

Original Research Article

Comparison of Two Different Doses of Fentanyl in Attenuation of Haemodynamic Responses during Laryngoscopy & Endotracheal Intubation

Abhijit Mohite¹, Divakar Patil², Jyotsna Paranjpe², Vikas Kumar¹, Jitendra Dorkar³, Kavita Jadhav⁴

¹PG Student, ²Professor, ³Assistant Professor, ⁴Senior Resident,
Dept of Anaesthesia, B.V.D.U. Medical College & Hospital, Sangli, Maharashtra.

Corresponding Author: Abhijit Mohite

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ABSTRACT

Introduction: Pressor responses to laryngoscopy and intubation have been associated with sympathetic and parasympathetic responses like hypertension, tachycardia due to increased plasma catecholamine concentrations. Premedication with fentanyl attenuates pressor response to laryngoscopy and intubation.

Aims and Objectives: To evaluate and compare effects of 2 different doses of fentanyl 1mcg/kg and 2mcg/kg in attenuating pressor response to laryngoscopy and intubation.

Methods: 75 patients aged 18-60 years of either sex of ASA grade I and II scheduled for elective surgery under general anaesthesia were randomly divided into 3 groups. All patients were uniformly premedicated, 10 mins before induction. Group I received normal saline 5cc (control group), Group II received Inj. Fentanyl 1mcg/kg and Group III received Inj. Fentanyl 2mcg/kg IV. After induction with thiopentone and succinylcholine; laryngoscopy and intubation was done. HR, SBP, DBP were recorded for all three groups before premedication (baseline), during laryngoscopy & intubation and 30 seconds, 1 min, 2min, 5min and 10min after intubation. Data was analyzed and compared with paired 't' test.

Results: HR and BP levels were lower during and after laryngoscopy and intubation than baseline levels in Group II and III than Group I. But in Fentanyl 2 mcg/kg group amount of increase in HR, SBP, DBP were lower compared to 1 mcg/kg without any adverse effects.

Conclusion: Fentanyl 2 mcg/kg is more effective than 1 mcg/kg in attenuating pressor response to intubation and provides more stable hemodynamic profile without any adverse effects.

Keywords: Fentanyl, Laryngoscopy, Endotracheal Intubation, Haemodynamic response.

INTRODUCTION

Laryngoscopy and intubation in the lightly anaesthetized patient is associated with significant increase in HR and BP for short duration, which was well tolerated by healthy patients but not in patient with cardiovascular disease. These changes occur from reflex sympathetic discharge resulting from pharyngeal and laryngeal stimulation with increase in plasma

concentration of epinephrine and norepinephrine. [1,2] The pressure response to laryngoscopy and endotracheal intubation has been recognized since long. In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and intubation. [3] The rise in pulse and blood pressure are usually transitory, variable and unpredictable. These changes are of no consequence and are well

tolerated by healthy individuals. But in patients with hypertension, heart disease and coronary artery disease, the pressure response can result in an increase in the cardiac workload. [4] The pressure response also assumes great significance in neurosurgical patients. [5]

Many methods have been identified to attenuate these responses including intravenous and inhalational agents, narcotics, vasodilators, adrenergic and calcium blockers. [6-10] Fentanyl citrate has been identified as an effective agent in this regard. Fentanyl is effective in blunting pressure response to laryngoscopy and intubation with different potency and different dose titration. [11] Of course it would have some side effects like respiratory depression and chest wall rigidity. But with doses used in clinical setting to attenuate this pressure response, side effects are minimal.

This study was therefore designed to compare the two different doses of fentanyl citrate that is 1microgram/kg and 2microgram/kg in attenuation of hemodynamic effects during laryngoscopy and intubation.

