

## Original article

**Comparative study between Intravenous fentanyl & Intravenous fentanyl with lignocaine for attenuation of haemodynamic responses during laryngoscopy: Our experience from TNMC and BYL Nair ch. Hospital, Mumbai, Maharashtra****Dr. Anand Subhashrao Nirgude<sup>1</sup>, Dr. Laxmikant Kisan Pawar<sup>2</sup>, Dr. Anant A. Takalkar<sup>3</sup>**

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**Corresponding author: Dr. Anant A. Takalkar*****ananttakalkarpsm@gmail.com*****Abstract**

**Introduction:** Laryngoscopy, Endotracheal intubation of the trachea stimulates laryngeal and tracheal sensory receptors, resulting in a marked increase in the elaboration of sympathetic amines (adrenaline & noradrenaline). There are various noxious stimuli which can cause haemodynamic instability during general anaesthesia viz. Laryngoscopy, endotracheal intubation, skin incision, insertion of trocar, organ manipulation. Both drugs lignocaine & fentanyl are standard of care & routinely used. **Objective:** To study the effect of Intravenous fentanyl & Intravenous fentanyl with lignocaine for attenuation of haemodynamic response to noxious stimuli viz. laryngoscopy, intubation & skin incision with respect to heart rate, Systolic blood pressure, Diastolic blood pressure and mean arterial pressure. **Methodology:** An open observational comparative study was conducted in ASA-1 patients at department of anaesthesiology at TNMC and BYL Nair ch. Hospital, Mumbai at tertiary care centre. The patients were randomly divided into two groups (fentanyl group and fentanyl with lignocaine group). The fentanyl group received 2mcg/kg and the fentanyl with lignocaine group received 2mcg/kg fentanyl & 1.5mg lignocaine. Hemodynamic variables were recorded. **Results:** Mean age was 40.13yrs+/-8.99 in fentanyl group and 45.08+/-9.352 in fentanyl plus lignocaine. There were 18 males and 22 females in fentanyl group and 15 males and 25 females in fentanyl plus lignocaine group. The rise in heart rate was seen after intubation and skin incision was more with fentanyl plus lignocaine group ( $p < 0.01$ ). There was no significant difference between fentanyl and fentanyl plus lignocaine group after giving drugs. The rise in SBP was seen after intubation and skin incision was more with fentanyl plus lignocaine group ( $p < 0.01$ ). The rise in DBP was seen after intubation and skin incision was more with fentanyl plus lignocaine groups ( $p < 0.01$ ).

**Conclusion:** The haemodynamic response was attenuated at various time interval and the heart rate, blood pressure, post laryngoscopy and post intubation were more attenuated in fentanyl group than in fentanyl plus lignocaine group and it was proven statistically significant.

**Key words:** Laryngoscopy, Endotracheal intubation, IV fentanyl, fentanyl plus lignocaine, hemodynamic variables etc.

**Introduction**

Induction of anaesthesia and endotracheal intubation often creates a period of

hemodynamic instability in ASA 1 patients. In spite of much progress in anaesthesia the problem of pressure response is still unsolved. Laryngoscopy, Endotracheal intubation of the trachea stimulates laryngeal and tracheal sensory receptors, resulting in a marked increase in the elaboration of sympathetic amines (adrenaline & noradrenaline). Laryngoscopy, endotracheal intubation stimuli manifest as circulatory disturbances such as hypertension, tachycardia & cardiac disturbances which are known as Pressure Response.<sup>1,2,3</sup>

Various methods to attenuate the pressure response are: sufficient depth of anaesthesia, duration of laryngoscopy less than 15sec, IV opioids, iv opioid with lignocaine, iv opioid with propofol, inhalational anaesthesia, vasodilators like Nitroglycerin, Calcium channel blockers, beta blockers, iv or topical lidocaine. There are various noxious stimuli which can cause haemodynamic instability during general anaesthesia viz. Laryngoscopy, endotracheal intubation, skin incision, insertion of trocar, organ manipulation. Both drugs lignocaine & fentanyl are standard of care & routinely used.<sup>3</sup>

