Original Research Article

A randomized double blind comparative study of intravenous magnesium sulphate and intravenous lignocaine for attenuation of haemodynamic response to laryngoscopy and tracheal intubation

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Abstract

Background: Even though the elevation in blood pressure and heart rate due to laryngoscopy and intubation are brief, they may have detrimental effects in high risk patients including myocardial infarction, cardiac failure, intracranial haemorrhage and increase in intracranial pressure. Laryngoscopy and tracheal intubation induces changes in circulating catecholamine levels significantly and also it is associated with elevation of blood pressure and heart rate. **Methods:** This is a Prospective Randomized Double Blind Study conducted in Sri Sathya Sai Institute of Higher Medical Sciences; Total 70 Patients (Group A – 35, Group A – 35). All the subjects` included after informed consent, blood samples and urine samples are collected from the all the subjects. Hb, Blood sugar, Serum urea, Serum creatinine, Coagulation profile, Serology, Blood grouping and Rh typing and Urine analysis was measured by laboratory standard methods. Along with Chest X- ray and ECG-for patients over 40 years of age. **Results:** This study was evaluated In Lignocaine group (group A) heart rate at Baseline, Post-induction, 1min, 3min, 5min and 10min after laryngoscopy were 86.70±12.65, 83.51±10.63, 94.82±11.65, 87.14±9.68 and 86.70±12.65. In Magnesium group (group B) the baseline mean heart rate was 89.57±16.23 which reduced to 85.62±13.03 after induction. 1 min after laryngoscopy the mean heart rate increased to 98.45±16.90. At 3, 5 and 10 minute from the time of laryngoscopy mean heart rates were 91.80±10.86, 86.05±9.51 and 81.37±8.96. **Conclusion:** In Magnesium sulphate group significant and consistent attenuation of sympathetic response as compared to lignocaine group was noted at 1 and 3 minutes. Among the two study groups I.V Magnesium sulphate appears to be superior over I.V. lignocaine in attenuating the sympathetic responses to laryngoscopy and intubation and is statistically significant.
Key Words: ECG, laryngoscopy, Magnesium and X- ray.

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Received Date: 02/11/2020 Revised Date: 08/12/2020 Accepted Date: 19/01/2021
DOI: https://doi.org/10.26611/10151728

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 24 February 2021

INTRODUCTION

Laryngoscopy and intubation are standard methods for general anaesthesia technics and in these technic hemodynamic variable alterations particularly catecholamine concentrations. Increase sensory nervous system activation and laryngeal reflex are causes of elevated levels of catecholamines leads to hypertension, tachycardia and arrhythmia endotracheal intubation[1-3]. The circulatory responses to laryngeal and tracheal stimulation following laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation[4]. Even though the elevation

How to site this article: Madhu Kumar B S, Prameela V S, Sunil Chhabria, Brijesh K, Srikanta Murthy TN. A randomized double blind comparative study of intravenous magnesium sulphate and intravenous lignocaine for attenuation of haemodynamic response to laryngoscopy and tracheal intubation. *MedPulse International Journal of Anesthesiology.* February 2021; 17(2): 83-89. http://medpulse.in/Anesthsiology/index.php

in blood pressure and heart rate due to laryngoscopy and intubation are brief, they may have detrimental effects in high risk patients including myocardial infarction, cardiac failure, intracranial haemorrhage and increase in intracranial pressure [5]. The intubation period as one of the greatest risk phase in the surgical patients with coronary artery disease and patients with intracranial aneurysms. The techniques of laryngoscopy and tracheal intubation are not confined only to the operating room, but are also employed for non-anaesthetic purposes. Few instances are diagnostic laryngoscopy, fibreoptic bronchoscopy, where intubation may be required for prevention of aspiration and protection of airway and during mechanical ventilation[6-8]. All these procedures can also produce sympathetic response and one should keep in mind that many of these patients are critically ill and are at increased risk. Hence it is important to find an effective means of attenuating sympathetic response to laryngoscopy and tracheal intubation. Many strategies have been advocated to minimise these adverse hemodynamic responses and aimed at different levels of the reflex arc[9]. There are various techniques by which intubation related stress response can be attenuated, all of which depend on reduction in input stimuli or the blockade of adrenergic responses, deep anaesthesia, topical anaesthesia, use of ganglion blockers, beta blockers, antihypertensive agents like phentolamine, sodium nitroprusside, nitroglycerine, calcium channel blockers. Clonidine, an α 2 adrenoreceptor agonist attenuates adrenergic hemodynamic stress response[10-12]. Based on this background the present study was evaluated study to compare the effectiveness of intravenous lignocaine and magnesium sulphate in attenuating the haemodynamic response associated with the powerful stimulus of laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS

This is a Prospective Randomized Double Blind Study conducted in Surgical Complex of the Sri Sathya Sai Institute of Higher Medical Sciences. A total 70 subjects are included again grouped into the sampled patients were randomly allocated to either Lignocaine (Group A) 35 subjects or Magnesium (Group B) group 35 subjects. All the subjects were recruited in the study after obtaining their informed consent after obtaining of ethical clearance from the institute. Patients with various elective surgical procedures, under general anaesthesia, belonging to ASA class I and II, Patients aged between 20 to 60 years of both the sex, Patients belonging to ASA physical status class I and II, Mallampatti grade I and II and Elective surgeries under general anaesthesia were included in this study and patients with Patient refusal, Patients with hypertension, cardiac, coronary, renal, hepatic, cerebral diseases, peripheral vascular diseases and electrolyte imbalance, Patients with heart rate < 60bpm, systolic blood pressure <100 mm of Hg, Presence of 1st, 2nd or 3rd degree heart block, Patients with difficult airway and obese patients or those who require more than one attempt for laryngoscopy and intubation, Patients with endocrinal disease like hypothyroidism, hyperthyroidism, diabetes mellitus, Pregnant and nursing women were excluded.

Cases were divided into two groups with 35 cases in each group.

Lignocaine group (Group A): Patients received 1.5mg/kg of preservative free 2% lignocaine intravenously 90 seconds before laryngoscopy.

Magnesium group (Group B): Patients received 30 mg/kg of magnesium 90 seconds prior to laryngoscopy.

The following cardiovascular parameters were recorded in all patients " Heart rate [HR] in beats per minute, Systolic blood pressure [SBP] in mm of Hg , Diastolic blood pressure [DBP] in mm of Hg, Mean blood pressure[MBP] in mm of Hg" along with cardiovascular parameters were monitored in the following time interval " Base line (before giving study drug), Post induction (Pre laryngoscopy), One min after laryngoscopy and intubation, Three minutes after laryngoscopy and intubation, Five minutes after laryngoscopy and intubation and Ten minutes after laryngoscope and intubation.

Premedication:

All the patients were visited the day before surgery and pre anaesthetic counselling was done. All patients received Diazepam 5mg orally at night on the day before surgery. On the day of surgery intravenous line was secured with 18G IV cannula and base line HR, SBP, DBP were recorded, Inj. Glycopyrolate5mcg/kg i.v, Inj .Phenargan 0.25mg/kg i.v pre medications were given 15 minutes before induction. On entering the OT pulse oximeter, non-invasive blood pressure and ECG monitors was connected. I.V. infusion of RL/NS/DNS solution was started.

Anaesthetic technique:

Randomly selected 35 patients were given IV. Lignocaine 1.5mg/kg 90 seconds prior to laryngoscopy and 35 randomly selected patients were given IV Magnesium sulphate 30mg/kg. The study solution was prepared in a 5 ml syringe by an anaesthesiologist who handed over the syringe in a coded form to the attending anaesthesiologist who records the parameters after injecting the drug. Laryngoscopy was done at the end of 3 mins after vecuronium injection using rigid laryngoscope with standard Macintosh blade. Heart rate, systolic and diastolic blood pressure were recorded post induction and at 1, 3, 5 and 10 minute intervals from the onset of laryngoscopy. Patients were connected to closed circuit and anaesthesia was maintained with oxygen (50%), air (50%), isoflurane 1% and non-depolarizing muscle relaxant vecuronium

bromide at a dose of 0.05 mg/kg i.v. and IPPV. Adequacy of ventilation was monitored by EtCO2 and SPO2 was maintained at 99-100%. Positioning and surgery was withheld till the completion of recording upto 10 miniutes.

