Original article:

Comparison of Fentanyl, Lignocaine and Placebo on Attenuation of Cardiovascular Responses to Laryngoscopy and Intubation: A Comparative Study

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Abstract

Introduction: The pressor response which is an element of enormous spectrum of stress response during laryngoscopy and intubation following general anaesthesia is due to sympathoadrenal activity. The plan of this study was to do a comparative study of Lignocaine (Xylocaine), fentanyl and placebo for the attenuation of the cardiovascular response to direct laryngoscopy and intubation during general anaesthesia

Material and Methods: One hundred fifty patients aged 20–60 years of either sex and weighing between 35-80 kgs of Anaesthesiology department at the Shri Guru Ram Rai Institute of Medical & Health Sciences, Dehradun physical status 1and 2 undergoing surgeries under general anesthesia and requiring orotracheal intubation were enrolled in this prospective, randomized double‑blind study. Relevant clinical signs and symptoms like pulse rate, blood pressure, respiratory rate were noted. All the selected patients were divided into three groups consisting of 50 patients each.

Results: After intubation, incidence of tachycardia (HR>100/min) was significantly lower in fentanyl group ($p<0.05$) in comparison of placebo and lignocaine group. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly high in comparison to baseline value in placebo group and lignocaine group compare to fentanyl group ($p<0.05$).

Conclusions: Findings of the present study suggested that attenuation of the pressor response was seen both with lignocaine and fentanyl. Further, among both drugs, fentanyl was more consistent, reliable and effective attenuation of haemodynamic response to laryngoscopy and endotracheal intubation in comparison of lignocaine. However, more studies on larger population are required to compare the effects of lignocaine and fentanyl in attenuation of pressor response to laryngoscopy and tracheal intubation.

Key words: Pressor Response, Larngoscopy, Fentanyl, Blood Pressure.

INTRODUCTION

The pressor response which is an element of enormous spectrum of stress response during laryngoscopy and intubation following general anaesthesia is due to sympathoadrenal activity as proofed by increased heart rate (HR), blood pressure, and serum catecholamine concentrations explained in 1940 by Reid and Brace.[1]Thesehemodynamic alterations are generally transitory, changeable, and unpredictable. These changes may be of no consequence in healthy individuals, but either or both may be harmful in patients with hypertension, myocardial ischemia, cerebrovascular diseases, and those with raised intraocular pressures.[2] Further reducing the cardiovascular response, anesthesia induction for patients at risk must also gratify the

following requisites: it must be applicable despite patient collaboration, prevent impairment of cerebral blood flow, and also prevent stimulation of the patient; it should neither be time-consuming nor affect the duration or modality of the ensuing anesthesia.[3]

The diverse process of attenuation of the response to laryngoscopy and intubation are still in the hunt from the date of its recognition. Various studies have been made in order to achieve this haemodynamic response to laryngoscopy and intubation. A variety of drugs and techniques have been used from time to time for attenuating the stress response including opioids lidocaine, beta blockers calcium channel blockers vasodilators α2 agonists. Nevertheless, no modality was devoid of negative aspects and limitations and the look for ideal drug persist. No single agent has been recognized as the most suitable for this purpose. Amongst the suggested procedures, intravenous lidocaine or fentanyl appear to best to fulfil the above-stated criterion.[2, 3]

Lignocaine is a medication used to numb tissue in a specific area. It is an amide (-NHCO-) synthetic local anaesthetic. Lidocaine was discovered in 1946 and went on sale in 1948.[4] It is on the World Health Organization's List of Essential Medicines, the most efficient, safe and sound medicines needed in a health system The use of lignocaine is well recognized in treatment of patients with ventricular dysarrthmias and as prophylaxis in curing of ventricular tachyarrthmia as especially in connection with myocardial infarction and mechanical irritation of cardia. The principal metabolic pathway of lignocaine is oxidative dealkalysation in the liver to monoethylglylcinexylidide followed by hydrolysis of this metabolite to xylidide. Monoethylglycinexylidide has about 80% of the activity of lignocaine for defence against cardiac dysarrythmias.

Lignocaine prevents (conduction blockade)which is a transmission of the nerve impulse by inhibiting passage of sodium ions through ion selective sodium channels in nerve membrane.[5]Lignocaine molecule itself is a specific receptor to the sodium channel.

