Original Article

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To Find Optimal Time for Intravenous Fentanyl (1.5μg/Kg) to Attenuate Hemodynamic Response to Laryngoscopy and Intubation

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Abstract

Background: Laryngoscopy is often accompanied with a haemodynamic pressor response, which could be hazardous and needs to be suppressed. The aim is to find optimal timing for intravenous low dose Fentanyl (1.5μg/Kg) to attenuate hemodynamic response to laryngoscopy and intubation. **Subjects and Methods:** The study was conducted on 100 adult patients for elective surgery under general anaesthesia and endotracheal intubation. The haemodynamic changes (Heart rate and Blood Pressure) were noted after administering intravenous Fentanyl at 3 (Group I) or 5 minutes (Group II). **Results:** Changes in haemodynamic parameters were more significant in Group I as compared to Group II. **Conclusion:** Fentanyl when given 5 minutes before intubation effectively attenuates the haemodynamic response to laryngoscopy and endotracheal intubation.

Keywords: Low Dose Fentanyl, Haemodynamic Response, Endotracheal Intubation

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Introduction

Laryngoscopy for endotracheal intubation is a painful invasive stimulus in anaesthesia, often accompanied with a haemodynamic pressor response, first described by Reid and Brace in 1940.[1] Hypertension and tachycardia is due to reflexsympathetic discharge and increased plasma norepinephrine concentration.[2,3]This could be hazardous in patients with hypertension, coronary heart disease, intracranial pathology and hyperactive airways, hence there is a need to suppress it. Many attempts have been made to attenuate this response, like swift, gentle and quick laryngoscopy by an experienced anaesthetist, intubating in deep plane of anaesthesia, using a myriad variety of drugs including local anaesthetics, ganglion blockers,arterial dilators, venodilators, beta blockers, alpha 2 agonist, calcium channel blockersand opioids. Opioids, especially Fentanyl, are being used increasingly to effectively attenuate the stress response to laryngoscopy and intubation and its efficacy has been proved by many studies. Fentanyl is a commonly used drug in anaesthesia practice and low dose rarely cause any side effects. Administration of Fentanyl at the right time before intubation reduces the dose necessary to mask adverse hemodynamic responses to tracheal intubation.[4–22]

Aim

To find the optimal time for injection of intravenous low dose Fentanyl (1.5 μg/kg) to attenuate haemodynamic response to laryngoscopy and intubation during induction of anaesthesia

Subjects and Methods

The study was conducted at a community hospital from January to March 2020, after approval from Ethical committee. We studied 100 patients posted for elective surgery under general anaesthesia and endotracheal intubation. All patients were assessed in pre-anaesthesia check-up clinic as routinely done in our hospital, and written informed consent obtained from those enrolled in the study

Inclusion Criteria

All patients between 18-65 years, ASA physical status I & II and modified Mallampatti score I & II

Exclusion Criteria

Patient with anticipated difficult airway, obesity, full stomach, emergency surgery, hypertension, coronary artery disease, valvular heart disease, cerebrovascular accidents, chronic

renal failure, on antihypertensive or cardiac drugs and in whom intubation time exceeded 15 seconds.

Blocked randomization was used to assign patients into 2 groups-

Group I: 50 patients were given i/v Fentanyl (1.5 μg/kg) 3 minutes before intubation

Group II: 50 patients were given i/v Fentanyl (1.5 μg/kg) 5 minutes before intubation

Preoperatively Tab. Diazepam 5mg and Tab. Ranitidine 150 mg was given the night before and 2 hours prior to surgery. In Operating Room, standard multi-parameter monitor (ECG, NIBP, Pulse Oximeter) was connected to patient and average of first two BP values recorded 3 minutes apart before induction noted as baseline values.

