



Comparative Study Between Infusion Fentanyl and Magnesium Sulphate in Attenuation of Hemodynamic Response During Laryngoscopy and Intubation

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KEYWORDS

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ABSTRACT:

Background: Laryngoscopy & endotracheal intubation are an integral part of general anaesthesia. There is increase in heart rate and blood pressure as a sequel of direct laryngoscopy and endotracheal intubation. Fentanyl a synthetic μ -receptor agonist is used to attenuate the laryngoscopy & intubation response. Magnesium sulphate(MgSO₄) is a cerebral depressant, is used to attenuate intubation-induced vasopressor response.

Aims & Objectives: 1. To compare the efficacy of IV infusion Fentanyl 2 μ g/kg and MgSO₄ 20mg/kg in the attenuation of hemodynamic response to laryngoscopy & intubation.

2. To evaluate any side effects associated with the use of these drugs.

Materials and Methods:A prospective randomized study was conducted on 100 ASA grade I and II patients of either sex between the age group 18-60 years undergoing elective and emergency surgeries under general anaesthesia. The study population was divided into 2 groups with 50 patients in each group. Group F received IV infusion Fentanyl 2 μ g/kg dose in 20cc NS over 10 mins in infusion pump. Group M received IV infusion MgSO₄ 20mg/kg dose in 20cc NS over 10 mins in infusion pump.

Results: The heart rate, systolic & diastolic blood pressure, mean arterial pressure decreased in both the groups receiving MgSO₄ & Fentanyl. The response to laryngoscopy and intubation with increased parameters was seen in both groups, greater increase in fentanyl as compared to MgSO₄.

Conclusion:Both Fentanyl and MgSO₄ are effective in the hemodynamic attenuation during laryngoscopy, MgSO₄ significantly & effectively attenuates hemodynamic responses & intubation in comparison to fentanyl.

Introduction:

Laryngoscopy and endotracheal intubation are an integral part of general anaesthesia which induces a variety of responses in the cardiovascular, respiratory and other systems. King and colleagues had first described the reflex circulatory responses to direct laryngoscopy and tracheal intubation in 1951, after

which there have been numerous studies discussing about both the response and the manoeuvres by which it may be attenuated.^[1]

Increase in heart rate and blood pressure are well documented sequelae of direct laryngoscopy and endotracheal intubation in normotensive individuals. The magnitude of hemodynamic changes observed may



be dependent on various factors such as depth of anaesthesia, whether any measures are taken prior to airway manipulation, the anaesthetic agent used, the duration of laryngoscopy and intubation.^[2]

Pressor response to intubation is exaggerated in hypertensive patients even though rendered normotensive preoperatively by antihypertensive medications and may result in intra-operative myocardial infarction, acute L.V.F, dysrhythmias. Such hemodynamic changes can also alter the balance between myocardial oxygen demand and supply and can precipitate myocardial ischaemia in patients with coronary artery disease, valvular heart disease, hypertension, cerebrovascular disease.^[3]

Fentanyl is a synthetic pure μ -receptor agonist with shorter time to peak analgesic effect, larger safety margin, minimal respiratory depression at analgesic doses, rapid termination of effect after small bolus doses and relative cardiovascular stability. This drug has been used to attenuate the laryngoscopy and intubation response in most of the patients.^[4]

I.V. Magnesium Sulphate (MgSO_4) has been extensively tried with reasonable margin of safety in management of pregnancy induced hypertension. It is a cerebral depressant which acts by blocking N-methyl D-aspartate (NMDA) receptor in CNS and by decreasing sympathetic outflow. It is used to attenuate intubation-induced vasopressor response by blocking the release of catecholamines from both adrenal medulla and from nerve terminals.^[4] Catecholamine release inhibition and vasodilation properties of MgSO_4 prompted us to study its effect on pressor response to laryngoscopy and intubation.

The present study was undertaken to compare the efficacy of IV infusions of Fentanyl and MgSO_4 in attenuation of the hemodynamic response occurring during laryngoscopy and intubation and to study the side effects of the drugs used.

Materials and Methods:

This prospective clinical randomized double-blind study was conducted on **100** ASA grade I and II patients of either sex between the age group 18-60 years undergoing elective and emergency surgeries under

general anaesthesia(GA) and whose trachea was intubated. The study was conducted after approval from the ethical committee and with the informed consent given by the patient.