Aims and Objectives:

1. To observe the cardiovascular response to direct laryngoscopy and oral endotracheal intubation ASA physical status I and II, normotensive individuals; in respect of following parameters,
 - i. Pulse rate
 - ii. Systolic arterial blood pressure
 - iii. Diastolic arterial blood pressure
 - iv. Mean arterial blood pressure
2. To observe, if there is any role of intravenous fentanyl administration before laryngoscopy and endotracheal intubation; in attenuating the changes in above mentioned parameters.
3. To study the side effects of fentanyl.

MATERIALS AND METHODS

After obtaining approval from the institutional ethical committee, we studied

75 patients posted for surgery under general anaesthesia and requiring orotracheal intubation. We have conducted the study over a period of two years and analysed the data statistically. These patients were randomly divided into three groups.

Group I – Normal saline 5 cc. (control group)

Group II – Inj. Fentanyl 1mcg/kg IV

Group III - Inj. Fentanyl 2mcg/kg IV.

All patients belonged to ASA I & II of both sexes aged 18-60 years were included in this double blinded parallel grouped comparative randomized study.

Exclusion Criteria:

- Patient's refusal.
- Known allergy to the trial drugs.
- ASA III or more.
- Emergency surgeries.
- Patients with difficult intubation.
- Patients with bronchospastic disease.
- Patients on beta blockers.

A detailed pre-anaesthetic evaluation of each case was done after noting the medical history, a thorough systemic examination was carried out to detect the presence of any systemic disorder. Routine and special investigations were done accordingly. All patients were kept nil by orally 6-8hrs prior to surgery. All patients were premedicated with Inj Glycopyrrolate 0.2 mg iv, Inj Ondansetron 4mg iv, Inj Ranitidine 50 mg iv and Inj Midazolam 1mg i.v 10 min before giving study drug. Baseline Pulse, blood pressure, SPO₂, ECG were recorded before premedication.

Group I received normal saline, Group II received Inj Fentanyl 1mcg/kg i.v and Group III received inj. fentanyl 2mcg/kg i.v. All the agents were diluted in 5 ml distilled water and injected i.v slowly over 1 minute. After 3 min of oxygenation and administration of the study drugs, induction was done with Thiopentone sodium 5% i.v till the loss of eyelid reflexes and Inj suxamethonium 2mg/kg i.v. Laryngoscopy and intubation was

performed 90 seconds after the administration of succinylcholine. All the patients were intubated with Macintosh curve blade laryngoscope within a period of 15 seconds and we have excluded the patient who had taken more than 15 seconds for intubation. Total time taken for intubation after injection of study drug was 5 minutes in all patients. Anaesthesia was maintained with O₂-N₂O (50%-50%) & sevoflurane 1%. Injection vecuronium was used for muscle relaxation. Patients were not stimulated during the observation period and surgery was allowed to start after 15 min of intubation.

Pulse, blood pressure, oxygen saturation were monitored continuously and recorded before giving the study drug (baseline), during laryngoscopy and intubation then after 30 seconds and 1,2,5,10 minutes post-intubation. The patient's ECG (lead II) was monitored by the attending anesthetist for arrhythmias and ST-T changes.

At the end of surgery anaesthesia was reversed with inj. neostigmine 0.05 mg/kg i.v and inj. glycopyrrolate 0.08 mg/kg i.v. All the patients were monitored in recovery room for the pulse, blood pressure and SPO₂. Patients were observed intraoperatively and postoperatively for any complication like arrhythmias, bradycardia, nausea, vomiting, respiratory depression, sedation, muscular rigidity and pruritus. Unpaired 't' test was used for analysis of data between groups. Results were considered significant for P values < 0.05. The Statistical software namely SPSS 11.0 were used for the analysis of the data.

OBSERVATIONS AND RESULTS

All three groups were comparable with respect to age, sex and weight (Tab: 1). Baseline SBP, DBP and MAP were comparable between all three groups. Increase in SBP, DBP and MAP during intubation was more in group I and II compare to group III, which was clinically and statistically very highly significant (P<0.001). Even 10 minutes after intubation SBP in group I was significantly higher compare to group II and III (P<0.001) (Tab:3). Statistically significant difference in DBP between three groups also last up to 10 min after intubation (Tab:4).

