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Efficacy of Intravenous Fentanyl Citrate 2 Microgram/Kg Body Weight Administered before Laryngoscopy and Endotracheal Intubation to Attenuate Hemodynamic Response in Normotensive Individuals

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Abstract

Introduction: Laryngoscopy and intubation results in a stimulation of larynx, pharynx, epipharynx and trachea, which are extensively innervated by autonomic nervous system. The parasympathetic supply is via the vagus and sympathetic supply via superior cervical ganglion. Fentanyl seem to provide minute to minute haemodynamic control from intubation to recovery. *Aims and Objective:* To determine efficacy of intravenous fentanyl 2 microgram / kg body weight administered before laryngoscopy and endotracheal intubation in attenuating the changes in the hemodynamic parameters in normotensive individuals. *Methods:* Sixty normotensive patients of both sexes, aged between 18-65 years belonged to ASA physical status 1, free from intercurrent cardiovascular and neurological disease were posted for elective surgical procedures under general anaesthesia requiring orotracheal intubation were selected. Patients were informed. Written consent was obtained and the study protocol was approved by the Institutional Ethical committee. *Results:* When compared with control group, the rise in pulse rate in group II was significantly smaller ($p<0.001$) at all instances except at 30 sec ($p>0.5$), increase in mean systolic blood pressure in group II was significantly smaller ($p<0.001$) at all instances except at 5 min, increase in diastolic blood pressure in group II was significantly smaller ($p<0.001$), rise in mean arterial pressure in group II was significantly smaller($p<0.001$) at all instances except 5 min, rise in rate pressure product in group II was significantly smaller ($p<0.05$). *Conclusion:* Thus fentanyl in addition to its narcotic analgesic activity is addition to anaesthesiologist's armamentarium for attenuation of sympathetic stimulation by laryngoscopy and endotracheal intubation.

Keywords: Fentanyl; Laryngoscopy; Endotracheal Intubation; Normotensive.

Introduction

Endotracheal intubation and artificial control of ventilation marked a new era in the history of anesthesia. This had resulted in better control of airway and ventilation making administration of anaesthesia safer. Most invasive stimuli in anaesthesia such as Endotracheal intubation, producing stress response in the form of tachycardia, hypertension and increased catecholamine levels [1,2].

Laryngoscopy and intubation results in a stimulation of larynx, pharynx, epipharynx and trachea, which are extensively innervated by autonomic nervous system. Stimulation of aforementioned areas results in stimulation of automatic nervous system which in turn leads to various cardiovascular changes, coughing, laryngospasm, bronchospasm, vomiting, pulmonary aspiration , increase in intracranial and intraocular pressures.

The cardiovascular changes include tachycardia, systematic arterial hypertension [3], and cardiac dysrhythmias including asystole, bradycardia in children, rise in cerebral blood flow, cerebral metabolism intracranial pressure, and rise in intra ocular pressure.

The cardiovascular changes mentioned above may be further aggravated peri-operative factors such as, light planes of general

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anaesthesia, hypoxemia and hypercarbia both of which may be produced during induction, laryngoscopy or intubation, higher level of anxiey in the preoperative period, poorly controlled systematic arterial hypertension, use of anticholinergic premedication, cardiovascular effects of induction anaesthetic agents themselves, reflex baroreceptor effects following sodium pentothal administration. The various adverse cardiovascular responses mentioned before may be reduced by deeper planes of general anaesthesia which also may be poorly tolerated.

Recently fentanyl, mu receptor agonist is a natural choice to attenuate pressor response during laryngoscopy and intubation because [4], Low dose fentanyl required to circulatory response to tracheal intubation, reduce the dose of thiopentone, rapid onset of action, extremely lipid soluble, provide cardiovascular stability throughout the operative period, block sympathetic stress response to surgical stimulation, rapid and potent analgesic, anxiolytic and sedative, decreasing concentration of inhaled agent requirement.

Considering all above fentanyl seem to provide minute to minute hemodynamic control from intubation to recovery. In this study an attempt has been made to evaluate the efficacy of injection fentanyl in attenuation of sympathetic during laryngoscopy and intubation.

