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Research Article

A Comparative Study Of Midazolam-Fentanyl And Midazolam-Pentazocine For Hemodynamic Control During Laryngoscopy And Intubation

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ABSTRACT

Context: Laryngoscopy and intubation are crucial yet noxious stimuli that provoke significant hemodynamic changes. Effective attenuation of these responses is vital, particularly in high-risk patients. This study compares the hemodynamic effects of midazolam-fentanyl and midazolam-pentazocine combinations during laryngoscopy and intubation.

Aims: To evaluate and compare the efficacy of midazolam-fentanyl and midazolam-pentazocine in attenuating heart rate, blood pressure, rate pressure product, mean arterial pressure and maintaining oxygen saturation during airway management.

Settings and Design: A prospective, randomized controlled study conducted at a tertiary care hospital.

Methods and Material: Sixty ASA grade I or II patients aged 18–60 years undergoing elective surgeries under general anaesthesia were randomized into two groups: Group F (midazolam 0.03 mg/kg + fentanyl 2 µg/kg) and Group P (midazolam 0.03 mg/kg + pentazocine 0.6 mg/kg). Hemodynamic parameters were recorded at baseline, pre-induction, and at five intervals up to 10 minutes post-intubation.

Statistical analysis used: Inter-group comparisons were conducted with t-tests and the Chi-square test; intra-group changes were analysed using repeated measures ANOVA, with $p<0.05$ considered significant.

Results: Group F showed significantly lower HR, BP, and RPP compared to Group P, particularly during induction and the immediate post-intubation phase ($p<0.05$). Group P exhibited higher fluctuations, indicating less haemodynamic stability. Oxygen saturation remained comparable between groups ($p>0.05$).

Conclusions: Midazolam-fentanyl demonstrated superior attenuation of hemodynamic responses compared to midazolam-pentazocine, making it a preferred option for patients requiring stable cardiovascular parameters during airway management. Future studies could explore strategies to enhance the efficacy of pentazocine in such contexts.

Keywords*: laryngoscopy, endotracheal intubation, Haemodynamic changes , fentanyl, pentazocine.*

INTRODUCTION

Laryngoscopy and endotracheal intubation are cornerstone techniques in modern anaesthesia, critical care and trauma management. Established as the standard for tracheal intubation since the early 20th century, direct laryngoscopy is associated with high success rates exceeding 99% in elective and emergency settings.[1,2] Despite its usefulness, laryngoscopy and intubation are potent noxious stimuli that provoke significant haemodynamic responses, including hypertension, tachycardia and arrhythmias.[3] These responses are mediated by vagus (cranial nerve X) and glossopharyngeal (cranial nerve IX) nerve activity, which involves reflex sympathetic activation and leads to catecholamine release.[4] Though such responses are usually tolerable in normotensive individuals, they can pose morbid threats in patients having cardiovascular or cerebrovascular diseases.

The attenuation of these haemodynamic changes is crucial for safe and uneventful intubation. Various pharmacological strategies, such as the use of opioids, benzodiazepines, beta-blockers and calcium channel blockers, have been implemented, with non-pharmacological techniques like gentle laryngoscopy.[5] Among opioids, fentanyl is known for its rapid onset and effective attenuation of sympathetic responses and has been extensively studied.[6] Pentazocine is a relatively less studied mixed agonist-antagonist opioid also demonstrated efficacy in blunting haemodynamic responses.[7]

This study evaluates the efficacy of intravenous midazolam-fentanyl and midazolam-pentazocine combinations in mitigating hemodynamic changes—heart rate (HR), blood pressure (BP), rate pressure product (RPP), mean arterial pressure (MAP), and oxygen saturation—during laryngoscopy and intubation under general anaesthesia. It aims to optimize anaesthetic induction protocols for high-risk patients by comparing these combinations.