Table: 1. Demographic data

	Group I	Group II	Group III
Age (years)	32.92±12.44	38.20±12.08	31.32±12.57
Sex (M/F)	13/12	12/13	10/15
Weight (kg)	58.12±9.84	62.72±9.87	51.68±8.47

Baseline mean heart rate in all three groups was comparable (P>0.05) to baseline. All three groups showed rise in HR after intubation. But difference in HR between two study groups (II & III) at any time interval was statistically insignificant (P>0.05). In Group I maximum rise in HR was 37.72% at 1 min post intubation which was significant as compare to baseline. In Group II maximum increased in HR was 24.26% at 30 sec post intubation whereas in group III HR increase by only 10.02% after intubation at 30 sec which was significantly smaller (p<0.001) as compare to baseline, also in group III there were significant (p<0.05) fall in HR by 3.44% and 8.52% at 5 min and 10 min post intubation respectively as compared to baseline.

Table: 2. Comparisons of Changes in Mean Heart Rate in Group I, II & III

Time	Group I (HR/ min)	Group I Percentage change from baseline	Group II (HR/min)	Group II Percentage change from baseline	Group III (HR/min)	Group III Percentage change from baseline
Baseline	80.08		77.8		80.2	
During Scopy	103.96	↑ 29.82	94.92	↑ 22	86.92	↑ 8.37
30 sec	107.12	↑ 33.89	96.68	↑ 24.26	88.24	↑ 10.02
1 min	110.28	↑ 37.72	95.8	↑ 23.13	86.76	↑ 8.17
2 min	106.6	↑ 33.11	91.48	↑ 17.58	83.48	↑ 4.08
5 min	97.44	↑ 21.67	85.8	↑ 10.28	77.44	↓ 3.44
10 min	90.64	↑ 13.18	78.88	↑ 1.38	73.36	↓ 8.52

Table: 3. Comparisons of Changes in Mean Systolic Blood Pressure between Group I, II and III

Time	Group I (mm of Hg)	Group I Percentage change from baseline	Group II (mm of Hg)	Group II Percentage change from baseline	Group III (mm of Hg)	Group III Percentage change from baseline
Baseline	127.24		132.24		120.56	
During scopy	151.32	↑ 18.92	150.28	↑ 13.64	127.56	↑ 5.80
30 sec	152.32	↑ 19.71	148.44	↑ 12.25	128.56	↑ 6.63
1 min	153.84	↑ 20.90	145.28	↑ 9.86	122.2	↑ 1.36
2 min	148.88	↑ 17.00	138.56	↑ 4.77	117.52	↓ 2.52
5 min	140.08	↑ 10.09	129.72	↓ 1.90	110.88	↓ 8.02
10 min	133.2	↑ 4.68	118.8	↓ 10.16	106.72	↓ 11.47

Table: 4. Comparison of Changes in Mean Diastolic Blood Pressure between Group I, II and III

Time	Group I (mm of Hg)	Group I Percentage change from baseline	Group II (mm of Hg)	Group II Percentage change from baseline	Group III (mm of Hg)	Group III Percentage change from baseline
Baseline	77.92		78.92		74.56	
During scopy	99.52	↑ 27.72	98.88	↑ 25.29	81.96	↑ 9.92
30 sec	101.16	↑ 29.82	97.68	↑ 23.77	82.48	↑ 10.62
1 min	101.32	↑ 30.03	93.8	↑ 18.85	77.8	↑ 4.34
2 min	97.08	↑ 24.58	88.16	↑ 11.70	73.28	↓ 1.78
5 min	91.2	↑ 17.04	81.84	↑ 3.69	68.56	↓ 8.04
10 min	85.96	↑ 10.31	72.6	↓ 8.00	64.44	↓ 13.57

Table: 5. Comparison of Changes in Mean Arterial Pressure between Group I, II and III