Fentanyl act at opioid receptors & predominantly act on mu receptors. Fentanyl brings haemodynamic stability during perioperative period by its action on cardiovascular & autonomic regulatory areas. It decreases sympathetic tone & increases parasympathetic tone. It is frequently used opioid that binds with the stereospecific receptors at many sites within the CNS, increases pain threshold, alter pain reception, inhibits ascending pain pathway & joints with hypnotic's agent to diminish hemodynamics response to tracheal intubation. Fentanyl inhibits pituitary adrenal response directly or indirectly via hypothalamus. It attenuates the response at 2mcg/kg IV given before laryngoscopy & intubation. Optimal time of administration is 5 minutes before laryngoscopy & intubation.<sup>3</sup>

Lidocaine is a class Ib antiarrhythmic, block the sodium channel in the cell membranes of the heart & reduces the rate of the rise of the of the action potential & hence the conduction velocity above all the his purkinje system & in the atrial & ventricular musculature. Lidocaine has a suppressive effect on the circulatory response such as pulse, blood pressure, intracranial pressure & intraocular pressure in a patient undergoing laryngoscopy & tracheal intubation. It has a direct myocardial depressant effect & finally an effect on synaptic transmission.<sup>4</sup>

We were taken up drugs both IV Lignocaine & IV fentanyl were routinely used to attenuate hemodynamic response as individual bolus before laryngoscopy. We were taken up combination of IV fentanyl & IV lignocaine to take advantages of synergistic effect on hemodynamic status. this study was taken up to compare opioid as inj. Fentanyl & iv lignocaine in propofol based anaesthesia to attenuate the hemodynamic response to laryngoscopy, endotracheal intubation, skin incision in ASA Grade-1 patients undergoing laparoscopic abdominal surgeries. Propofol was used as an induction agent. it was a universal induction agent.

### **Objective:**

To study the effect of Intravenous fentanyl & Intravenous fentanyl with lignocaine for attenuation of haemodynamic response to noxious stimuli viz. laryngoscopy, intubation & skin incision with respect to heart rate, Systolic blood pressure, Diastolic blood pressure and mean arterial pressure. Hence the object of the study is to compare which of the two combinations

of drugs offer better haemodynamic stability.

### Materials and methods

An open observational comparative study was conducted in ASA-1 patients at department of anaesthesiology at TNMC and BYL Nair ch. Hospital, Mumbai.

Patients were randomly assigned to undergo into two groups Viz. GROUP 1 & GROUP 2.

- GROUP 1: Comprise of 40 patients who received inj. Fentanyl 2mcg/kg.
- GROUP 2: Comprise of 40 patients who received inj. Fentanyl 2mcg/kg with inj. Lignocaine 1.5mg/kg IV 1minute prior to laryngoscopy.

Source of data:

The patients were randomly divided into two groups (fentanyl group and fentanyl with lignocaine group). The fentanyl group received 2mcg/kg and the fentanyl with lignocaine group received 2mcg/kg fentanyl & 1.5mg lignocaine. Hemodynamic variables were recorded at preoperatively, after giving study drugs, inductive anesthetic agents with propofol, after giving inj. Lignocaine, 1minute prior to laryngoscopy, at the time of laryngoscopy, intubation & every 1minute after intubation till 5minute & at skin incision.

Inclusion criteria:

- Adult aged between 18 to 65 years.
- ASA 1 patients Patient scheduled for Propofol based Abdominal Laparoscopic Surgery in general anaesthesia.
- Weight between 20 to 70 kg.

Exclusion criteria:

- ASA-2, ASA-3 & ASA-4 Patient with controlled & uncontrolled hypertension.
- Severe cardiac, cerebrovascular, respiratory disease.
- Hepatic & renal dysfunction.
- Bleeding & coagulation disorder.
- Anticipated difficult intubation with MPC 3 & 4 patients.
- Refusal to participate in study,
- Allergy to drugs.

Study period and place:

This was hospital based open randomized comparative study was conducted in department of anaesthesiology in Mumbai at tertiary care center after obtaining permission from institutional ethics and research committee at tertiary care center, Mumbai for a period of 2 year.

