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KEY WORDS: Fentanyl, Magnesium sulfate, Laryngoscopy, cardiovascular response.

"A COMPARATIVE STUDY BETWEEN INTRAVENOUS FENTANYL AND MAGNESIUM SULFATE IN ATTENUATION OF CARDIOVASCULAR RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION"

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ABSTRACT

Background and Objectives: Laryngoscopy and intubation are associated with stress response leading to hypertension, tachycardia and cardiac arrhythmias. It may be of no consequences in patients with normal cardiovascular status but undesirable in patients with comorbid conditions such as hypertension, coronary artery disease, cerebrovascular disease and thyrotoxicosis etc. Various pharmacological and non-pharmacological methods have been studied in attenuating this response. The present study is undertaken to compare the efficacy of Fentanyl and Magnesium sulphate in attenuating cardiovascular response to laryngoscopy and endotracheal intubation.

Methods: A prospective, randomized double blinded study was conducted among 100 ASA I/II adults patients undergoing electives surgeries under general anesthesia. Group A (n=50): received inj. fentanyl (2 g/kg) and Group B (n=50): received inj. Magnesium Sulfate 30mg/kg. Heart rate, systolic, diastolic and mean arterial pressure were measured at baseline, before induction, before intubation, just after intubation, 3, 5, 10, 15, 30 mins after intubation.

Results: Fentanyl showed more effective in attenuating the cardiovascular response to laryngoscopy and intubation compared to Magnesium Sulfate.

Conclusion: IV Fentanyl 2μg/kg is a better drug than Magnesium Sulfate 30mg/kg in controlling cardiovascular response to laryngoscopy and intubation.

INTRODUCTION

Endotracheal intubation includes Laryngoscopy and intubation. Endotracheal intubation is the trans-laryngeal placement of endotracheal tube into the trachea through the oral or nasal cavity. Since its introduction towards the end of the 19th century, laryngoscopy and intubation has been an integral part of anaesthetic management and critical care. The haemodynamic response during laryngoscopy were known since 1940 after its description by Reid & Brace[1]. This cardiovascular stress response is characterized by hypertension, tachycardia and cardiac arrhythmias. In 1951, King et al in their study described the circulatory response to endotracheal intubation was due to reflex sympathoadrenal stimulation[2].

These haemodynamic responses are usually transitory, variable and unpredictable. They are well tolerated in healthy individuals but undesirable in patients with comorbid conditions such as hypertension, coronary artery disease, cerebrovascular disease and thyrotoxicosis etc. Such alterations can lead to severe conditions such as ventricular failure, myocardial ischemia, ventricular dysrhythmias and cerebral hemorrhage.[3] Various pharmacological and non-pharmacological methods have been studied to attenuate this cardiovascular response. Pharmacological agents like lidocaine, opioids, beta blockers like esmolol, calcium channel blockers like diltiazem, magnesium sulfate, vasodilator like nitroglycerine and sodium nitroprusside have also been used. Fentanyl is a synthetic opioid derivative and it predominately act as an agonist on mu (μ) receptors and block the central mechanisms of integration of sensory input and found to be effective in blunting the pressor response to laryngoscopy and intubation[4,5]. Magnesium Sulphate has also been shown to attenuate the hemodynamic responses by blocking the release of catecholamines from both adrenergic nerve terminals and adrenal gland. In addition, it also produces vasodilation by acting directly on blood vessels. In high doses, it attenuates vasopressin mediated vasoconstriction.[6,7,8]

METHODOLOGY

A prospective, randomized double blinded study was conducted among 100 ASA I/II adults patients undergoing electives surgeries requiring general anesthesia. The study was conducted at SILCHAR MEDICAL COLLEGE AND HOSPITAL in Silchar, Assam from 01/06/2020 to 31/05/2021.

After obtaining Institutional Ethical Committee clearance and written informed consent from the patients. The study population was randomly divided into two groups with 50 patients in each group using computer generated randomized table.

Group A– Fentanyl (n=50): received Inj. fentanyl (2μg / kg).
Group B - Magnesium sulfate (n=50): received Inj. Magnesium sulfate (30 mg/kg).

