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COMPARISON OF COMBINATION OF INTRAVENOUS MAGNESIUM SULPHATE WITH LIDOCAINE 2% VERSUS INTRAVENOUS FENTANYL WITH LIDOCAINE 2% ON ATTENUATION OF CARDIOVASCULAR RESPONSE TO LARYNGOSCOPY AND INTUBATION- AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Laryngoscopy and tracheal intubation are invariably associated with certain stress responses due to the sympatho-adrenal stimulation. These cardiovascular and neurohumoral alterations may directly affect the physiology and increase the risk. Various drugs have been tried but no one drug has been considered ideal for blunting this pressor response.

Objectives: This comparative study was planned to evaluate and compare the efficacy of intravenous magnesium sulphate (30 mg/kg) along with lidocaine 2% versus intravenous fentanyl with lidocaine 2%, in attenuating the presser response to laryngoscopy and tracheal Intubation.

Methods and Materials: One hundred patients were randomised to receive either magnesium sulphate 30 mg/kg diluted in 100 ml saline (Group M) along with 2% lidocaine or Intravenous fentanyl 2mcg/kg along with lidocaine 2%.1 (Group F) 10 min before induction of anaesthesia . After laryngoscopy and intubation were performed, heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded pre-drug, after drug, at intubation, at intervals of 1min , 5 min, and 10 min post intubation.

Statistical analysis used: The collected data was analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data, descriptive statistics frequency analysis, percentage analysis was used for categorical variables, and for continuous variables the mean and SD was used. To find the significant difference between the bivariate samples in Independent groups the unpaired sample t-test was used. To find the significance in categorical data, Chi-Square test was used. In both the above statistical tools the probability value of 0.05 was considered as significant.

Results: There was a significant statistical difference in both the groups in terms of heart rate and blood pressure at one and five minutes after intubation.

Conclusion: Prophylactic administration of combination of magnesium sulphate and 2% lidocaine was found to be effective in attenuating hemodynamic responses to the stress effect of laryngoscopy and intubation as compared to intravenous Fentanyl.

Keywords: Laryngoscopy, tracheal intubation Magnesium sulphate, Fentanyl, pressor response.

INTRODUCTION

Direct laryngoscopy and endotracheal intubation are noxious stimuli and almost always associated with haemodynamic changes due to reflex sympathetic stimulation caused by laryngo-pharyngeal stimulation. It frequently induces a cardiovascular stress response characterized by hypertension, tachycardia and increased serum concentrations of catecholamines.[1] The reflex response seen in patients to laryngeal stimulation are transient and well tolerated in patients with normal cardiovascular status, but is undesirable in patients with pre-existing hypertension, coronary artery disease, valvular heart disease or cerebrovascular disease . Various non pharmacological and pharmacological methods have been used to attenuate the pressor stress response to laryngoscopy and endotracheal intubation. Non pharmacological methods like smooth and gentle intubation with a shorter duration of laryngoscopy, insertion of LMA have been used. Pharmacological methods like inhalational anaesthetics, topical and intravenous lidocaine, narcotics, calcium channel blocker, vasodilators and ß-blockers have also been attempted, but no one agent was found to be ideal .

Magnesium attenuates hemodynamic response by inhibition of catecholamine release from the adrenal medulla and also by reduction of the increased circulating norepinephrine when i compared to that of a control group [4] . It also has a systemic and coronary vasodilation effect by antagonizing calcium ion in vascular smooth muscle

Fentanyl is primarily a μ opioid receptor agonist, with an analgesic potency greater than Morphine, Pethidine and Alfentanil. Analgesia is produced by interaction with μ receptor at the supraspinal site. It also binds to a lesser degree to κ receptor at substantia gelatinosa of spinal cord. Due to stimulation of central nucleus, there is a fall in heart rate, which is dose dependent and also depends on speed of injection. There is also a fall in blood pressure, which is primarily due to the reduction in systemic vascular resistance, through centrally mediated reduction in systemic tone

Lignocaine has been used both as surface anaesthetic and also by intravenous route to depress haemodynamic response to intubation. .Lignocaine, when used systemically, has antagonistic action on sodium channels and NMDA receptors, reduces the release of substance P, has glycinergic action, which decreases the airway reactivity

The aim of this study was to compare the combination of intravenous (IV) magnesium sulphate (MgSo4) with Lidocaine 2% versus IV Fentanyl with Lidocaine 2% in attenuation of hemodynamic response to laryngoscopy and tracheal intubation.