Time	Group I (mm of Hg)	Group I Percentage change from baseline	Group II (mm of Hg)	Group II Percentage change from baseline	Group III (mm of Hg)	Group III Percentage change from baseline
Baseline	94.35		96.69		89.87	
During scopy	116.78	↑ 23.77	116.01	↑ 19.98	97.15	↑ 8.10
30 sec	118.21	↑ 25.28	114.59	↑ 18.51	97.83	↑ 8.85
1 min	118.81	↑ 25.92	110.95	↑ 14.74	92.59	↑ 3.02
2 min	114.34	↑ 21.18	104.95	↑ 8.54	88.03	↓ 2.04
5 min	107.49	↑ 13.92	97.79	↑ 1.13	82.66	↓ 8.02
10 min	101.70	↑ 7.79	87.99	↓ 8.99	78.53	↓ 12.61

Maximum rise in SBP in Group I was 20.90% at 1 min post intubation which was significant ($p < 0.05$) whereas in Group II rise in SBP was maximum (13.64%) during scopy which was statistically significant ($p < 0.001$) while in Group III rise in SBP was significantly smaller 6.63% at 30 sec post intubation. After intubation SBP started decreasing and at 10 min after intubation it was 11.41% lower than basal value in group III whereas in group I, it remained higher than baseline.

Similarly Group I showed more significant rise ($p < 0.05$) in DBP (30.03%) at 1 min post intubation. Also group II showed significant rise in DBP by 25.29% during scopy compared to group baseline, whereas in group III rise was significantly smaller ($p < 0.0001$). 10 min after intubation fall in DBP was 13.57%; significantly lower than basal value in Group III whereas in Group I, it was higher than baseline.

Similarly Group I showed more significant rise ($p < 0.05$) in MAP (25.92%) at 1 min post intubation. Also group II showed significant rise in MAP by 19.98% during scopy compared to group baseline, whereas in group III rise was significantly smaller ($p < 0.0001$). 10 min after intubation fall in MAP was significantly lower by 12.61% than basal value which was statistical significant ($p < 0.001$).

Adverse events observed during study: One of the 25 patients (of group III) had bradycardia which was not less than 60/min. One patient from group III had hypotension which was not considered significant (less than 20% deviation from baseline value). No other adverse effects i.e. rhythm disturbances, truncl rigidity or recall of laryngoscopy and intubation and respiratory depression were noted in any patient. No respiratory depression had been observed in any fentanyl treated patients.

DISCUSSION

The occurrence of adverse cardiovascular responses to laryngoscopy and tracheal intubation and its suppression by various methods/drugs is extensively reported in literature and it can be said that tracheal intubation is the most stressful condition during induction of general anaesthesia. This may be inferred from the fact that the depth of anaesthesia required to suppress the circulatory response to intubation is much higher (1.3 MAC) than that required to suppress the reflexes following surgical incision. [12]

Reid and Brace in 1940 were probably the first to recognize the problem when they reported electrocardiographic changes such as extrasystoles and conduction defects following intubation. [3] This was followed by a series of studies on this subject. Burstein et al (1950) suggested a possible mechanism for the same. [13] They postulated reflex stimulation of cardiac accelerator within the sympathetic or vagus nervous system. King et al (1954) reported tachycardia, hypertension and dysrhythmias following intubation. [14] Hortan (1955) had reported both tachycardia as well as bradycardia as possible outcome in his study. [15] Devault et al (1960) confirmed that the circulatory changes following intubation were due to sympathoadrenal discharge. [16] Even though Forbes and Dally (1970) had reported that these changes are transient and hence do not lead to long lasting damage in normotensive patients. [17] Prys Roberts et al (1971) had recommended prophylaxis with beta blockers to prevent hypertensive crisis. [18] Later Prys Robert et al (1973) demonstrated attenuation of cardiovascular responses with practolol. [19] From that time onward there has been several studies to find the efficacy of various agents to attenuate the pressor response.