SUBJECT AND METHODS

This prospective, randomized, controlled study was conducted at a tertiary care hospital with approval from the Institutional Ethics Committee and the Department of Anaesthesia. Sixty patients, aged 18–60 years, of American Society of Anesthesiologists (ASA) physical status grade I or II, undergoing elective surgical procedures under general anaesthesia, were included after obtaining written informed consent. Patients were randomly assigned to one of two groups (30 patients each). Group F received intravenous midazolam 0.03 mg/kg and fentanyl 2 µg/kg, while Group P received intravenous midazolam 0.03 mg/kg and pentazocine 0.6 mg/kg. Patients with ASA grade III or IV, pregnant women, those with difficult airways, and those with hypertension, diabetes mellitus, coronary artery disease or hypersensitivity to local anaesthetics were excluded. After a pre-anaesthetic evaluation, fasting for at least 8 hours was ensured. At the time of surgery, intravenous access and lactated Ringer's infusion were initiated. Standard monitoring was applied, including non-invasive BP, HR, electrocardiograph (ECG) and pulse oximetry. Premedication included intravenous glycopyrrolate 0.004 mg/kg, followed by the study drugs administered five minutes before induction. Anaesthesia induction was performed with intravenous propofol 2 mg/kg and vecuronium 0.1 mg/kg, with patients ventilated for three minutes before laryngoscopy and intubation using a Macintosh curved blade and a cuffed endotracheal tube. Intubation was completed within 15–20 seconds; those requiring longer were excluded. Anaesthesia maintenance involved 50% nitrous oxide in oxygen with intermittent vecuronium doses. Vital parameters, including HR, systolic and diastolic BP, MAP, RPP and SpO_2, were recorded at baseline, pre-induction and at five intervals up to 10 minutes post-intubation. Side effects, including bradycardia, tachycardia, hypertension or desaturation, were noted. Data were analysed using SPSS v22.0 (©IBM Inc.), with inter-group comparisons conducted using the Chi-square test for categorical variables and t-tests for continuous variables, and intra-group changes were analysed using repeated measures ANOVA, with $p<0.05$ considered statistically significant.

RESULTS

In this study comparing the haemodynamic effects of midazolam-fentanyl (Group F) and midazolam-pentazocine (Group P) during laryngoscopy and intubation, the mean age of participants was similar between groups (Group F: 38.97 ± 10.99 years; Group P: 36.47 ± 11.68 years; $P > 0.05$), with an equal gender distribution of 43.3% males and 56.7% females in both groups.

At baseline and T-0, Group P had significantly higher mean heart rates than Group F ($P < 0.05$), though no differences were observed at T-5, induction, or 7 minutes post-intubation. Both groups showed a significant rise in heart rate during induction and immediately post-intubation compared to baseline (Table 1).

Systolic BP was significantly higher in Group F at induction ($P < 0.05$), with no other significant inter-group differences observed. Diastolic BP and MAP followed a similar trend, showing significant differences only at induction ($P < 0.05$), while both groups exhibited significant deviations from baseline at several time points (Table 1).

RPP was significantly higher at T-0 in Group P ($P < 0.05$), but differences were insignificant at other intervals. SpO_2 remained comparable between groups across all time points, with no significant intra-group variations (Table 1).

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Table 1: Inter and intra-group comparison of heart rate, systolic BP, diastolic BP, Mean Arterial Pressure, Rate Pressure and Spo2 of the patients in Group F and Group P.

Heart rate (Per min)												
Groups		Baseline	T – 0	T–5	At induction	Post intubation	0min	1min	3min	5min	7min	10 min
F	**Mean**	80.17	81.17	83.6	87.7	92.77	92.43	88.4	85.93	83.2	81.97	78.17
	SD	12.9	14.21	17.59	17.01	16.35	16.79	15.23	13.93	13.52	13.48	12.93
	P-valu		0.565^{NS}	0.125 NS	0.006	0.001	0.001	0.003	0.021	0.184 NS	0.457 NS	0.320 NS

	e [Intra-group]											
P	Mean	88.7	95.37	92.5	87.83	102.5	99.87	98.77	94.83	91.77	88.67	88.37
	SD	19.07	20.39	20.05	17.34	20.28	18.15	18.33	17.48	17.76	17.91	17.59
	P-value [Intra-group]		0.005	0.157 NS	0.945 NS	0.001	0.001	0.002	0.038	0.270 NS	0.990 NS	0.903 NS
P-value [Inter-Group]		0.047	0.003	0.073 NS	0.977 NS	0.045	0.105 NS	0.021	0.033	0.040	0.107 NS	0.013
Systolic BP												
F	Mean	126.4	120.93	117.3	121.77	137.7	129.03	124.47	120.2	113.53	110.47	106.27
	SD	11.89	13.41	13.55	22.64	19.57	16.67	18.59	21.45	19.78	15.43	13.47
	P-value [Intra-group]		0.002	0.001	0.220 NS	0.001	0.299 NS	0.488 NS	0.060 NS	0.001	0.001	0.001
P	Mean	123.5	119.43	115.3	106.13	130.43	125.83	118.57	113.13	111.37	109.03	109.53
	SD	11.45	11.77	12.69	14.36	20.31	20.11	17.35	15.78	14.14	11.76	10.23
	P-value [Intra-group]		0.005	0.002	0.001	0.070 NS	0.554 NS	0.133 NS	0.001 NS	0.001	0.001	0.001
P-value [Inter-]		0.340 NS	0.647 NS	0.557 NS	0.002	0.164 NS	0.505 NS	0.209 NS	0.152 NS	0.627 NS	0.687 NS	0.295 NS
Diastolic BP												
F	Mean	78	75.33	75.1	76.77	84.97	81.03	77.67	74	69.57	69.5	66.33
	SD	8.04	11.16	12.7	15.77	9.06	9.46	14.79	14.8	14.67	13.25	11.67
	P-value [Intra-group]		0.007	0.091 NS	0.286 NS	0.005	0.105 NS	0.691 NS	0.050	0.001	0.001	0.001

P	Mean	78.33	75.53	75	66.5	84.43	81.33	75.77	72.13	69.9	69.83	69.27
	SD	7.95	9.49	10.14	13.47	16.31	16.07	15.36	11.23	11.19	9.63	10.33
	P-value [Intra-group]		0.003	0.032	0.001	0.020	0.242 NS	0.274 NS	0.001	0.001	0.001	0.001
P-value [Inter-]		0.873 NS	0.941 NS	0.973 NS	0.009	0.876 NS	0.930 NS	0.627 NS	0.584 NS	0.922 NS	0.912 NS	0.307 NS
MAP												
F	Mean	96.47	92.52	91.3	93.77	103.97	99.27	98.07	93.47	87.43	85.77	83.17
	SD	9.62	10.5	11.92	17.51	11.43	11.78	17.86	19.36	16.46	13.56	12.25
	P-value [Intra-group]		0.002	0.019	0.309 NS	0.002	0.182 NS	0.587 NS	0.288 NS	0.001	0.001	0.001
P	Mean	94.6	91.47	89.59	81.5	101.43	97.47	91.63	87.53	86	84.73	83.93
	SD	7.61	8.56	9.1	12.36	16.53	16.79	14.72	11.72	11.45	8.59	10.03
	P-value [Intra-group]		0.002	0.003	0.001	0.022	0.334 NS	0.231 NS	0.001	0.001	0.001	0.001
P-value [Inter-]		0.408 NS	0.675 NS	0.538 NS	0.003	0.493 NS	0.633 NS	0.133 NS	0.156 NS	0.697 NS	0.726 NS	0.792 NS
Rate Pressure product												
F	Mean	10149.73	9795.13	9802.4	10677.8	12681.73	11963	14343.07	10386.43	9492.33	9085.8	8336.27
	SD	2000.87	1930.55	2490.59	3282.74	2812.35	2915.09	20158.06	2779.83	2475.38	2086.58	1874.18
	P-value [Intra-group]		0.162 NS	0.280 NS	0.304 NS	0.001	0.001	0.253 NS	0.615 NS	0.105 NS	0.007	0.001
P	Mean	15039.23	11321.97	10623.6	9364	13311.77	15959.03	11677.03	13392.07	10153.8	9696.4	9691.9

	SD	23237.67	2260.51	2424.7	2150.41	3054.03	18611.9	2591.89	14271.54	2130.41	2353.36	2147.64
	P-value [Intra-group]		0.389^{NS}	0.305 NS	0.193^{NS}	0.682^{NS}	0.866^{NS}	0.426^{NS}	0.745^{NS}	0.261 NS	0.222 NS	0.220 NS
P-value [Inter-]		0.256^{NS}	0.007	0.201 NS	0.072^{NS}	0.409^{NS}	0.250^{NS}	0.475^{NS}	0.262^{NS}	0.272 NS	0.292 NS	0.012
SPO2												
F	**Mean**	99.77	99.93	99.9	99.93	99.97	100	100	100	100	100	99.97
	SD	0.57	0.25	0.3	0.25	0.18	0	0	0	0	0	0.18
	P-value [Intra-group]		0.999^{NS}	0.999 NS	0.999^{NS}	0.999^{NS}	0.999^{NS}	0.999^{NS}	0.999^{NS}	0.999 NS	0.999 NS	0.999 NS
P	**Mean**	99.7	99.83	99.93	99.97	100	100	100	100	100	100	100
	SD	0.53	0.46	0.25	0.18	0	0	0	0	0	0	0
	P-value [Intra-group]		0.999^{NS}	0.999 NS	0.999^{NS}	0.999^{NS}	0.999^{NS}	0.999^{NS}	0.999^{NS}	0.999 NS	0.999 NS	0.999 NS
P-value [Inter-]		0.642^{NS}	0.302^{NS}	0.647 NS	0.561^{NS}	0.321^{NS}	0.633^{NS}	0.999^{NS}	0.999^{NS}	0.999 NS	0.999 NS	0.321 NS

Values are mean and SD, P-value [Inter-group] by independent sample t test, P-value [Intra-group] by repeated measures ANOVA [RMANOVA}. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant. NS:not significant

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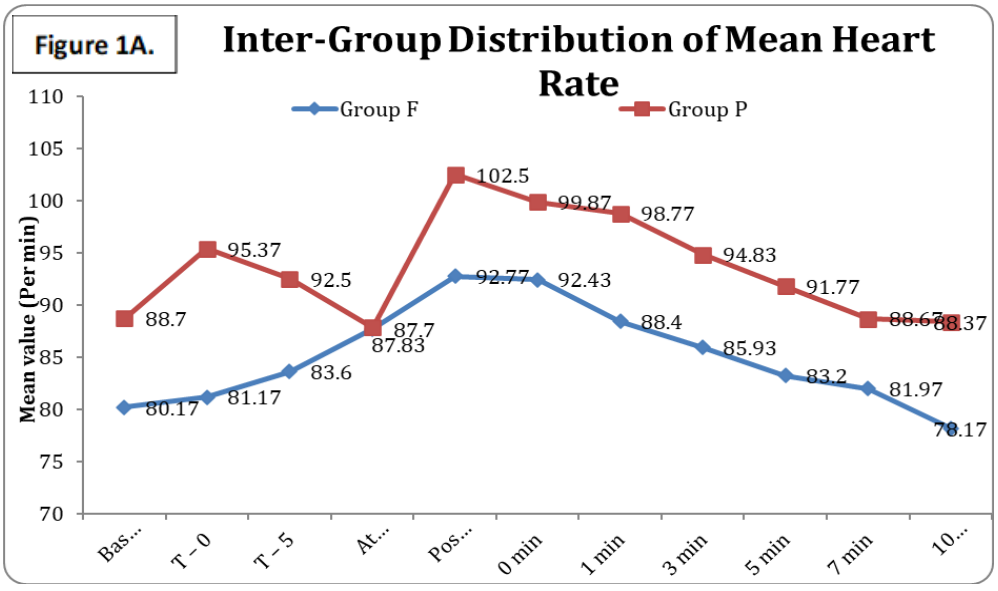
Figure 1(A-F):Graphical representation of inter-group comparison of heart rate, systolic BP, diastolic BP, Mean Arterial Pressure, Rate Pressure and Spo2 of the patients in Group F and Group P.



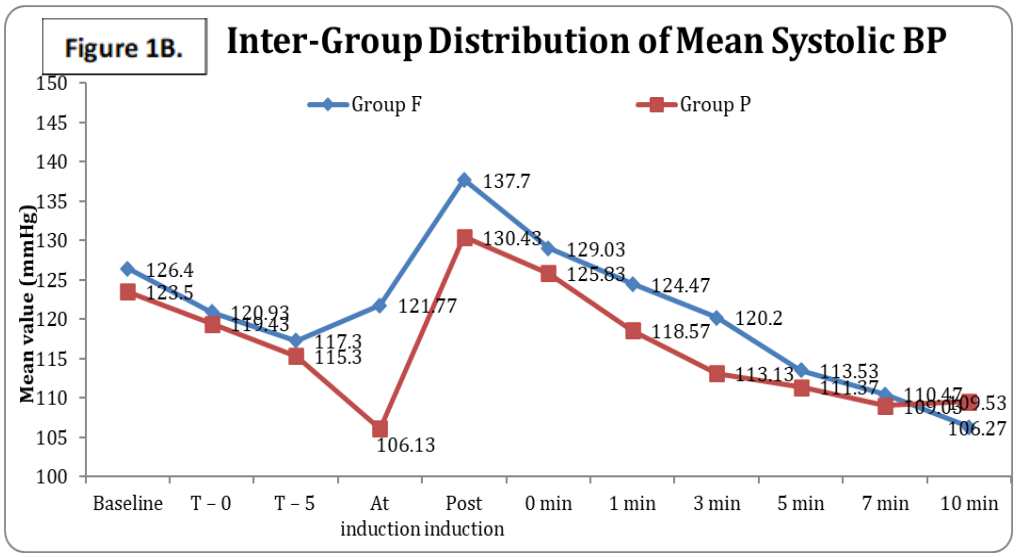


Figure 1B.
Inter-Group Distribution of Mean Systolic BP
Group F
Group P
Mean value (mmHg)
150
145
140
135
130
125
120
115
110
105
100
126.4
123.5
120.93
119.43
117.3
115.3
121.77
106.13
137.7
130.43
129.03
125.83
124.47
118.57
120.2
113.13
113.53
111.37
110.47
109.09
109.53
106.27
Baseline
T – 0
T – 5
At induction
Post induction
0 min
1 min
3 min
5 min
7 min
10 min

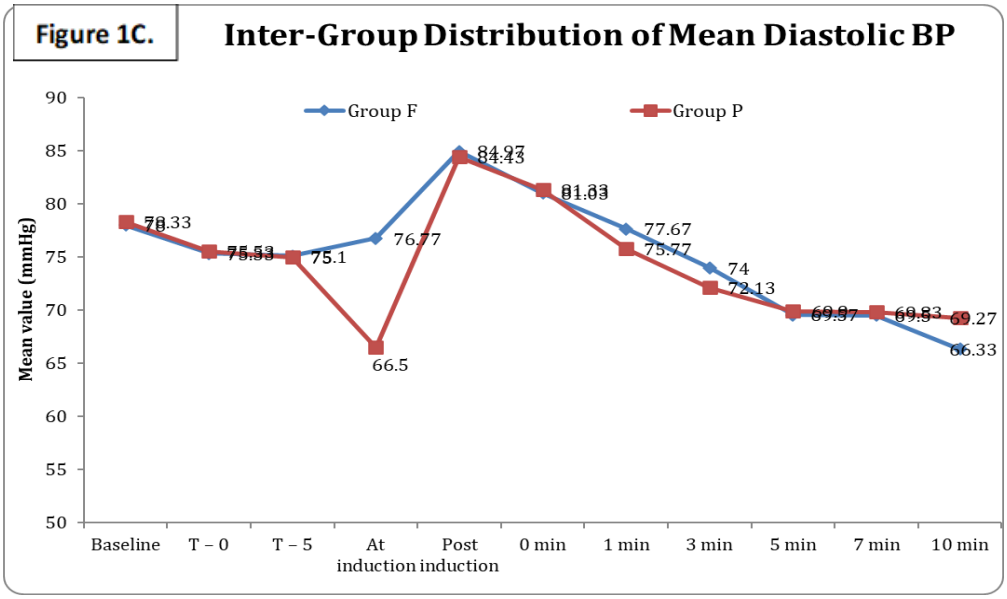


Figure 1C.
Inter-Group Distribution of Mean Diastolic BP
Group F
Group P
Mean value (mmHg)
90
85
80
75
70
65
60
55
50
78.33
75.1
76.77
66.5
84.27
84.43
81.33
77.67
75.77
74
72.13
69.83
69.27
66.33
Baseline
T – 0
T – 5
At induction
Post induction
0 min
1 min
3 min
5 min
7 min
10 min

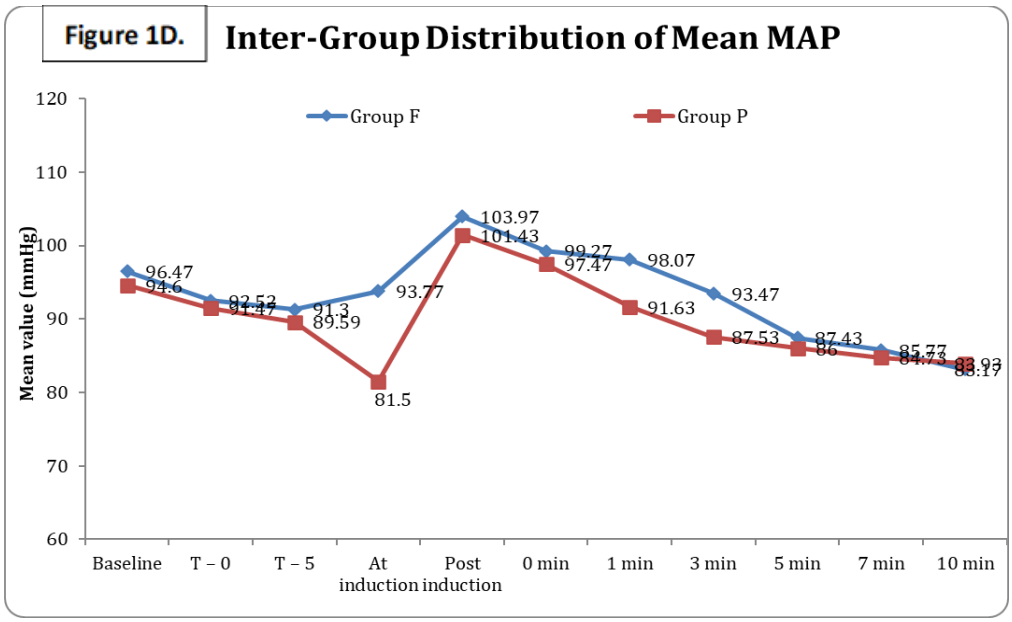
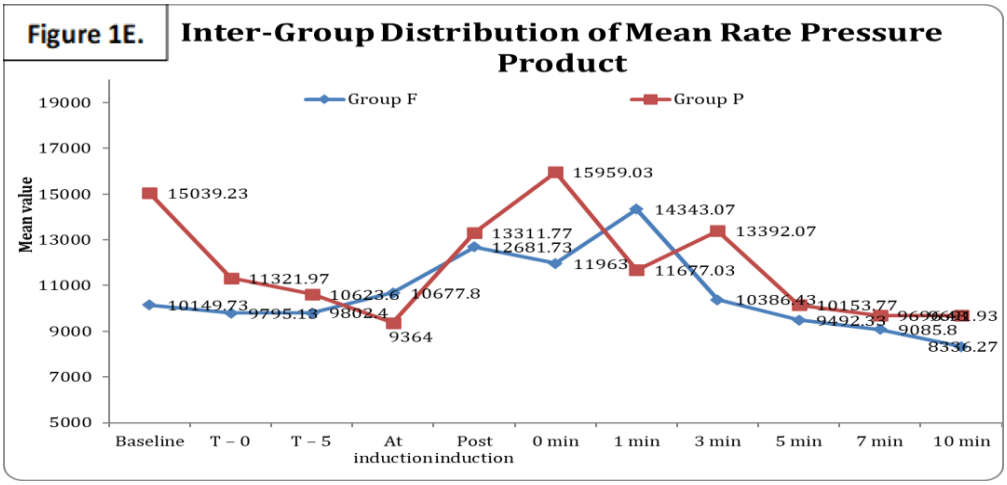
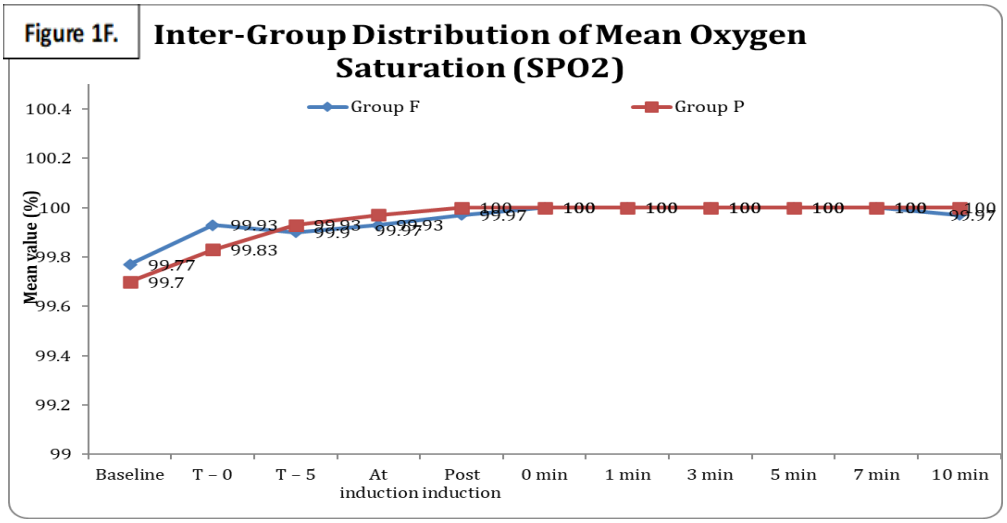


Figure 1D.
Inter-Group Distribution of Mean MAP
Group F
Group P
Mean value (mmHg)
120
110
100
90
80
70
60
96.47
94.6
92.53
91.47
91.3
89.59
93.77
81.5
103.97
101.43
99.27
97.47
98.07
91.63
93.47
87.53
87.43
86
85.77
84.73
83.93
83.17
Baseline
T – 0
T – 5
At induction
Post induction
0 min
1 min
3 min
5 min
7 min
10 min





DISCUSSION

This study compares hemodynamic responses to midazolam-fentanyl (Group F) and midazolam-pentazocine (Group P) during laryngoscopy and intubation, which aligns with and contrasts various prior studies. The comparable age and sex distribution between groups mirrors the demographic balance in studies by Adnet et al. and Heidegger et al., ensuring reliable outcome comparison.[1,2] Group F exhibited more excellent heart rate stability, consistent with Akheela and Chandra's findings on fentanyl's efficacy in blunting cardiovascular responses.[8] Del Río Vellosillo et al. also noted fentanyl's superiority over other opioids in maintaining hemodynamic stability.[9] Group F's lower heart rate at T-0 and post-induction aligns with Feng et al. and Gupta and Tank, who highlighted fentanyl's role in mitigating tachycardic responses to intubation.[4,5]

The SBP and DBP trends in Group F, characterized by significant attenuation at induction and post-induction, mirror results from studies by Hassani et al. and Hoda and Khan, which documented fentanyl's efficacy in hypertensive patients.[3,10] Conversely, pentazocine's comparatively higher SBP and DBP align with Kothari, Sharma, Sadafule, and Karhade, who reported pentazocine's limited ability to attenuate pressor responses.[7,11] The MAP trends observed in this study, where Group F achieved superior control, are consistent with observations by Lee et al. and Swarnamba et al., who emphasized fentanyl's robust hemodynamic effects.[6,12] The higher RPP in Group P at T-0 resonates with findings by Pang et al. and Ugur et al., indicating that pentazocine's analgesic properties might not sufficiently suppress the sympathetic surge associated with laryngoscopy.[13]

The absence of significant differences in SpO2 between the groups at all time points aligns with findings by Collins and Levitan et al., who reported that fentanyl and pentazocine do not impair oxygenation during intubation.[14] Intra-group analysis revealed fentanyl's ability to maintain hemodynamic stability for longer post-induction, consistent with Janeway, who emphasized its benefits in geriatric and high-risk patients.(15)] Additionally, Miller, Poole-Wilson, and Langer highlighted fentanyl's role in modulating myocardial oxygen demand, supporting its observed advantages in this study.[16,17]

LIMITATION

Pentazocine's limited attenuation of hemodynamic responses aligns with findings by Gunalan, Akheela, and Chandra, who noted its inability to entirely suppress stress responses during laryngoscopy, likely due to its partial agonist activity

at opioid receptors.[8,18] In contrast, fentanyl consistently demonstrated superior control of SBP, DBP, MAP, and heart rate, as shown in studies by Albertin et al. and del Río Vellosillo et al.. In contrast, pentazocine underperformed, particularly during laryngoscopy and intubation.[9]

CONCLUSION

This study's results reinforce the existing body of evidence suggesting fentanyl's superiority over pentazocine in achieving hemodynamic stability during laryngoscopy and intubation. These findings are consistent with extensive literature, including studies by Swarnamba et al., Ugur et al., and others, while also highlighting the limitations of pentazocine in this context. Further research could explore combining pentazocine with other agents or optimizing dosing regimens to improve its efficacy in such scenarios.[6,13]

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