OBJECTIVES

- To evaluate a hypothesis of which drug has better hemodynamic control by comparing heart rate, systolic blood pressure, diastolic blood pressure , and Mean arterial pressure to laryngoscopy and endotracheal intubation .
- To evaluate the effectiveness of the timing of administration of both the drugs involved in the study.

METHODS AND MATERIALS

This study was undertaken in the department of Anesthesiology at our institution from period of November 2021 to May 2022. Informed written consent was obtained from all patients. The preoperative serum magnesium values were monitored for the patients in both groups.

One hundred patients between the age group of 18-50 years of either gender, of ASA (American Society of Anesthesiologists) 1 and 2 physical status, scheduled for elective surgeries under general anaesthesia with endotracheal

intubation were selected. Patients were randomly allocated by computer generated randomisation table into two groups with 50 patients in each group. Group F (n =50) received intravenous Fentany l 2 mcg/kg 5 minutes before intubation. Group M (n=50) received 30 mg/kg of intravenous Magnesium sulphate in 100ml normal saline (NS), intravenously 5 minutes before intubation.

Both groups received preservative free lignocaine 2% at 1.5 mg/kg 90 seconds prior to laryngoscopy. Patients allergic to or having any contraindications to the study drugs, anticipated difficult airway and emergency surgical procedures requiring rapid sequence induction were excluded from the study.

On the day prior to surgery, a detailed pre-anesthetic evaluation and routine pre-operative investigations were done. Demographic (age, gender, weight) and vital parameters were recorded.

In the operating room, basal parameters-heart rate (HR), systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial pressure(MAP), baseline ECG and oxygen saturation were recorded.

These parameters were recorded at induction and every minute thereafter till 10 mins post intubation. The study drugs were administered by a trained anaesthesiologist. Five minutes before induction, patients in Group M received 30mg/kg of MgSO4 in 100ml saline while those in Group F received intravenous Fentanyl at 2 mcg/kg.

After pre-oxygenation for 3 min, all patients received Inj protocol 2mg/kg. After confirming adequacy of mask ventilation, Inj.Vecuronium 0.1mg/kg was given intravenously. Ninety seconds before intubation, patients in both groups received preservative free 2% lignocaine 1.5mg/kg.

A qualified consultant anesthesiologist, performed gentle laryngoscopy and intubated the patient with appropriate sized cuffed endotracheal tube in all patients. The tube was secured after confirming proper placement.

Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure & Mean Arterial Pressures (MAP) were recorded at induction and at 1 minute, 5 minutes and 10 minutes after intubation.

Any adverse effects were observed for and treated accordingly. Anaesthesia was maintained with 33%oxygen and 66% air(1:3) with sevoflurane titrating to maintain MAC of 1.0 and intermittent boluses of vecuronium (0.02 mg/kg). At the end of surgery, inhalational agents were turned off. Residual neuromuscular blockade was reversed with Inj. Neostigmine 50 mcg/kg and Inj.Glycopyrrolate 10 mcg/kg slow IV. Patients were extubated when awake and had adequate spontaneous respiratory efforts.

The collected data was analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables, and for continuous variables the mean and SD was used.

To find the significant difference between the bivariate samples in independent groups the Unpaired sample t-test was used and to find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value of 0.05 was considered as significant.

RESULTS
Demographic Data

Table 1a: Comparison of demographic data

GROUP		N	Mean	SD
Age	Group F	50	37	12
	Group M	50	41	10

Table 1b: Comparison of demographic data
Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	Lower	Upper
Age	Equal variances assumed	3.069	.083	-1.779	98	.078	-4.0400	2.2714	-8.5476	.4676

Table 2: Gender Distribution

			GROUP		
			Group F	Group M	Total
Gender	Female	Count	28	26	54
		%	56.0%	52.0%	54.0%
	Male	Count	22	24	46
		%	44.0%	48.0%	46.0%
Total		Count	50	50	100
		%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	p-value		
Pearson Chi-Square	.161a	1	.688		

In group–M (n=50) the age group ranged from 18–50 yrs. and the mean age with standard deviation was 41.0±10 with P-0.78 and sex distribution is 26 male: 24 females with a p value of 0.688.