Inclusion criteria:

Age :18-60 years, Either Sex, ASA class I and II, Mallampati Grade I and II, Elective & emergency surgeries under GA

Exclusion criteria:

Cardiac, renal, hepatic, cerebral diseases & peripheral vascular diseases, Pregnancy & lactating mothers, Uncontrolled hypertension, Heart Rate(HR)<60bpm and Systolic Blood Pressure(SBP)<100mmHg, Patients with difficult airway, Obese patients (BMI>30), Patients with full stomach

The study population was divided into 2 groups with 50 patients in each group:

1. Group **F** received IV infusion **Fentanyl 2 $\mu\text{g/kg}$** dose in 20cc NS over 10 mins in infusion pump
2. Group **M** received IV infusion **MgSO_4 20mg/kg** dose in 20cc NS over 10 mins in infusion pump

Sample selection was done using the Closed Envelope Method. The computer randomly allocated each subsequent participant into Group M or Group F. The patients were informed priorly about the chances of them getting either of the drug and only those who consented were taken up for the study. After patient was taken to the Operation theatre, monitors were connected and basal vital parameters i.e., HR, SBP, Diastolic Blood Pressure(DBP), Mean Arterial Pressure(MAP) and SpO_2 were recorded. IV access was established using a 20G cannula.

Infusion was started as mentioned above and the patient was preoxygenated with 100% O_2 via facemask at the 2nd minute of infusion. After 7 mins of infusion, patient was induced with Propofol 2mg/kg dose. Inhalational agent Sevoflurane at **1%** was added to Oxygen after confirming ventilation, neuromuscular blockade was achieved using Atracurium 0.5mg/kg dose followed by



laryngoscopy & trachea was intubated with appropriately sized cuffed ETT under the supervision of Consultant.

HR, SBP, DBP, MAP & SpO₂ were recorded at the following stages-Every 2 minutes during the infusion, At the time of induction (7th minute), Pre intubation, Post-intubation, Time increments of 1, 3, 5, 10 minutes post intubation.

Statistical analysis:

The data was analyzed using the sample size estimate software G Power 3.1.9.2. The statistical test which was used is Repeated major ANOVA within and between.

Results:

Table 1 shows that the age, sex and ASA grading distributions in both groups were not significantly different from one another ($p < 0.05$). There was a significant difference between the 2 groups in terms of Height (cm) ($p = 0.003$), with the median Height (cm) being highest in the Group M. There was a significant difference between the 2 groups in terms of Weight (Kg) ($p = 0.037$), with the mean Weight (Kg) being highest in the Group F. There was a significant difference between the 2 groups in terms of BMI (Kg/m²) ($p = < 0.001$), with the mean BMI (Kg/m²) being highest in the Group F.

Figure 1 shows changes in heart rate over the period of time. Patients in Group M had a mean baseline HR of 84.9 bpm while the mean baseline HR of patients in Group F was 79.8 bpm. Baseline HR was higher in Group M with a t value of 1.941 and a p value of 0.056 which was not statistically significant. Heart rate at induction (7 minutes post infusion): Patients in Group M had mean HR of 80.49 bpm at 7 minutes post infusion, while the mean HR of patients in Group F was 70.49 bpm. Group M showed a decrease in HR by 5% from the baseline as compared to Group F which showed a greater decrease in HR by 11.2 % from baseline which was statistically significant ($p < 0.05$). Heart rate at the end of infusion (10 minutes post infusion): Patients in Group M had a mean HR of 79.76 bpm at the end of infusion, while the mean HR of patients in Group F was 69.25 bpm. Group M showed a decrease in HR by 5.9% from the baseline as compared

to Group F which showed a decrease of 13.8% from baseline which was statistically significant ($p < 0.05$). Heart rate post intubation: Patients in Group M had a mean HR of 87.94 bpm post intubation, while the mean HR of patients in Group F was 91.47 bpm. Group F had an exponential increase in HR by 15.3% from the baseline as compared to Group M which showed a slight increase of 4.6% from the baseline. The HR was seen to decrease gradually at 1, 3, 5 and 10 mins post intubation in both Group M and Group F which was seen to be statistically significant ($p < 0.05$) at all timepoints post intubation.

