

COMPARATIVE STUDY OF EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE AND INTRAVENOUS FENTANYL IN ATTENUATING THE HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND INTUBATION

Patta Saroj¹, Allu Satyanarayana², Potti Sharah Suhasini³, Bevara Krishna Chaitanya⁴, Juvvala Kranthi⁵

¹Associate Professor, Department of Anaesthesiology, Andhra Medical College.

²Professor and HOD, Department of Anaesthesiology, Andhra Medical College.

³Senior Resident, Department of Anaesthesiology, Andhra Medical College.

⁴Senior Resident, Department of Anaesthesiology, Andhra Medical College.

⁵Post Graduate, Department of Anaesthesiology, Andhra Medical College.

ABSTRACT

AIM

To compare the haemodynamic response to laryngoscopy and intubation with intravenous MgSO₄ and intravenous fentanyl.

METHODS

Fifty adult patients were divided into two groups randomly into group M and group F. Patients of group M received 30 mg/kg body weight of IV MgSO₄ and group F received IV fentanyl 1.5 µg/kg 5 minutes before intubation.

RESULTS

IV Fentanyl showed greater degree of haemodynamic stability i.e. rise in heart rate, mean arterial pressure during laryngoscopy and intubation compared to IV MgSO₄. IV fentanyl showed side effects like respiratory depression, nausea and vomiting.

CONCLUSION

IV fentanyl is a better drug in controlling haemodynamic response to laryngoscopy and intubation.

KEYWORDS

Hemodynamic response, laryngoscopy, Fentanyl, Magnesium Sulphate.

HOW TO CITE THIS ARTICLE: Saroj P, Satyanarayana A, Suhasini PS, et al. Comparative study of effect of intravenous magnesium sulphate and intravenous fentanyl in attenuating the haemodynamic responses to laryngoscopy and intubation. J. Evid. Based Med. Healthc. 2016; 3(30), 1360-1367. DOI: 10.18410/jebmh/2016/311

INTRODUCTION: Laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response characterised by hypertension, tachycardia and increased serum concentrations of catecholamines¹ (Ronald D Miller) which are transient and are considered innocuous in patients with normal cardiovascular status. This response is undesirable in any patient with heart disease and may prove to be dangerous in patients with pre-existing hypertension, coronary artery disease, valvular heart disease, cerebrovascular disease, abdominal aortic aneurysm, dissecting aortic aneurysm, pheochromocytoma, pre-eclamptic toxemia etc. A variety of agents have been used to attenuate this response. No single agent has been established as the most appropriate for this purpose. The aim of the study is to compare IV MgSO₄ and IV fentanyl in attenuation of haemodynamic responses to laryngoscopy and tracheal intubation.

AIM: To compare the attenuation of haemodynamic changes to laryngoscopy and intubation with IV bolus fentanyl 1.5 µg/kg and IV magnesium sulphate 30 mg/kg.

OBJECTIVES:

- To evaluate a hypothesis, which drug has better haemodynamic control by comparing Heart rate, Systolic Blood pressure, Diastolic Blood pressure, and Mean arterial pressure to laryngoscopy and intubation in general anaesthesia?
- Effectiveness of timing of the study drug administration.
- To evaluate the side effects and safety of study drugs

MATERIALS AND METHODS: After approval from hospital ethical committee, a prospective randomised comparative study was conducted on adult patients undergoing elective surgeries under general anaesthesia.

This study was conducted on 50 adult patients of both sex divided randomly to two groups.

Group-M patients were given Inj. MgSO₄ - 30 mg/kg IV 5 min before intubation.

Group-F patients were given Inj. Fentanyl - 1.5 µg/kg IV 5 min before intubation.

Financial or Other, Competing Interest: None.
Submission 16-03-2016, Peer Review 25-03-2016,
Acceptance 09-04-2016, Published 14-04-2016.
Corresponding Author:
Dr. Patta Saroj,
Door No. 10-4-18, Asilmetta, A. V. Post,
Visakhapatnam-530003, Andhra Pradesh, India.
E-mail: saroj_patta@yahoo.com
DOI: 10.18410/jebmh/2016/311

Inclusion Criteria: Forty patients scheduled for elective noncardiac surgery under general anaesthesia entered this randomised placebo controlled study. Subjects aged between 18 and 50 years of either sex and of physical status ASA I and II entered the study. All the patients were normotensive and had a normal heart rate, ECG, haemoglobin and electrolytes preoperatively. The procedure to be undertaken was explained and informed consent obtained from all the patients and randomly assigned to receive a pre-induction dose of IV MgSO₄ - 30 mg/kg; or IV fentanyl -1.5 µg/kg.

