

Fentanyl Versus Lidocaine Intravenously to Attenuate Hemodynamic Effects of Endotracheal Intubation

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Abstract

Background and objectives: Hemodynamic changes to laryngoscopy and endotracheal intubation may increase morbidity in the perioperative period. Those changes may become significant in patients with uncontrolled hypertension or heart diseases. In this study, we compared the efficacy of intravenous fentanyl and intravenous lidocaine in attenuating the hemodynamic responses during laryngoscopy and intubation. **Methods:** A total of 100 adult patients, American Society of Anesthesiologists physical status I and II from both gender aged 18 to 65 years undergoing various elective surgeries under general anesthesia, were included in this prospective, randomized, single-blind study. The patients were randomly divided into two equal groups, Group F received 1mcg/kg fentanyl IV 3 minutes before intubation, group L received 1mg/kg lidocaine IV 3 minutes before intubation. Patients in both groups were anesthetized with the same technique. heart rate, systolic, diastolic and mean blood pressure were monitored and recorded before giving the study drug, 3 minutes after giving the study drug, 3 minutes after intubation then 6 minutes after intubation. **Results:** We evaluated 100 patients including 49 males and 51 females, 62 American Society of Anesthesiologists physical status I and 38 American Society of Anesthesiologists physical status II, there were significant differences between the two groups 3 and 6 minutes after intubation, F group had less rise in heart rate, systolic, diastolic and mean blood pressure than L group 3 minutes after induction and endotracheal intubation. **Conclusions:** we concluded that fentanyl 1mcg/kg IV had more and faster effect in blunting stress response to laryngoscopy and endotracheal intubation as compared to lidocaine 1mg/kg IV.

Keywords: Fentanyl; Lidocaine; Hemodynamic response; Laryngoscopy; Endotracheal intubation.

Introduction

Laryngoscopy and orotracheal intubation are potent stressful stimuli that provoke hemodynamic response like tachycardia and hypertension, these responses can be transient and harmless in healthy patients, but it may prove hazardous amongst patient with underlying cardiac disease, or hypertensive disease and its sequelae that can lead to myocardial ischemia, ventricular arrhythmia, left ventricular failure, and cerebral hemorrhage. The mechanisms of the responses to laryngoscopy and orotracheal intubation are proposed to be by somatovisceral reflexes¹. Induction of anesthesia and endotracheal intubation often produces a period of hemodynamic instability for hypertensive patients and regardless of the level of preoperative blood pressure control, many patients with hypertension display an accentuated hypotensive response to induction of anesthesia, followed by an exaggerated hypertensive

response to endotracheal intubation. Endotracheal intubation of the trachea stimulates laryngeal and tracheal sensory receptors, resulting in a marked increase in the elaboration of sympathetic amines (adrenaline and noradrenaline), this sympathetic stimulation results in tachycardia and elevation of blood pressure².

Stimulation of proprioceptors at the base of the tongue during laryngoscopy induces impulse dependent increases of systemic blood pressure, heart rate, and plasma catecholamine concentrations. Subsequent orotracheal intubation recruits additional receptors that elicit augmented hemodynamic and epinephrine responses as well as some vagal inhibition of the heart³.

These events are especially detrimental in individuals who have limited myocardial reserve due to coronary artery disease, cardiac dysrhythmia, cardiomyopathy, congestive heart failure, hypertension, and geriatric population⁴.

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Thus, diverse classes of drugs and different techniques such as; local anesthetics, opioids, calcium channel blockers, short acting β -adrenergic blockers, and their combinations have been used to prevent hemodynamic responses induced by laryngoscopy and endotracheal intubation⁵⁻⁷.

Fentanyl is a phenylpiperidine of the 4-amino piperidine series, structurally related to, but not derived from pethidine⁸. Fentanyl is a frequently used opioid that joins with hypnotic agents to diminish hemodynamic responses to tracheal intubation^{9, 10}

Lidocaine is an amide (-NHCO-) synthetic local anesthetic¹¹. Lidocaine has a suppressive effect on the circulatory responses in patients undergoing laryngoscopy and tracheal intubation¹².

Patients and methods

This is a prospective, randomized, single-blind study carried out in the Rzgary teaching hospital and Sardem private hospital in Erbil city from July 2017 to January 2018. Informed consent was obtained from patients. The study population consisted of 100 patients who were randomly divided into two groups of (n 50) patients in each group, F & L groups, American Society of Anesthesiologists physical status I & II, male and female adults between the ages of 18-65 years scheduled for various elective surgical procedures. Patients with predicted difficult intubation, modified Mallampati Class III or IV, refusal or inability to understand the procedure, allergy to any of the study drugs, body mass index (BMI) >30, history of respiratory distress, gastroesophageal reflux, neurological, cardiovascular, cerebrovascular, respiratory, hepatic or renal diseases, anticipated difficult airway and pregnant ladies were excluded from the study. The patients' demographic data such as sex and age were recorded and then patients were randomly divided into two groups (fentanyl group and lidocaine group). In the operating room, patients were attached to the following monitors; electrocardiography, noninvasive blood pressure monitor, pulse oximeter. The baseline values (pre-anesthetic reading) for systolic blood pressure (SBP), diastolic blood pressure (DBP), ; mean arterial pressure (MAP) and heart rate (HR) were recorded, Fentanyl group received 1mcg/kg fentanyl IV three minutes before

