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Original Article

The Haemodynamic Response to Endotracheal Intubation at Different Time of Intravenous Fentanyl Given During Induction in Elective Surgeries

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ABSTRACT

Introduction: Fentanyl is a potent short acting synthetic opioid agonist which is similar to morphine and confers analgesic effect at a greater extent. Fentanyl targets opioid receptors present in brain neuroanatomical structures that better hold the speaking, pain and emotions and so on.

Aim: The main aim was to study and compare the effects of fentanyl at varying time intervals before anaesthesia induction on haemodynamic response to laryngoscopy and endotracheal intubation and side effects of the drugs in patients undergoing surgical procedures under general anaesthesia.

Materials and Method: Study population (50 patients) was randomly divided by computer generated numbers into 2 groups with 25 patients in each group. Group F5: received Inj. Fentanyl 2µg/kg 5 min before Anaesthesia induction. Group F10: received Inj. Fentanyl 2µg/kg 10 min before Anaesthesia induction. Standard monitors like ECG, NIBP, and pulse-oximeter were applied and baseline parameters [SpO2, Heart rate (HR), Systolic blood pressure (SBP), and Diastolic blood pressure (DBP), Mean arterial pressure (MAP)] were recorded.

Results: The difference in mean HR, systolic blood pressure, mean diastolic blood pressure, mean arterial pressure were increased compared with baseline and statistically highly significant with p value of <0.0001after anaesthesia induction, 1min, 2min, 3min, 5min and 10min of endotracheal intubation. No significant changes occurred in HR, SBP at baseline and after premedication inn between the groups. An increase in the HR, SBP was observed in both the groups after intubation However, in group F5 the increase was seen to a lesser extent and lower compared to group F10 at all time points. The changes observed with regard to DBP, MAP and RPP were same as that seen in SBP, indicating that successful suppression of stress response was achieved in group F5.

Conclusion: Our results indicated that 5 minutes prior to induction was the most effective injection time of fentanyl at a dose of 2 mcg/kg to prevent the hemodynamic responses to tracheal intubation.

Key Words: *Fentanyl, laryngoscopy, endotracheal intubation, haemodynamic response.*

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INTRODUCTION

Laryngoscopy and tracheal intubation result in a stress response characterized by increased activity of the sympathoadrenal axis caused by the inevitable stimulation of laryngopharynx. [1] Stimulation of the sympathoadrenal axis leads to an increase in the levels of circulatory catecholamines, which in turn causes a rise in heart rate (HR) and blood pressure(BP), It is important especially in high-risk patients with a significant coronary artery or cerebrovascular diseases. This can precipitate myocardial oxygen imbalances, and often dysrhythmias**.** This response reaches its maximum level within 1 minute and ends within 5-10 minutes after intubation.[2]

Numerous efforts have been made and are still in process to attenuate the haemodynamic response; Among the recommended procedures intravenous lignocaine[3], esmolol[4], fentanyl and dexmedetomidine[5]are commonly used drugs.

Fentanyl is a potent short acting synthetic µ-selective opioid agonist that potentially blunt the laryngoscopy reflex.[6]Fentanyl targets opioid receptors present in brain neuroanatomical structures.The timing of fentanyl administration was also found important during induction in order to obtain the most stable haemodynamic status.[7]

This study was designed to study and compare the effects of fentanyl at varying time intervals before anaesthesia induction on haemodynamic response to laryngoscopy and endotracheal intubation and side effects of the drugs in patients undergoing surgical procedures under general anaesthesia

AIMS AND OBJECTIVES

The objectives were

1. To study the effectiveness of iv fentanyl 2µg/kg in attenuating the haemodynamic response to direct laryngoscopy and intubation at 5 and 10 minutes before anaesthesia induction.
2. To observe the effects of drugs during intra operative and postoperative period.

MATERIALS AND METHODS

After obtaining institutional ethical committee approval of Government Medical College Kota, Rajasthan, this study was done from July 2020 to Aug. 2023. Written informed consent was obtained from all the patients and their relative before starting the study.

Inclusion Criteria:

Adult patients scheduled for elective surgeries under general anaesthesia with ASA Grade I or II and Mallampati airway assessment - Grade I or II were included in this study.

Exclusion Criteria:

Patient with history of known allergies to study drugs or anaesthetic drugs used in the study and patients in whom laryngoscopy and intubation proved to be prolonged >60seconds and patients with negative consent were excluded in this study.

Study population (50 patients) was randomly divided by computer generated numbers into 2 groups with 25 patients in each group.