Exclusion Criteria Included:

- Heart rate of less than 60 beats per minute.
- Systolic blood pressure of less than 100 mm Hg.
- Presence of first, second or third degree heart block.
- Congestive heart failure or myocardial infarction within the previous three to six months.
- History of bronchospastic disease or asthma.
- Significant hepatic or renal disease.
- Ingestion of any beta blocking drug in the past 24 hours.
- Demographic data including age, sex, weight and ASA physical status were recorded.

All patients were premedicated with 1 mg of inj. midazolam and 0.2 mg of inj. glycopyrrolate, inj. diclofenac, inj. ranitidine intramuscularly 45 minutes to 1 hour before induction of anaesthesia.

On arrival to the operating room, after a resting period of five minutes, patient's baseline heart rate, mean systemic arterial blood pressure, pulse oximetry, arterial pressure were recorded and designated as pre-induction basal value or B.

Patients were then pre-oxygenated with 100% oxygen for three minutes. At time zero, the study medication was administered intravenously over 15 secs., followed by induction of anaesthesia with Thiopentone 3 to 5 mg/kg and succinylcholine 1.5 mg/kg. Direct laryngoscopy and tracheal intubation 4 mins after time zero. Anaesthesia was maintained with Oxygen: Nitrous oxide (33%: 66%) and 0.1% Halothane using Bain's circuit. Neuromuscular blockade was achieved with Vecuronium -0.08 mg/kg

(loading dose) and 0.02 mg/kg (incremental dose). Heart rate and blood pressure were recorded every five minutes from zero time, after study drug, immediately after intubation, at every 5 min interval for next 30 minutes. Surgery did not commence in any patient until the study protocol was completed. Any deleterious cardiovascular events are noted. Analgesia was provided either with intravenous fentanyl (1 µg/kg body weight) or 1 mg midazolam.

At the end of the surgery, residual neuromuscular block was antagonised with appropriate doses of inj. neostigmine (0.05 mg/kg) and inj. glycopyrrolate (0.01 mg/kg). The extubation was performed when respiration was spontaneous and adequate. Parametric data including weight, baseline heart rate and arterial pressure were compared using unpaired student's t test. Changes in heart rate and arterial pressure were analysed using unpaired student's t test. A statistical significance level of $P < 0.05$ was chosen.

RESULTS AND ANALYSIS: In group-M (n=25) the age group ranged from 18–50 yrs. and the mean age with standard deviation is 33.40 ± 9.9 with $P=0.105$ and sex distribution is 9 male: 11 females and the mean weight is 54.40 ± 5.2 kg (range 61–70 kg) ($P=0.255$)

In group-F (n=25) the age group ranged from 18–50 yrs and the mean age with standard deviation is 28.80 ± 7.3 $P=0.106$, and sex distribution is 12 males: 8 females and the mean weight is 56.95 ± 8.3 kg (range 58–72 kg). ($P=0.257$).

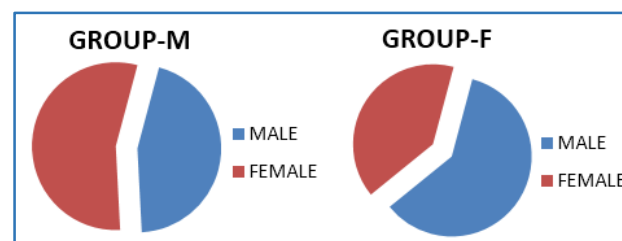


Fig. 1: Demographic data

Changes in Heart Rate: The changes in the heart rate are given in the Figure 2.

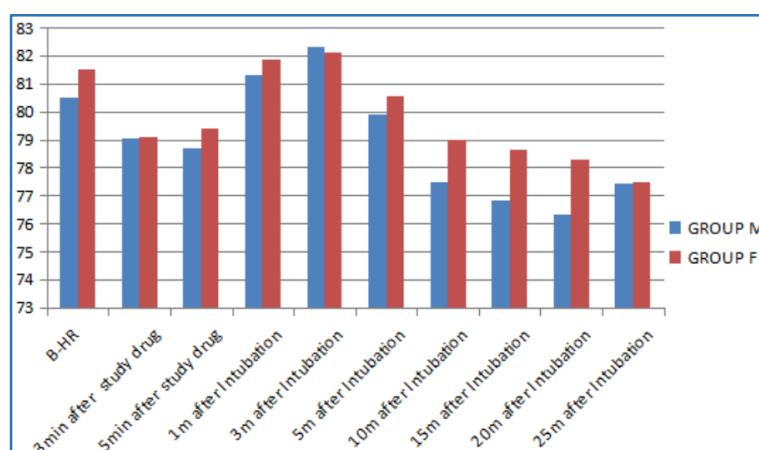
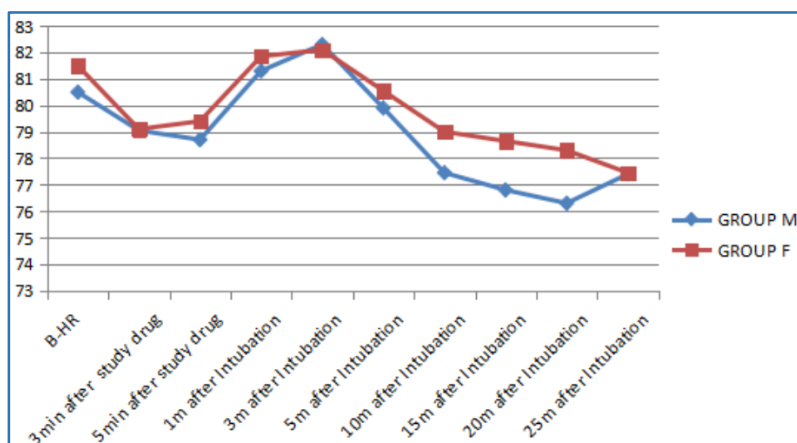