Figure 2 shows changes in SBP over the period of time. Patients in Group M had mean baseline SBP of 132.18 mmHg while the mean baseline SBP of patients in Group F was 130.00 mmHg. The Baseline SBP of Group M was higher as compared to that of Group F with a t value = -0.632 and $p = 0.529$ which was not statistically significant. Patients in Group M had a mean SBP of 106.12 mmHg at 7 minutes post infusion, while the mean SBP of patients in Group F was 102.31 mmHg. Group M showed a decrease in SBP by 19.2% from the baseline as compared to that of Group F which showed a decrease of 21% from the baseline which was statistically significant ($p < 0.05$). Patients in Group M had a mean SBP of 108.88 mmHg at the end of infusion, while the mean SBP of patients in Group F was 102.94 mmHg. Group M showed a decrease in SBP by 17% from the baseline as compared to that of Group F which showed a greater decrease of 19.8% from the baseline which was statistically significant ($p < 0.05$). Patients in Group M had a mean SBP of 127 mmHg post intubation, while the mean SBP of patients in Group F increased to 140.51 mmHg. Group F showed an increase in SBP by 9.1% from baseline as compared to that of Group M which continued to show a decline of the SBP from baseline by 3.3% however there was an increase from the pre-intubation value of 110.47 mmHg which was statistically significant ($p < 0.05$). Group M showed statistically significant values only at 3, 5 and 10 minutes post intubation ($p < 0.05$) whereas Group F showed statistically significant values at all timepoints post intubation ($p < 0.05$). There was no significant drop in the BP at 1 minute post intubation in both the groups.



Figure 3 shows changes in DBP over the period of time. Patients in Group M had a mean baseline DBP of 80.86 mmHg while the mean baseline DBP of patients in Group F was 74.82 mmHg. The Baseline DBP of Group M was higher as compared to that of Group F with a t value = -2.628 and p value = 0.010 which was statistically significant ($p < 0.05$). Patients in Group M had a mean DBP of 65.67 mmHg at 7 minutes post infusion while the mean DBP of patients in Group F was 58.71 mmHg. Group M showed a decrease in the DBP by 18.5% from the baseline in comparison to Group F which showed a decrease in DBP by 21% from the baseline which was statistically significant ($p < 0.05$). Patients in Group M had a mean DBP of 66.80 mmHg at the end of infusion while the mean DBP of patients in Group F was 59.84 mmHg. Group M showed a decrease in the DBP by 17.2% from the baseline as compared to Group F which showed a decrease by 19.1% from the baseline which was statistically significant ($p < 0.05$). Patients in Group M had a mean DBP of 78.02 mmHg post intubation, while the mean DBP of patients in Group F was 85.02 mmHg. Group F showed a greater increase in DBP by 15.6% from the baseline as compared to Group M which still showed a decrease of DBP by 3% from the baseline but with an increase from the pre-intubation value of 68.24 mmHg which was statistically significant ($p < 0.05$). Group M showed statistically significant values at 3, 5 and 10 mins post intubation ($p < 0.05$) whereas Group F did not show statistically significant values post immediate intubation.

Figure 4 shows changes in MAP over the period of time. Patients in Group M had a mean baseline MAP of 98.37 mmHg while the mean baseline MAP of patients in Group F was 93.73 mmHg. The Baseline MAP of Group M was higher as compared to that of Group F with t value = -1.729 and p value = 0.087 which was statistically not significant. Patients in Group M had a mean MAP of 79.69 mmHg at 7 minutes post infusion, while the mean MAP of patients in Group F was 73.73 mmHg. Group M showed a decrease in MAP by 18.6% from the baseline as compared to Group F which showed a decrease in MAP by 21.1% from the baseline which was statistically significant ($p < 0.05$). Patients in Group M had a mean MAP of 80.92 mmHg at the end of infusion, while the mean MAP of patients in Group F was 75.24 mmHg. Group M showed a decrease in MAP

by 17.4% from baseline as compared to Group F which showed a decrease in MAP by 18.7% from the baseline which was statistically significant ($p < 0.05$). Patients in Group M had a mean MAP of 93.73 mmHg post intubation, while the mean MAP of patients in Group F was 103.49 mmHg. Group F showed a sharp increase in the MAP by 11.8% from the baseline as compared to Group M which continued to show a decrease in the MAP by 4.3% from the baseline but an increase from the pre-intubation value of 82.51 mmHg which was statistically significant ($p < 0.05$). Group M showed statistically significant values at 3, 5, 10 mins post intubation, Group F did not show any statistically significant values except immediate post intubation. Figure 5 shows changes in SpO₂ over the period of time. There was no significant difference between any of the timepoints as compared to the Baseline timepoint in terms of SpO₂ (%) except at 2 minutes post infusion from the baseline ($p < 0.05$).