induction, Lidocaine group received 1mg/kg lidocaine IV three minutes before induction. The Hemodynamic variables (SBP), (DBP), (MAP) and (HR) were monitored three minutes after giving study drugs and prior to induction and performing endotracheal intubation. All patients in both groups were anesthetized with the same technique, Anesthesia was induced by Propofol given in 2mg/kg dose with rocuronium 0.6 mg/kg followed by intubation after 1 minute. Then a laryngoscopy was performed by an anesthetist with a standard Macintosh laryngoscope blade and the trachea was intubated with an appropriate size cuffed endotracheal tube within a period of 15 seconds. Failure to intubate in this period and difficult intubation cases were excluded from this study and the patient was ventilated with oxygen. Hemodynamic variables (SBP), (DBP), (MAP) and (HR) were recorded 3 minutes and six minutes after induction and performing endotracheal intubation. All results were expressed as mean \pm SD. Hemodynamic variables in the present study were analyzed by using statistical package for social sciences (SPSS), sampling size done by convenience sampling method. p-values \leq 0.05 were considered significant. The study had been approved by ethical committee of Kurdistan Board for Medical Specialties.

Results

Regarding patient's gender, ASA physical status I & II and age there were no significant differences between study groups, p-value (0.31, 0.68, 0.82) respectively, Table 1.

Table (1) Relationship between study groups and different parameters.

Demographic data	Study groups		p-value
	Fentanyl	Lidocaine	
Male: Female	22:28	27:23	0.31
ASA I: ASA II	32: 18	30:20	0.68
Age groups	< 20 years	4	4
	20 –30 years	21	24
	> 30 years	25	22

Regarding Systolic Blood Pressure there were no significant difference between the study groups in baseline measurement (SBP1 p-value=0.58) and 3 minutes before intubation (SBP2 p-value=0.81), 3 minutes after intubation (SBP3) was significantly higher in group L as compared to

group F (p-value 0.03), 6 minutes after intubation (SBP4), significant difference was observed, more increase in group F than in group L, Table 2.

Table (2): Mean SBP of both fentanyl and lidocaine groups over different timings.

Variable	Group F mean \pm SD	Group L mean \pm SD	p-value
SBP 1	125.8 \pm 14.9	127.2 \pm 13.3	0.58
SBP 2	126.4 \pm 15	125.7 \pm 13.5	0.81
SBP 3	130.1 \pm 18.9	137 \pm 14.2	0.03
SBP 4	131.1 \pm 17.4	123.7 \pm 13.5	0.01

Regarding diastolic blood pressure between the study groups, differences in baseline measurement (DBP1 p-value =0.4), 3 minutes before intubation (DBP2 p-value =0.41) and 3 minutes after intubation (DBP3 p-value =0.12) were statistically insignificant, 3 minutes after induction and endotracheal intubation mean (DBP4) in group F(78.52 \pm 12.4) in group L(73.34 \pm 9.87) p-value= 0.01) which is significant shows more increase in (DBP) in group F than in group L, Table 3.

Table (3): Mean DBP of both fentanyl and lidocaine groups over different timings.

Variables	Group F mean \pm SD	Group L mean \pm SD	p-value
DBP 1	73.92 \pm 12.0	75.78 \pm 9.95	0.40
DBP 2	74.18 \pm 11.96	75.60 \pm 8.35	0.41
DBP 3	75.74 \pm 15.8	80.36 \pm 13.1	0.12
DBP 4	78.52 \pm 12.4	73.34 \pm 9.87	0.01

There were no significant differences between the study groups regarding baseline mean blood pressure (MAP1), 3 minutes before intubation (MAP2) and 3 minutes after intubation (MAP3), (p-value =0.43, 0.71,0.08) respectively. Six minutes after induction and endotracheal intubation (MAP4) there was significant change in blood pressure (p-value =0.009), Table 4.

Table (4): Mean MAP of both fentanyl and lidocaine groups over different timings.

Variable	Group F Mean \pm SD	Group L Mean \pm SD	p-value
MAP 1	90.86 \pm 12.5	92.60 \pm 10.1	0.43
MAP 2	91.24 \pm 12.4	92.02 \pm 9.25	0.71
MAP 3	93.76 \pm 16.1	98.84 \pm 12.6	0.08
MAP 4	95.74 \pm 13.5	89.78 \pm 10.3	0.009

There were no significant differences between the study groups regarding baseline heart rate (HR1), 3 minutes before intubation (HR2) and 6 minutes after intubation (HR4), (p-value =0.79, 0.06, 0.93) respectively. While there was significant difference between the study groups 3 minutes after intubation (HR3, p-value =0.02), Table 5.