Fig. 2: Changes in heart rate at various specified timings in two groups



Graph 1: Changes in heart rate at various specified timings in two groups

After arrival into the operation theatre heart rates were recorded just before study drug (B-HR). In group-M heart rates ranged from 68–90 beats per min with a mean±SD of 80.5±7.45 and is compared with group-F in which heart rate ranged from 62–94 beats per min with a mean±SD of 81.5±9.22. There is no statistical difference in both the groups as the P value -0.708 (P>0.05).

At time 3 mins after the given study drug, the mean±SD of heart rate were 79.05±8.04 & 79.10±10.93 in the group M & F respectively. There is no statistical difference in both the groups. (P-0.98). At time 5 mins after the given study drug, the mean±SD of heart rate were 78.05±9.5 & 79.4±11.59 in the group M & F respectively. There is no

statistical difference in both the groups. (P-0.836). At time 1, 3, 5, 10 and 15 mins after intubation, there was no statistically significant difference.

Initially, fall in heart rate is noted 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. This insignificant rise is below the baseline heart rate. And there is no significant difference between MgSO₄ & Fentanyl. MgSO₄ is as good as fentanyl in attenuating the heart rate as the P value is >0.05.

Changes in Systolic Blood Pressure: The changes in the Systolic blood pressure are given in the Figure 3.

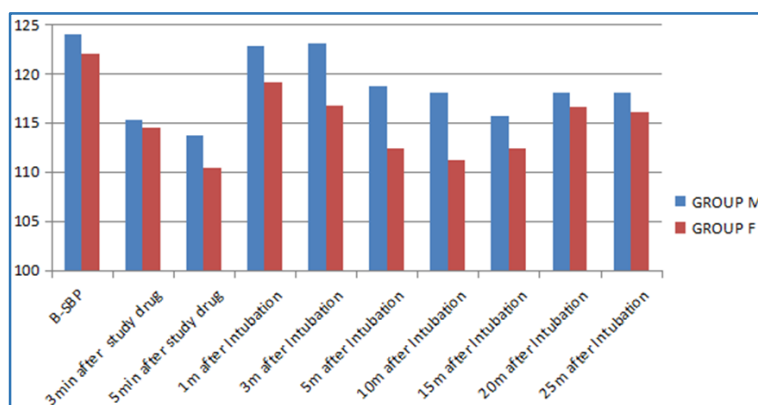
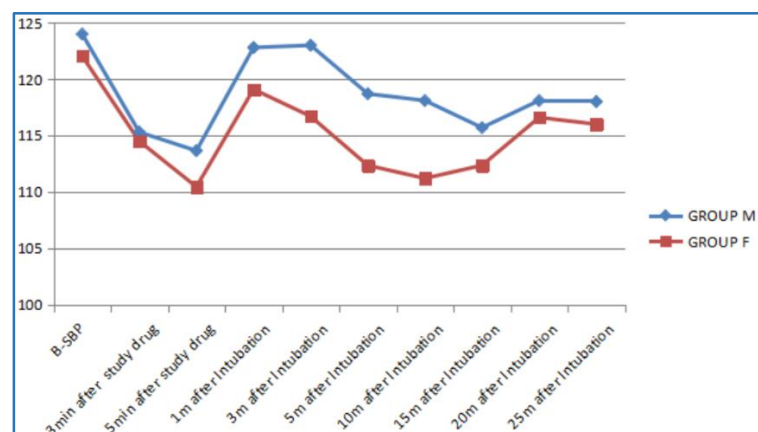


Fig. 3: Changes in systolic blood pressure at various specified timings in two groups



Graph 2: Changes in systolic blood pressure at various specified timings in two groups

After arrival into the operation theatre, heart rates were recorded just before study drug (B-SBP). In group-M, systolic blood pressures ranged from 106-140 mmHg with a mean \pm SD of 124 ± 9.81 and is compared with group-F in which systolic blood pressures ranged from 110-138 mmHg with a mean \pm SD of 122.05 ± 11.54 . There is no statistical difference in both the groups as the P value is 0.568 ($P > 0.05$). There was no statistical significant difference after 1, 3, 5, 15, 20 and 25 minutes after intubation.