Discussion:

Laryngoscopy and intubation are known to cause an increase in heart rate and blood pressure.^[5] These responses are transitory and variable and may not be significant in otherwise normal individuals. However, in patients with cardiovascular compromise like hypertension, ischemic heart disease, and cerebrovascular disease and in patients with intracranial aneurysms, even these transient changes in hemodynamics can result in potentially deleterious effects.^[6] These are by far the most important indications for attenuation of hemodynamic response to laryngoscopy and tracheal intubation. Many methods like the use of inhalational anaesthetic agents, Lidocaine^[6], Opioids, direct-acting vasodilators^[7], α -2 agonists, Calcium-channel blockers^[8], and β -blockers have been tried by various authors for blunting hemodynamic responses to laryngoscopy and intubation. However, all such manoeuvres had limitations. The search for the ideal technique or agents for attenuation of hemodynamic changes is still continuing.

MgSO₄ in a bolus dose of 20-50 mg/kg was observed to attenuate the adverse haemodynamic responses without any hypotension or bradycardia by directly blocking the release of catecholamines from both adrenal gland and



adrenergic nerve terminals and indirectly through negative feedback mechanism.^[9]

Fentanyl is advocated for attenuation of sympathetic response to laryngoscopy and intubation. Blunting of sympathetic response is dose dependent. At high doses, Fentanyl produces tissue accumulation and thus patients may require mechanical respiratory support.^[10] Fentanyl at 6 µg/kg completely abolishes, whereas at 2 µg/kg significantly attenuates arterial pressure and heart rate increase during laryngoscopy and intubation

In the present study Baseline HR was higher in Group M with a t value of 1.941 and a p value of 0.056 which was not statistically significant. The study done by Gunalan et al.^[11] showed comparative evaluation of the administration of Dexmedetomidine and Fentanyl for the stress attenuation during laryngoscopy and intubation. It showed non significant values of baseline HR when compared between Fentanyl and Dexmedetomidine.

Group M showed a decrease in HR by 5% from the baseline as compared to Group F which showed a greater decrease in HR by 11.2 % from baseline which was statistically significant ($p < 0.05$). This was similar to a study done by Panda et al.^[12] who conducted a research to determine the minimum effective dose of MgSO₄ for attenuating hemodynamic response and they observed that HR decreased following induction, with a short spike after intubation

Group M showed a decrease in HR by 5.9% from the baseline as compared to Group F which showed a decrease of 13.8% from baseline which was statistically significant ($p < 0.05$). Gunalan et al.^[11] noticed similar observations with Fentanyl 2µg/kg wherein a decrease in the HR was seen after the start of the drug from baseline value of 81.97 bpm to 79.20 bpm at the end of the drug infusion

The HR was seen to decrease gradually at 1,3,5 and 10 mins post intubation in both Group M and Group F which was seen to be statistically significant ($p < 0.05$) at all timepoints post intubation. Similar results were found by Panda et al.^[12] who showed statistically significant value for MgSO₄ post intubation. The HR

post intubation increased to 75.3 bpm from the pre-intubation value of 65.7 bpm.

The Baseline SBP of Group M was higher as compared to that of Group F with a t value = -0.632 and $p = 0.529$ which was not statistically significant. Group M showed statistically significant values only at 3, 5 and 10 minutes post intubation ($p < 0.05$) whereas Group F showed statistically significant values at all timepoints post intubation ($p < 0.05$). There was no significant drop in the BP at 1 minute post intubation in both the groups. Honarmand et al.^[13] also observed that the rise in SBP was statistically significant at 1, 3 and 5 minutes post intubation in all 3 groups receiving MgSO₄ at 30mg/kg, 40mg/kg and 50mg/kg doses.

The Baseline DBP of Group M was higher as compared to that of Group F with a t value = -2.628 and p value = 0.010 which was statistically significant ($p < 0.05$). Group M showed statistically significant values at 3, 5 and 10 mins post intubation ($p < 0.05$) whereas Group F did not show statistically significant values post immediate intubation. The observations in our study were similar to that of Honarmand et al.^[13] which showed statistically significant values at 1, 3 and 5 minutes post intubation.

