Original Article

Role of Intravenous Fentanyl and Lignocaine for Attenuation of Stress Response in Endotracheal Intubation - A Comparative Study

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Abstract

Background: *Laryngoscopy and tracheal intubation is invariably associated with a reflex sympathetic pressor response resulting in elevated heart rate and blood pressures. This may prove detrimental in high risk patients. Many drugs have been suggested in modifying in haemodynamic responses to laryngoscopy and intubation.*

Objective: *To assess efficacy of two drugs Fentanyl and Lignocaine and to assess which one is more effective to attenuate haemodynamic response to direct laryngoscopy and endotracheal intubation.*

Methods: *A total number of 60 patients ASA class I and II were selected randomly as per inclusion and exclusion criteria in two groups, 30 patients in each group. Group F received Fentanyl 1.5mg/kg IV 5min before intubation and group L received Lignocaine 1.5mg/kg IV 90 sec before intubation. Per-operative data were recorded at 1min, 2min, 5min and 10min after intubation.*

Result: *The mean heart rate(HR), systolic(SBP), diastolic(DBP), mean(MAP) arterial pressure and rate pressure product(RPP) before starting anaesthesia were similar in group- F(Fentanyl) and L(Lignocaine). But the values were significantly lower in group F(Fentanyl) at 1, 2, 5 and 10 minute than group L(Lignocaine).*

Conclusion: *Fentanyl 1.5mcg/kg is superior to Lignocaine 1.5mg/kg for attenuation of haemodynamic response (HR, SBP, DBP, MAP and RPP) to laryngoscopy and endotracheal intubation.*

Keywords: *Fentanyl, lignocaine, laryngoscoy, endotracheal intubation.*

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Introduction

Intubation is associated with a cardiovascular response of elevated blood pressure and pulse, occasional dysrhythmias, cough reflexes, increased intracranial pressure and increased intraocular pressure. If no specific measures are taken to prevent hemodynamic response, the HR can increase from 26%-66% depending on the method of induction, and SBP can increase from 36%-45%[1].

In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and intubation. The hypertensive response to anesthetic induction with endotracheal intubation may be harmful in patients with cardiovascular disease, increased intracranial pressure, or anomalies of the cerebral vessels[2].

Activation of sympathetic nervous system may cause coronary artery vasoconstriction, reducing the myocardial oxygen supply which in turn predispose to myocardial ischaemia. This condition is also aggravated by hypercoagulable state in the postoperative period-a stress response byADH[3].

Stress may be reduced by modifying or controlling the response to stress[4]. Several agents and

regimens have been devised to control this stress induced haemodynamic responses. These are Local anesthetics, Ganglion blockers, Vasodilators, Beta-bockers, Inhalational anaesthetics, Calcium channel blockers. But none of these gained wide spread popularity. Narcotics can also attenuate pressor response and can maintain proper depth of anaesthesia with inhalational or intravenous anaesthetic agent. As such administration of one or the other analgesic is needed during surgery. If a small dose of fentanyl, administered 5 minutes before intubation can prevent this hemodynamic response, it would be worth.[5] Few studies have shown that fentanyl is effective in blunting pressor response to laryngoscopy and endotracheal intubation. We undertook a study comparing the effect of Fentanyl (1.5µg/kg) or Lignocaine (1.5 mg/kg), a most widely used drug for attenuation of hemodynamic response. There are some studies about preventing stress response due to tracheal intubation with either Esmolol or Fentanyl or lignocaine and there are some comparative studies with Esmolol versus Fentanyl, Esmolol versus Lignocaine. But there are very limited study about comparing the effects of Fentanyl and Lignocaine. So we have taken this study to see the role of intravenous Fentanyl and Lignocaine for attenuation of stress response in tracheal intubation. It will help us to choice the better one to prevent per-operative MI, excessive bleeding & help for better recovery of the patient, ultimately patients good outcome.

Result and observation

Table I *Distribution of the patients by age & body weight of groups*

Mean ± SD	Group-F	Group-L	p value*
Age (inyears)	33.13 ± 8.57	34.37 ± 8.29	0.054
Weight(inkg)	54.80 ± 7.52	56.00 ± 8.51	0.100

*Chi-square test was done to measure the level of significance.

Mean ages of the patients of group F and group L were 33.13 ± 8.57 and 34.37 ± 8.29 years respectively. Mean weights of the patients of group F and group L were 54.80 ± 7.52 and 56.00 ± 8.51 kg respectively. No statistically significant difference was observed among groups at 0.05 level in term of age & Mean weights of the patients of group F and group L.