Hence, to blunt these responses, various methods have been tried like topical application of local anaesthetic,

infiltration or nerve blocks, α adrenergic blockers, vasodilators, calcium channel blockers, α 2 agonists. [20-26] But these drugs have no role for induction and maintenance of anaesthesia and also cause dangerous complication.

In our study patients were randomly distributed into three groups and there was no statistically significant difference in the distribution of age, sex and weight of patients in both the groups (Tab-1).

U.M. Kautto et al (1982) [4] studied effect of fentanyl in two different doses i.e. 2 mcg/kg (F2 group) and 6 mcg/kg (F6 group) for attenuation of circulatory response to laryngoscopy and intubation. . Kautto et al showed that, a significant increase ($p < 0.001$) in pulse rate, SBP, DBP & MAP were observed only in control group. In that study, all above mentioned parameters didn't increase significantly in both fentanyl groups, and with 6mcg/kg they remained fairly stable during whole observation period. It was concluded that fentanyl 2 mcg/kg significantly attenuated the increase in haemodynamic parameters during laryngoscopy and intubation and fentanyl 6 mcg/kg completely abolished these responses. The results of our present study are comparable with the results obtained by U.M. Kautto. In our study, in group III increase in all above haemodynamic parameters above baseline during scopy and all the intervals post intubation were significantly smaller ($p < 0.0001$) than group I and II.

Chung and Evans (1985) [27] studied 28 surgical patients aged (65-84) randomly assigned to either a control group (12) induced with thiopentone alone and a treatment group (16) induced with 3 mcg/kg fentanyl IV followed by thiopentone. Study showed that no significant increase in HR, SBP, DBP & MAP above baseline at any level in study group while in control group rise in these parameters were 2-4 times significantly

above the baseline at 1 and 2 min post intubation. It was concluded that, 3 mcg/kg IV fentanyl significantly attenuate cardiovascular stress response to intubation. The results of our present study are comparable with the result obtained by Chung and Evans. We found that all these parameters rose significantly above the baseline at each instances from laryngoscopy, in all three groups but in both fentanyl groups, the rise was significantly smaller ($p < 0.001$) as compared to control group. Also better attenuation obtained in group III as compare to group II without any significant adverse effects.

William M. Splinter [28] used fentanyl in two different doses i.e. 1.5 mcg/kg and 3 mcg/kg in geriatric patients, above 64 years. It was showed that fentanyl in both doses reduced the rises in HR, SBP, DBP & MAP significantly ($p < 0.05$). The higher dose, 3 mcg/kg of fentanyl resulted in more dramatic attenuation. Our results of present study are comparable with the results obtained by William et al. With fentanyl 1 mcg/kg and 2 mcg/kg IV, we got increase in all these haemodynamic parameters were significantly smaller ($p < 0.001$) compared to control group.

Only one of all 75 patients had bradycardia which was not clinically significant (< 60 /min). Similarly only one patient from group III had hypotension which was not considered significant (less than 20% baseline). No respiratory depression had been observed in any fentanyl treated patients.

Based on the comparative study and in the light of observations made in the present study, between group II and group III in regards to haemodynamic response to laryngoscopy and intubation, we conclude that intravenous fentanyl 2 mcg/kg body weight provides better attenuation of haemodynamic response to laryngoscopy and endotracheal intubation. Considering incidence and severity of side

effects which were in clinical limits, the 2 mcg / kg body wt of fentanyl is an appropriate dose for the purpose.

CONCLUSION

Based on the comparative study and in the light of observations made in the present study, between group II and group III in regards to haemodynamic response to laryngoscopy and intubation, we conclude that intravenous fentanyl 2 mcg/kg body weight provides better attenuation of haemodynamic response to laryngoscopy and endotracheal intubation. Considering incidence and severity of side effects which were in clinical limits, the 2 mcg / kg body wt of fentanyl is an appropriate dose for the purpose. Since this is an observational study- depending on clinical parameters, we recommend for biochemical and physicochemical evidences to support as ongoing study.

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