Group F5: received inj. **Fentanyl** 2 µg/kg 5 min before Anaesthesia induction.
Group F10: received inj. **Fentanyl** 2 µg/kg 10 min before Anaesthesia induction.

Study Method:

Patients were premedicated 30 min before anaesthesia induction with inj. ondansetron 0.15 mg/kg iv and inj. glycopyrrolate 4µg/kg iv and inj fentanyl 2 µg/kg iv was given 5min or10min before induction according to respective groups. After premedication all the patients were preoxygenated with 100% oxygen by mask for 3 minutes. Induction was achieved with inj. propofol 2 mg/kg iv till loss of eyelash reflex and inj. succinylcholine 2mg/kg was given iv. After 30 seconds, Laryngoscopy was done using standard macintosh blade. Oral Intubation with appropriate size, high volume low pressure, disposable, portex cuffed endotracheal tube was done within 30 seconds. After checking bilateral air entry equal, endotracheal tube was fixed and positive pressure ventilation was started. Heart rate, SBP, DBP, MAP were recorded for baseline, after premedication, after induction, after laryngoscopy and intubation at 1, 2, 3, 5 and 10 minutes. Anaesthesia was maintained with 50% O_2 + 50% N_2O + Sevoflurane. For muscle relaxation inj. Atracurium 0.5 mg/kg iv was given as loading dose and 0.1 mg/kg maintenance dose. Intraoperative vitals were monitored.

An observation was made related to adverse effects of drugs, laryngospasm, bronchospasm or desaturation and anaesthesia related problems.

STATISTICAL ANALYSIS

All patients data were recorded in the proforma of study. Data were expressed as mean value ± standard deviation (SD). Quantitative data were analysed using 't'-test and qualitative by chi square test. Statistical calculations were carried out using statistical package for the social sciences (SPSS version 22.0). Changes in haemodynamic variables from baseline and a comparison of means were analysed by unpaired t-test for each time interval. P-value < 0.05 was considered statistically significant. P value < 0.001 was considered highly significant. P value > 0.05 was considered as not-significant.

RESULTS

Demographic distribution (Age, Weight, Height, Gender) between Group C and Group D were comparable.

Table 1 Demographic Distribution

Parameters	Group F5	Group F10	P Value
Age	43±10.24	45.1±9.20	0.499
Weight	60.55±6.59	61.65±8.62	0.653
Height	151.05±6.89	152.2±7.41	0.614

Table 2: Parameters

Parameters	Group F5	Group F10	P Value
Mallampatti Grade (I &II)	9 &11	11 & 9	0.752
ASA Grade (I & II)	12 & 8	9 & 11	0.527
Mean Duration of Surgery(MIN)	90.85±30.30	94±31.56	0.749

There was no significant difference between both groups in terms of Mallampatti Grade (I &II), ASA Grade (I & II) and Mean Duration of Surgery.

Table 3: Changes in Mean Heart Rate:

Time Interval	Group F5	Group F10	P Value
Baseline	76.4±3.56	76.75±4.02	0.7723
After Pre-medication	77.6±4.69	77.85±4.20	0.8600
After Anaesthesia Induction	80.65±3.28	87.55±2.98	<0.0001
1 min after of Endotracheal Intubation	87.5±2.24	96.9±2.63	<0.0001
2 min after of Endotracheal Intubation	87.9±2.79	97.1±3.48	<0.0001
3 min after of Endotracheal Intubation	80.35±5.92	94.2±6.45	<0.0001
5 min after of Endotracheal Intubation	80.2±2.82	87.4±3.57	<0.0001
10 min after of Endotracheal Intubation	79.7±4.60	84.85±2.70	<0.0001

The difference in mean HR was increased compared with baseline heart rate and statistically highly significant with p value of <0.0001 in patients after anaesthesia induction, 1 minute, 2 minute, 3 minute, 5 minute and 10 minutes of endotracheal intubation.

Table 4: Changes in Mean Systolic Blood Pressure (mm of Hg):

Time Interval	Group F5	Group F10	P value
Baseline	122.15±5.13	122.25±2.71	0.9390
After Pre-medication	123.7±3.25	123.6±2.60	0.9150
After Anaesthesia Induction	125.1±3.01	138.7±5.24	<0.0001
1 min after Endotracheal Intubation	126.7±2.79	162.2±5.36	<0.0001
2 min after Endotracheal Intubation	127.7±2.30	163.6±2.46	<0.0001
3 min after Endotracheal Intubation	126.6±3.90	154.45±2.89	<0.0001
5 min after Endotracheal Intubation	125.7±3.51	132.75±5.00	<0.0001
10 min after Endotracheal Intubation	124.7±2.73	132.35±6.49	<0.0001

The difference in mean systolic blood pressure was increased compared with baseline systolic blood pressure and statistically has highly significant value in participants after anaesthesia induction, 1 minute, 2 minute, 3 minute, 5 minute and 10 minutes of endotracheal intubation.