Fentanyl is a phenylpiperidine of the 4-amino piper dine series, structurally correlated to, but not derived from pethidine. Fentanyl has a rapid onset and short duration of action. It is a potent, synthetic narcotic analgesic. Which is highly lipid soluble, has a low molecular weight and is a synthetic opioid agonist which is widely used as an intravenous analgesic supplement, the component of inhalation anaesthesia, balanced anaesthesia and neurolept analgesia and also as a lone anaesthetic. As an analgesic, it is 75 to 125 times more potent than morphine. The onset of effect is 1-2 minutes and the duration is 1 hour after intravenous administration. As a result, it has proved ideal for control of the short-lived haemodynamic sequelae, associated with laryngoscopy and intubation.

The plan of this study was to do a comparative study of Lignocaine (Xylocaine), fentanyl and placebo for the attenuation of the cardiovascular response to direct laryngoscopy and intubation during general anaesthesia.

MATERIAL AND METHODS

After obtaining Ethical Committee approval and patients informed consent, one hundred fifty patients aged 20–60 years of either sex and weighing between 35-80 kgs of Anaesthesiology department at Shri Guru Ram Rai Institute of Medical & Health Sciences, Dehradun physical status 1and 2 undergoing surgeries under general anesthesia and requiring orotracheal intubation were enrolled in this prospective, randomized double‐blind study. Patient with ASA grade I Normotensive and Normal ECG is included in this study and the Patients with a history of regular medication, alcoholism, past history of myocardial ischemia, hypertension, cerebrovascular

accident or eclampsia has been excluded from the study. Patients careful pre-anaesthetic evaluation was done by taking history and by clinical examination. Relevant clinical signs and symptoms like pulse rate, blood pressure, respiratory rate were noted. All the selected patients were divided into three groups consisting of 50 patients each.

Group-: Received Fentanyl 4µg /kg body weight.

Group-II: Received Lignocaine (xylocaine) 1.5 mg /kg body

weight Group-III: Received normal saline.

Premedication of the patient with intra-muscular atropine 0.01mg/ kg, pentazocine 0.5mg/kg i.v Midazolam 0.01mg /kg half an hour prior to induction. With a close-fitting face-mask using Bains Circuit, all the patients were pre-oxygenated with 100% oxygen for 5L/ minutes. For all patients induction of anaesthesia was standardized with thiopentone 5 mg/kg i.v. and were relaxed with succinylcholine 2mg/kg i.v. and intubated. Maintained with 3L/min of oxygen and 5L/min of nitrous oxide. For the first five minutes post-intubation no additional agents were given, nor was any surgical stimulus given to these patients. Additionally, anaesthesia in all three groups of patients was carried out as per the requirement. All patients who needed a second try at intubation were expelled from the study. The heart rate, blood pressure, and SPO2 were recorded at the following time intervals.

"B" Baseline value- during the time of pre-anaesthetic check up one day priorly.

"0" Just prior to intubation.

"1" One minute after intubation

"2 Two minutes after intubation

"3" Three minutes after intubation

"4" Four minutes after intubation

"5" Five minutes after intubation

At the end of a monitored period which is of 5 minutes time, the patient has been cleaned and draped, surgery is commenced

RESULTS

After intubation, incidence of tachycardia (HR>100/min) was significantly lower in fentanyl group ($p<0.05$) in comparison of placebo and lignocaine group. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly high in comparison to baseline value in placebo group and lignocaine group compare to fentanyl group ($p<0.05$).

Comparison of Heart Rate

Table 1 and 2 shows that p value for heart rate was insignificant basal and prior to intubation at 0 minute. However, p value for heart rate was statistically significant for 1^{st}, 2^{nd},3^{rd},4^{th} and 5^{th} minute between group I and group II. ($p<0.05$)

There was an insignificant difference for heart rate of baseline and 0 minute in group II and group III. Whereas, p value for the heart rate was statistically significant at 1^{st}, 2^{nd}, 3^{rd} and 4^{th}minute for group II and group III. Further, there was an insignificant p value for heart rate at 5^{th} minute for group II and group III.

It is evident from table 2 that p value was insignificant for baseline heart rate and 0 minute heart rate for group III and group I. Whereas, there was statistically significant difference in heart rate at 1st, 2nd, 3rd, 4th and 5th minute for group III and group I.

Comparison of Systolic Blood Pressure

Compared with baseline value, changes in systolic blood pressure in group I and group II was statistically insignificant for group I and group II. Further, p value was statistically significant at 1st, 2nd, 3rd and 4th minute for SBP in group I and group II. Whereas p value was insignificant for SBP at 5th minute in group I and group II.