At time 3 mins after the given study drug, the mean \pm SD of systolic blood pressures were 115.3 ± 8.36 & 114.5 ± 12.82 in the group M & F respectively. There is no statistical difference in both the groups. ($P=0.817$).

At time 5 mins after the given study drug, the mean \pm SD of systolic blood pressures were 113.65 ± 6.98 & 110.45 ± 12.467 in the group M & F respectively. There is no statistical difference in both the groups. ($P=0.323$).

There is rise in systolic blood pressure after intubation in both the groups, but below the baseline systolic BP level which is not significant when compared to baseline systolic blood pressure, but there is a significant difference between MgSO₄ & fentanyl group at 3 mins to 10 mins after intubation, where there is more fall in systolic BP in fentanyl group when compared to MgSO₄ group as the P value is <0.05 . ($P=0.041$, 0.016, & 0.008)

Changes in Diastolic Pressure: The changes in the diastolic blood pressures are given in the Figure 4.

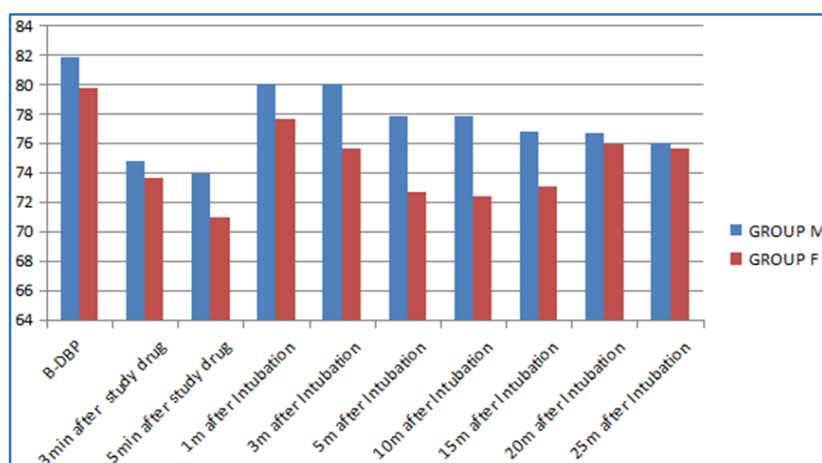
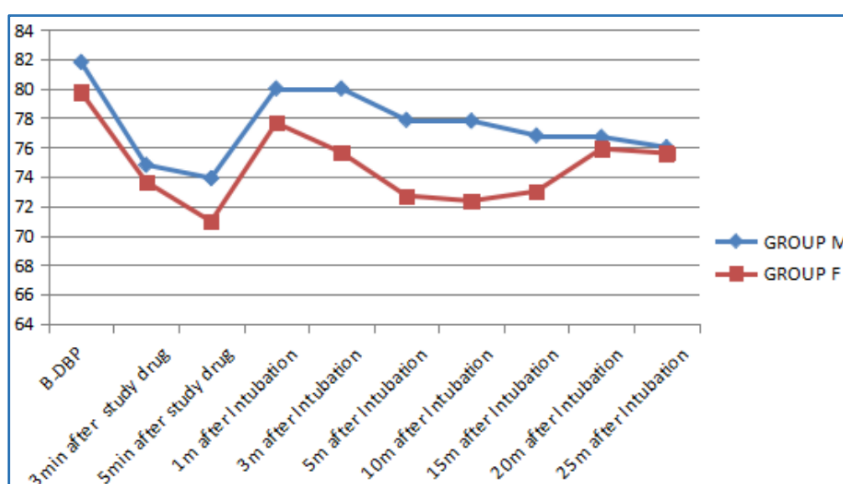


Fig. 4: Changes in diastolic blood pressure at various specified timings in two groups



Graph 3: Changes in diastolic blood pressure at various specified timings in two groups

After arrival into the operation theatre, diastolic blood pressures were recorded just before study drug, base line value (B-DBP). In group M, diastolic blood pressures ranged from 66 mmHg to 90 mmHg with a mean \pm SD of 81.8 ± 8.18 and is compared with group F in which diastolic BP ranged from 60 mmHg to 100 mmHg with a mean \pm SD of 79.75 ± 9.24 . There is no statistical difference in both the groups as the P value is 0.462 ($P > 0.05$). No statistical significant difference after 1, 3, 5, 10, 15, 20 and 25 minutes after intubation.