TABLE 5: Changes in Mean Diastolic Blood Pressure:

Time Interval	Group F5	Group F10	P value
Baseline	79±2.47	77±4.01	0.0652
After Pre-medication	79.4±2.84	78.5±3.17	0.3503
After Anaesthesia Induction	80.3±2.85	89±3.01	<0.0001
1 min after Endotracheal Intubation	81.25±1.48	92.55±3.98	<0.0001
2 min after Endotracheal Intubation	81.3±1.63	92.85±4.97	<0.0001
3 min after Endotracheal Intubation	79.55±1.90	91.15±4.36	<0.0001
5 min after Endotracheal Intubation	78.2±2.89	91.1±3.32	<0.0001
10 min after Endotracheal Intubation	77.8±2.59	88.2±4.05	<0.0001

The participants mean diastolic blood pressure was increased compared with baseline systolic blood pressure and statistically highly significant with p value of <0.0001 after anaesthesia induction, 1 minute, 2 minute, 3 minute, 5 minute and 10 minutes of endotracheal intubation.

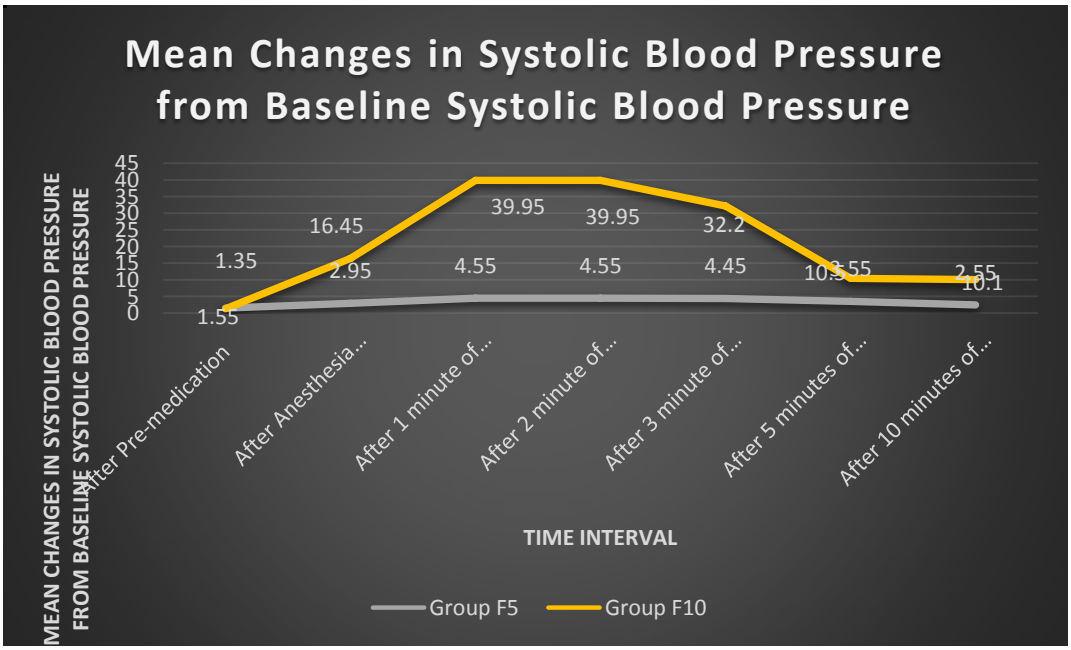

Figure 1: Comparison of Mean Changes in SBP at different intervals from SBP at Baseline

The mean SBP increase was found to be significantly least in group F5 with p value of <0.0001 (HS) as compare to group F10 at all point of time.