The Baseline MAP of Group M was higher as compared to that of Group F with t value = -1.729 and p value = 0.087 which was statistically not significant. Group M showed a decrease in MAP by 17.4% from baseline as compared to Group F which showed a decrease in MAP by 18.7% from the baseline which was statistically significant ($p < 0.05$). Montazeri et al.^[14] and Honarmad et al.^[13] observed statistically significant values ($p < 0.05$) just before intubation. Group M showed statistically significant values at 3, 5, 10 mins post intubation unlike Panda et al.^[12] which showed statistically insignificant value for MAP after 2 and 5 minutes post intubation. In our study, Group F did not show any statistically significant values except immediate post intubation.

There was no significant difference between any of the timepoints as compared to the Baseline timepoint in terms of SpO₂ (%) except at 2 minutes post infusion from the baseline ($p < 0.05$).



One drawback of our study was, we selected patients who had Mallampati score of Grade 1 and 2. Patients with Mallampati Grade 3 and 4 or any anticipated difficult airway patients were excluded from our study. Also, the laryngoscopy and intubation were performed only by an experienced anaesthesiologist within the minimum time.

Conclusion: Both Fentanyl and MgSO₄ are effective in the hemodynamic attenuation during laryngoscopy, but MgSO₄ in the dose of 20µg/kg is better in the mean reduction of the hemodynamic parameters. MgSO₄ significantly and effectively attenuates the hemodynamic responses to laryngoscopy and intubation in comparison to Fentanyl.

References:

1. Kamewad A, Sharma V, Kamewad S, Popli V. Haemodynamic response to endotracheal intubation: direct versus video laryngoscopy. *Int J Res Med Sci*. 2016 Dec 1;4.
2. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. *Br J Anaesth*. 1987 Mar;59(3):295–9.
3. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. *Anesthesiology*. 1977 Dec;47(6):524–5.
4. Zhang J, Wang Y, Xu H, Yang J. Influence of magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy: A meta-analysis of randomized controlled studies. *Medicine (Baltimore)*. 2018 Nov;97(45):e12747.
5. Mahajan L, Kaur M, Gupta R, Aujla KS, Singh A, Kaur A. Attenuation of the pressor responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine versus magnesium sulphate under bispectral index-controlled anaesthesia: A placebo-controlled prospective randomised trial. *Indian J Anaesth*. 2018 May;62(5):337–43.
6. Stoelting RK. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lidocaine. *Anesth Analg*. 1978 Apr;57(2):197–9.
7. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. *Anesth Analg*. 1979 Apr;58(2):116–9.
8. Mikawa K, Nishina K, Maekawa N, Obara H. Comparison of nicardipine, diltiazem and verapamil for controlling the cardiovascular responses to tracheal intubation. *Br J Anaesth*. 1996 Feb;76(2):221–6.
9. Comparison of intravenous magnesium sulphate and lidocaine for attenuation of cardiovascular response to laryngoscopy and endotracheal intubation in elective surgical patients at Zewditu Memorial Hospital Addis Ababa, Ethiopia. [cited 2021 Dec 4].
10. Martin DE, Rosenberg H, Aukburg SJ, Bartkowski RR, Edwards MW, Greenhow DE, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982 Aug;61(8):680–4.
11. Gunalan S, Venkatraman R, Sivarajan G, Sunder P. Comparative Evaluation of Bolus Administration of Dexmedetomidine and Fentanyl for Stress Attenuation During Laryngoscopy and Endotracheal Intubation. *J Clin Diagn Res JCDR*. 2015 Sep;9(9):UC06–9.
12. Panda NB, Bharti N, Prasad S. Minimal effective dose of magnesium sulfate for attenuation of intubation response in hypertensive patients. *J Clin Anesth*. 2013 Mar 1;25(2):92–7.
13. Honarmand A, Safavi M, Badiei S, Daftari-Fard N. Different doses of intravenous Magnesium sulfate on cardiovascular changes following the laryngoscopy and tracheal intubation: A double-blind randomized controlled trial. *J Res Pharm Pract*. 2015 Jun;4(2):79–84.
14. Maziar, Heidari M, Dahmardeh M, Mirtajani SB, Jahangirifard A. Comparison of Dexmedetomidine, Lidocaine, and Fentanyl in Attenuation Hemodynamic Response of Laryngoscopy and Intubation in Patients Undergoing Cardiac Surgery. *Anesthesiol Res Pract*. 2020;2020:4814037.