At time 3 mins after the given study drug, the mean \pm SD of diastolic blood pressures were 74.8 ± 6.40 & 73.65 ± 6.26 in the group M & F respectively. There is no statistical difference in both the groups. ($P=0.569$).

At time 5 mins after the given study drug, the mean \pm SD of diastolic blood pressures were 73.9 ± 7.79 & 70.05 ± 8.14 in the group M & F respectively. There is no statistical difference in both the groups. ($P=0.249$).

There is rise in diastolic blood pressure after intubation in both the groups, (at 1 min to 3 mins after intubation) but

below the baseline diastolic BP level which is not significant, finally the graph of diastolic blood pressure showed a fall at 5 mins after intubation.

But there is a significant difference between MgSO₄ & fentanyl group at 5 mins to 10 mins after intubation, where there is more fall in diastolic BP in fentanyl group when

compared to MgSO₄ group as the P value is <0.05. (P-0.025, & 0.008).

Changes in Mean Arterial Pressure: The changes in the Mean arterial pressure are given in the Figure 5.

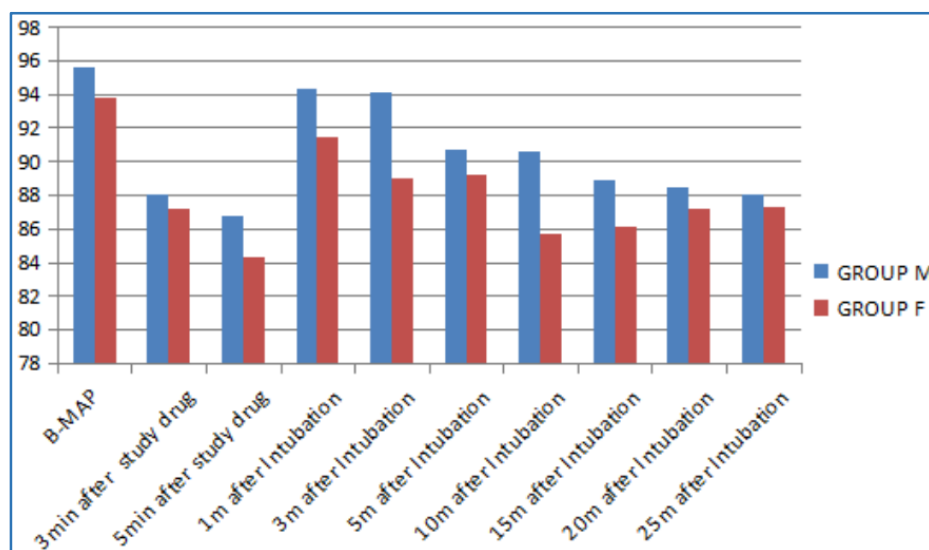
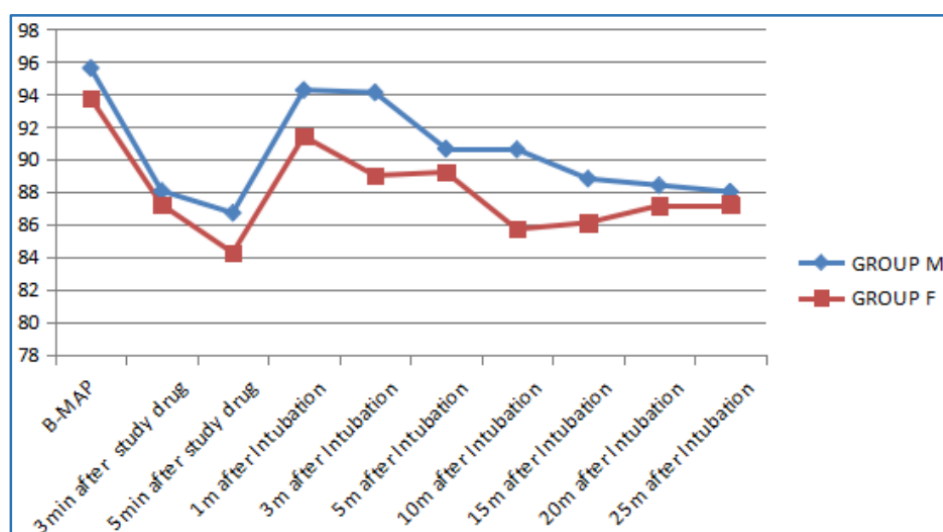


Fig. 5: Changes in mean arterial pressure at various specified timings in two groups



Graph 4: Changes in mean arterial pressure at various specified timings in two groups

After arrival into the operation theatre, mean arterial pressures were recorded just before study drug, named base line value (B-MAP). In group M, mean arterial pressures ranged from 83 mmHg to 103 mmHg with a mean±SD of 95.6±8.61 and is compared with group F in which mean arterial pressures ranged from 73 mmHg to 106 mmHg with a mean±SD of 93.75±9.38. There is no statistical difference in both the groups as the P value is 0.52 (P > 0.05).