Sample size:

The comparative study was conducted in two groups. According to the rule of normal distribution statistical parameters for all the groups like mean, standard deviation and coefficient of variation were calculated for the quantitative data.

$$n \geq \frac{(Z1 - \alpha/2 \sqrt{2pq} + Z1 - B \sqrt{p1q1 + p2q2})^2}{(p1 - p2)^2}$$

$$(p1 - p2)^2$$

$$(Z1 - \alpha/2) = 1.96 \text{ (level of significance 5\% or 95\% confidence interval)} \quad Z1 - b = 0.84 \text{ (power of 80\%)}$$

P1=proportion in group with Fentanyl

P2=proportion in group with Fentanyl plus Lidocaine

$$Q1 = 100 - p1; \quad p- = p1 + p2 \div 2; \quad q = 100 - p- \quad Q2 = 100 - p2$$

Group A (40) in which patients will receive Fentanyl.

Group B (40) in which patients will receive Fentanyl with Lidocaine.

To exclude the dropouts sample size is taken as 40 each. (Considering Mean and standard deviation Diastolic Pressure)<sup>5,6</sup>

Study procedure:

Availability of Study Material Confirmed. Permission from Hospital Ethical Committee for Study Procedure taken. Informed Valid Written Consent for Surgery & Anaesthesia procedure was Taken. Tab Pantoprazole 40mg & Tab Alprazolam 0.25mg 1HS and 1tab 2hrs Prior To Surgery with Sip of Water as Premedication given. All Patient were Fasted For 8hrs.

Upon Arrival of The Patient to The Operating Room, Consent & Fasting State were Checked & 18G Iv Cannula was Secured Over the Non-Dominant Hand. Standard ASA Monitoring Like Pulse Oximetry (Saturation Probe), Non-Invasive Blood Pressure (NIBP), Electrocardiography (ECG) was Attached to The Patient & Baseline Reading Noted. Patient with Secured Iv Line was Injected With 10ml/Kg Ringer Lactate Solution as preloading. In This Study Two Drugs opioid (fentanyl) & opioid (fentanyl) with Lignocaine was used In Propofol Based Anaesthesia In Laparoscopic Abdominal Surgeries. They studied For Their Effectiveness, In Attenuating Hemodynamics Response to Noxious Stimuli; Viz. Laryngoscopy, Endotracheal Intubation & skin incision.

GROUP 1: Comprised of 40 patients who will receive inj. Fentanyl 2mcg/kg GROUP 2: Comprised of 40 patients who will receive inj. Fentanyl 2mcg/kg with inj. Lignocaine 1.5mg/kg IV 1minutes prior to laryngoscopy.

The student was doing the study, observed & note the hemodynamic parameter. Senior anaesthesiologist (SR/SMO/CONSULTANT) did laryngoscopy and other student was injected drugs as per theater protocol.

Induction & maintenance: 3minutes after inj. Fentanyl both the groups patients were preoxygenate with 100% oxygen for 5minutes & were induced with inj. Propofol 2-2.5mg/kg slow IV in both the groups till loss of consciousness. This was followed by inj. Vecuronium 0.1mg/kg for muscle relaxation to facilitate endotracheal intubation. After assisting ventilation for 3minute & after noting apnea, assessment of tone of abdominal muscle laryngoscopy done after inj. Lignocaine 1min. prior to laryngoscopy in group-2 & endotracheal intubation was performed with appropriate size endotracheal tube.

Bilateral air entry confirmed, ETCO<sub>2</sub> reading noted & endotracheal tube secured with adhesive tape. Anaesthesia was maintained with oxygen 40% & air on IPPV using close circuit circle absorber & muscle relaxation using inj. vecuronium at fixed intervals throughout the procedure.

Vital parameters like HR, SBP, DBP & MAP were recorded at following events:

- Preoperative – prior to study drug administration (POP)
- Post study drug administration (PoSD)
- Induction with inj. Propofol (IND)
- administration of Lignocaine IV (PoSD2)
- Laryngoscopy (LYNG)
- Intubation (INTUB)
- Every 1minute after intubation
- Skin incision (INC).