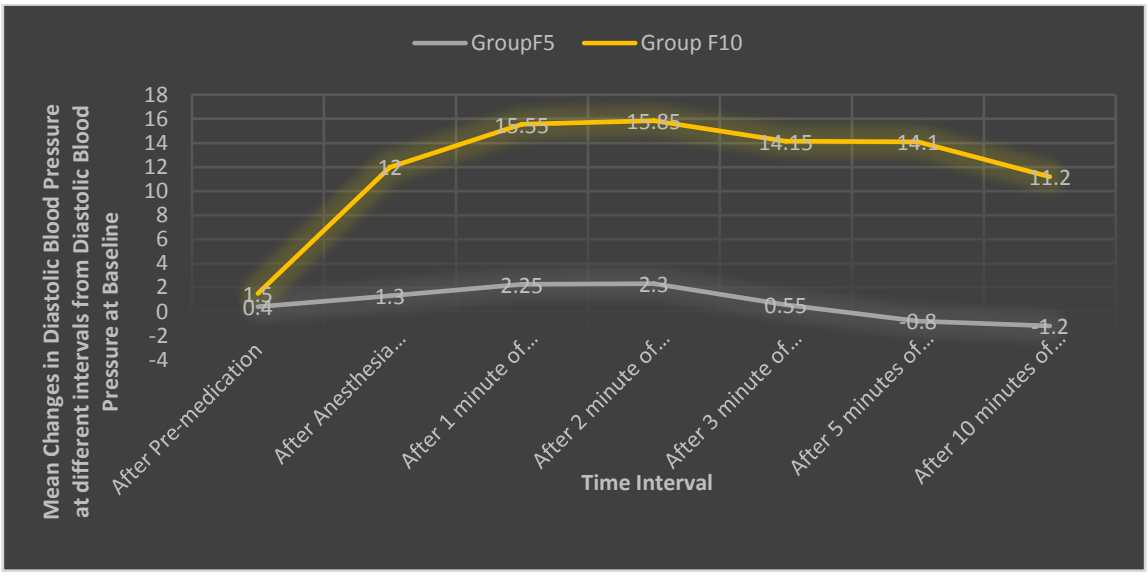

Figure 2: Comparison of Mean Changes in DBP at different intervals from DBP at Baseline

The mean DBP increase was found to be significantly least in group F5 with p value of <0.0001 (HS) as compare to group F10 at all point of time.

Table 6: Changes in Mean MAP

Time Interval	Group F5	Group F10	P value
Baseline	93.38±2.04	92.08±2.63	0.0888
After Pre-medication	94.17±2.40	93.53±2.24	0.3888
After Anaesthesia Induction	95.23±1.95	105.57±2.54	<0.0001
1 min after Endotracheal Intubation	96.4±1.31	115.77±3.48	<0.0001
2 min after Endotracheal Intubation	96.77±1.27	116.43±3.27	<0.0001
3 min after Endotracheal Intubation	95.23±1.67	112.25±2.64	<0.0001
5 min after Endotracheal Intubation	94.03±2.36	104.98±1.91	<0.0001
10 min after Endotracheal intubation	93.43±1.90	102.92±3.40	<0.0001

The participants mean arterial pressure was increased compared with baseline arterial pressure were statistically highly significant with p value of <0.0001 after anaesthesia induction, 1 minute, 2 minute, 3 minute, 5 minute and 10 minutes of endotracheal intubation. The MAP increase was found to be significantly least in group F5 with p value of <0.0001 (HS) at all point of time.