At time 3 mins after the given study drug, the mean±SD of mean arterial pressures were 88.05±6.61 & 87.2±7.33 in the group M & F respectively. There is no statistical difference in both the groups. (P-0.702).

At time 5 mins after the given study drug, the mean±SD of mean arterial pressures were 86.7±6.61 & 84.25±9.39 in

the group M & F respectively. There is no statistical difference in both the groups. (P-0.346). There was no statistically significant difference after 1, 3, 5, 10, 15, 20 and 25 minutes after intubation.

There is rise in mean arterial blood pressure after intubation in both the groups, (at 1 min to 3 mins after intubation) but below the baseline level which is not significant, finally the graph of mean arterial blood pressure showed a fall at 5 mins after intubation.

But there is a significant difference between MgSO₄ & fentanyl group at 3 mins after intubation, where there is more fall in mean arterial BP in fentanyl group when compared to MgSO₄ group as the P value is <0.05. (P-0.04)

DISCUSSION: Direct laryngoscopy and tracheal intubation frequently induce cardiovascular stress response, characterised by hypertension, tachycardia and increased serum concentrations of catecholamines. This sympathoadrenal response to laryngoscopy and tracheal intubation results in an increase in cardiac work load which in turn may culminate in perioperative myocardial ischaemia and acute heart failure in susceptible individuals. Adrenergic responses that produce in transient but intense increase in heart rate and blood pressure have been observed during stressful perioperative or intraoperative stimuli. Patients with underlying coronary artery disease are at significant risk of developing myocardial ischaemia and infarction from these intense, although transient, hyperadrenergic states because of sudden increase in myocardial oxygen demand.

Slogoff and Keats reviewed and concluded that²:

1. Myocardial ischaemia was significantly more frequent in patients who developed tachycardia (heart rate >100 bpm).
2. Myocardial ischaemia was most likely to occur during intubation, skin incision or other surgical stimuli such as sternal splitting.
3. The incidence of postoperative myocardial infarction was almost threefold higher in patients with intraoperative myocardial ischaemia.

Anaesthesiologists utilise several pharmacological modalities to eliminate the haemodynamic consequences that occur during endotracheal intubation. Drugs such as inhalational anaesthetic agents, lidocaine, vasodilators (Sodium nitroprusside, nitroglycerin), narcotic analgesics (morphine, fentanyl), and beta blockers have been used during intubation with variable degrees of success. No single agent has been established as the most appropriate for this purpose. Deep inhalational anaesthesia has the disadvantage that it acts by causing myocardial depression, and it causes a rise in intracranial pressure which is undesirable in neurosurgical patients. Topical lidocaine anaesthesia, as in a study by Robert K. Stoelting (1978) is contraindicated in patients with full stomach,³ while intravenous lidocaine is found to reduce the incidence of dysrhythmias only with minimal effect on blood pressure response to tracheal intubation as seen in a study by Mounir N Abou Madi et al (1977).⁴ Antihypertensive agents like sodium nitroprusside are potent agents and require continuous intra-arterial blood pressure monitoring (Robert K Stoelting, 1979).⁵ Beta adrenergic blockade though effective, had to be used with a generous dose of atropine according to Prys-Roberts et al.⁶ But atropine has detrimental effects in patients with coronary artery disease as it causes increased myocardial oxygen consumption. Intravenous metoprolol is found to be a useful method in reducing both heart rate and blood pressure after laryngoscopy and intubation (A. J. Coleman and C. Jordan, 1980).⁷

Intravenous propranolol caused significant attenuation of tachycardia seen during skin incision and sternotomy in patients undergoing coronary artery bypass grafting (CABG).

The administration of propranolol and other beta adrenergic antagonists as shown to be associated with less severe intraoperative haemodynamic instability. However, because of their long half-life the effects far outlast the clinical need. Adverse effects, should they occur, could lead to problems of management as a result of their long duration of action.

Esmolol, a cardio selective beta adrenergic antagonist has been shown to be of benefit in the treatment of patients with acute myocardial infarction for controlling the cardiovascular response to tracheal intubation, when used as a continuous infusion technique. However, the dose regimen and time required for preparation of an infusion adds a degree of complexity to the induction process.