Table II *Comparison of groups in term of heart rate(Heart rate at different follows up period)*

Heart rate	Group		p value*
	Group-F	Group-L	
Before induction			
0 minute	90.63 ± 12.39	91.93 ± 7.87	0.348
After intubation			
1 minute	111.37 ± 25.49	118.57 ± 12.18	0.001
2 minute	100.17±10.69	114.60 ± 17.52	<0.001
5 minute	87.17 ± 11.10	87.17 ± 11.10	<0.001
10 minute	83.40 ± 10.00	86.80 ± 8.73	0.426

*Chi-square test was done to measure the level of significance

Table shows the mean heart rate before induction and after intubation among the patients of different groups in different follows up period. Significance differences were observed among groups in term of heart rate at 1 minute, 2 minute and 10 minute.

Table III *Comparison of groups in term of systolic blood pressure(Systolic blood pressrue at different follows up period)*

Systolic BP	Group		p value*
	Group-F	Group-L	
Before induction			
0 minute	122.13 ± 8.11	125.47 ± 8.74	0.447
After intubation			
1 minute	142.13 ± 11.02	152.90 ± 11.50	0.002
2 minute	135.90 ± 8.73	145.07 ± 9.90	0.003
5 minute	120.17 ± 8.65	131.13 ± 13.58	0.000
10 minute	117.97 ± 10.60	121.50 ± 12.12	0.111

*Chi-square test was done to measure the level of significance

Table shows the mean systolic blood pressure before induction of anaesthesia and after intubation among the patients of different groups in different follows up period. Significant differences were observed among groups at 1 minute, 2 minute, 5 minute and 10 mimute.

Table IV: *Comparison of groups in term of diastolic blood pressure(Diastolic blood pressrue at different follows up period)*

Diastolic BP	Groups		p
	Group-F	Group-L	value*
Before induction			
0 minute	80.87 ± 7.24	80.83 ± 9.40	.981
After intubation			
1 minute	101.17 ± 6.24	113.60 ± 14.55	.000
2 minute	93.37 ± 11.08	104.43 ± 15.68	.005
5 minute	86.07 ± 8.86	91.63 ± 12.79	.012
10 minute	77.33±7.32	80.53 ± 9.73	.244

*Chi-square test was done to measure the level of significance

Table shows the mean diastolic blood pressure before induction and after intubation among the patients of different groups in different follows up period. Significance differences were observed among groups at 1 minute, 2 minute, 5 minute and 10 minute.

Table V *Comparison of groups in term of mean arterial pressure(Mean arterial pressure at different follows up period)*

Mean arterial pressure	Groups		p
before induction	Group-F	Group-L	value*
0 minute	94.62± 5.11	95.71± 7.63	0.837
After intubation			
1 minute	114.82 ± 6.41	126.70 ± 12.51	0.000
2 minute	107.54 ± 7.82	117.98 ± 12.87	0.001
5 minute	97.43 ± 7.86	104.80 ± 12.78	0.002
10 minute	90.88 ± 7.38	94.19 ± 8.63	0.376

*Chi-square test was done to measure the level of significance

Table shows the mean arterial blood pressure before and after induction among the patients of different groups in different follows up period. Significance differences were observed among groups at 1 minute, 2 minute 5 minute and 10 minute.

Table VI *Comparison of groups in term of rate pressure product(Rate pressure product at different follows up period)*

Rate pressure product	Group		p
before induction	Group-F	Group-L	value
0 minute	11076.0±1741.5	11507.7±966.6	.281
After intubation			
1 minute	15801.3±3670.1	18134.2±2325.6	.000
2 minute	13601.0±1605.2	16618.1±2764.7	.000
5 minute	10508.0±1710.2	12922.8 ±1640.6	.000
10 minute	9836.2±1409.0	10548.9±1514.4	.145

*Chi-square test was done to measure the level of significance

Table shows the mean rate pressure product before and after induction among the patients of different groups in different follows up period. Significance differences were observed among groups at 1 minute, 2 minute, 5 minute and 10 minute.

Table VII *Distribution of assessment of intubation conditions by groups*

Assessment	Group		p
	Group-F	Group-L	value*
Excellent	27 (90.0)	22 (73.3)	0.233
Good	3 (10.0)	8 (26.7)	
Total	30 (100.0)	30 (100.0)	

*Chi-square test was done to measure the level of significance. #Figure within parentheses indicates in percentage.

Table shows the clinical assessment of patients after induction of drugs among groups. Maximum patients of all groups show excellent result. No significant difference was observed in term of assessment results among groups at 5% level.