After completion of surgery, achieving complete hemostasis & placement of dressing at the site of surgery, residual neuromuscular blockade was antagonizing with the combination of

inj. Neostigmine 0.05mg/kg & inj. glycopyrrolate 0.08mg/kg. Inhalational anaesthetic agent stopped & 100% o<sub>2</sub> administered. The patient was extubated after complete endotracheal suctioning & complete reversal of power, tone, reflexes. All patients were monitored in recovery room. All the vital parameters HR, SBP, DBP & MAP were monitored carefully from preoperatively to post extubation period.

### Statistical analysis:

The qualitative data represented in the form of frequency and percentage. Among qualitative data, nominal data included age, gender of the patients and analyzed using chi-square test. Quantitative data represented using mean  $\pm$  SD. Quantitative data include mean heart rate, diastolic blood pressure, systolic blood pressure, mean arterial pressure measurement. Quantitative data analyzed using paired t-test and ANOVA if groups more than three. Result was graphically represented when deemed necessary. All analysis done using SPSS software version 25.

### Results

**Table 1: Sociodemographic information of the patients**

	Fentanyl (mean $\pm$ SD)	Fentanyl plus lignocaine (mean $\pm$ SD)	P value
Age in years	40.13 $\pm$ 8.899	45.08 $\pm$ 9.352	0.018
Weight in kg	57.83 $\pm$ 8.421	60 $\pm$ 7.385	0.235
Gender			
Male	18	15	0.4
Female	22	25	
Total	40	40	

Mean age was 40.13yrs  $\pm$  8.99 in fentanyl group and 45.08  $\pm$  9.352 in fentanyl plus lignocaine. Mean weight was 57.83kg  $\pm$  8.421 and 60 kg  $\pm$  7.385 in fentanyl plus lignocaine. There were 18 males and 22 females in fentanyl group and 15 males and 25 females in fentanyl plus lignocaine group.

**Table 2: Intergroup comparison of mean heart rate**

Time	Mean $\pm$ SD		P value
	Fentanyl	Fentanyl plus lignocaine	
HR After giving drugs	62.09 $\pm$ 3.201	62.25 $\pm$ 3.365	0.379
HR 1min after intubation	76.25 $\pm$ 3.176	79.13 $\pm$ 4.363	0.001
HR 2min after intubation	75.85 $\pm$ 2.617	77.85 $\pm$ 3.704	0.007
HR 3min after intubation	74.70 $\pm$ 2.198	76.98 $\pm$ 4.142	0.003

HR 4min after intubation	75.85+/-2.617	78.05+/-3.816	0.004
HR 5min after intubation	75+/-2.679	78.05+/-3.816	0.001
HR At skin incision	78.75+/- 3.586	82.20+/-5.450	0.001

It is seen that though there was no significant difference in heart rate after giving drugs, there was significant difference in heart rate at 1 min, 3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in heart rate was seen after intubation and skin incision was more with fentanyl plus lignocaine group ( $p < 0.01$ ).

**Table 3: Intergroup comparison of mean arterial pressure**

Time	Mean +/- SD		P value
Drugs	Fentanyl	Fentanyl plus lignocaine	
MAP After giving drugs	75.83+/-2.560	76.22+/-3.463	0.563
MAP 1min after intubation	93.21+/-2.557	99.06+/-1.914	<0.001
MAP 2min after intubation	93.01+/-2.627	98.98+/- 1.968	<0.001
MAP3min after intubation	89.833+/-3.594	95.508+/-2.861	<0.001
MAP 4min after intubation	90.033+/-3.134	95.4+/-2.470	<0.001
MAP 5min after intubation	88.48+/-2.981	93.23+/-3.03	<0.001
MAP At skin incision	92.433+/-3.218	96+/-3.248	< 0.001

There was significant difference in mean arterial pressure at 1 min, 3 min, 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in MAP was seen after intubation and skin incision was more with fentanyl plus lignocaine group. But in this study, there was no significant difference between fentanyl and fentanyl plus lignocaine group after giving drugs

**Table 4: Intergroup comparison of systolic blood pressure**

Time	Mean +/- SD	P value
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Drugs	Fentanyl	fentanyl plus lignocaine	
SBP After giving drugs	96.70+/-2.954	99.30+/-5.254	0.008
SBP 1min after intubation	118.95+/-5.002	124.60+/-3.954	<0.001
SBP 2min after intubation	118.95 +/-5.002	124.55+/-4.025	<0.001
SBP3min after intubation	116.20+/-4.957	122.53+/-4.107	<0.001
SBP 4min after intubation	118.60+/-4.986	124.60+/-3.954	<0.001
SBP 5min after intubation	113.75+/-5.027	118.00+/-5.853	0.001
SBP At skin incision	116.00+/-4.815	121.00+/-5.584	<0.001