Aims and Objectives

The aim of present study was to determine efficacy of intravenous fentanyl 2 microgram / kg body weight administered before laryngoscopy and endotracheal intubation in attenuating the changes in the hemodynamic parameters in normotensive individuals.

Material and Methods

The study was carried out on sixty normotensive adult patients of both sexes, aged between 18-65 years belonged to ASA physical status 1, free from intercurrent cardiovascular and neurological disease were posted for elective surgical procedures under general anaesthesia requiring orotracheal intubation were selected during study duration. Patients were informed and written consent was obtained both for the conduct of study as well as for administration of general anaesthesia. The study protocol was approved by the Institutional Ethical committee. Patients were randomly assigned into one of the two groups I and II comprising 30 patients in each group.

Exclusive criteria: Pre-existing systematic arterial hypertension , treated or otherwise, menstruating , pregnant and lactating women, any drug therapy, that would interface with the cardiovascular system in the previous 48 hours, patients having significant cardiovascular disease, presence of significant respiratory disease, pre-existing neurological and neuromuscular disorder , anticipated difficulty in mask ventilation or oral endotracheal intubation patients who require more than 20 seconds for performance of laryngoscopy and intubation were also excluded. Malnutrition, significant anemia (Hb< 9 gm%) and morbid obesity, drug dependence, diabetes mellitus, patients is not willing to participate in the study were also excluded from the study.

All patients were examined and assessed pre-operatively on the day before surgery. All patients were premedicated with intramuscular Glycopyrrolate 4 microgram / kg 30 minutes before induction.

Continuous ECG monitoring , pulse rate , systolic blood pressure, diastolic blood pressure, mean arterial pressure , rate pressure product, respiratory rate, depth of respiration were measured and recorded on arrival of patient in anaesthetic room.

Intravenous line was secured for all patients. Preoxygenation with 100% oxygen was carried out for 3 minutes. General anaesthesia was induced with inj. thiopentone sodium 4-5 mg / kg IV till loss of eyelash reflex over 30 seconds.

Following 30 seconds one of the test medications was given as a bolus intravenously. Patients were allotted one of the two groups by randomization.

For Group I – normal saline IV

Group II – Inj. Fentanyl 2 mcg / kg IV

All the solutions were diluted appropriately to make upto 10 ml. This was followed by Inj. Succinylcholine 1.5-2 mg / kg IV.

Intubation was done exactly after 90 seconds. Direct laryngoscopy and oral endotracheal intubation was performed. Intubation was performed by same anaesthesiologist in all the patients. Patients in whom intubation took more than one attempt or took more than 20 seconds were excluded from the study. Anaesthesia was maintained with oxygen, nitrous oxide, sevoflurane on closed circuit with controlled ventilation with pancuronium bromide as muscle relaxant.

On each instant pulse rate, blood pressure was recorded from multipara monitor. Electrocardiographic monitoring was done continuously. The person making the recordings was kept blind regarding the administered drug. Pulse rate , systolic blood pressure, diastolic blood pressure, mean arterial pressure, rate pressure product were recorded

1. Before premedication
2. During laryngoscopy and intubation
3. 30 seconds, 1 minute, 2 minute and 5 minutes after intubation

Statistical Analysis

The data obtained from the study were organized and analyzed statistically. Descriptive statistics such as mean, SD and percentage was used. Chi-square test for categorical variable and Analysis Of Variance (ANOVA) tests for continuous variables. Comparison between groups was done by using student's t test. A p-value of less than 0.05 was considered significant. Data analysis was performed by using software SPSS 16.0

Results

There was no significant difference in the demographic data between the groups regarding age, sex, and weight of the patients (p>0.05).

When group I and II were compared from baseline value to the subsequent time interval it was showed that increase in pulse rate in group II was significantly smaller (p<0.001) during scopy, at 1 min , 2 min and 5 min post intubation compared to group I. At 30 seconds changes in group II compared to group I were not significant (p<0.05). As at 30 sec. postinubation there is maximum sympathetic stimulation, so low dose of fentanyl i.e. 2 / kg is ineffective in attenuation of sympathetic overactivity (Table 1).