In group–F (n=50) the age group ranged from 18–50 yrs and the mean age with standard deviation was 37.0±12 with p value of 0.78, and sex distribution is 22 males: 28 females with a p value of 0.688 which was not significant.

COMPARISON OF HEART RATE IN BOTH GROUPS

Table 3a: Comparison of heart rate

Group Statistics

GROUP		N	Mean	SD
HR T0	Group M	50	85.8	14.9
	Group F	50	88.4	13.2
HR T1	Group M	50	85.3	13.2
	Group F	50	93.3	12.9
HR T5	Group M	50	82.4	15.1
	Group F	50	87.1	9.9
HR T10	Group M	50	79.1	15.1
	Group F	50	80.6	10.6

Table 3b: Comparison of heart rate

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
HR T0	Equal variances assumed	.382	.538	-.952	98	.343	-2.6800	2.8146	-8.2656	2.9056
HR T1	Equal variances assumed	.006	.940	-3.072	98	.003	-8.0000	2.6040	-13.1675	-2.8325
HR T5	Equal variances assumed	5.084	.026	-1.842	98	.069	-4.7000	2.5519	-9.7643	.3643
HR T10	Equal variances assumed	2.552	.113	-.566	98	.572	-1.4800	2.6127	-6.6649	3.7049

After arrival into the operation theatre heart rates were recorded just before the study drugs were administered. In group–M heart rates ranged from 68–102 beats per min with a mean±SD of 85.8±14.9 and is compared with group–F in which heart rate ranged from 62–94 beats per min with a mean±SD of 88.4±13.2 . There is no statistical difference in both the groups with p value -0.343(P>0.05). 1min after intubation, the mean±SD of heart rate were 93.3±12.9 and 85.3±13.2 in Group F and Group M respectively which is statistically significant with a p value of 0.003 (p value <0.05). 5 mins and 10 minutes after intubation, the mean±SD of heart rates were 82.4 ±15.1 and 87.1± 9.9 in groups M and F and79.1± 15.1and 80.6±10.6 in groups M and F and respectively which was statistically insignificant as P value was >0.05.

COMPARISON OF MEAN BLOOD PRESSURE IN BOTH GROUPS

Table 4a: Comparison of Mean Blood Pressure

GROUP		N	Mean	SD
MAP T0	Group M	50	94.6	22.1
	Group F	50	101.4	16.5
MAP T1	Group M	50	93.4	19.5
	Group F	50	107.0	15.7
MAP T5	Group M	50	81.5	13.0
	Group F	50	98.5	15.2
MAP T10	Group M	50	81.8	15.6
	Group F	50	89.4	14.1

Table 4b: Comparison of Mean Blood Pressure

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	Lower	Upper
MAP T0	Equal variances assumed	3.436	.067	-1.740	98	.085	-6.7800	3.8970	-14.5135	.9535
MAP T1	Equal variances assumed	3.809	.054	-3.835	98	.0002	-13.6000	3.5464	-20.6378	-6.5622
MAP T5	Equal variances assumed	.336	.564	-6.016	98	.0005	-16.9800	2.8226	-22.5813	-11.3787
MAP T10	Equal variances assumed	.019	.891	-2.559	98	.012	-7.6000	2.9702	-13.4943	-1.7057

The mean arterial pressures were recorded just before the study drugs were administered. There was no statistical difference in both the groups with a p value of 0.52 (P >0.05). At 1 minute and 5 minutes after intubation, the mean±SD of mean arterial pressures were 107.0±15.7 and 93.4±19.5 in the group M & F respectively with a p value of 0.0002 and 0.0005 respectively. There was no significant difference in both the groups at 10 minutes post intubation.