**Table 1:** Demographic characteristics of study participants in two groups:

Parameters	F (n = 51)	M (n = 49)	p value
Age (Years)	40.47 ± 13.09	38.12 ± 12.99	0.396 ¹
Age			
18-30 Years	11 (21.6%)	17 (34.7%)	0.334 ²
31-40 Years	17 (33.3%)	11 (22.4%)	
41-50 Years	9 (17.6%)	11 (22.4%)	
51-60 Years	14 (27.5%)	10 (20.4%)	
Gender			
Male	28 (54.9%)	23 (46.9%)	0.426 ²
Female	23 (45.1%)	26 (53.1%)	
ASA Grade			
I	37 (72.5%)	37 (75.5%)	0.736 ²
II	14 (27.5%)	12 (24.5%)	
Weight (Kg)***	62.63 ± 8.18	59.16 ± 8.19	0.037 ³
Height (cm)***	160.69 ± 6.21	164.59 ± 6.52	0.003 ¹
BMI (Kg/m²)***	24.27 ± 3.32	21.83 ± 3.07	<0.001 ³
BMI***			
<18.5 Kg/m ²	4 (7.8%)	8 (16.3%)	0.014 ²
18.5-22.9 Kg/m ²	14 (27.5%)	21 (42.9%)	
23.0-24.9 Kg/m ²	8 (15.7%)	12 (24.5%)	
25.0-29.9 Kg/m ²	24 (47.1%)	8 (16.3%)	
30.0-34.9 Kg/m ²	1 (2.0%)	0 (0.0%)	

***Significant at $p < 0.05$, 1: Wilcoxon-Mann-Whitney U Test, 2: Chi-Squared Test, 3: t-test

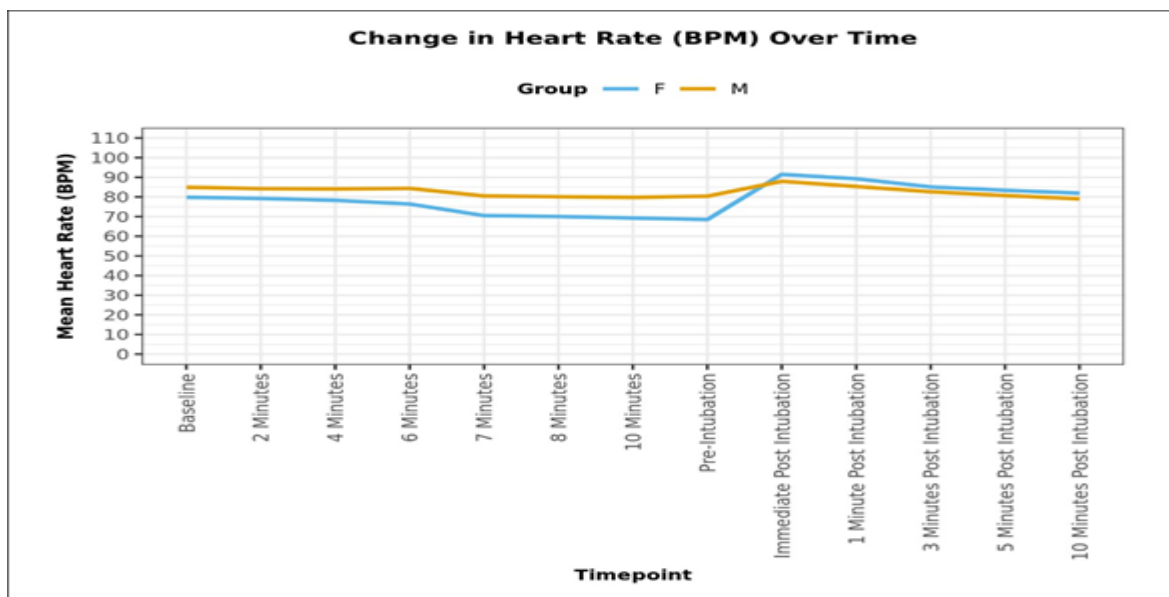
Figure 1: Changes in heart rate over the time