There was significant difference in systolic blood pressure after giving drugs and at 1 min, 3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in SBP was seen after intubation and skin incision was more with fentanyl plus lignocaine group ( $p < 0.01$ )

**Table 5: Intergroup comparison of diastolic blood pressure**

Time	Mean +/- SD		P value
Drugs	Fentanyl	Fentanyl plus lignocaine	
DBP after giving drugs	65.40+/-3.601	64.70+/-3.466	0.378
DBP 1min after intubation	80.35+/-3.101	86.30+/-2.919	<0.001
DBP 2min after intubation	80.05+/-3.186	86.20+/- 2.821	<0.001
DBP3min after intubation	76.65+/-4.560	82.00+/-3.843	<0.001
DBP 4min after intubation	75.75+/-3.848	80.80+/-2.963	<0.001
DBP 5min after intubation	75.85+/-3.827	80.85+/-2.931	<0.001
DBP At skin incision	80.65+/- 3.800	83.50+/-3.289	0.001

There was no significant difference in diastolic blood pressure after giving drugs in fentanyl and fentanyl plus lignocaine group. There was significant difference in diastolic blood pressure at 1 min, 3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus

lignocaine group. The rise in DBP was seen after intubation and skin incision was more with fentanyl plus lignocaine groups ( $p < 0.01$ ).

### Discussion

In this study There were 80 patients, 40 pts were in group fentanyl and 40 pts were in group that received fentanyl plus lignocaine. similarly, in study of attenuation of hemodynamic response to laryngoscopy and tracheal intubation with fentanyl lignocaine nebulization and recombination of both: A Randomized Control Trial had 96 patients.<sup>7</sup>

In study of comparison of fentanyl and fentanyl plus lidocaine on attenuation of hemodynamic responses to tracheal intubation in controlled hypertensive patients undergoing general anaesthesia there were 37 patients including 15 males 22 females with men age of  $56.08 \pm 10.85$  years.<sup>8</sup>

In a study Intravenous Low Dose Fentanyl versus Lignocaine in Attenuating the Hemodynamic Responses during Endotracheal Intubation: A Randomized Double-Blind Study The age range was 18–60 years for control and study groups. The mean values of age in years with standard deviations are  $42.63 \pm 9.27$ ,  $43.17 \pm 11.7$ , and  $44.93 \pm 9.78$  for control, lignocaine, and fentanyl groups respectively.<sup>9</sup>

In this study Both groups were comparable with respect to demographic and operational factors. mean age was  $40.13 \pm 8.899$  years and  $45.08 \pm 9.352$  years in fentanyl and fentanyl plus lignocaine respectively. similarly in study of attenuation of hemodynamic response to laryngoscopy and tracheal intubation with fentanyl, lignocaine nebulization and combination of both : a RCT 39 had patients of either sex in the age group of 18-65 years and mean was  $36.03 \pm 10.17$  and  $37.02 \pm 14.64$  and there were 12 males 20 females and 9 males and 23 females in fentanyl and fentanyl plus lignocaine group while remaining were in lignocaine group while in our study there were 18 females and 22 males and 15 females 25 males in respective groups.

In a study Intravenous Low Dose Fentanyl versus Lignocaine in Attenuating the Hemodynamic Responses during Endotracheal Intubation, 60% of the patients were male and 40% of the patients are females, Lignocaine group had 53% of male and 47% of female patients and Fentanyl group contained 60% of male and 40% of female patients.<sup>9</sup>

In a study Intravenous Low Dose Fentanyl versus Lignocaine in Attenuating the Hemodynamic Responses during Endotracheal Intubation in the control group is 40–70 kg. Mean value of weight is  $53.33$  with a standard deviation of  $\pm 5.72$ . in study groups, weight ranges for lignocaine and fentanyl groups are 40–70 kg respectively. Mean values and standard deviations of weight are  $56.3 \pm 6.83$  and  $55 \pm 5.8$  kg, respectively. With regard to weight, the difference between the three groups is not statistically significant ( $P > 0.05$ ).<sup>9</sup>