Statistical Analysis

The normal distribution of data checked by using Kolmogorov Smirnov test. All the characters descriptively summarized. The mean and standard deviation about the arithmetic mean were used. Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent, Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Post-hoc Tukey test has been used to find the significance pair wise. Chi-square /Fisher exact test has been used to find the homogeneity of samples on categorical scale. Randomization code has been generated to allocate patients to treatment groups by Graphpad Software.

RESULTS

Table 1: Shows the mean and standard deviation (SD) values of subject's characteristics were analysed the patients Age distribution of patients Lignocaine (Group A) and Magnesium (Group B) groups. There was no statistically significant difference between the groups with regard to age and so they are comparable. (p=0.66) and in between the gender significantly more in males group a and group B (77.1% and 71.4%) compared to females (22.9% and 28.6%) P – 0.58.

Table 1: comparison between patient characteristics

	Group	N	Mean	p-value
Age	A	35	38.03(12.84)	0.66
	B	35	39.23(9.46)	
Gender	A	35	27: 8	p= 0.58
(Male, Female)	B	35	25: 10	

Table 2: Shows the mean and standard deviation (SD) values of subject's Heart rate (bpm) was analysed by using independent students test, in lignocaine group heart rate at baseline, Post- induction, there was a significantly reduced levels of heart rate at Baseline, Post-induction, 1min, 3min, 5min and 10min after laryngoscopy were 86.70±12.65, 83.51±10.63, 105.51±10.03, 94.82±11.65, 87.14±9.68 and 86.70±12.65. In Magnesium group (group B) the baseline mean heart rate was 89.57±16.23 which reduced to 85.62±13.03 after induction. 1 min after laryngoscopy the mean heart rate increased to 98.45±16.90. At 3, 5 and 10 minute from the time of laryngoscopy mean heart rates were 91.80±10.86, 86.05±9.51 and 81.37±8.96. The mean heart rate touched the baseline at around 5 minutes. Intergroup comparison between the groups, there was a statistically significant levels at 1 minute value after laryngoscopy, in in magnesium group was statistically significantly lower compared to lignocaine group (P<0.05). 3minute, 5 minute and 10 minutes values were lower in magnesium group but statistically not significant when compared to lignocaine group.

Table 2: Comparison of Heart rate (bpm) in the groups studied

Heart Rate	Group	N	Mean	SD	Mean diff.	95% CI of difference		t	df	p-value
						Lower	Upper			
Baseline	A	35	86.70	12.65	2.86	-4.14	9.87	0.81	67	0.41
	B	35	89.57	16.23						(NS)
Post Induction	A	35	83.51	10.63	2.11	-3.56	7.78	0.74	68	0.46
	B	35	85.62	13.03						(NS)
1 min	A	35	105.51	10.03	-7.05	-13.68	-.42	-2.12	68	0.03*
	B	35	98.45	16.90						
3 min	A	35	94.82	11.65	-3.02	-8.40	2.34	-1.12	68	0.26
	B	35	91.80	10.86						(NS)
5 min	A	35	87.14	9.68	-1.08	-5.66	3.49	-0.47	68	0.63
	B	35	86.05	9.51						(NS)
10 min	A	35	82.68	9.27	-1.31	-5.66	3.03	-0.60	68	0.54
	B	35	81.37	8.96						(NS)

Table 3:

In Magnesium group the post induction SBP was significantly lower compared to its baseline (P=0.008). Also at 5 min and 10 minutes value were significantly lower (p=0.001 and p<0.001 respectively) when compared to its baseline but this fall was not clinically significant (SBP < 25% from the baseline). Where as in Lignocaine group statistically significant fall in SBP compared to baseline was seen only after post induction and 10min following laryngoscopy Intergroup comparison between the two groups showed that the SBP at 1, 5 and 10 minute after laryngoscopy in magnesium group were statistically significantly lower compared to lignocaine group (P<0.05). At 3 minute SBP was lower in magnesium group but not statistically significant when compared with lignocaine group.

