

"Comparative Efficacy of Different Doses of Fentanyl on Cardiovascular Responses to Laryngoscopy and Tracheal Intubation"

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## ABSTRACT

**Background**: This study was conducted to determine an effective bolus dose of fentanyl, which would attenuate the cardiovascular response to laryngoscopy and tracheal intubation.

**Materials and Methods:** A randomised double blind controlled study was carried out on 50 healthy adult patients (ASA I and II) undergoing elective surgery under general anaesthesia. The patients were randomly allocated into two groups of 25 each i.e. group A and group B receiving fentanyl 3  $\mu$ g/kg, 5  $\mu$ g/kg intravenously three minutes before intubation respectively. The pulse rate, systolic blood pressure was recorded at induction,

during intubation and at 1,3, 5 min post intubation.

**Results**: The study showed that both the doses were equally effective in blunting the pulse rate response, but the  $5\mu g / kg$  proved significantly effective in blunting the blood pressure response. The rate pressure product, a measure of cardiac O<sub>2</sub> consumption was found to be significantly lower in fentanyl  $5\mu g/kg$  compared to fentanyl  $3\mu g/kg$ .

**Conclusion**: So, we conclude that both blood pressure and rate pressure product were completely abolished by a bolus dose of fentanyl  $5\mu g$  /kg in comparison with fentanyl  $3\mu g$ /kg following laryngoscopy and intubation.

#### Keywords: Cardiovascular response, Fentanyl, Pulse rate

# **INTRODUCTION**

Laryngoscopy and tracheal intubation can cause tachycardia, hypertension, dysarrhythmias, perioperative myocardial ischaemia, acute heart failure, and cerebrovascular accidents in susceptible individuals [1] .These responses are due to intense sympathetic discharge caused by stimulation of upper respiratory tract, evidenced by rise in catecholamine's. Various drugs and techniques like, topical and IV Lignocaine, deepening level of anaesthesia, adrenergic blockers, vasodilators like, alpha blockers, and opioids have been used [1]. Fentanyl, a synthetic opioid which attenuates the cardiovascular response by its action on opioid receptors, effects on cardiovascular system, preventing the increase in plasma concentrations of catecholamines and decreasing the central sympathetic vasoregulatory outflow. We conducted a randomized double blind controlled study to determine the effective dose of fentanyl to attenuate the cardiovascular effects of laryngoscopy and tracheal intubation.

# **MATERIALS AND METHODS**

We conducted a randomized double blind controlled study on 50 ASA physical status I and II patients, aged between 20-60 years, scheduled for elective surgery requiring general anaesthesia. Institutional ethical committee approval and informed consent was obtained. Patients with history of hypertension, angina, coronary artery disease, recent myocardial infarction, congestive cardiac failure, heart blocks, cardiac pace maker, chronic obstructive pulmonary disease, pregnant and nursing women, anticipated difficult airway and patients on treatment with anti-hypertensive and anti arrhythmic drugs were excluded from study. All the patients were randomly allocated in a double blind fashion and using a sealed envelope technique to one of the two groups, fentanyl 3µg/kg (group A), fentanyl 5µg/kg (group B) each containing 25 patients. All the patients were premedicated with Inj.glycopyrrolate 0.2 mg intramuscularly and midazolam 0.05mg/kg IM, 30 min prior to

induction of anaesthesia. On arrival to operation theatre, a base line pulse rate, systolic blood pressure, diastolic blood pressure and oxygen saturation were recorded. Based on randomization patients received either fentanyl 3µg/kg or fentanyl 5µg/kg in pre-prepared five ml saline, 3-4 min prior to laryngoscopy and tracheal intubation. All patients received a dose of inj.thiopentone 3-5mg/kg till the abolition of eyelash reflex, followed by inj.vecuronium 0.1mg/kg to facilitate laryngoscopy and tracheal intubation and ventilated for at least three min with 100% oxygen. Laryngoscopy was performed with macintosh blade and orotracheal intubation was completed within 30sec with appropriate size endotracheal tube. Anaesthesia was maintained with N<sub>2</sub>0 in oxygen (60:40), vecuronium, IPPV and isoflurane as per requirement. At the end of anaesthesia, the neuromuscular blockade was antagonised with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.02 mg/kg intravenously. Patients were extubated when respiration was deemed sufficient and patients were able to obey simple commands.

Intraoperatively pulse rate, systolic blood pressure, and diastolic blood pressure were recorded at following time intervals.

- Tb Base line value i.e. prior to induction
- Ti During laryngoscopy and intubation
- T1 At 1min postintubation
- T3 At 3min postintubation

T5 - At 5min post intubation, mean arterial pressure (MAP) and rate pressure product (RPP) were calculated subsequently.

## **STATISTICAL ANALYSIS**

Demographic data was analysed using student t-test. Unpaired t-test was applied to observe the changes in mean rate pressure product with different doses of fentanyl using open epi soft ware version 2.3.1.The comparison was considered significant, if p-value was less than 0.05 (p <0.05) and p< 0.001 was considered highly significant.