When group I and II were compared from baseline value to the subsequent time interval it was showed that increase in systolic blood pressure in group II was significantly smaller (p<0.001) during scopy, 30 sec, 1 min., 2 min a post intubation compared to group I. At 5 min, fall in systolic blood pressure in group II was insignificant (p>0.05) compared to group I (Table 2).

When group I and II were compared, the increase in mean diastolic blood pressure in group II during scopy, 30 sec, 1 min, 2 min were significantly smaller (p<0.001) than group I and fall in diastolic blood pressure at 5 min in group II was insignificant (p>0.05) compared to group I (Table 3).

When group I and II were compared rise in mean MAP in group II was significantly smaller (p<0.0001) during scopy, 30 sec, 1 min, 2 min post intubation, compared to group I. Fall in mean arterial pressure in group II at 5 min was not significant (p>0.05) compared to group I (Table 4).

When group I and II were compared, rise in mean rate pressure product in group II during scopy, 30 sec, 1 min, 2 min was significantly smaller (p<0.0001)than group I. At 5 min., fall in mean rate pressure product in group II by 264.93 (2.91%) which was not significant (p>0.05), while there was rise in mean rate pressure product in group I which was insignificant (Table 5).

Table 1: Changes in mean pulse rate

Group	Mean Baseline Pulse rate (per min)	During laryngoscopy	After Laryngoscopy and Intubation			
			30 sec	1 min	2 min	5 min
I	79.4 ±5.7	101± 5.7	109.96± 5.7	110.4± 5.6	110.0± 5.07	85.0±5.5
II	78.73± ±5.4452	97.86 ± 7.9391*	107.4± 4.9032[a]	99.73± 5.1120**	99.73± 5.3715**	79.3± 5.3648**

'a': Not significant compared to changes in control group (p>0.05), *: Statistically significant compared to changes in control group (p<0.05), **: Highly significant compared to changes in control group (p<0.001)

Table 2: Changes in Mean Systolic Blood Pressure (SBP)

Group	Mean Baseline SBP (mmHg)	During laryngoscopy	After Laryngoscopy and Intubation			
			30 sec	1 min	2 min	5 min
I	115.6 ± 8.0925	127.93± 8.1110	145.6±8.3111	157.6±8.2110	147.53±8.2992	110.73±7.9564
II	115.73± 7.9608	123.866 ±7.084*	139.6±7.8623 **	134.73±7.9391**	133.6 ±9.0118**	111.53±8.4311**

'a': Not significant compared to changes in control group (p>0.05), *: Statistically significant compared to changes in control group (p<0.05), **: Highly significant compared to changes in control group (p<0.001)

Table 3: Changes in Mean Diastolic Blood Pressure (SBP)

Group	Mean Baseline DBP (mmHg)	During laryngoscopy	After Laryngoscopy and Intubation			
			30 sec	1 min	2 min	5 min
I	73.73 ±3.6287	91.666± 3.7539	112.06±4.2176	113.6±3.7655	105.73±3.777	73.8±3.8720
II	74.06± 3.7318	86.06 ±4.2176*	101.46±3.9630 **	95.66±4.1716**	94.73 ±3.9473**	73.26±4.0166[a]

'a': Not significant compared to changes in control group (p>0.05), *: Statistically significant compared to changes in control group (p<0.05), **: Highly significant compared to changes in control group (p<0.001)

Table 4: Changes in mean arterial pressure (MAP)

Group	Mean Baseline MAP	During laryngoscopy	After Laryngoscopy and Intubation			
			30 sec	1 min	2 min	5 min
I	87.65 ±4.5024	103.726± 4.4657	123.21±4.6781	128.23±4.5225	119.63±4.7017	86.07±4.6261
II	87.92± 4.3914	98.67 ±4.3697**	114.17±4.5058 **	108.65±4.6219**	107.58 ±4.6760**	85.98±4.5887[a]

'a': Not significant compared to changes in control group (p>0.05), *: Statistically significant compared to changes in control group (p<0.05), **: Highly significant compared to changes in control group (p<0.001)

Table 5: Changes in mean rate pressure product (RPP)