L. G Wilson, B. H. Meiklejohn and G. Smith have concluded that intravenous lignocaine may not be the agent of choice for attenuating the sympathoadrenal responses to laryngoscopy and tracheal intubation with myocardial ischaemia.⁸

U. A Carabine, P. M. C Wright, J. P Howe and J. Moore concluded that in a study that clonidine partially attenuates the blood pressure and heart rate responses to tracheal intubation.⁹

Vigorite C, Giordano A, Ferraro P et al (1991) showed the haemodynamic effects of magnesium sulphate on normal human heart where Mg as a calcium antagonist reduces myocardial contractile force.¹⁰

Magnesium produces vasodilatation by directly acting on the blood vessels and by interfering with a wide range of vasoconstrictor substances. Because of its dual action of calcium antagonist and vasodilator properties along with antiarrhythmic effects and the ability of magnesium to inhibit the release of catecholamines, it has been used as an agent in attenuating the intubatory responses.

Douglas W. W Rubin RP studied the mechanism of magnesium inhibiting the catecholamine release from the adrenal medulla and the role of calcium in stimulus-secretion coupling.¹¹

James MFM, Beer RE, Esser J. D showed that intravenous magnesium sulphate inhibits catecholamine release associated with tracheal intubation.¹²

Fentanyl, the short acting opioid analgesic is very effective in attenuating the cardiovascular, hormonal and metabolic responses and inhibiting the catecholamine release to stress response like surgical stimuli, laryngoscopy and intubation. According to N. Dahlgren et al (1981), fentanyl though effective in attenuation in pressor response may cause postoperative respiratory depression and nausea and vomiting.¹³

Oliver HG, Wilder S et al studied the sensory changes and analgesia after abdominal hysterectomy by comparing the anaesthetic supplementation with fentanyl versus magnesium.¹⁴ He showed that the quality of sedation and analgesia is higher with fentanyl than with magnesium but apart from associated respiratory depression and postoperative nausea and vomiting, chest rigidity, its procurement in India is difficult due to rigid narcotic regulation.¹⁴

K. Montazeri MD, M Fallah in 2005 studied various doses of MgSO₄-Response Study in suppressing cardiovascular responses to laryngoscopy and endotracheal intubation. Different doses of MgSO₄ of 10 mg/kg, 20 mg/kg, 30 mg/kg, 40 mg/kg, & 50 mg/kg were given prior to intubation. Among all magnesium groups, he showed that the group who received 30 mg/kg before intubation had less cardiovascular response.¹⁵

In our study, of comparison between MgSO₄ & fentanyl in attenuating haemodynamic responses to laryngoscopy and intubation, the same IV MgSO₄ dose of 30 mg/kg were given prior to intubation as the present dosage is the optimal dose in attenuation of intubatory responses with minimum side effects like bradyarrhythmias and hypotension.

Similar results were observed by Dilip Kothari, Amrita Mehrotra et al in 2008. The study was conducted to compare the effects of magnesium sulphate and fentanyl on circulatory changes during intubation and anaesthesia. Group MgSO₄ received 20 mg/kg before induction followed by 10 mg/kg, total of 30 mg/kg were given intravenously. Group fentanyl received 1.25 mcg/kg, followed by 0.5 mcg/kg were given IV. There is insignificant rise in heart rate and mean arterial blood pressure to laryngoscopy, but fentanyl showed greater haemodynamic stability.¹⁶

They concluded that though magnesium is not superior to the actions of potent short-acting opiate fentanyl, it could be a safe and cheaper alternative to fentanyl as it may not have side effects of respiratory depression, postoperative nausea and vomiting like opioids.

Fentanyl plays an important role in balanced general anaesthesia by virtue of meeting all aspects of balanced anaesthesia like narcosis, analgesia and attenuation of stress responses, but apart from associated respiratory depression, chest rigidity and postoperative nausea and vomiting, its availability is difficult in India due to rigid narcotic regulation.

Magnesium is a popular drug in prevention of convulsions as it has been extensively used in prevention and treatment of convulsions in eclampsia. Recent studies showed that its role as analgesic during intraoperative and postoperative period in attenuating haemodynamic responses to laryngoscopy and intubation.

Oliver et al used similar doses as adjuvant to general anaesthesia in abdominal hysterectomies. A clinically insignificant rise in heart rate observed after injection of magnesium sulphate, which further observed stabilised near to baseline values.¹⁴

Ability of magnesium sulphate to inhibit acetylcholine release from vagus nerve in intact animal has been attributed to this effect.

In our study statistically insignificant ($P > 0.05$) fall in blood pressure immediately after the injection, but later in the course of the study significant rise was observed up to 5 mins after intubation. No significant changes were observed during rest of the study period in both the groups except at 5 to 10 mins after intubation. A significant difference was observed between two groups in which group F (fentanyl)

has showed smoother and stable blood pressure than group M(MgSO₄) to intubation.

Our results are in accordance with Puri et al to observe significant fall in MAP after MgSO₄ at pre-induction stage with a sudden rise in postintubation period.¹⁷

James et al also observed the similar results in patients pre-treated with IV MgSO₄. The stability with MgSO₄ could be attributed to its antagonistic activity on calcium and NMDA receptor, or inhibition of catecholamine release, or vasodilator effect of the ion, or a combination of all these.¹²

Fentanyl suppresses the nociceptive stimulation or centrally decreases the sympathetic tone, shorter duration of action, and a very good analgesic with good property of postoperative analgesia.