Discussion

The hypertensive response to anesthetic induction with endotracheal intubation may be harmful in patients with cardiovascular disease, increased intracranial pressure, or anomalies of the cerebral vessel[2]. Instrumentation of pharynx and tracheal intubation may result in tachycardia, hypertension and increased catecholamine concentration that may evoke life threatening condition among susceptible individuals specially those with cardiovascular disease[6]. Activation of sympathetic

nervous system may cause coronary artery vasoconstriction, reducing myocardial oxygen supply which in turn predispose to myocardial ischaemia. This condition is aggravated by hypercoagulable state in the postoperative period- a stress response by ADH[3]. Intubation is associated with a cardiovascular respose of elevated blood pressure and pulse, occasional dysrrhythmias, cough reflexes, increased intracranial pressure, and increased intraocular pressure. If no specific measures are taken to prevent hemodynamic response, the HR can increase from 26%-66% depending on the method of induction, and SBP can increase from 36%-45%.

Stress may be reduced by modifying or controlling the response to stress[4]. Premedication is used to provide sedation, anxiolysis and to enhance quality of induction, maintenance and recovery from anesthesia. A recent study has suggested that different premedication may lead to an alteration in sympathoadrenal stress responses during intubation and surgery[7]. Several agents and regimens have been deviced to control this stress induced hemodynamic responses. These are Local anesthetics, Ganglion blockers, Vasodilators, Opioids, Deep inhalational anesthesia, Large dose of thiopental sodium. But none of them gained wide spread popularity. Local anesthetic in large dose may cause cardiac depression, Vasodilator and Ganglion blocker cause hypotension and reflex tachycardia, Deep inhalational anesthesia cause intracranial hypertension, large dose thiopental causes cardiac depression. These effects are not desirable and limit their usefulness.

A prospective randomized double blind study was performed by Bakiye Ugur et al[8] to investigate the effects of Esmolol, Lidocaine, Fentanyl, on 120 (ASA I&II), divided into 4 equal groups. Group C received 5% dextrose 5ml, group-E ESmolol 1.5mg/ kg IV, group-F fentanyl 1mcg/kg IV, and group-L lignocaine 1.5mg/kg IV 2 min before endotracheal intubation. HR, MAP, and RPP were recorded before and after induction of anesthesia, immediately after intubation and 1, 3, 5, 7 and 10 min after intubation. An increase in HR was observed immediately after intubation in all groups except the group-E. The decrease in HR began 3 min after intubation, occurred earliest in group-E, and was significant in all groups 10 min after intubation ($p<0.0083$). MAP increased after intubation in all groups but was lower in fentanyl group. MAP decreased first in the group-E 3 min after intubation and than in other grup 5 min after intubation ($p<0.05$). Calculated RPP increased immediately after intubation in all groups compared with baseline values. Increased RPP values began to decrease first in the group-E 3 min after intubation ($p<0.05$). They concluded that Esmolol 1.5 mg/kg can be given 2 min before laryngoscopy and intubation to prevent RPP and tachycardia and can be beneficial when administered before layngoscopy and tracheal intubation in patients with tachycardia.

A double blind, randomized, controlled, study was designed by A Malde and et al.[1] to compare the efficacy of single bolus doses of Fentanyl (2Âµg/ kg) or Lignocaine (1.5 mg/kg) for attenuation of pressor response to laryngoscopy and endotracheal intubation (ETI). Ninety patients received either fentanyl or lignocaine or saline 5 minutes before intubation. The fentanyl group showed significantly lesser rise (5.46%) in HR compared to lignocaine (16.23%) ($p=0.018$) and Control group (43.68%) ($p=0.000$). The rise persisted for 2, 5 and 10 minutes in fentanyl, lignocaine & control groups respectively. The fentanyl group showed significant decrease in SBP after administration, which came back to normal at 1 to 3 minutes following intubation and again decreased 4 minutes after intubation. They conclude that Lignocaine and fentanyl both attenuated the rise in pulse rate, though fentanyl was better. Lignocaine attenuated the rise in blood pressure with intubation whereas fentanyl prevented it totally.

A prospective randomized double blind study was performed by Gurulingappa et al[9]. Seventy five ASA I and II status normotensive patients scheduled for elective surgical procedures were selected randomly and divided into three groups of 25 each. All patients received premedication with pentazocine 0.05mg/kg i.v., atropine 0.01mg/ kg intramuscularly and midazolam 0.01mg/kg i.v. half an hour prior to induction. Induction of anesthesia was standardized for all patients who received, thiopentone 5 mg/kg i.v. and and were relaxed with succinylcholine 2mg/kg i.v. The first group received fentanyl 4mcg/kg i.v bolus, the second group received lignocaine 1.5mg i.v bolus and then

third group received placebo (normal saline), 5 minutes before laryngoscopy and intubation. HR, SBP, DBP were recorded noninvasively before induction 0 postinduction, 1,2,3,4 and 5 minutes from the onset of laryngoscopy. After intubation incidence of tachycardia (HR>100/min) was significantly greater in placebo and lignocaine group than in fentanyl group ($p<0.05$). Rise in SBP and DBP were also statistically significant in placebo and lignocaine group than in fentanyl group ($p<0.05$).They concluded that attenuation of pressor response is seen both with lignocaine and fentanyl. Of the two drugs fentanyl 4mgicrogram i.v. bolus provides a consistent, reliable and effective attenuation as compared to lignocaine 1.5mg/kg iv. bolus.