In our study, the mean weight in our study was  $57.83 \pm 8.421$  and  $60 \pm 7.385$  in fentanyl and fentanyl plus lignocaine group while it was comparable in the study attenuation of hemodynamic response to laryngoscopy and tracheal intubation with fentanyl lignocaine nebulization and combination of both: a RCT 39 mean weight was  $58.17 \pm 8.36$  and  $57.70 \pm 7.41$  in the two groups.<sup>7</sup>

### Intergroup comparison of heart rate:

There was significant difference in heart rate at 1 min, 3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in heart rate was seen after intubation and skin incision was more with fentanyl plus lignocaine group.

A highly statistically significant difference was observed among all groups at subsequent assessments up to 5 min in our study. In study intravenous low dose fentanyl versus lignocaine



in attenuating haemodynamic response during endotracheal responses: a double-blind study by Ranithkumar R, heart rate increases 33 % in lignocaine 26 % in fentanyl. Both lignocaine and fentanyl attenuated heart rate significantly. Suppression in rise in heart rate is statistically highly significant when compared with lignocaine. it remains till 5 min.<sup>9</sup>

#### **Intergroup comparison of mean arterial pressure:**

There was significant difference in MAP at 1 min, 3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in MAP was seen after intubation and skin incision was more with fentanyl plus lignocaine group.

In the study intravenous low dose fentanyl vs lidocaine in suppressing hemodynamic response during endotracheal intubation fentanyl is highly significant in attenuating pressure response.<sup>9</sup>

Map increase to limit in lignocaine 13.8% while fentanyl to only 6.5%. p value of 0.01 with lignocaine and 0.001 in fentanyl. It reached preinduction level over 7 min in lignocaine group and 5 min in fentanyl group the attenuation of MAP by fentanyl highly significant when compared with lignocaine p value of 0.001.

#### **Intergroup comparison of systolic blood pressure:**

In our study There was significant difference in systolic blood pressure after giving drugs and at 1 min,3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in SBP was seen after intubation and skin incision was more with fentanyl plus lignocaine group.

In a study of low dose intravenous fentanyl vs lidocaine in attenuating haemodynamic response, fentanyl is highly significant in attenuating systolic blood pressure response at subsequent assessment up to 7 min than lignocaine.<sup>9</sup>

It also shows maximum increase compared to preinduction was 14.5% in lignocaine and 7.2% in fentanyl, difference was statistically significant, fentanyl was better.

#### **Intergroup comparison of diastolic blood pressure:**

There was no significant difference in diastolic blood pressure after giving drugs in fentanyl and fentanyl plus lignocaine group.

There was significant difference in diastolic blood pressure at 1 min, 3 min 5 min after intubation and at skin incision in fentanyl and fentanyl plus lignocaine group. The rise in DBP was seen after intubation and skin incision was more with fentanyl plus lignocaine group. A significant difference is seen in all groups at 1, 3, 5, 7 min interval.

The maximum increase in diastolic blood pressure was 12.6 in lignocaine and 6% in fentanyl. p values of 0.01 with lignocaine and 0.001 with fentanyl seen. A statistically highly significant difference seen by fentanyl than lignocaine p value < 0.01.

Similarly study by Miller CD and Warren showed that lignocaine was not effective in suppressing haemodynamic response to laryngoscopy and intubation.<sup>7</sup>

But there are many studies showing lignocaine is effective in suppressing hemodynamic response to laryngoscopy and intubation.

Also, study titled comparative study of fentanyl and fentanyl plus lignocaine in attenuating haemodynamic response to tracheal intubation showed there is no difference and both fentanyl and fentanyl plus lignocaine are effective in suppressing stress response to tracheal intubation in controlled hypertensive subjects.<sup>8</sup>

#### **Conclusion:**

It was concluded that haemodynamic response was attenuated at various time interval and the heart rate, blood pressure, post laryngoscopy and post intubation was more attenuated in

fentanyl group than in fentanyl plus lignocaine group and it was proven statistically significant.

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