Hence both the groups are compared in attenuating the haemodynamic responses to laryngoscopy and intubation. Forty ASA I and II grade patients were randomly allocated to receive IV MgSO₄-30 mg/kg [Group-M] and IV fentanyl 1.5 µg/kg [Group-F] five minutes prior to intubation in elective surgeries. Heart rate and blood pressure were recorded every five minutes from zero time, after study drug, immediately after intubation, at every 5 min interval for next 30 minutes.

Mean arterial blood pressures at 3 minutes after intubation in group M is 94.1 ± 7.51 when compared to group F is 89 ± 7.64 . There is significant rise in mean arterial blood pressure in group M when compared to group F ($p = 0.04$), where the raised mean arterial pressures after intubation showed fall and reached below the baseline values 5 min after intubation. In our study, adverse effects like hypotension is not observed in either of the groups, but bradycardia was seen in one patient in group M, treated with inj. atropine.

CONCLUSION: Based on our findings we conclude that IV fentanyl showed a greater degree of haemodynamic stability, that is good control on rise in heart rate and mean arterial pressures during laryngoscopy and intubation compared to IV MgSO₄, despite to its side effects like respiratory depression and nausea and vomiting.

REFERENCES:

1. Ronald D Miller. Miller's anesthesia. Elsevier health sciences, 7th edn. 2010;vol 2:pgs 1645.
2. Slogoff S, Keats AS. Does perioperative myocardial ischaemia lead to postoperative myocardial infarction? *Anesthesiology* 1985;62(2):107-114.
3. Robert K, Stoelting. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lidocaine. *Anaesthesia Analgesia* 1978;57(2):197-199.
4. Mounir N-Abou-Madi, Hugo Keszler, Joseh M Yacoub. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous dose of lidocaine. *Canadian Society Anaesthesia Journal* 1977;24(1):12-18.

5. Robert K, Stoelting. Attenuation of blood pressure responses to laryngoscopy and tracheal intubation with sodium nitroprusside. *Anaesthesia Analg* 1979;58(2):116-119.
6. Prys-Roberts, Greene LT, Meloche R, et al. Studies of anaesthesia in relation to hypertension-II. Haemodynamic consequences of induction and endotracheal intubation. *British Journal of Anaesthesia* 1971;43(6):541-547.
7. Coleman AJ, Jordan C. Cardiovascular responses to anaesthesia. *Anaesthesia* 1980;35(10):972-978.
8. Wilson IG, Meiklejohn BH, Smith G. Intravenous lignocaine and sympathoadrenal responses to laryngoscopy and intubation. The effect of varying time on injection. *Anaesthesia* 1991;46(3):177-180.
9. Carabine UA, Allen RW, Moore J. Partial attenuation of the pressor response to endotracheal intubation. A comparison of the effects of intravenous clonidine and fentanyl. *Eur J Anaesthesiol* 1992;9(4):325-329.
10. Vigorito C, Giordano A, Ferraro P, et al. Hemodynamic effects of magnesium sulfate on the normal human heart. *Am J Cardiol* 1991;67(16):1435-1437.
11. Douglas WW, Rubin RP. The effects of alkaline earths and other divalent cations on adrenal medullary secretion. *J physiol* 1964;175(2):231-241.
12. James MF, Beer RE, Esser JD. Intravenous magnesium sulfate inhibits catecholamine release associated with tracheal intubation. *Anesth Analg* 1989;68(6):772-776.
13. Dahlgren N, Messeter K. Treatment of stress response to laryngoscopy and intubation with fentanyl. *Anaesthesia* 1981;36(11):1022-1026.
14. Wilder Smith OH, Lars AN, Gaumann D, et al. Sensory changes and pain after abdominal hysterectomy: a comparison of anaesthetic supplementation with fentanyl versus magnesium or ketamine. *Anesth Analg* 1998;86(1):95-101.
15. Montazeri K, Fallah M. A dose-response study of magnesium sulfate in suppressing cardiovascular responses to laryngoscopy & endotracheal intubation. *Journal of Research in Medical Sciences* 2005;10(2):82-86.
16. Dilip Kothari, Amrita Mehrotra, Bhanu Choudhary, et al. Effect of intravenous magnesium sulfate and fentanyl citrate on circulatory changes during anaesthesia and surgery: a clinical study. *Indian Journal of Anesthesia* 2008;52(6):800-804.
17. Puri GD, Marudhachalam KS, Chari P, et al. The effect of magnesium sulphate on haemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with coronary artery disease. *Anesth Analg* 1998;87(4):808-811.