Figure 2: Changes in systolic BP over the time

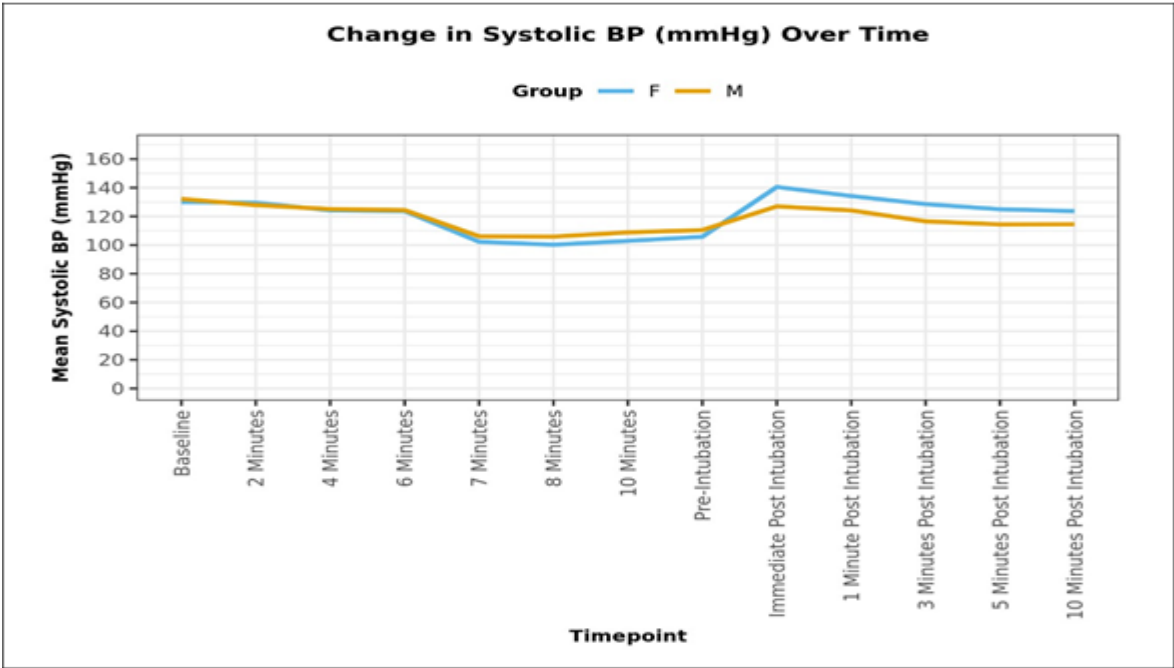


Figure 3: Changes in diastolic BP over the time