A prospective double blind study was carried out by Dr. Rupal B. Shah and et al[10]. 40 patients of ASA grade I and II aged 20-50 years were selected for elective surgery requiring general anaesthesia for endotracheal intubation. They were divided into 2 groups. Group-1: Lignocaine hydrochloride group. Here patients received inj. Lignocaine hydrochloride 1.5 mg/ kg i.v. bolus 3 min prior to induction. Group-2: Fentanyl citrate group. Here patients received injection Fentanyl citrate 2 mcg/ kg i.v. bolus 3 min prior to induction. All patients were pre-oxygenated with 100% O_2 for 3 min before induction. Induction was achieved with injection Thiopentone sodium 5 mg/kg i.v. and injection succinylcholine 2 mg/kg was given i.v. IPPV given with 100% O_2 and after adequate relaxa-tion laryngoscopy and intubation was done. Anaesthesia was maintained with O_2(33%), N2O(67%), Isoflurane(0.5-1.0%) and injection Vecuronium bromide. Peri-operative vitals and complications were recorded. Changes in mean pulse rate(HR) and MAP was significant after intubation and intraoperatively with mean pulse rate, MAP being higher in group-1 than group-2. Thus Fentanyl citrate provides better haemodynamic stability by increasing sedation, analgesia and depth of anaesthesia. They concluded that Fentanyl citrate is safer and more effective in attenuation of haemodynamic response to laryngoscopy and intubation.

In this prospective study sixty patients have been randomly selected into one of the two groups by a computer generated random number table and by card sampling. Each patient has been given cards to take any one blindly from two groups. There were no significant differences between two groups in age, body weight, gender and ASA grading. Before induction of anaesthesia heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), rate pressure product (RPP) and mean arterial pressure (MAP) were not statistically significant($p>0.05$) in three groups.

One minute after intubation, these parameters were significantly raised ($p<0.05$) in all groups. The findings of our study are comparable to those of Bakiye et al[8], who found a rise in HR, MAP and RPP, just after and 1 min after intubation and also comparable to those of King et al[11] who found a rise of HR, SBP, DBP, RPP and MAP 1 min after intubation. They also found gradual return of these parameters to baseline as anaesthesia deepened.

Our study demonstrated highly significant reduction in HR,SBP, DBP, RPP and MAP in group F compared with group L, at 1, 2. 5 and 10 minutes after intubation. The reduction of HR, SBP, DBP, MAP and RPP were significantly more in group F (Fentanyl) than those of group L (Lignocaine) (fig I-V). In our study five minutes after intubation, HR, SBP, DBP, RPP and MAP returned to almost baseline values in Fentanyl group but in Lignocaine group it took 10 min to return to base line.These findings are in agreement with that of Bakiye Ugur et al[8]. It is also comparative with that of A Malde and et al.[1] who found that Lignocaine and fentanyl both attenuated the rise in pulse rate, though fentanyl was better. Lignocaine attenuated the rise in blood pressure with intubation whereas fentanyl prevented it totally. Our study is also comparable to those of Gurulingappa et al[9] found that Rise in HR, SBP and DBP were statistically significant in lignocaine group than in fentanyl group ($p<0.05$), and also coparable to those of Dr. Rupal B. Shah and et al[10] who showed that changes in mean pulse rate(HR) and MAP was significant after intubation and intraoperatively with mean pulse rate, MAP being higher in group-1(Lignocaine) than group-2(Fentanyl).

We observed that both Fentanyl and Lignocaine attenuated the HR, SBP DBP MAP and RPP, but the attenuation was more in Fentanyl group. The decrease in SBP and RPP were significantly higher in Fentanyl group than in Lignocaine group.

The dose of Fentanyl and Lignocaine evaluated in this study did not cause any adverse effects. This study has one limitation-we only tested the 1.5 mcg/kg Fentanyl and 1.5 mg/kg Lignocaine and administered the anaesthetic agents through the intravenous route. Therefore the results of the study are applicable to the doses tested in combination with the anaesthesia induction technique used.

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