COMPARISON OF SYSTOLIC BLOOD PRESSURE IN BOTH GROUPS

Table 5a: Comparison of Systolic Blood Pressure

GROUP		N	Mean	SD
SBP T0	Group M	50	123.9	25.4
	Group F	50	130.0	21.9
SBP T1	Group M	50	123.8	24.3
	Group F	50	136.2	22.1
SBP T5	Group M	50	108.2	15.0
	Group F	50	126.5	17.6
SBP T10	Group M	50	108.0	18.2
	Group F	50	117.7	17.0

Table 5b: Comparison of Systolic Blood Pressure
Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
SBP T0	Equal variances assumed	.823	.366	-1.289	98	.201	-6.1200	4.7495	-15.5453	3.3053
SBP T1	Equal variances assumed	.825	.366	-2.658	98	.009	-12.3600	4.6493	-21.5863	-3.1337
SBP T5	Equal variances assumed	1.057	.306	-5.605	98	.0005	-18.3200	3.2686	-24.8063	-11.8337
SBP T10	Equal variances assumed	.247	.620	-2.741	98	.007	-9.6600	3.5238	-16.6528	-2.6672

After arrival into the operation theatre, systolic blood pressure was recorded just before study drugs were administered and there was no significant difference noted in both the groups.

There was a statistically significant difference at 1, 5, and 10 minutes after intubation in both the groups. At time 1 min after the study drugs were administered, the mean±SD of systolic blood pressures were 123.8±24.3 and 136.2±22.1 in the group M & F respectively with a p value of .009. After 5 mins of the given study drugs, the mean±SD of systolic blood pressures were 108.2±15.0 and 126.5±17.6 in the group M & F respectively with a p value of .0005. There was a statistical significant rise in the SBP in the Group F as compared to Group M.

COMPARISON OF DIASTOLIC BLOOD PRESSURE IN BOTH GROUPS

Table 6a: Comparison of Diastolic Blood pressure

GROUP		N	Mean	SD
DBP T0	Group M	50	81.1	22.0
	Group F	50	88.2	15.6
DBP T1	Group M	50	78.8	18.1
	Group F	50	89.1	16.4
DBP T5	Group M	50	69.6	12.3
	Group F	50	80.3	14.6
DBP T10	Group M	50	69.2	15.3
	Group F	50	72.8	14.9

Table 6b: Comparison of Diastolic Blood pressure
Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	p-value	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
DBP T0	Equal variances not assumed	6.632	.012	-1.862	88.297	.066	-7.1000	3.8134	-14.6779	.4779
DBP T1	Equal variances assumed	.309	.580	-2.992	98	.004	-10.3200	3.4490	-17.1645	-3.4755
DBP T5	Equal variances assumed	2.357	.128	-3.990	98	.0005	-10.7400	2.6920	-16.0822	-5.3978
DBP T10	Equal variances assumed	.354	.553	-1.165	98	.247	-3.5200	3.0212	-9.5154	2.4754

After arrival into the operation theatre, systolic blood pressure was recorded just before study drugs were administered and there was no significant difference noted in both the groups.

There was a statistically significant difference after 1and 5 minutes, of intubation in both the groups. At time 1 min after the study drugs were administered, the mean±SD of diastolic blood pressures were 78.8±18.1 and 89.1±16.4 in the group M & F respectively with a p value of .004.

After 5 mins of the given study drugs, the mean±SD of diastolic blood pressures were 69.6±12.3 and 80.3±14.6 in the group M & F respectively with a p value of .0005 . There is a statistical significant rise in the DBP in the Group F as compared to Group M.

DISCUSSION

During direct laryngoscopy, proprioceptors are stimulated by the pressure exerted at the base of
tongue which results in increase in heart rate, blood pressure and increase in plasma catecholamine concentration[3] .Insertion of the endotracheal tube was found to exaggerate this response by somato-visceral reflex followed by rapid decrease of SBP and HR while plasma catecholamine concentration regress more slowly. This reflex sympathetic response produced is usually well tolerated in healthy individuals but can be fatal in patients with ischemic heart disease, hypertension or raised intracranial pressure. Therefore it is important to take measures to attenuate the pressor response during laryngoscopy and intubation.

Magnesium is a non-competitive inhibitor of inositol triphosphate gated calcium channels and thus functions as an endogenous calcium antagonist by affecting its uptake and distribution. At the neuromuscular junction, it inhibits calcium mediated release of acetyl choline from the presynaptic nerve terminal. In central nervous system, it exerts its depressant effect by inhibition of N-methyl-D-aspartate glutamate receptor and inhibition of catecholamine release.