Patients were preoxygenated for 3 minutes. Inj.Glycopyrrolate (0.2mg) and Inj.Midazolam (40μg/kg) was given at 0 minutes. Inj.Fentanyl (1.5μg/kg) was given 3 minutes or 5 minutes before laryngoscopy according to the assigned study group. Inj.Propofol 2mg/kg was given at 3^{rd}minute followed by Inj.Vecuronium 0.1mg/kg. All patients were ventilated using bag and mask with 100% oxygen for 3 minutes. Laryngoscopy and intubation was done at 6^{th} minute and time taken for same was noted. If laryngoscopy time exceeded 15 seconds, that patient was excluded from statistical analysis.

After confirmation of tube position, anesthesia was maintained with 67% nitrous oxide, 33% oxygen and 1% Isoflurane. Any kind of stimulation was avoided for 5 minutes after intubation. The values of haemodynamic parameters - Heart rate and NIBP (systolic, mean and diastolic) were recorded in a proforma at baseline, pre-intubation, during intubation and every one minute upto 5^{th} minute after intubation. The baseline and 1 minute post-intubation values of heart rate and NIBP were compared.

Data Entry and Analysis

The data was entered in EPI 6 statistical software and analyzed using SPSS10 for Windows software. Continuous data were expressed as mean + Standard Deviation (SD) and simple percentages were calculated for dichotomous variables. Student's 't' test was used to test for statistical significance of differences observed between and within groups in case of continuous variables. P value of 0.05 was considered as statistical level of significance and p value greater than 0.05 was considered insignificant.

Results

Out of one hundred patients enrolled, two (one in each group) were excluded from statistical analysis because time taken for laryngoscopy exceeded 15 seconds.

Baseline Haemodynamic Parameters - There was no significant difference in baseline values of heart rate and noninvasive blood pressure (systolic, diastolic and mean) among the groups, as shown in [Table 1] below.

Haemodynamic Parameters at 1 minute post-intubation - It is clear from [Table 2] below that in Group I there were statistically significant changes in all haemodynamic parameters when compared to baseline values. In contrast, Group II showed statistically significant change only in heart rate. Also, it is seen that the changes were more evident in Group I as compared to Group II and statistically significant, with p values <0.007 at 1 minute post-intubation.

Systolic Blood Pressure - The rise at 1 minute post-intubation as compared to baseline was statistically significant in Group I while it was minimal in Group II

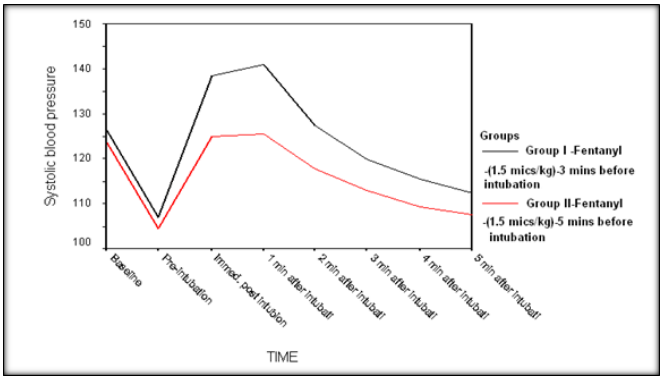

Figure 1: Systolic Blood Pressure

D iastolic Blood Pressure - The rise at 1 minute post-intubation when compared to baseline was statistically significant only in group I [Table 4].

Mean Blood Pressure – As seen in [Table 5], the rise in mean blood pressure at 1 minute post-intubation when compared to baseline was statistically significant only in group I.

Heart Rate Change –[Table 6] shows that an increase in heart rate from baseline was statistically significant in Group I, it did not return to baseline until 5^{th} minute and remained well above group II. In group II, the rise from baseline was significant but less than that in group I. Also in Group II, values remained significantly closer to baseline and returned closer to baseline much earlier after intubation as compared with Group I.