Group	Mean Baseline RPP	During laryngoscopy	After Laryngoscopy and Intubation			
			30 sec	1 min	2 min	5 min
I	9174 ±894.3227	12910.26±985.0869	15932.26±1167.0837	17407.06±1257.253	16231.73±1163.9296	9415.73±887.4132
II	9109.73±888.4631	12132.4 ±994.1252**	15001.73±1125.153 **	13431.33±996.4007**	13326.8 ±1201.7459**	8844.8±883.7614*

'a': Not significant compared to changes in control group (p>0.05), *: Statistically significant compared to changes in control group (p<0.05), **: Highly significant compared to changes in control group (p<0.001)

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 required to suppress the circulatory response to intubation is much higher (1.3 MAC) than that required to suppress the reflexes following surgical incision [5].

Number of methods are advocated to suppress the reflex cardiovascular effects of intratracheal intubation. It is believed that fentanyl suppresses the hemodynamic response by increasing the depth of anesthesia and decreasing sympathetic discharge [6].

A low dose of fentanyl was employed in the present study because large dose of fentanyl often leads to muscular rigidity, bradycardia, respiratory depression, nausea, and vomiting [7].

Fentanyl and fentanyl plus lidocaine are effective in decreasing the hemodynamic response to tracheal intubation, however, neither fentanyl nor fentanyl plus lidocaine could inhibit all hemodynamic responses, furthermore fentanyl plus lidocaine was not more effective than fentanyl alone [8,9].

Further, unlike Fentanyl (2µg / kg IV 5 min before laryngoscopy and intubation), Nalbuphine was not found to be effective in controlling the heart rate post induction and intubation as it affects a slight increase in heart rate itself after drug administration [10].

Discussion

Changes in Pulse Rate

U.M Kautto et al(1982) [11] studied effect of IV fentanyl in two different Dose i.e. 2 microgram / kg and 6 microgram / kg for attenuation of circulatory response to laryngoscopy and intubation and showed that, a significant increase (p<0.001) in pulse rate was observed only in control group, whereas in another study, it was observed that, hemodynamic responses to intubation in hypertensive patients were controlled effectively in the fentanyl 2 mcg / kg groups as well [8]. We also found the similar results with inj. fentanyl 2 microgram / kg body weight in significant attenuation of increase in pulse rate during laryngoscopy and pulse rate.

Changes in Systolic Blood Presure

The mean baseline systolic blood pressure was 115.6 ± 8.0925. After laryngoscopy and intubation, in control group there was a classical pressor response and mean systolic blood pressure showed maximum increase to 157.6 ± 8.2110, a rise by 42 (36.33%) at 1 min. At 5 min of post intubation there was significant fall in systolic blood pressure by 4.87(4.21%). These findings were parallel to the study done by P Agarwal et al [12].

U.M. Kautto (1982) [11] studies showed that systolic

pressure in F6 group did not rise above control level after intubation and decreased thereafter gradually to 18% lower than the control value after 5 min. In control group($p<0.001$) and F2 group ($p<0.02$), systolic pressure increased significantly after intubation compared with baseline values, but the elevation in F2 group was significantly less than the control group ($p<0.05$). It was concluded that 2 microgram / kg fentanyl IV, significantly attenuate the increase in arterial pressure after laryngoscopy and intubation. Our study also showed increase in mean systolic blood pressure significantly smaller ($p<0.001$) during scopy, 30 sec, 1 min, 2 min post intubation compared to control group. At 5 min with fentanyl 2 microgram / kg IV, fall in systolic blood pressure was below baseline but it was not significant ($p>0.05$).

Chung and Evans (1985) [13] studies showed that, increase in systolic blood pressure was significantly smaller in fentanyl group at 1 min post intubation. Systolic blood pressure rose by 56 mm of Hg in control group and increase of 15 mm of Hg in fentanyl group. In fentanyl groups systolic blood pressure was lower than baseline value at 5 min post intubation. It was concluded that, 2 microgram / kg IV fentanyl significantly attenuate cardiovascular stress response to intubation. In our study also, similar results were observed with 2 microgram / kg IV 23.87mm of Hg in group II.