It also shows modulatory effects on sodium and potassium currents, thus influencing membrane potential. It stabilizes haemodynamics by inhibition of catecholamine release from the adrenal medulla and peripheral adrenergic nerve endings and direct blockade of catecholamine receptors. It has antiarrhythmic properties related to L-type calcium channel antagonism. MgSO4 has onset of 2-3 minutes and acts for a duration of 30 min by IV route.

In a study conducted by Mahajan et al., 30 mg per kg of MgSO4 was used to study pressor response to laryngoscopy and intubation. It was found to attenuate pressor response well with better haemodynamic stability than dexmedetomidine 1mcg per kg. Panda et al. conducted a study to ascertain minimal effective dose of MgSO4 for attenuation of intubation response in hypertensive patients. They compared 30 mg/kg, 40 mg/kg and 50 mg/kg of MgSO4 with lignocaine 1.5 mg/kg (control group). HR was in decreasing trend post induction with a brief increase after intubation in all groups. MAP was well maintained in 30 mg/kg group throughout the study period where as in 40 mg/kg group it showed significant decrease from 3rd minute post intubation till the end of study period and in 50 mg/kg group, it decreased after induction and remained lower. 40 mg/kg and 50 mg/kg groups required significantly more interventions to manage hypotensive episodes than 30 mg/kg group. It was concluded that 30 mg /kg was the optimum dose of MgSO4 to prevent pressor response for laryngoscopy and intubation in hypertensive patients, with better cardiac stability. From the inferences of literature

search, we chose to use 30mg/kg of magnesium sulphate in our study.

Lignocaine acts by NMDA receptor antagonism, sodium channel antagonism and suppression of atrioventricular nodal activity. Intravenous lignocaine has its onset in 1-2 minutes with duration of action for 1 hour. It has proved ideal for control of short lived haemodynamic sequelae, associated with laryngoscopy and intubation. There are various studies with lignocaine being used intravenously to study its effect on pressor response during intubation.

In a study, intravenous lignocaine was used in doses of 0.75 mg and 1.5 mg per kg and cardiovascular response pre and post intubation were compared. It was found that in the group where 0.75 mg per kg lignocaine was used DBP and HR showed significant rise. In the group where 1.5 mg per kg was used, changes in BP and HR were statistically not significant. Stoelting RK confirmed that 1.5 mg per kg of lignocaine given 90 seconds prior to intubation was safe. In our study we used 2% lignocaine 1.5 mg per kg intravenously, 90 seconds prior to intubation.

Fentanyl is primarily a μ opioid receptor agonist, with an analgesic potency greater than Morphine, Pethidine and Alfentanil. Analgesia is produced by interaction with μ receptor at supraspinal site. It also binds to a lesser degree to κ receptor at substantia gelatinosa of spinal cord. Due to stimulation of central nucleus, there is a fall in heart rate, which is dose dependent and also depends on speed of injection. There is also a fall in blood pressure, which is primarily due to the reduction in systemic vascular resistance, through centrally mediated reduction in systemic tone.

In our study we saw that the heart rate, systolic and diastolic blood pressure had significantly decreased in the magnesium sulphate group as compared to the fentanyl group especially 1 minute and 5 minutes post intubation. Misganaw A, Sitote M in their study showed that magnesium with lignocaine 2% showed a significant decrease in the heart rate , Systolic and Diastolic blood pressure at 1, and 5 minutes as compared to the fentanyl group post intubation

In a study done by Panda and colleagues, where lignocaine 1.5 mg /kg was used 90 seconds before intubation, similar trend of HR was seen. HR was seen reaching the baseline value at intubation followed by a decreasing trend till 10th minute post intubation. In a study by Nooraei and colleagues, where lignocaine 1.5 mg/kg used 3 minutes prior to intubation, HR showed a statistically significant rise following intubation in initial 3 minutes and reached basal value in 4th and 5^{th} minute which was statistically insignificant.

In a study by Panda et al. which compared various doses of MgSO4 (30,40 and 50 mg/kg), the heart rate did tend to decrease after induction, after a brief rise post intubation in all 3 groups.

Hence we conclude that a combination of Magnesium sulphate with preservative free lidocaine 2% would be more effective in attenuating the hemodynamic response as compared to the combination of intravenous Fentanyl with preservative free lidocaine 2%. There were no significant side effects in both the groups . As the sample size and duration of study was limited, more research is required to reach a definitive result.

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