Table 3 shows that comparing the baseline value and one minute after intubation systolic blood pressure in group II and group III was statistically insignificant. Whereas, at second, third and forth minute, high significant difference was observed. However, after fifth minute difference was slight only.

In group I &III difference in systolic blood pressure was significant as compared to baseline values. At first, second, third fourth and fifth minute statistically high significant difference in systolic blood pressures was observed.

Comparison of Diastolic Blood Pressure

It is evident from figure 1 that there was statistically significant difference in baseline values of diastolic blood pressures among group I & II ($P<0.05$) but no significant difference was seen just before intubation.

Further, results revealed that at 1st and 2nd minutes, there was statistically high significant difference in mean diastolic blood pressure but at 3rd minute no significant difference was observed. In addition, statistically significant difference was recorded at 4th and 5th minute.

In group II and III ($P<0.05$) statistically significant difference was seen in baseline diastolic blood pressures and just before intubation but at first minute statistically no significant difference was observed. Whereas at second, third, fourth and fifth minute high significant difference in mean diastolic blood pressure was seen.

No significant difference among groups I and III ($P>0.05$) was seen in baseline DBP but it became highly significant just before and at 1st to 5th minutes after intubation.

Table 1: Comparison of changes in heartbeat of each group.

	Baseline	0 minute	1 minute	2 minute	3 minute	4 minute	5 minute
Group I Fentanyl 4mcg/kg	80±6.4	83±7.5	80±5.7	86±4.6	85±4.4	84±2.8	82±2.4
Group II Lignocaine 1.5 mg/kg	79±5.4	82±4.3	83±2.7	89±1.6	88±2.6	90±2.9	89±2.3
Group III Placebo (normal saline)	77±2.6	83±2.8	87±2.9	100±3.6	96±3.5	93±3.2	89±2.2

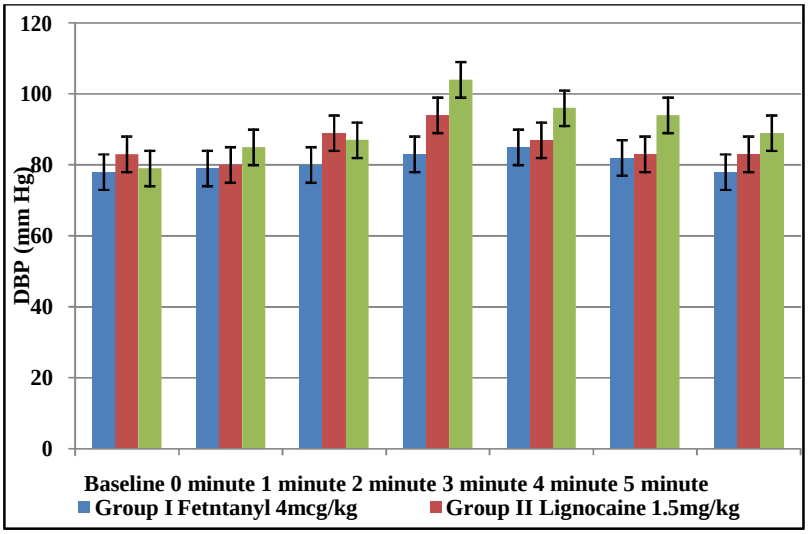
Table 2: The p value of heart beat in each group.

	Group I vs Group II	Group II vs Group III	Group III vs Group I
Baseline	p<0.05	p<0.05	p>0.05
0 minute	p<0.05	p>0.05	p<0.05
1 minute	p<0.05	p<0.05	p<0.05
2 minute	p>0.05	p<0.05	p<0.05
3 minute	p<0.05	p<0.05	p<0.05
4 minute	p<0.05	p<0.05	p<0.05
5 minute	p<0.05	p<0.05	p>0.05

Table 3: Comparison of systolic blood pressure of each group.

	Baseline	0 minute	1 minute	2 minute	3 minute	4 minute	5 minute
Group I Fentanyl 4mcg/kg	130±5.4	124±6.3	125.2±6.8	130±3.88	132±4.8	134±7.4	132±4.68
Group II Lignocaine 1.5 mg/kg	134±5.4	122±5.8	127.8±5.8	136±4.26	143±5.46	139±6.4	134±6.7
Group III Placebo (normal saline)	129±5.5	127±5.9	129±5.78	164±7.6	169±4.88	153±6.29	135±4.9

Fig. 1: Comparison of diastolic blood pressure of each group.