William M. Splinter et al (1989) [14] used fentanyl in two different dose i.e. 1.5 microgram / kg and 3 microgram / kg in geriatric patients, above 64 years. It was showed that fentanyl in both doses reduced the rises in systolic blood pressure significantly ($p<0.05$). Our results of present study are also shows that increase in the mean systolic blood pressure which was significantly smaller ($p<0.01$) compared to control group.

Changes in Diastolic Blood Pressure

U.M. Kautto (1982) [11] studies showed that diastolic pressure did not increase significantly after intubation in F6 Group, whereas the increase in control and F2 group was significant ($p<0.001$) compared to baseline value. The increase was highest in control group and differed significantly from F2 group ($p<0.01$) and F6 group ($p<0.001$). It was concluded that 6 microgram / kg fentanyl prevented the arterial pressure increase during scopy and intubation and even a small dose of fentanyl 2 microgram / kg, significantly attenuated this response. In our study, in group II increase in diastolic blood pressure above baseline during scopy, 30 sec, 1 min, 2 min post intubation were significantly smaller ($p<0.001$) than group I.

Chung and Evans (1985) [13] studies showed that increase in diastolic blood pressure was significantly smaller in the fentanyl group at 1 min post intubation. Diastolic blood pressure increased by 42 mm of Hg in control group compared to 20 mm of Hg in the fentanyl group. In our study, increase in diastolic blood pressure in group II (fentanyl 2 microgram / kg IV) were significantly smaller ($p<0.001$) at 1 min post intubation. Diastolic blood pressure increased by 39.87 mm of Hg increase in control group compared to 21.6 mm of Hg increase in group II.

Willam M Splinter et al (1989) [14] studies showed that fentanyl in both doses reduced the rises in diastolic blood pressure significantly ($p<0.05$). It was concluded that low dose fentanyl attenuate the haemodynamic response to laryngoscopy and intubation and decreased incidence of marked fluctuations in blood pressure. Similar results were obtained in our study, fentanyl group II showed increase in diastolic blood pressure above baseline which was significantly smaller ($p<0.001$) than group I. The average increase in blood pressure by 40-50% have been observed [6], comparable results were obtained in our study also. Probably of no consequence in healthy individuals with regards to transitory hypertension and tachycardia, these may be hazardous to individuals those are having with history of diabetes, preeclampsia, myocardial insufficiency or cerebrovascular diseases [1].

Changes in Mean Arterial Pressure

William M. Splinter et al (1989) [14] studied was found that with both doses fentanyl reduced the rises in mean arterial pressure significantly ($p<0.05$), during laryngoscopy and intubation. In our study, causes rise in mean arterial pressure which was significantly smaller ($p<0.001$) as compared to group I.

Changes in Rate Pressure Product

This is the product of heart rate and systolic blood pressure and is considered one of the parameters determining myocardial oxygen demand.

U. K. Kautto (1982) [11] studied showed that, with fentanyl 2 mcg / kg IV following thiopentone sodium, there was significant attenuation of increase in rate pressure product during laryngoscopy and intubation. Fentanyl 6 mcg / kg IV completely abolished these responses. In our study fentanyl 2 microgram / kg caused rise in rate pressure product during scopy, 30 sec, 1 min, 2 min, which was

significantly smaller than control group.

Based on comparison between groups and results obtained, we came to a conclusion point that, intravenous fentanyl 2 mcg / kg is safe and effective for attenuation of haemodynamic response to laryngoscopy and intubation. Similar comparable results also obtained in another study[15] showing more stable hemodynamic profile without any adverse effects.

Conclusion

We found that use of intravenous fentanyl 2 mcg / kg is safe and effective for attenuation of haemodynamic response to laryngoscopy and intubation. It is concluded that, intravenous fentanyl citrate even in low dose of 2 microgram / Kg body weight provide a simple, safe and effective method of attenuation of the haemodynamic response to laryngoscopy and intubation.

Thus fentanyl in addition to its narcotic analgesic activity is addition to anaesthesiologist's armamentarium for attenuation of sympathetic stimulation by laryngoscopy and endotracheal intubation.

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