Discussion

Many studies reported a beneficial effect of Fentanyl as adjuvant to barbiturate induction. Dahlgren et al, [14] (1981) showed that 5μg/kg of Fentanyl given before intubation effectively

Table 1: Baseline Haemodynamic Parameters

Haemodynamic	Group I		Group II		T test (p value)
	Mean	SD	Mean	SD	
Systolic BP (mm Hg)	126.53	13.79	123.74	12.51	0.30*
Diastolic BP (mm Hg)	73.48	8.25	73.39	5.92	0.95*
Mean BP (mm Hg)	92.39	10.08	91.18	7.86	0.51*
Heart Rate (beats/min)	80.51	10.24	82.86	10.74	0.27*

(*p> 0.27, p value of significance being < 0.05)

Table 2: Haemodynamic Parameters at 1 minute post-intubation

Haemodynamic parameter	Group I	Group II	T test (p value)
	Mean + SD	Mean + SD	
Systolic BP (mm Hg)Φ	141.12 + 22.99*	125.35 + 18.31	$<0.001^{\Phi}$
Diastolic BP (mm Hg)Φ	82.65 + 15.19*	75.22 + 10.92	0.007^{Φ}
Mean BP (mm Hg)Φ	104.41 + 17.77*	94.31 + 13.57	0.002^{Φ}
Heart Rate (beats/min)Φ	99.80 + 13.37*	90.98 + 12.47*	0.001^{Φ}

(*significant at p = 0.05 within group) Φ significant at p = 0.05 between two groups

Table 3: Systolic Blood Pressure (SBP) €

SBP (mm Hg)	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	126.53	13.79	123.74	12.51
Pre-intubation	107.12*	11.20	104.41*	12.85
During intubation	138.49*	24.60	124.94	22.02
2 min post-intubation	127.43	16.24	117.82	19.33
3min post-intubation	119.90*	17.00	113.12*	16.03
4 min post-intubation	115.35*	15.79	109.16*	15.60
5 min post-intubation	112.47*	12.96	107.57*	12.63

(* significant at p = 0.05) € compared with the corresponding baseline value

Table 4: Diastolic Blood Pressure (DBP) €

Diastolic BP (mm Hg)	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	73.48	8.25	73.39	5.92
Pre-intubation	64.06*	11.07	61.80*	8.76
During intubation	81.39*	16.79	76.04	12.72
2 min post-intubation	71.65	12.98	69.27	9.96
3min post-intubation	67.55	10.80	65.45	9.79
4 min post-intubation	66.33	11.50	65.73	9.53
5 min post-intubation	65.43	11.03	64.00*	9.28

(*significant at p = 0.05) € compared with the corresponding baseline value

Table 5: Mean Blood Pressure (MBP) €

Mean BP (mm Hg)	Group I		Group II	
	Mean	Std. deviation	Mean	Std. deviation
Baseline	92.39	10.08	91.18	7.86
Pre-intubation	78.94*	10.72	76.98*	9.35
During intubation	102.57*	19.20	93.18	16.06
2 min post-intubation	91.41	13.60	87.90	12.39
3min post-intubation	87.02	12.88	83.00	11.09
4 min post-intubation	85.73	16.47	81.53*	10.15
5 min post-intubation	81.37*	11.41	78.94*	9.23

(*significant at p=0.05) € compared with the corresponding baseline value

Table 6: Heart Rate (HR) Φ

Heart rate (beats per min)	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	80.51	10.24	82.86	10.74
Pre-intubation	76.16*	9.51	77.14*	10.38
During intubation	95.90*	13.42	88.43*	12.86
2 min post-intubation	94.00*	10.15	89.24*	10.64
3min post-intubation	90.65*	11.50	85.98*	9.65
4 min post-intubation	88.82*	11.19	82.63	9.77
5 min post-intubation	85.65*	10.85	81.45	9.70

(*significant at p = 0.05 level) Φ compared with the corresponding baseline values