Table 3: Comparison of Systolic Blood Pressure (SBP) (mm Hg) in the two groups studied

SBP	Group	N	Mean	SD	Mean diff.	95% CI of difference		t	df	p-value
						Lower	Upper			
Baseline	B	35	128.20	13.54	-3.40	-9.76	2.96	-1.06	68	0.29(NS)
	A	35	131.60	13.12						
Post Induction	B	35	115.62	8.46	-2.20	-7.31	2.91	-0.85	68	0.39(NS)
	A	35	117.82	12.58						
1 min	B	35	137.34	14.83	-12.37	-19.90	-4.84	-3.27	68	0.002*
	A	35	149.71	16.67						
3 min	B	35	129.60	12.88	-6.17	-13.55	1.20	-1.66	68	0.10(NS)
	A	35	135.77	17.68						
5 min	B	35	116.17	7.59	-9.48	-14.95	-4.02	-3.46	68	0.001*
	A	35	125.65	14.31						
10 min	B	35	113.00	7.82	-8.91	-13.91	-3.91	-3.55	68	0.001*
	A	35	121.91	12.58						

Table 4: Comparison of Diastolic Blood Pressure (DBP) (mm Hg) in the two groups studied, In Magnesium group the post induction DBP values was significantly lower compared to its baseline with P value of 0.02. At 1 minute there was slight increase in mean DBP with P=0.03 which returned near baseline value by 3minute. At 5 min and 10 minutes values were significantly lower (P=0.02 and P=0.001 respectively) when compared to its baseline but this decrease was not clinically significant. Where as in Lignocaine group statistically significant increase in DBP compared to baseline was seen only at 1 minute after laryngoscopy with P value of <0.001.

Table 4: Comparison of Diastolic Blood Pressure (DBP) (mm Hg) in the two groups studied

DBP	Group	N	Mean	SD	Mean diff.	95% CI of difference		t	df	p-value
						Lower	Upper			
Baseline	B	35	81.20	9.64	2.54	-1.51	6.59	1.25	68	0.21 (NS)
	A	35	78.65	7.17						
Post Induction	B	35	75.14	8.74	0.17	-3.54	3.88	.09	68	0.92 (NS)
	A	35	74.97	6.70						
1 min	B	35	86.77	10.93	-4.17	-8.94	0.60	-1.74	68	0.08 (NS)
	A	35	90.94	8.97						
3 min	B	35	80.54	6.95	-2.80	-6.11	0.51	-1.68	68	0.09 (NS)
	A	35	83.34	6.94						
5 min	B	35	75.37	7.36	-3.57	-6.62	-0.52	-2.33	68	0.02*
	A	35	78.94	5.23						
10 min	B	35	73.45	6.55	-5.05	-8.15	-1.95	-3.25	68	0.002*
	A	35	78.51	6.44						

Table 5: Shows the Comparison of Mean Blood Pressure (MBP) (mm Hg) in two groups studied. In Magnesium group the post induction MBP was significantly lower compared to its baseline (P<0.001). Also at 5 min and 10 minutes value were significantly lower (p=0.003 and p<0.001 respectively) when compared to its baseline but this levels are reduced. Where as in lignocaine group statistically significant fall in MBP compared to baseline was seen only after post induction and 10min following laryngoscopy. However there was statistically significant increase in MBP seen at 1 minute after laryngoscopy in lignocaine group with P<0.001. Intergroup comparison between the two groups showed that the MBP at 1 minute after laryngoscopy in magnesium group was statistically significantly lower compared to lignocaine group (P=0.03). At 3, 5 and 10 minutes MBP was lower in magnesium group but not statistically significant when compared with lignocaine group.

Table 5: Comparison of Mean Blood Pressure (MBP) (mm Hg) in two groups studied

MBP	Group	N	Mean	SD	Mean difference	95% CI of difference		t	df	p-value
						Lower	Upper			
Baseline	B	35	100.42	9.19	3.20	-0.82	7.22	1.58	68	0.11
	A	35	97.22	7.60						(NS)
Post Induction	B	35	91.17	8.13	2.05	-1.55	5.66	1.13	68	0.25
	A	35	89.11	6.94						(NS)
1 min	B	35	104.66	11.82	-6.02	-11.47	-0.56	-2.20	68	0.03*
	A	35	110.68	11.01						