Inclusion Criteria

- Patients between age 18-60 years
- Patients of both sexes
- Patients of ASA grade I&II
- Informed consent form

Exclusion Criteria

- Refusal to informed consent
- Age <18 and >60 years
- Patient with anticipated difficult airway
- Patient of ASA grade III&IV
- History of hypersensitivity to study drug.
- Pregnant and lactating mother
- Patient with any disorders of cardiovascular system, respiratory system, renal system, hepatic and neuromuscular conditions.

Pre anaesthetic evaluation included history taking, general examination, systemic examinations were conducted and investigations like complete blood count, KFT, LFT, CXR, ECG was done. Patients were kept NPO for 8 hours prior surgery. All patients were given tablet alprazolam 0.5 mg orally at bed time on the previous night of the surgery.

On arrival of the patient in the operating room, patient's body weight, fasting status, consent and preoperative evaluation were checked. A 20-gauge intravenous cannula was secured and connected to IV fluid ringer lactate. The patient was then connected to Mindray A5 anaesthesia machine which recorded heart rate, SPO2, non-invasive measurements of SBP, DBP, MAP, EtCO2 and continuous ECG monitoring. The

baseline systolic, diastolic blood pressure, mean arterial pressure and heart rate was recorded. After recording the baseline reading, all patients were being premedicated with inj. glycopyrrolate (0.005mg/kg), ondansetron 4mg iv and ranitidine 50mg iv before giving the study drug. Patients in group A received inj. Fentanyl 2 g/kg body weight diluted to 10 ml normal saline intravenously over 10 min and patients in group B received inj. Magnesium sulfate 30 mg/kg diluted to 10 ml with normal saline over 10 minutes.

The patients were then preoxygenated for 3 minutes and anesthesia was induced with propofol. Endotracheal intubation was facilitated with IV Atracurium 0.5mg/kg three minutes prior to laryngoscopy and intubation. Laryngoscopy and oral intubation was performed using appropriate sized Macintosh blade. Anesthesia was maintained using 60% nitrous oxide and 40% of oxygen with isoflurane and inj. Atracurium. Hemodynamic parameters of patients including systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were recorded before induction, just before intubation, just after intubation, 3 mins, 5 mins, 10 mins, 15 mins and 30 mins after intubation. Side effects, if any were also recorded. At the end of the surgical procedure patient was reversed with neostigmine 0.05 mg/kg body weight and glycopyrrolate 0.5mg.

RESULTS

All data are presented as Mean ± SD (Standard Deviation). All Quantitative data are assessed using Student's t - test to analyse changes over a period of time. Qualitative data are assessed using Fisher exact Test or Chi- square test.

- p>0.05 – Statistically Not Significant (NS)
- p≤0.05 – Statistically Significant (S)
- p<0.001 – Statistically Highly Significant (HS)
- p<0.0001 - Statistically Extremely Significant (ES)

Data analysis was carried out using Microsoft word and Excel was used to generate graphs, tables etc

Table 1:-Comparison of demographic parameters between two groups

Demographic parameters	Group A (FENTANYL) N=50 MEAN±SD	Group B (MgSO4) N=50 MEAN±SD	P-Value
Age (Yrs)	37.20±10.59	38.32±11.04	0.60
Weight	61.7±7.4	62.7±8.6	0.40
SEX	Male=23(46%) Female=27(54%)	Male=22(44%) Female=28(56%)	0.99
ASA status(I/II)	I-52% II-48%	I-56% II-44%	0.10

Table 2: - Comparison of mean heart rate between two groups

	Heart Rate (beats/min)				P-value
	Group A (FENTANYL) N=50		Group B (MgSO4) N=50		
	Mean	SD	Mean	SD	
HR T0 (Baseline)	85.26	5.61	86.56	7.07	0.139
HR T (Before Induction)	84.82	5.72	85.46	6.55	0.707
HR T1 (Before Intubation)	74.68	6.45	76.16	4.25	0.178
HR T2 (Just After Intubation)	92.68	5.41	94.36	3.96	0.797
HR T3 (3mins After Intubation)	88.36	5.31	89.32	4.47	0.331
HR T4 (5mins After Intubation)	85.84	4.41	84.52	3.41	0.113
HR T5 (10mins After Intubation)	84.90	3.95	84.94	8.40	0.975
HR T6 (15mins After Intubation)	84.64	4.47	84.80	8.64	0.907
HR T7(30mins After Intubation)	84.94	4.60	84.68	8.55	0.850

The mean HR decrease observed just before intubation after giving study drug, but there was rise in mean heart rate after intubation in both the groups which was not statistically significant. (p value >0.05). Magnesium sulfate was as good as fentanyl in attenuating the heart rate as the P value is > 0.05.