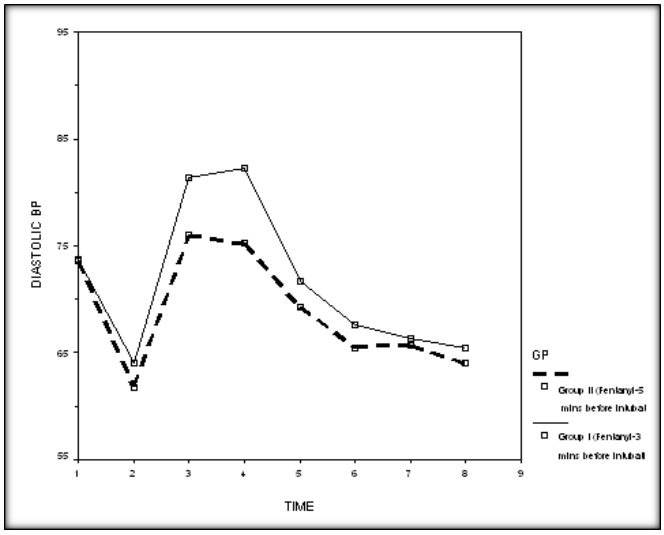

Figure 2: Diastolic Blood Pressure

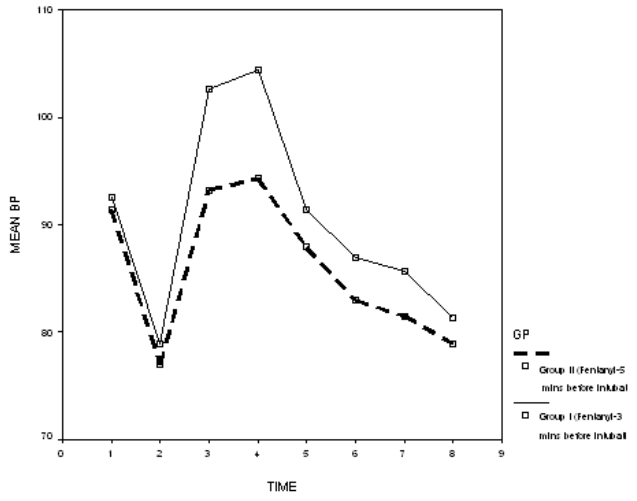

Figure 3: Mean Blood Pressure

reduces hemodynamic stress responses to intubation in neurosurgical patients.

Black et al, [12](1984) and Kay et al, [13](1985) found complete attenuation of haemodynamic intubation response with 5μg/kg Fentanyl.

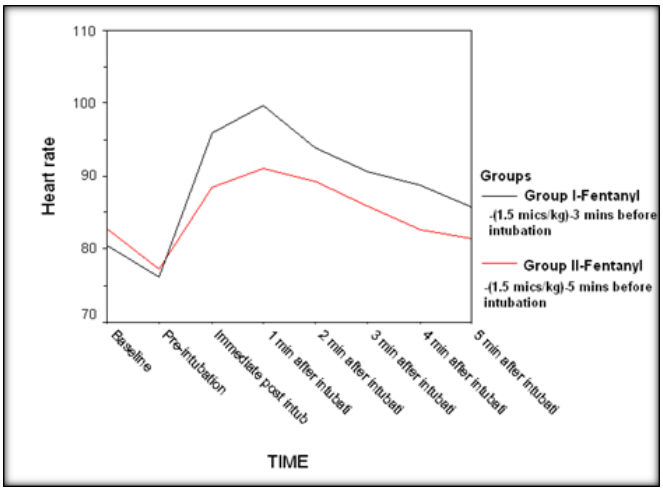

Figure 4: Heart Rate

By using 8μg/kg Fentanyl bolus, Martin et al, [17] demonstrated that Fentanyl abolishes both heart rate and blood pressure increases related to tracheal intubation during induction with Thiopentone.

Splinter et al, [11] noticed that both 1.5μg/kg and 3μg/kg Fentanyl attenuated the response to laryngoscopy and intubation in geriatric patients and that a dose of 1.5 μg/kg effectively blunted increase in circulatory parameters.

Chung and Evans, [4] found attenuation of increase in heart rate and arterial pressure during the first minute after intubation with 3μg/kg Fentanyl in geriatric patients when compared with controls.

Ko et al, [21] (1998) studied effect of Fentanyl (2μg/kg) given at 1, 3, 5 or 10 min before tracheal intubation and concluded that the most effective time is 5 min before intubation. In their study the 1 min post-intubation systolic arterial pressure values increased significantly relative to baseline values in patients who received Fentanyl 1 min or 10 minutes before intubation. But these haemodynamic values were not significantly different relative to their baseline values in patients who received Fentanyl 3 min or 5 minutes before intubation. However the heart changes were not seen in patients who received Fentanyl 5 minute before intubation only.