3 min	B	35	97.86	8.82	-3.28	-7.73	1.15	-1.47	68	0.14
	A	35	101.15	9.77						(NS)
5 min	B	35	93.16	7.74	-0.30	-4.16	3.54	-0.15	68	0.87
	A	35	93.46	8.40						(NS)
10 min	B	35	90.67	7.76	0.76	-2.98	4.52	0.40	68	0.68
	A	35	89.90	7.95						(NS)

DISCUSSION

The sequence of induction of anaesthesia, laryngoscopy and tracheal intubation are associated with marked haemodynamic changes and autonomic reflex activity which may be a cause of concern in many high risk patients because it is associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias 13. These potentially dangerous changes disappear within 5 minutes of onset of laryngoscopy. Although these responses of blood pressure and heart rate are transient and short lived they may prove to be detrimental in high risk patients especially in those with cardiovascular disease, increased intracranial pressure or anomalies of the cerebral blood vessels 14. Many factors influence the cardiovascular changes associated with laryngoscopy and intubation. Age, drugs, depth of anaesthesia, hypoxia, hypercarbia etc., influence the pressor response. These variations in heart rate decrease with increasing age. Young patients show more extreme changes, Marked fluctuations in haemodynamic responses are often seen in geriatric patients 15. In addition to attenuation of cardiovascular responses to laryngoscopy and intubation, Lignocaine prevents rise in intracranial pressure and rise in intraocular pressure associated with laryngo tracheal stimulation. It also suppresses cough related to extubation. The ability of magnesium ions to inhibit the release of catecholamines from both the adrenal glands and peripheral adrenergic nerves terminals and also produces vasodilation, directly. Many studies have showed that MgSO4 can attenuate cardiovascular responses to endotracheal intubation[16-18]. The study was made to compare magnesium with lignocaine to find out whether it can be used as a suitable alternative to lignocaine or not. This clinical study is a randomized, prospective, double blind study, patients randomly allocated into two groups based on Patients belonging to Group A received 1.5mg/kg of lignocaine intravenously 90 seconds prior to laryngoscopy and intubation and In Group B patients received intravenous magnesium sulphate 30mg/kg 90 seconds prior to laryngoscopy and intubation. Similarly previously used similar dose of lignocaine and found it to be effective in attenuation of sympathetic responses of laryngoscopy and intubation 19. Another studies also done by using optimal dose of magnesium sulphate for attenuation of hemodynamic response to laryngoscopy and intubation and concluded that 30mg/kg as optimal dose and smaller dose was less effective and larger doses resulted in complications[20-22]. Both the groups were well matched for demographic data and no statistically significant difference were found between groups with regard to age and gender. In lignocaine group, the heart rate decreased from baseline after induction, which was not statistically significant (P=0.77) and there was statistically significant increase following intubation only at 1 min and 3 min (P<0.001 and P=0.002) and At 5 minute heart rate was still above baseline and reached below baseline at 10 minute but these were not statistically significant (P=1.00 and P=0.44). Similarly another study reported that there was statistically significant increase in heart rate from baseline in lignocaine group at 1 and 3 minutes followed by statistically non-significant increase at 5 minute and They found statistically significant increase in mean heart rate after 1 min (P=0.001) and at 2 min (P=0.027) followed by statistically non-significant increase at 3, 4 and 5 minutes (P= 0.68, P=0.51, P=0.579)[23-24]. In magnesium group the mean heart rate decreased from the baseline to post induction and it was statistically not significant (P=0.35). After intubation the mean heart rate increased at 1 and 3 minutes, however the increase in heart rate from baseline was statistically significant only at 1 min (P<0.001). It gradually reached the baseline by 5 minutes and was statistically significantly below baseline by 10 min (P=0.009) but this was not clinically significant. Our results correlated with the study noted that the significant increase in heart rate from base line at 1 min followed by non-significant increase at 3 min and fall below baseline at 5 minute both of which were not statistically significant[25]. This was comparable to another study found that there was statistically significant difference in mean heart rates between magnesium and lignocaine groups at 1 minute after laryngoscopy (P<0.05). This can be attributed to the fact that the above mentioned authors have evaluated the difference in heart rate as % change from baseline whereas we have calculated the p values taking into consideration the difference in heart rate between both the groups at each given time interval. In lignocaine group, mean systolic blood pressure decreased from baseline after induction, which was statistically significant (P=0.004) but clinically not significant. There was statistically significant increase following intubation at 1 min P<0.001 followed by non-statistically significant increase at 3 min with P=1.00. At 5 minute and 10 minute systolic blood pressures were below baseline but statistically significant only at 10 minute

