was performed under succinylcholine[18].

Nitrous oxide may increase the tone of sympathetic nervous system. The directaction of Nitrous oxide is negative inotropism which is offset by increased sympathetictone. Halothane has potency to decrease the heart rate but at concentration used formaintenance it does not appreciably change the

heart rate [19].

Nasotracheal intubation comprises of three distinct phases a) nasopharyngealintubation b) direct laryngoscopy to identify the vocal cords and c) Passage of tracheal tube into the trachea. Nasopharyngeal intubation causes significant pressor response. This response in heightened by the passage of tracheal tube in the larynx and trachea in our study we included only direct laryngoscopy andorotracheal intubation.

Laryngoscopy alone may produce most of the cardiovascular responses reported after laryngoscopy and tracheal intubationduringanaesthesiaThe most significant laryngoscopic factor influencing cardiovascular responses is found to be the duration of laryngoscopy. A linear increase in heart rate and mean arterial pressure during the first 45 seconds has been observed. Further prolongation has little effect. As the duration of laryngoscopy is normally less than 30 seconds, the results of studies in which it takes longer than this have less clinical relevance. The force applied during laryngoscopy has only minor effect. In our study the duration of laryngoscopy and intubation was limited to 20 seconds.

Adequate care was taken to achieve the required depth of anesthesia avoidinghypoxia and hypercarbia which can influence e the hemodynamic variations. Excluding hypoxia and hypercarbia other contributory causes of hypertension and tachycardia could be continued manifestation of anxiety concerning anesthesia and surgery, glycopyrrolate premedication, reflex baroreceptor effect after thiopentone and possible effect of suxamethonium.But they seem to be less important than laryngotracheal stimulation during laryngoscopy and intubation.

Attenuation of sympathetic responses during laryngoscopy and intubation is ofprime concern to the anaesthetist more so in high risk subjects as mentioned earlier.Many strategies have been recommended which include minimising the duration oflaryngoscopy to less than 20 seconds, topical application of local anaesthetics, iv?-blockers, calcium channel blockers, Clonidine, Sodium Nitroprusside, lignocaine. No single drug or technique is satisfactory. Each technique has advantages and disadvantages, the most obvious being that the prevention often outlasts the stimulus.

In group NL the basal value of Systolic blood pressure, Diastolic blood pressure, and Mean arterial pressure was 1117.50 mm Hg, mm 77.35 Hg, and 94.55 mm Hg respectively. Following laryngoscopy and intubation, the maximal rise in Systolic blood pressure (SBP) was found to be 38.30 mm Hg, that of Diastolic blood pressure (DBP) was 20.45 mm Hg and that of Mean arterial pressure (MAP) was 22.33 mm Hg. These elevated pressure readings started coming down by 3 minutes. However they remained above the baseline value even at the end of 5 minutes and reached baseline at 10 mins.

Stanley Tam employing inj. Lignocaine 1.5 mg / kg i.v 3 minutes before laryngoscopy and intubation to blunt the pressor responses, found out the maximal increase in SBP was(15)12 mm Hg, DBP was 9 mm Hg and MAP to be 11 mm Hg. Mounir Abou- Madi et al [18] noticed the change in SBP by 30 mm Hg, change in the DBP was 22 mm Hg. CD Miller37noticed a increase in SBP to be 33 mm Hg, DBP to be 37 mm Hg. Splinter et al. noticeda change in SBP to be 26 mm Hg, DBP to be 41 mm Hg and change in MAP to be 44 mmHg.

In group ML Inj. $MgSO_4$ 30mg / kg i.v. 3 minutes before laryngoscopy and intubation was used to blunt the pressor response, the basal value of Systolic blood pressure (SBP), Diastolic blood pressure (DBP), and Mean arterial pressure (MAP) was 117.30 mm Hg, mm 78.95 Hg, and 91.45 mm Hg respectively. Following laryngoscopy and intubation, the maximal rise in Systolic blood pressure (SBP) was found to be 17.03mm Hg, that of Diastolic blood pressure (DBP) was 11.30 mm Hg and that of Mean arterial pressure (MAP) was 11.9 mm Hg. These elevated pressure readings started coming down by 3 minutes. However they remained above the baseline value even at the end of 5 minutes and reached baseline at 10 mins

In the study of Dr. Santosh Kumar using $MgSO_4$ i.v 30mg / kg 3 minutes before laryngoscopy and intubation to blunt the pressor responses, found out the maximal increase in SBP was 5 mm Hg, DBP was 4 mm Hg and MAP to be 4mm Hg. In K.Montazeri et al study employing $MgSO_4$ i.v 30mg / kg 3 minutes before laryngoscopy and intubation to blunt the pressor responses, found out the maximal increase in MAP to be 20 mm Hg

In group CL Inj clonidine 3µg / kg i.v. 3 minutes before laryngoscopy and intubation was used to blunt the pressor response, the basal value of Systolic blood pressure (SBP), Diastolic blood pressure (DBP), and Mean arterial pressure (MAP) was 122.15 mm Hg, mm 83.90 Hg, and 96.5d5 mm Hg respectively. Following laryngoscopy and intubation, the maximal rise in Systolic blood pressure (SBP) was found to be 16.35mm Hg, that of Diastolic blood pressure (DBP) was6.70 mm Hg and that of Mean arterial pressure

(MAP) was 12.75 mm Hg. These elevated pressure readings started coming down by 3 minutes. However they remained above the baseline value even at the end of 5 minutesand at 10minutes difference Of MAP between basal and 10 min after intubation was 4 mm hg

In study done by In Marco P Zalunardo [20] with clonidine 3 u / kg the difference of MAP between basal and 10 min after intubation was 21.1.

## Conclusion

With respect to attenuation of blood pressure responses, there were no significant differences between clonidine & lignocaine group and $MgSO_4$ & lignocaine group during at different times after laryngoscopy and intubation.

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