In our study, group I had an increase in mean systolic blood pressure from baseline (126.5 + 13.7 mm Hg) to 1 min post-intubation (141.12 + 23 mm Hg) which is statistically significant. This finding was in concordance to the study by Ko et al (140 + 20 mm Hg). In group II, the increase from baseline (126.5 + 13.7 mm Hg) to 1 min post-intubation (125.35 + 18.31 mm Hg) was lower and not statistically significant. When compared between the groups, this rise was more in group I (141.12 + 23 mm Hg) than group II (125.35 + 18.31 mm Hg) and was statistically significant. This finding was also in accordance with the study by Ko et al, Chung et al and Splinter et al. [11]

In group I, increase in mean blood pressure from baseline (92.39 + 10.08 mm Hg) to 1 min post-intubation (104.41 + 17.77 mm Hg) was statistically significant and in concordance to the study by Ko et al (110 + 16 mm Hg). In group II, increase in mean blood pressure from baseline (92.39 + 10.08 mm Hg) to 1 min post-intubation (94.31 + 13.57 mm Hg) was minimal and not statistically significant. When compared between the groups this rise was more in group I (104.41 + 17.77 mm Hg) than group II (94.31 + 13.57 mm Hg) and was statistically significant, similar to the study by Ko et al.

In group I, increase in mean diastolic blood pressure from baseline (73.48 + 8.25 mm Hg) to 1 min post-intubation (82.65 + 15.19 mm Hg) was statistically significant and in concordance to study by Ko et al (94 + 14 mm Hg). In group II, the increase from baseline (73.39 + 5.92 mm Hg) to 1 min post-intubation (75.22 + 10.92 mm Hg) was minimal and not statistically significant. When compared between the groups, this rise in mean systolic blood pressure was more in group I (82.65 + 15.19 mm Hg) than group II (75.22 + 10.92 mm Hg) and was statistically significant. This finding was also in accordance with the study by Ko et al.

In group I there was statistically significant increase in mean heart rate from baseline (80.5 + 10.2) to that recorded at 1 minute post-intubation (99.8 + 13.4), in concordance to study by Ko et al (92 + 19). In our study this increase in heart rate was more compared to the study by Ko et al. This may be attributed to the smaller dose of Fentanyl (1.5 μg/kg) used in the present study, indicating importance of optimal time of injection of Fentanyl especially when smaller dose is used. Patients in group II showed a minimal increase in mean heart rate from baseline (82.9 + 10.7) to that recorded at 1 minute post-intubation (90.9 + 12.5). This increase in heart rate was not statistically significant. This finding was also in accordance with the study by Ko et al.

Previous investigators have given Fentanyl from 1 to 10 minutes before intubation but right timing of injection before intubation has not been well mentioned. Our study showed that Fentanyl when given in a dose of 1.5 μg/kg, 5 minutes before intubation, most effectively attenuated the increase in all four haemodynamic parameters (systolic BP, diastolic BP, mean arterial pressure and heart rate).

Several limitations must be addressed regarding the design of this study. We studied 100 scheduled surgical patients allocated into 2 groups, and the sample size might have been insufficient for exploring statistical significance. As our study included only ASA I and II patients, extending these results to other ASA classes cannot be assumed and needs further study

in those particular groups. Collection of haemodynamic data was not blinded in our study. However, the haemodynamic data was stored in the memory of the monitor and outcomes were assessed using the clinical parameters. No subjective measures were used as outcome in this study reducing bias and error. To the best of our knowledge, no published study has established a link between brief changes in blood pressure, heart rate or intracranial pressure and long term clinical outcomes. This should also be addressed in future studies.

Conclusion

Optimal time of injection of intravenous low dose Fentanyl (1.5 μg /kg to adequately attenuate hemodynamic response to laryngoscopy and endotracheal intubation was found to be 5 minutes before intubation.

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