P=0.002. Our results were consistent with study done by Navid nooraei *et al.*[44], who found a similar statistically significant increase in systolic blood pressure in lignocaine group at 1 min (P=0.0001), 2 min (P=0.001) from baseline after intubation. Though the mean systolic blood pressure was above baseline at 5 min it was not statistically significant (P=0.582) which is in accordance with our study. In magnesium group the mean systolic blood pressure decreased from the baseline to post induction and it was statistically significant (P<0.001) and After intubation the systolic blood pressure increased at 1 and 3 minutes, this increase from baseline was statistically significant only at 1 min (P=0.008), gradually reached the below baseline by 5 minutes and was statistically significantly below baseline by 5 min and 10 min (P=0.001 and P<0.001) however it was not clinically significant. Similarly another study noted a similar statistically significant increase in systolic blood pressure in magnesium group only at 1 min (P=0.011) followed by a stable systolic blood pressure as compared to baseline 26. In lignocaine group, mean diastolic blood pressure decreased from baseline after induction, which was not significant statistically (P=0.036) and clinically. There was statistically significant increase following intubation at 1 min P<0.001 followed by non-statistically significant increase at 3 min and 5 min with P=0.08 and P=1.00 respectively. At 10 minute diastolic blood pressures were below baseline but statistically not significant P=1.00. similarly another study found that statistically significant increase in diastolic blood pressure at 1 minute (P=0.046) followed by stable DBP and In magnesium group the mean diastolic blood pressure decreased from the baseline to post induction and it was statistically significant (P=0.02). After intubation there was a statistically significant increase in the diastolic blood pressure at 1 minute with P=0.03. It gradually reached the below baseline by 3 minutes and was statistically significantly below baseline by 5 min and 10 min (P=0.02 and P=0.001), however it was not clinically significant. No statistically significant increase in DBP from baseline at 1, 2, 3, 4 and 5 minutes 27. Along with the mean blood pressure decreased in lignocaine group from baseline after induction, which was statistically significant (P=0.001) but clinically not significant. There was statistically significant increase following intubation at 1and5 min P<0.001 followed by non-statistically significant increase at 3 and 10 min with P=0.40. Statistically significant difference in mean blood pressure at 1 after intubation followed by no statistically significant difference in the mean blood pressure at 3, 4 and 5 minute and Statistically significant increase in mean blood pressure from baseline in lignocaine group at 1 minute followed by statistically non-significant increase at 5 minute and In magnesium group the mean blood pressure decreased from the baseline to post induction and it was statistically significant (P<0.001) but not clinically significant 28. After intubation the mean blood pressure increased at 1 minute, this increase from baseline was neither statistically significant (P=0.43) nor clinically. It gradually reached the below baseline by 3 minutes and was statistically significantly below baseline by 5 min and 10 min (P=0.003 and P<0.001) however it was not clinically significant. Statistically significant difference in mean blood pressure only at 1 after intubation followed by no statistically significant difference in the mean blood pressure at 2, 3, 4 and 5 minute. In another similar study conducted study in 150 patients undergoing CABG receiving either magnesium sulphate 50mg/kg or lignocaine 1.5mg/kg andomly also showed similar statistically significant difference between lignocaine and magnesium groups in mean blood pressure after intubation (P=0.049) only at 1 minute.

CONCLUSION

On the basis of the present observation it can be concluded that Intravenous lignocaine and intravenous magnesium sulphate both significantly attenuates the sympathetic response to laryngoscopy and tracheal intubation, Intravenous magnesium sulphate at 30mg/kg is more efficient than lignocaine 1.5mg/kg in attenuating the sympathetic response to laryngoscopy and intubation and Hence we conclude that intravenous magnesium sulphate 30mg/kg 90 seconds prior to laryngoscopy and intubation is superior to lignocaine 1.5mg/kg prior to laryngoscopy and intubation.

ACKNOWLEDGEMENT

It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

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Source of Support: None Declared
Conflict of Interest: None Declared