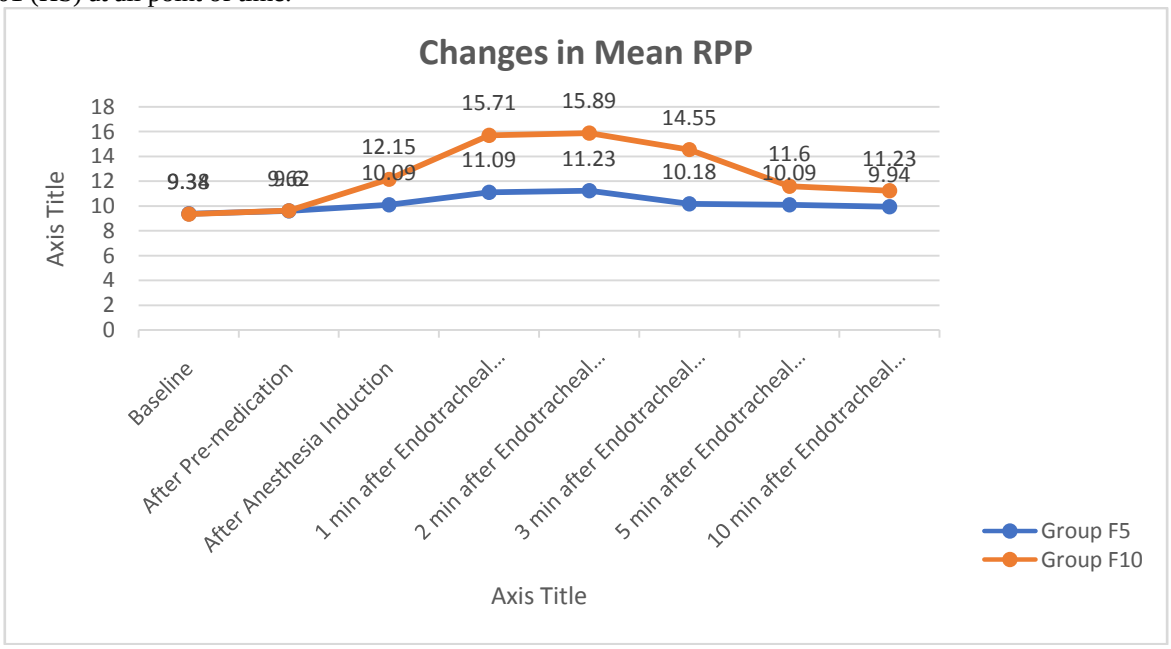

Figure 3: comparison of changes in mean RPP between both groups

The participants have difference in mean Rate pressure product was increased compared with baseline arterial pressure and statistically highly significant with p value of <0.0001 after anaesthesia induction, 1 minute, 2 minute, 3 minute, 5 minute and 10 minutes of endotracheal intubation in comparison of both groups. RPP increase was found to be significantly least in group F5 with p value of <0.0001 (HS) at this point of time.

DISCUSSION

After induction of anaesthesia, laryngoscopy and tracheal intubation result in a stress response characterized by increased activity of the sympathoadrenal axis caused by the inevitable stimulation of laryngopharynx.[8] This heightened response is found to begin within 5 second. A peak response is seen in 1–2 min, returning to baseline within 5 min.[9]

Among the various opioids used, fentanyl has been extensively studied as it has a good analgesic property along with the opposing the hemodynamic instability during laryngoscopy and intubation. Also, compared to other commonly used opioids, it has a relatively short time of onset and duration making it ideal for this purpose. A number of studies have been carried out to determine the appropriate dose of fentanyl required to achieve an adequate suppression of the hemodynamic response. Also, many authors have looked into the efficacy of using combination of drugs with fentanyl. However, studies specifically dwelling into the timing of administration of fentanyl are very scarce. Hence the present

study was carried out to determine the timing of administration before intubation and the effect on various hemodynamic parameters which determine the response.

There was no statistically significant difference between these groups with regards of age, weight and height (Tables 1) which helped for comparison making the groups comparable. Both the groups had similar sex distribution, Mallampatti grade distribution, ASA grade. (Tables 2)

Comparing groups with each other, the variation in baseline HR, SBP, DBP and MAP after anaesthesia induction, 1 minute, 2 minute, 3 minute, 5 minute and 10 minute of Endotracheal Intubation, the differences were statistically highly significant between group F5 & F10.

Similar to this study, **Cheng Yeonteong, chien-chung Huang(2020)**[10] conducted a prospective, double-blind, randomised-controlled clinical trial. The study included 145 patients over 20 years belonging to ASA physical class I and II, undergoing elective surgeries. In this study fentanyl 2 mcg/kg was administered at 1, 2, 3 minutes before intubation. Recordings of haemodynamic parameters were carried out for 10 minutes after induction. fentanyl 2 mcg/kg administered 2 minutes before intubation showed lesser haemodynamic responses than the groups in which fentanyl was given 1 and 3 minutes prior ($p < 0.05$).

Similar study, fentanyl 2 mcg/kg was administered at 1, 3, 5, or 10 min prior to tracheal intubation, carried out by Ko et al. Comparing HR and BP between baseline and 1 minute post-intubation. [11]Ko et al concluded that "Our study showed that fentanyl, at a dose of mcg/kg given 5 minutes before intubation, most effectively attenuated the increases in all four circulatory variables. Fentanyl given at 1 and 10 minutes preintubation did not protect against increases in arterial blood pressure or HR."

The study by **Seong-Hoon K and Dong-Chan Kim (1998)** [12]also shows results similar with findings of our study that SAP, DAP and MAP were higher 1 min after intubation compared to baseline within the groups in both the studies.

In a dose finding study, **Yukari (2013)** [13] found that fentanyl 2 mcg/kg and 4 mcg/kg is the optimal dose in normotensive patients and those with hypertension to reduce the stress response to tracheal intubation.

CONCLUSION

Our results indicate that 5 minutes prior to induction is the most effective injection time of fentanyl at a dose of 2 mcg/kg to prevent the hemodynamic responses to tracheal intubation. Fentanyl given at 5 minutes before induction resulted in lesser increase in HR, SBP, DBP and MAP compared to 10 minutes prior to induction. Compared with both groups, group F5 had best Hemodynamic stability.(Group F5 received Inj. Fentanyl 2 microgram/kg 5 minutes before anaesthesia induction).

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