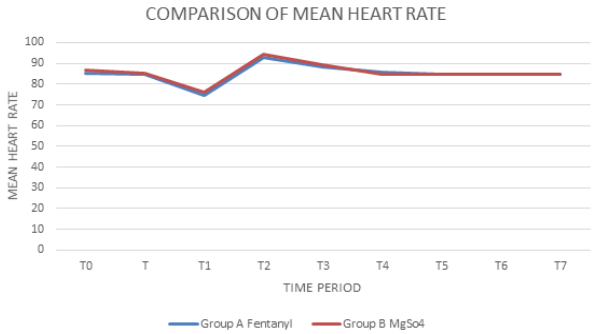

Figure 1 – Line diagram showing comparison of mean heart rate between the two groups.

Table 3: - Comparison of mean arterial pressure between the two groups.

	MAP				P value
	Group A (FENTANYL) N=50		Group B (MgSO4) N=50		
	Mean	SD	Mean	SD	
MAP(mmHg) T0 (Baseline)	97.18	4.12	97.92	3.92	0.359
MAP(mmHg) T (Before Induction)	95.70	4.49	96.80	3.97	0.198
MAP(mmHg) T1 (Before Intubation)	83.26	5.49	84.18	3.27	0.310
MAP(mmHg) T2 (Just After Intubation)	90.50	5.30	90.36	3.32	0.875
MAP(mmHg) T3 (3mins After Intubation)	84.96	4.58	90.96	3.30	0.000
MAP(mmHg) T4 (5mins After Intubation)	85.46	4.62	91.90	3.62	0.000
MAP(mmHg) T5 (10mins After Intubation)	86.40	3.46	92.00	3.24	0.000
MAP(mmHg) T6 (15mins After Intubation)	91.96	4.16	93.34	4.28	0.105
MAP(mmHg) T7(30mins After Intubation)	94.10	4.01	95.38	3.07	0.716

The fall in mean MAP values in group A (Fentanyl) at 3 mins, 5 mins and 10 mins after intubation were statistically highly significant (p=0.000) compared to group B (MgSO4).

DISCUSSION

Laryngoscopy and intubation have been an integral part of anaesthetic management and critical care since their introduction towards the end of 19th century. In 1940 (Reid & Brace),[1] the circulatory responses to laryngeal and tracheal stimulation were shown and presented to the world. King et al, (1951)[2] have described the circulatory responses to laryngeal and tracheal stimulation following laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation. These manifestations are mainly due to stress response in the form of laryngosympathetic stimulation. The usual manifestations include hypertension, tachycardia and cardiac arrhythmias. These changes are usually transitory, variable and unpredictable. In a healthy individual, these haemodynamic responses are of no consequence and well tolerated but undesirable in patients with comorbid conditions such as hypertension, coronary artery disease, cerebrovascular disease and thyrotoxicosis etc. Such alterations can lead to severe conditions such as ventricular failure, myocardial ischemia, ventricular dysrhythmias and cerebral hemorrhage.[3]

This is by far the most important indication for attenuating the haemodynamic response to laryngoscopy and tracheal intubation.

The study population consisted of 100 patients divided equally in two groups. Patients in group A received inj. Fentanyl 2µg/kg and group B received inj. Magnesium sulfate 30mg/kg.