DISCUSSION

Increase of blood pressure, heart rate and cardiac disarrhythmias have been found associated with laryngoscopy and endotracheal intubation.[6] All these cardiac markers may disappear after short time; nevertheless they may be induce harmful effects in patients suffering from various chronic diseases like anomalies of cerebral vessels, increased intracranial pressure and cardiovascular diseases.[7]

Fentanyl

Fentanyl acts on autonomic and cardiovascular regulatory areas which in turn lead to haemodynamic stability during perioperative period. It has been found associated with increase parasympathetic tone and decrease sympathetic tone.[8] Studies suggested that action of fentanyl is executed mainly by two receptors opioid receptors and μ receptors.[8,9]

Pituitary adrenal response is inhibited by fentanyl via hypothalamus. Fentanyl attenuates the response at 2μg/kg given before laryngoscopy and intubation. Optimal time of administration is 5 minutes before laryngoscopy and intubation.[10]In the present study 4μ g / kg were used and the efficacy was compared with lignocaine and placebo group. Similarly, Yushi U et al[11]recorded that 2 μ g/kg fentanyl was efficient enough to suppress the hemodynamic response for endotracheal intubation instead of response to the laryngoscopy.

It has been suggested in the study that supplementation of anesthetic induction with fentanyl 2 μ g/kg can significantly induce the increase of heart rate and blood pressure after laryngoscopy and intubation. However, it has been found that fentanyl 6 μ g/kg leads to completely decreased blood pressure responses.[12]

Alike, Gupta S et al observed that fentanyl in bolus dose of 2 μ g/kg before surgery are effective in sustaining the hemodynamic responses to suppress the hemodynamic response for endotracheal intubation like blood pressure and heart rateS instead of response to the laryngoscopy. On the other hand, low doses of fentanyl should be employed to side effects of large doses as large doses lead to various disorders like bradycardia, nausea, muscular rigidity and vomiting. Moreover, postoperative respiratory depression may be caused by administration of large doses of fentanyl especially in surgery of short duration.[12,13] Me Clain DA et al observed the apnoeic episodes in four patients out of seven patients who had received 3.2-6.5 μ g/kg fentanyl.[14]

Lignocaine

Studies have suggested that the sodium channels in the cell membranes of the heart are blocked or reduced by the action of lignocaine which in turn leads to increase of action potential results in decrease of conduction velocity in atrial and ventricular muscles.

Various studies recorded administration of intravenous lignocaine causes blunting increase in pulse rate, blood pressure, intraocular pressure and intracranial.

Researchers suggested that the possible mechanisms of action of lignocaine may include a direct myocardial depressant effect, a peripheral vasodilating effect along with an effect on synaptic transmission.[8]Lev R et al[15] suggested that a prophylactic intravenous does 1.5 mg/kg of lidocine leads to optimal intubation within 3 minutes. Moreover, they did not record any harmful side effects of prophylactic lidocaine.[15]

Wang YM et al[16] reported that the space between 1-3 minutes before laryngoscopy and tracheal intubation is the most optimal time for the administration of intravenous lidocaine to attenuate the increase of intraocular pressure.

Further, Wilson IGet al[17]observed that there was a significant increase of heart rate irrespective of the timing of administration of intravenousadministration of lignocaine 2nd, 3rd or 4th minutes before tracheal intubation in all groups. However, they did not record any significant increase in mean artrial pressure in response to intubation in lignocaine group before intubation, but increase of 19 % in MAP compared to baseline values was recorded in the placebo group.

In addition, Mollick MT et al[18] recorded that combination of intravenous lignocaine with pethidine sustained the normal sympathetic responses to endotracheal intubation and laryngoscopy with in 5 minute after intubation. However, the patients of only lignocaine group did not sustain their sympathetic responses to normal within 5 minute after laryngoscopy and endotracheal intubation.

Bachofen M[2] suggested that administration of fentanyl can significantly decrease blood pressure. Whereas, no significant effect of lidocaine was observed on the pressure response in patients with fentanyl group.

Malde AD et al[19] showed 1.5 mg/kg of lignocaine and 2 µ g/kg of fentanyl can attenuate rise of heart rate with 5 minutes after the administration. Though, the effect of fentanyl was better than the effect of lignocaine.

CONCLUSIONS

Findings of the present study suggested that attenuation of the pressor response was seen both with lignocaine and fentanyl. Further, among both drugs, fentanyl was more consistent, reliable and effective attenuation of haemodynamic response to laryngoscopy and endotracheal intubation in comparison of lignocaine. However, more studies on larger population are required to compare the effects of lignocaine and fentanyl in attenuation of pressor response to laryngoscopy and tracheal intubation.

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