	Group A	Group B	
Age (yrs)	36.5	35.2	
Gender	(Male:Female)	16:9	
Weight (kg)	58.6	59.25	
ASA( I/II)	19/6	20/5	

[Table/Fig-1]: Demographical profile of the study group

Groups	HR		MAP		RPP		
	А	В	А	В	А	В	
Time intervals							
Base	85.12	90	93.52	94.68	10499.36	11037.60	
line(Tb)	±12.10	±14.5	±7.8	± 6.5	±1923.20	±1744.65	
Ti	91.20	86.84	100.96	90.4	11613.6	10107.28	
	±10.93	±7.88	±8.32	± 6.89**	±2222.73	±1250.72*	
T1	87.40	84.72	94.24	87.24	10502.88	9680.24	
	±11.72	±9.42	±8.5	±5.72**	±2073.93	±945.69	
T2	83.68	80.8	88.12	82.56	9393.6	8480.16	
	±10.72	±9.29	±6.8	±4.8**	±1788.8	± 899.91*	
Т3	80	76.24	83.12	78.36	8415.52	7632.32	
	±9.85	±8.66	± 6.37	±3.85**	±1315.35	±875.42*	

[Table/Fig-2]: Changes in the mean heart rate, mean arterial blood and mean rate pressure product in both the groups

NS-not singnificant(p>0.005),S-Significant\*(p<0.005) between the groups,

HS-Highly significant\*\* (p<0.001) between the groups,

## RESULTS

The two groups were comparable in patient characteristics [Table/ Fig-1]. There was no statistically significant difference in mean pulse rate throughout study time between the fentanyl 3µg and fentanyl 5µg groups (p>0.05). Mean arterial pressure decreased significantly after induction of anaesthesia in fentanyl 5µg group compared to fentanyl 3µg group and remained so till 5min postintubation. There was a significant fall in the rate pressure product during intubation, 3min and 5min postintubation with fentanyl 5µg group compared to fentanyl 3µg group [Table/Fig-2]. None of the cases in our study showed any untoward side effects.

## DISCUSSION

Laryngoscopy and tracheal intubation are considered to be stressful and cause exaggerated cardiovascular response. Although transient hypertension and tachycardia are usually of little consequence, they may be hazardous, especially in patients with persistent hypertension, limited coronary and myocardial reserve, or cerebrovascular diseases [1,2]. Reflex changes in the cardiovascular system after laryngoscopy and intubation lead to an average increase in blood pressure by 40-50% and 20% increase in heart rate [3].

Sympatho-adrenal cardiovascular response to laryngoscopy and intubation may be attenuated by several methods and drugs. Opioids administered in moderate to high dose, have been suggested as a means of blunting this response [4-6]. Opioids are widely used to control the neurovegetative response to intubation; a linear relationship exists between increasing opioid dose and cardiovascular response reduction [7]. Fentanyl produce analgesia and stable hemodynamics by modulating stress response through receptor mediated actions on hypothalamic-pituitary-adrenal axis.

In our study, we chose two different doses of fentanyl 3 µg /kg and 5 µg /kg, as doses in excess of 5 µg /kg showed late onset of side effects in earlier studies and smaller doses of  $\leq 2$  µg /kg did not completely abolish the cardiovascular response.

In a randomized controlled study conducted by lyer and Russel, on patients undergoing coronary artery surgery were randomly given 0, 2, 5, 10 or 15  $\mu$ g /kg of fentanyl with induction of anaesthesia. A progressive attenuation of the MAP rise was found as the dose of

fentanyl increased. Increase in heart rate after intubation was more difficult to block and if heart rate is to be kept below 100 bpm, a dose of at least 10  $\mu$ g /kg should be used [8].

Dalhgren et al., reported that fentanyl 5  $\mu$ g/kg administered IV in conjunction with thiopental three and one –half minutes prior to laryngoscopy and tracheal intubation, found attenuation of BP and HR responses and there was no associated increase in ICP ,hypotension, chest wall stiffness, or postoperative respiratory depression [9]. In a study of elderly patients, Chung and Evan's found fentanyl 3  $\mu$ g/kg IV effective in attenuating the blood pressure and heart rate response to laryngoscopy and tracheal intubation [10].

In another study by Splinter et al., studied effects of lidocaine and fentanyl 1.5  $\mu$ g/kg and 3  $\mu$ g/kg for hemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients. A high incidence of stable hemodynamic variables was observed in both the fentanyl group. Hypotension was observed 2min postintubation, in patients who received fentanyl 3  $\mu$ g/kg [11].

Kautto et al., in his study concluded, that supplementation of anaesthetic induction with fentanyl 2  $\mu$ g/kg significantly attenuated the increase in heart rate, arterial pressure and rate pressure product after laryngoscopy and intubation, and fentanyl 6  $\mu$ g/kg completely abolished pressure responses [12], these results correlates with our study.

Kovac in his review of article for controlling the hemodynamic response to laryngoscopy and endotracheal intubation summarized that, fentanyl in doses of 5 $\mu$ g/kg and 8  $\mu$ g/kg produced respiratory depression and delayed awakening in short surgical cases. Care should be taken when administering fentanyl to geriatric patients. The recommended IV doses found to be effective in attenuating the BP and HR responses to laryngoscopy and tracheal intubation are fentanyl 5 to 6  $\mu$ g /kg in young healthy patients and fentanyl 1.5  $\mu$ g /kg to 3.0  $\mu$ g /kg in elderly patients administered 3-4 minutes prior to laryngoscopy and tracheal intubation [13].

In our study anaesthetic induction with fentanyl 3  $\mu$ g/kg significantly attenuated the increase in mean arterial blood pressure and rate pressure product, while fentanyl 5 $\mu$ g/kg completely abolished cardiovascular responses to laryngoscopy and tracheal intubation. While there was no statistically significant difference in the pulse rate response in both the groups. Limitations of our study are-we chose only young healthy and patients without any co-morbid conditions. We emphasise on the need for further study involving larger group and older patients with co-morbid conditions.

#### CONCLUSION

To conclude, fentanyl 5µg/kg as a single bolus dose found to be more effective in controlling rise in mean arterial pressure and the rate pressure product compared to fentanyl 3µg/kg.

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