Heart Rate (HR)
The Mean Baseline Heart Rate of group A was 85.26±5.61 whereas in group B it was 86.56±7.07, which was not statistically significant (p value=0.139). Before induction (T), mean heart rate in group A was 84.82±5.72 and group B was 85.46±6.55, which on comparison was again not significant with p value of 0.707. Before intubation (T1) i.e., after the study drug was being administered, the mean heart rate came down to 74.68±6.45 in group A and to 76.16±4.25 in group B. But on comparing the two groups, it was not statistically significant (p value=0.178). Just after intubation (T2), the mean heart rate group A was 92.68±5.41 and that in group B to 94.36±3.96. It was observed that there was increase in mean HR just after intubation in both the group but it was not statistically significant (P value=0.797). From 3 mins after intubation till the entire intraoperative period, the mean HR in both the groups stabilized at near the baseline value and there was no significant difference in the heart rate of both the groups.

Mean Arterial Pressure (MAP)
The baseline MAP of group A and group B were 97.18±4.12 and 97.92±3.92 respectively. On comparing, it was found to be statistically non-significant (p value= 0.359). The mean MAP before induction (T), before intubation (T1) and just after intubation (T2) in both the groups were compared and was found to be statistically non-significant (p value>0.05). At 3 mins after intubation (T3), the mean MAP reduced to 84.96±4.58 in group A whereas in group B it was 90.96±3.30. At 5 mins after intubation (T4), the mean MAP in group A and group B were 85.46±4.62 and 91.90±3.62 respectively and at time 10 mins after intubation (T5), the mean MAP in group A and group B were 86.40±3.46 and 92.00±3.24. The fall in mean MAP in group A at 3 mins, 5 mins and 10 mins after intubation were statistically highly significant compared to group B (p value<0.001). From 15 mins after intubation till the entire intraoperative period, the mean MAP in both the groups stabilized at near the baseline value and there was no significant difference in the mean MAP of both the groups (p value>0.05).

Saroj Patta et al[9] compared fentanyl 1.5µg/kg with magnesium sulphate 30 mg/kg for hemodynamic attenuation during laryngoscopy and intubation. Their study showed that initially there is fall in heart rate at 3 mins after the study drug further there is rise in heart rate after intubation in both the groups which is not statistically significant. But there was statistically significant fall in SBP in fentanyl group at 3 mins, 5 mins and 10 mins after intubation compared to magnesium sulfate. Also, there was statistically significant fall in mean DBP at 5 mins and 10 mins after intubation in fentanyl group compared to magnesium sulfate. There was also significant fall in mean MAP at 3 mins after intubation in fentanyl group compared to magnesium sulfate. Their study concluded that Fentanyl 1.5µg/kg was more effective in attenuation of cardiovascular response to laryngoscopy and intubation when compared to magnesium sulphate 30 mg/kg. In our study we used Fentanyl 2µg/kg and magnesium sulphate 30mg/kg. In our result we found significant fall in mean MAP at 3 min, 5 mins and 10 mins after intubation in Fentanyl group compared to magnesium sulfate and our result was almost comparable to their study.

Dilip Kothari et al[10] conducted a study to compare the effects of fentanyl and Magnesium sulfate on circulatory changes during intubation and anaesthesia. Magnesium sulfate (Group M, n=30) received 20mg/kg 5 mins before induction, 10 mg/kg 5 mins before skin incision and 10 mg/kg every 30 mins interval and Fentanyl citrate (Group F, n=30) received 1.25 mcg/kg, 0.5 mcg/kg and 0.5 mcg/kg at similar time intervals. They found that there was significant rise in heart rate and mean arterial pressure to laryngoscopy, but fentanyl showed greater haemodynamic stability. They concluded that magnesium is not superior to the action of short acting opiate Fentanyl in haemodynamic attenuation during laryngoscopy and intubation. Our study was comparable to the findings of their study in the hemodynamic attenuation caused by Fentanyl and Magnesium sulfate.

Side Effects
In our study, we noted bradycardia in subjects belong to group A and tachycardia in group B. PONV was seen in both the groups. There was no incidence of hypotension in either of the groups. These side effects were transient and did not require any intervention.

CONCLUSION
From this study it was observed that fentanyl caused better attenuation of cardiovascular response to laryngoscopy and intubation as compared to magnesium sulfate. It provided more stable HR, SBP, DBP and MAP during the stress response following laryngoscopy and intubation.

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Conflict of interest: Non declared
Ethical approval: The study was approved by the institutional ethics committee.

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