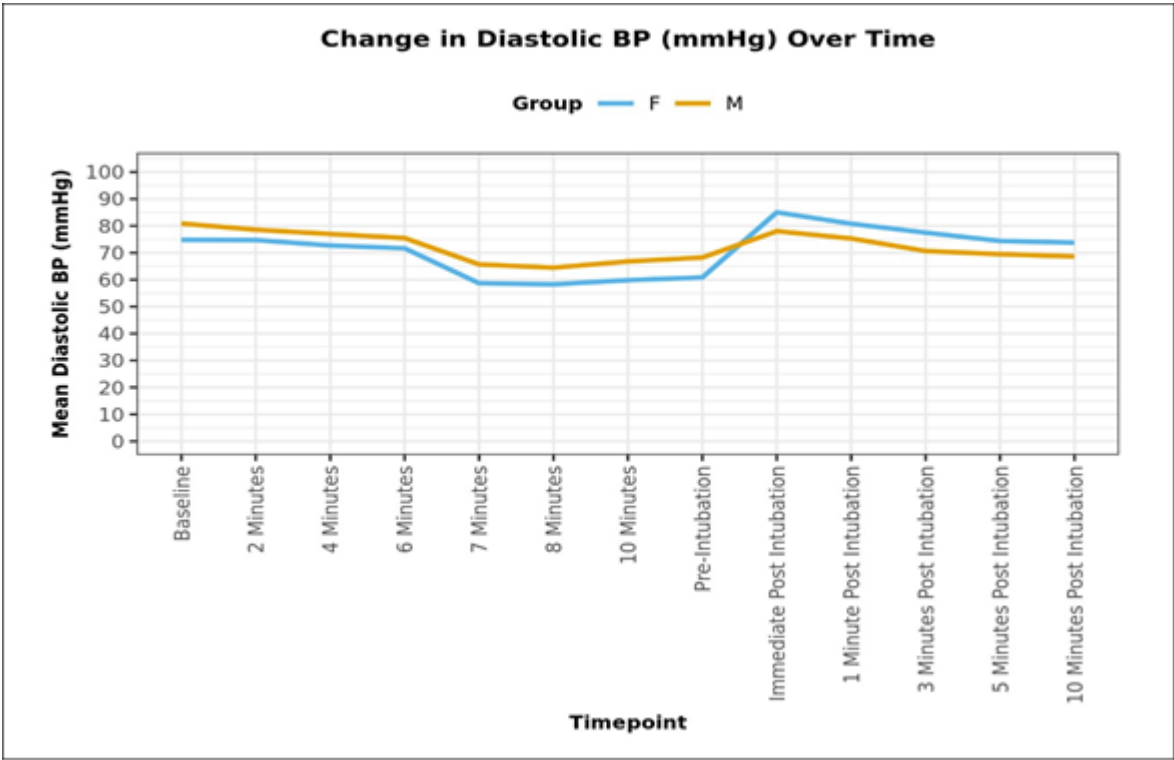




Figure 4: Changes in MAP over the time

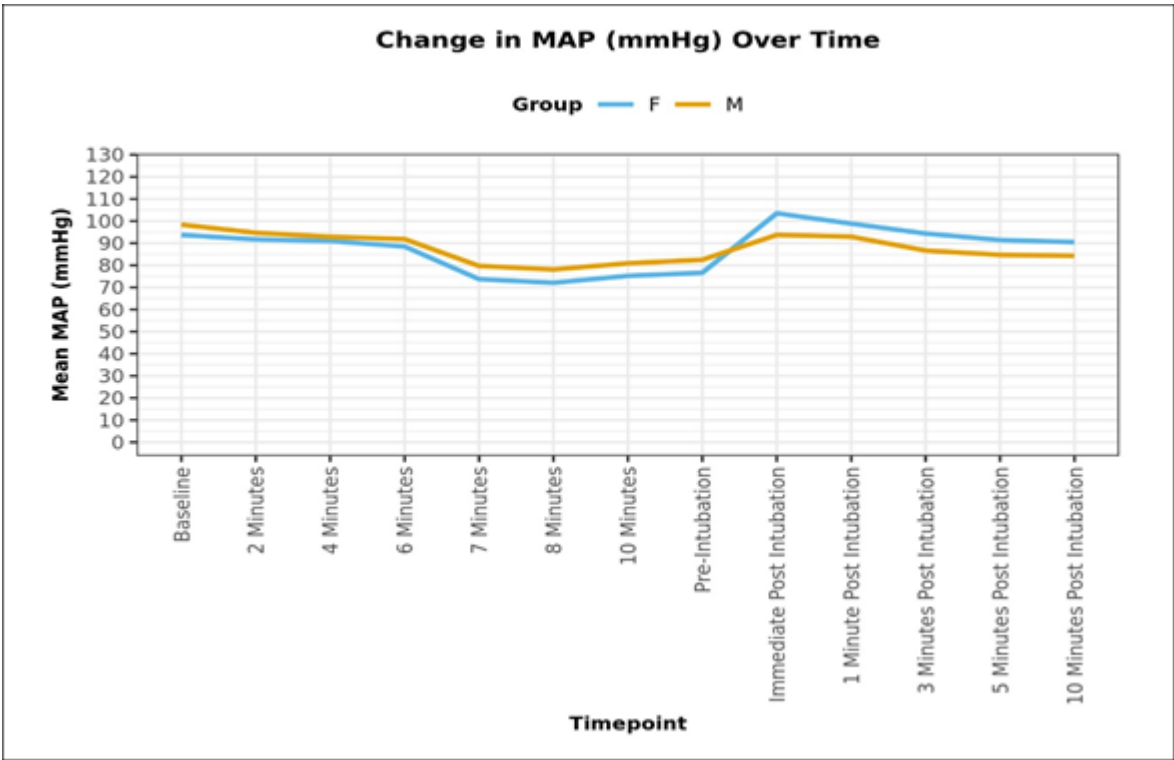


Figure 5: Changes in SpO2 over the period of time:

