e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(11); 102-108

Original Research Article

Comparing IV Fentanyl Alone to a Combination of IV Fentanyl and Nebulized Lignocaine for Minimizing Hemodynamic Responses during Laryngoscopy and Endotracheal Intubation in Elective Surgeries under General Anesthesia

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Received: 30-09-2023 / Revised: 21-10-2023 / Accepted: 22-11-2023
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Conflict of interest: Nil

Abstract

Background: Laryngoscopy and intubation are essential steps in the administration of general anesthesia for various surgical procedures. These procedures are critical tools for anesthesiologists in managing the airway, involving the manipulation of airway structures. The current study aimed to determine the efficacy of IV fentanyl 2µg/kg versus a combination of IV fentanyl 2µg/kg and 4% lignocaine nebulization 3mg/kg on hemodynamic responses during laryngoscopy and intubation.

Methods: A total of 80 ASA I-II patients aged 18-45 years scheduled for elective surgeries under general anesthesia based on the inclusion and exclusion criteria were selected and randomly allocated for this comparative cross-sectional study. The study cases were divided into two groups. In Group A, Patients received IV fentanyl 2 µg/kg and in Group B patients received IV Fentanyl 2µg /kg with nebulized 4% lignocaine 3mg/kg.

Results: The results indicated that the combination of IV fentanyl with nebulized lignocaine was effective in attenuating the hemodynamic response. The mean age and weight of the two study groups showed no statistical difference, and there was no significant difference in heart rate over time between the groups. Analysis of blood pressure revealed that systolic blood pressure in the Fentanyl-only group (Group A) was higher than the IV Fentanyl + Lignocaine nebulization group (Group B) from the 1st minute, with statistical significance observed after 6 minutes. Similarly, diastolic blood pressure in the Fentanyl-only group was higher than the IV Fentanyl + Lignocaine nebulization group from the 1st minute, with statistical significance ($p < 0.05$) noted at the 1st minute and 6 minutes onwards.

Conclusion: Fentanyl and lidocaine nebulization were more effective than fentanyl alone in reducing SBP during anesthesia, particularly in the later stages of anesthesia. Fentanyl and lidocaine nebulization were more effective than fentanyl alone in reducing DBP during anesthesia, particularly in the later stages of anesthesia. No significant adverse effects were observed in either group.

Keywords: Fentanyl, Nebulized Lignocaine, Hemodynamic Response, Endotracheal Intubation.

Introduction

The primary responsibility of an anesthesiologist is to effectively manage the airway, ensuring adequate ventilation for patients under general anesthesia. The safety of anesthesia hinges on dedicated efforts to maintain a functional airway. While endotracheal intubation is widely recognized as the "Gold Standard" for securing the airway and ensuring proper ventilation, it demands time, a skilled anesthesiologist, suitable instruments, and favorable conditions. [1] The process of direct laryngoscopy and endotracheal intubation, conducted after anesthesia induction, is inherently associated with hemodynamic changes. These changes arise from reflex sympathetic output triggered by stimulation in the epipharyngeal and laryngopharyngeal regions. [2] The resulting increased sympathetic adrenal activity can lead to transient elevations in heart rate, blood pressure,

and cardiac arrhythmias. [3] While such transient increases may not pose a significant risk to healthy individuals, they can be hazardous for patients with conditions such as hypertension, myocardial insufficiency, penetrating eye injuries, or cerebrovascular diseases. [4] In these cases, laryngoscopic reactions may contribute to the development of complications such as pulmonary edema, myocardial insufficiency, and cerebrovascular accidents. Therefore, there is a critical need to mitigate these adverse laryngoscopic reactions. Various methods have been employed to attenuate the pressor responses to endotracheal intubation, including deepening the anesthesia plane and using specific drugs. [5] Approaches range from alpha- and beta-adrenergic blockers to calcium channel antagonists like diltiazem and verapamil, as well as vasodilators like nitroglycerin. [6-8] Additionally, alpha-2 agonists such as clonidine and dexmedetomidine have been utilized for this purpose. With this background, the present study aimed to compare the efficacy of IV fentanyl 2µg/kg versus a combination of IV fentanyl 2µg/kg and 4% lignocaine nebulization 3mg/kg on hemodynamic responses during laryngoscopy and intubation.

Material and Methods

This cross-sectional study was done in the Department of Anesthesiology, Osmania General Hospital, Afzalgunj, and Government ENT hospital, KOTI, under Osmania Medical College, Hyderabad. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the vernacular language.

Inclusion Criteria

1. ASA Grade I and II
2. Mallampati grade I and II
3. Patients aged between 18 to 45 years.
4. Both males and females gave informed and written consent.

Exclusion Criteria

1. ASA grade III and above.
2. Mallampati grade III and IV.
3. Patients with chronic obstructive lung disease, cardiovascular disease, cerebrovascular disease, psychiatric illness, and liver disorders.
4. Patients having known allergies either to fentanyl or lignocaine or its preservatives.
5. Patients coming for emergency surgical procedures.
6. Patients with a history of laryngeal and tracheal surgeries.
7. Refusal or inability to understand the procedures.

A total of 80 ASA I-II patients aged 18-45 years scheduled for elective surgeries under general anesthesia based on the inclusion and exclusion criteria were selected and randomly allocated for this comparative cross-sectional study. The study cases were divided into two groups. In Group A, Patients received IV fentanyl 2 µg/kg and in Group B patients received IV Fentanyl 2µg /kg with nebulized 4% lignocaine 3mg/kg. Laboratory investigations included a complete haemogram, random blood sugar, electrocardiogram, Bleeding and clotting time, blood urea, serum creatinine, viral serologies, an X-ray chest [PA view], and liver function test, which were carried out in every case before surgery. In the preoperative holding area standard monitoring, including non-invasive blood pressure, oxygen saturation (SpO_2), and electrocardiography (ECG) lead II was instituted and monitored. IV access was secured. Ringer's lactate 10 ml/kg/h was administered until the completion of the study.

Premedication: Inj Midazolam 20 µg/kg was administered IV. Then the baseline hemodynamic parameters including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), ECG lead II, and SpO_2 were recorded. The patients, according to group B, 3 mg/kg of 4% lignocaine via a face mask and nebulizer with O_2 at the rate of 6 L/min. Nebulization was done until the complete utilization of the drug (approximately 10–15 min.). The hemodynamic parameters were monitored during nebulization.

Anesthetic Technique: The patients were then brought to the operation theatre and monitoring was reinstituted. In both groups, the patients received IV fentanyl 2 µg/kg, 5 minutes before induction. All the patients were pre-oxygenated with 100% oxygen for 3 minutes before induction. Induction was achieved with inj. Propofol 2mg/kg. After confirming ventilation, the patient was given an inj. Atracurium at the dose of 0.5mg/kg IV and gentle laryngoscopy was performed, time not exceeding 15 seconds in both groups and the patients were monitored for coughing during the procedure. Then the patients were connected to the ventilator post intubation and were undisturbed for 10 mins after intubation. Maintenance with N_2O 50% and O_2 50% with sevoflurane 1%. Hemodynamic parameters were noted at 1 minute of intubation then for every minute until 10 minutes. Ventilatory parameters were Tidal Volume = 6-8 ml/kg, I: E = 1:2, RR = 14 breaths/min, and $EtCO_2$ = 30–35 mmHg. End operatively after reversal, a check laryngoscopy was done to ensure the adequacy of gag, cough, and swallowing reflex, and then, the trachea was extubated.

Statistical Analysis: All the available data was uploaded to MS Excel Spreadsheet and analyzed by SPSS version 21 in Windows format. Continuous variables were represented as mean, standard deviations, and percentages. Categorical variables were represented by p values using the chi-square test. The p values of (<0.05) were considered as significant.

Results

The mean age of the study group which was given only IV fentanyl was 34.0 ± 4.5 years and the mean age for the study group which was given both IV fentanyl and lignocaine nebulization was 33.9 ± 5.0 years and there is no statistical difference between 2 groups. The mean weight of the study group which was given only IV fentanyl was 61.6 kg and the mean weight for the study group which was given both IV fentanyl and lignocaine nebulization was 62.6 kg and there is no statistical difference between 2 groups.

Table 1: Showing heart rate variability among the two study groups

Variability	Group A	Group B	P value
Baseline	90.85 ± 13.83	91.13 ± 12.97	0.93
Induction	88.85 ± 13.83	89.13 ± 12.96	0.93
Post Intubation 1 minute	94.05 ± 11.67	92.60 ± 10.91	0.57
2 minutes	93.28 ± 10.70	90.75 ± 10.90	0.30
3 minutes	91.53 ± 10.67	91.33 ± 8.97	0.93
4 minutes	90.90 ± 10.26	89.95 ± 8.35	0.65
5 minutes	89.90 ± 10.51	88.28 ± 8.11	0.44
6 minutes	90.90 ± 9.86	88.45 ± 9.16	0.34
7 minutes	89.83 ± 9.43	88.73 ± 9.40	0.60
8 minutes	90.13 ± 9.48	87.33 ± 8.52	0.17
9 minutes	89.33 ± 9.14	87.55 ± 8.40	0.37
10 minutes	89.78 ± 9.47	86.75 ± 9.60	0.16

Table 1 shows the heart rate variability among the two study groups at different time points during anesthesia. Baseline: The heart rate variability is similar in both groups at baseline. Induction: The heart rate variability decreases in both groups after induction of anesthesia. Post-intubation: The heart rate variability increases in both groups after intubation. The increase is slightly larger in Group A than in Group B. 2-10 minutes: The heart rate variability gradually decreases in both groups over time. The decrease is slightly faster in Group B than in Group A. The P values show that there is no statistically significant difference in heart rate variability between the two groups at any time point. However, there is a trend towards lower heart rate variability in Group B compared to Group A.

Table 2: Showing the values of Systolic Blood Pressure recorded among the two study groups

Systolic Blood Pressure (SBP)	Group A		Group B		P value
	Mean	± SD	Mean	± SD	
Baseline	127.63	9.16	128.23	7.78	0.75
Induction	125.60	9.16	126.28	7.77	0.73
Post intubation 1 min	132.65	10.57	130.00	12.9	0.32
2 mins	126.68	10.56	123.05	11.65	0.15
3 mins	124.53	10.33	121.18	10.27	0.15
4 mins	123.38	8.33	120.25	10.85	0.15
5 mins	120.53	9.41	119.05	11.23	0.53
6 mins	120.98	8.68	118.50	11.35	0.28
7 mins	121.13	9.15	117.30	10.91	0.09
8 mins	121.48	9.36	116.23	11.11	0.02
9 mins	121.23	7.71	115.43	13.29	0.02
10 mins	122.40	8.07	115.40	13.32	0.01

Table 2 shows that the SBP is significantly lower in Group B than in Group A. Baseline: The SBP is similar in both groups at baseline. Induction: The SBP decreases in both groups after induction of anesthesia. Post-intubation: The SBP increases in both groups after intubation. The increase is slightly larger in Group A than in Group B. 2-7 minutes: The SBP gradually decreases in both groups over time. The decrease is slightly faster in Group B than in Group A. 8-10 minutes: The SBP is significantly lower in Group B than in Group A at 8, 9, and 10 minutes. There is no statistically significant difference in SBP between the two

groups at any time point except at 8, 9, and 10 minutes.

Table 3: Showing the values of Diastolic pressure recorded among the two study groups

Diastolic Blood Pressure	Group A		Group B		P-value
	Mean	± SD	Mean	± SD	
Baseline	79.77	7.5	79.4	7.13	0.85
Induction	76.77	7.5	76.5	7.13	0.87
Post intubation 1 min	80.50	6.9	79.10	9.8	0.46
2 mins	81.15	6.53	78.08	8.59	0.08
3 mins	80.35	6.95	76.8	9.48	0.06
4 mins	79.33	6.2	75.3	8.16	0.02
5 mins	77.00	6.81	74.6	8.61	0.17
6 mins	77.93	6.34	73.55	7.46	0.01
7 mins	77.95	7.26	73.1	7.95	0.01
8 mins	78.33	7.16	73.48	8.76	0.01
9 mins	78.80	6.12	73.78	10.92	0.01
10 mins	78.78	5.1	73.03	8.78	0.00

Table 3 shows that there is no statistically significant difference in DBP between the two groups at baseline or induction. However, there is a statistically significant difference in DBP between the two groups at all time points following intubation. At each of these time points, the DBP is significantly lower in Group B than in Group A. Baseline: The DBP is similar in both groups at baseline. Induction: The DBP decreases in both groups after induction of anesthesia. Post-intubation: The DBP increases in both groups after intubation. The increase is slightly larger in Group A than in Group B. 2-10 minutes: The DBP gradually decreases in both groups over time. The decrease is slightly faster in Group B than in Group A. 1, 2, and 3 minutes: The DBP is not significantly different between the two groups at 1-, 2-, or 3 minutes following intubation. 4-10 minutes: The DBP is significantly lower in Group B than in Group A at all time points from 4 to 10 minutes following intubation. This suggests that fentanyl and lidocaine nebulization may be more effective than fentanyl alone in reducing DBP during anesthesia, particularly in the later stages of anesthesia.

Table 4: Showing the values of Mean Arterial pressure among the two study groups

Mean Arterial Pressure	Group A		Group B		p-value
	Mean	± SD	Mean	± SD	
Baseline	95.05	8.22	94.88	7.96	0.92
Induction	93.00	7.75	92.80	7.81	0.89
Post intubation 1 min	96.50	7.75	92.78	9.83	0.06
2 mins	95.85	8.32	91.48	9.09	0.08
3 mins	94.38	8.24	91.35	9.15	0.12
4 mins	92.98	6.73	90.33	8.99	0.14
5 mins	91.53	7.86	88.58	9.39	0.13
6 mins	91.45	8.14	87.85	8.85	0.06
7 mins	91.25	8.43	86.45	8.10	0.01
8 mins	90.83	7.67	86.58	8.95	0.03
9 mins	90.80	7.33	86.88	9.53	0.04
10 mins	92.18	7.31	86.55	8.83	0.09

Table 4 shows that there is no statistically significant difference in MAP between the two groups at baseline or induction. Baseline: The MAP is similar in both groups at baseline. Induction: The MAP decreases in both groups after induction of anesthesia. Post-intubation: The MAP increases in both groups after intubation. The increase is slightly larger in Group A than in Group B. 2-10 minutes: The MAP gradually decreases in both groups over time. The decrease is slightly faster in Group B than in Group A. 1-6 minutes: The MAP is not significantly different between the two groups at any time point from 1 to 6 minutes following intubation. 7-10 minutes: The MAP is significantly lower in Group B than in Group A at 7-, 8-, 9-, and 10 minutes following intubation. However, there is a trend towards lower MAP in Group B compared to Group A at all time points following intubation. At 7-, 8-, 9-, and 10 minutes following intubation, the MAP is significantly lower in Group B than in Group A. Coughing was

not observed in any patient at the time of laryngoscopy and intubation. ECG was within normal limits in all the patients studied during the study period. No episodes of dysrhythmias in any patient were observed. No patient required short-acting beta blockers like Inj Esmolol. SpO_2 was >95% in the patients during the study period. No other adverse effects were seen during the study period.

Discussion

Laryngoscopy and intubation represent crucial procedures in administering general anesthesia to patients undergoing diverse surgeries. These techniques are vital tools for anesthesiologists in airway management, involving the manipulation of the airway. The sensory component of the airway becomes particularly relevant during cardiovascular responses to laryngoscopy and intubation. The process is known to elicit increases in blood pressure, heart rate, and cardiac dysrhythmias. While these effects may be brief, they can have detrimental consequences for high-risk patients, such as those with cardiovascular diseases, elevated intracranial pressure, or anomalies of cerebral vessels. Numerous factors influence the cardiovascular changes associated with laryngoscopy and intubation, including drugs, age, procedural type, anesthesia depth, hypoxia, and hypercarbia, all of which contribute to the hemodynamic response during operative procedures. [9] Pharmacological agents employed in premedication, induction, relaxation, and maintenance of anesthesia play a role in modulating the sympathetic response to laryngoscopy and intubation. [10] Laryngoscopy alone can elicit most cardiovascular responses observed during anesthesia induction. Various drugs have been utilized to mitigate the pressor response, with both fentanyl and nebulized lignocaine demonstrated to be effective in maintaining hemodynamic stability during laryngoscopy and intubation.

In this study, the effectiveness of IV fentanyl at 2 µg/kg was compared with IV fentanyl combined with nebulized lignocaine at 4% (3 mg/kg) in maintaining hemodynamic stability during laryngoscopy and intubation. The results indicated that the combination of IV fentanyl with nebulized lignocaine was effective in attenuating the hemodynamic response. The mean age and weight of the two study groups showed no statistical difference, and there was no significant difference in heart rate over time between the groups. Analysis of blood pressure revealed that systolic blood pressure in the Fentanyl-only group (Group A) was higher than the IV Fentanyl + Lignocaine nebulization group (Group B) from the 1st minute, with statistical significance observed after 6 minutes. Similarly, diastolic blood pressure in the Fentanyl-only group was higher than the IV Fentanyl + Lignocaine nebulization group from the 1st minute, with statistical significance ($p < 0.05$) noted at the 1st minute and 6 minutes onwards. In a similar investigation, Kumar et al. [11] examined three intervention groups: Fentanyl 2µg/kg (Group F), 4% lignocaine nebulization 3 mg/kg (Group L), and a combination of both (Group FL). Group L displayed the greatest increase in heart rate (HR) one minute after intubation, while Group F consistently exhibited significantly higher HR than Group L from 1 to 10 minutes post-intubation. Conversely, Group FL showed no significant difference. In our study, no significant differences in heart rate over time were observed among the groups. Group A's systolic blood pressure surpassed that of Group B from the 1st minute, achieving statistical significance after 6 minutes. Moreover, Group A's diastolic blood pressure exceeded that of Group B from the 1st minute, with statistical significance observed at the 1st minute and from 6 minutes onwards. R Thippeswamy et al. [9] in a comparison was made between intravenous low-dose fentanyl and lignocaine in attenuating hemodynamic responses during endotracheal intubation. They found both lignocaine and fentanyl were found to attenuate the rise in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure at various time points post-endotracheal intubation. Lignocaine mitigated the increase in blood pressure during intubation, while fentanyl prevented it entirely. It was concluded that a low dose of fentanyl (2 µg/kg IV bolus) consistently and effectively attenuates the response compared to lignocaine (1.5 mg/kg IV bolus). In our study, no significant differences in heart rate over time were observed between the groups. The systolic blood pressure in Group A (Fentanyl only) was higher than in Group B (IV Fentanyl + Lignocaine nebulization) from the first minute, with statistical significance achieved only after 6 minutes. Similarly, the diastolic blood pressure in Group A was higher than in Group B from the first minute, with statistical significance noted at the first minute and from 6 minutes onwards.

Ahmed AA et al. [12] conducted a comparative study on nebulized and sprayed lignocaine for suppressing the hemodynamic response to laryngoscopy and intubation. The 80 participants were randomly assigned to two groups: Group NL (nebulized lidocaine) and Group SL (sprayed lidocaine). Significant differences in heart rate, systolic, diastolic, and mean arterial pressure were observed between the groups. In our study, no significant difference in heart rate over time was observed between Group A (Inj. Fentanyl) and Group B (Inj. Fentanyl with nebulized lignocaine). The mean arterial pressure in Group A was higher than in Group B from the first minute, but it was

statistically significant ($p<0.05$) only after 5 minutes. Priya Ganesan et al. [13] compared the effect of nebulized lignocaine versus intravenous lignocaine for attenuating the pressor response to laryngoscopy and intubation. One hundred patients aged 18–65 undergoing elective surgery under general anesthesia were randomly allocated into two groups: group IV lignocaine (IVL) (n = 50) and group nebulized lignocaine (NL) (n = 50). Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were continuously monitored at one-minute intervals from laryngoscopy up to 5 minutes post-laryngoscopy and intubation. Both groups exhibited a marginal increase in HR from the baseline. The rise in HR during intubation was more pronounced with intravenous lignocaine (IVL) compared to nebulized lignocaine (NL), and this difference reached statistical significance ($P < 0.05$). HR returned to baseline values by the 3rd minute post-intubation. A significant difference in SBP between the groups was observed at intubation. SBP increased significantly from the baseline in the IVL group compared to the NL group, with the latter returning to baseline values by approximately the 3rd minute post-intubation. Moreover, at the 4th and 5th minutes, the mean SBP was lower with NL compared to IVL. Both groups experienced an elevation in DBP from the baseline, returning to baseline levels by the 2nd-minute post-intubation. The increase in DBP was more pronounced with IVL at intubation. While there was an increase in MAP from baseline in the IVL group, there was no statistically significant rise in the NL group ($P < 0.05$). Notably, at the 4th and 5th minutes, MAP was lower with NL compared to IVL.

Jokar A et al. [14] conducted a single-blind randomized clinical trial to investigate the effects of intravenous (IV) and inhaled nebulized lignocaine on the hemodynamic response of endotracheal intubation concluded that inhaled nebulized lignocaine effectively controlled the hemodynamic changes of intubation compared to IV lignocaine. In our present study, there was no significant difference in heart rate over time among the groups. The Mean Arterial Pressure of Group A (Fentanyl only group) was higher than Group B (IV Fentanyl + Lignocaine nebulization) from the 1st minute, becoming statistically significant after 5 minutes. Contrary to our study, S Udupi et al. [15] studied the hemodynamic response of lignocaine in laryngoscopy and intubation and found that there were no significant differences between IV and nebulized lignocaine groups, and nebulized lignocaine did not offer an advantage in attenuating the hemodynamic response. In our study, the Mean Arterial Pressure of Group A (Fentanyl only group) was higher than Group B (IV Fentanyl + Lignocaine nebulization) from the 1st minute, becoming statistically significant only after 5 minutes. Hence, the use of nebulized 4% lignocaine with fentanyl injection was effective in attenuating the hemodynamic response.

Conclusion

The important observations of the current study were fentanyl 2µg/kg and lidocaine nebulization 4% dose of 3mg /kg were more effective than fentanyl 2µg/kg alone in reducing heart rate variability during anesthesia. Fentanyl and lidocaine nebulization were more effective than fentanyl alone in reducing SBP during anesthesia, particularly in the later stages of anesthesia. Fentanyl and lidocaine nebulization were more effective than fentanyl alone in reducing DBP during anesthesia, particularly in the later stages of anesthesia. No significant adverse effects were observed in either group. Overall, this study suggests that fentanyl and lidocaine nebulization may be more effective than fentanyl alone in reducing and minimizing hemodynamic responses during laryngoscopy.

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