Table (5): Mean HR of both fentanyl and lidocaine groups over different timings.

Variable	Group F Mean \pm SD	Group L Mean \pm SD	p-value
HR 1	89.46 \pm 13.4	88.78 \pm 15.8	0.79
HR 2	96.46 \pm 15.1	90.90 \pm 13.8	0.06
HR 3	100.7 \pm 15.2	107.2 \pm 11.3	0.02
HR 4	95.46 \pm 16.9	95.24 \pm 11.7	0.93

Discussion

Airway Manipulation like laryngoscopy and tracheal intubation had been observed to cause hemodynamic changes with increased heart rate, blood pressure and plasma catecholamines there are numerous methods to decrease these effects of laryngoscopy and tracheal intubation. The most common methods are: using inhaled anesthetics, sympathetic blockers, vasodilators, local anesthetics, narcotics^{13,14}.

In this study, patients randomly divided into the fentanyl (F) or the lidocaine (L) group, we did not include control groups to avoid the risk of hemodynamic changes during laryngoscopy and intubation also the intubation was performed when patient became fully relaxed and the duration of laryngoscopy and intubation was less than ¹⁵ seconds when performed in the first attempt.

Fentanyl 1 mcg/kg and lidocaine 1 mg/kg was used separately and shown different results in reducing the pressor responses. Although these drugs act in decreasing hemodynamic responses of laryngoscopy and tracheal intubation; both medications have shown slightly different outcomes. That is, the use of fentanyl has resulted in a slightly more rapid response than the use of lidocaine (shown 3 minutes after intubation).

Fentanyl produces hemodynamic stability throughout perioperative period by its action on cardiovascular and autonomic regulatory areas. It increases parasympathetic tone and decreases sympathetic tone¹¹.

Regarding our study, hemodynamic response to laryn-

gосcopy and intubation was not completely abolished in any of the groups. Fentanyl or lidocaine was effective in blunting the post-intubation increase in both heart rate and blood pressures, but both of them were comparable. Some studies like Hoda and Khan¹⁵, Parida et al.¹⁶, found IV fentanyl effective in blunting hemodynamic response to laryngoscopy and intubation. Black et al.¹⁷ and Kay et al.¹⁸ have shown complete attenuation of the hemodynamic response to intubation by IV fentanyl. Our study shows blunting but not the complete attenuation of the hemodynamic response to intubation. This may be due to a higher dose of fentanyl (5–6 µg/kg) used in these studies, unlike our study in which we used 1 µg/kg.

There are few studies for fentanyl does not agree with our study. Helfman et al, did not find any hemodynamic attenuation to intubation with either 200 mg lignocaine or 200 µg fentanyl, however, they intubated 2 minutes after study drug injection, their patients were ASA I, ASA IV while our patients were ASA I, ASA II¹⁹.

Lidocaine blocks the sodium channels in the cell membranes of the heart and reduces the rate of the rise of the action potential and hence the conduction velocity above all the His Purkinje system and in the atrial and ventricular musculature¹¹.

Malde and Sarode compared lignocaine (1.5mg/kg) and fentanyl (2 µg/kg) efficacy on hemodynamic stability, they found that lidocaine and fentanyl both attenuated the rise in heart rate, but fentanyl produced better results. Lidocaine attenuated the rise in blood pressure with intubation while fentanyl inhibits it totally, our results were in agreement with this study, but we found that fentanyl does not inhibit rise in blood pressure totally and this discrepancy may be due to a lower dose of fentanyl (1mcg/kg) we used in our study²⁰.

Lev & Rosen wrote a study on “Prophylactic lidocaine use preintubation”. They revealed that a dose of prophylactic lidocaine of 1.5 mg/kg given intravenously 3 minutes before intubation is optimal. No studies document any harmful effects of prophylactic lidocaine given preintubation²¹. There are some studies that have used the same dose of lidocaine that we used in our study, they showed that lidocaine (1mg/kg) IV given before induction and intubation are effective in suppressing the hemodynamic responses

to intubation^{22,23}.

Various studies have reviewed the effect of lidocaine to blunt hemodynamic responses to laryngoscopy and intubation. It is tried in various forms like viscous lidocaine, aerosol, orolaryngeal spray before induction of anesthesia, and inhalation of lidocaine prior to induction of anesthesia. Some studies note a response of intravenous lidocaine in blunting rises in pulse, blood pressure, intracranial and intraocular pressure. Aouad et al. showed that supplementing sevoflurane induction of anesthesia in children with IV lignocaine 2 mg/kg can suppress cough after tracheal intubation and thus improve intubating conditions. In addition, lidocaine minimizes blood pressure fluctuations after tracheal intubation²⁴.

While others showed no effect of intravenous lidocaine administered 1, 2, or 3 minutes before laryngoscopy, In Miller and Warren's study, intravenous lidocaine failed to attenuate the cardiovascular response to laryngoscopy and tracheal intubation irrespective of the timing of administration i.e. 1, 2, or 3 minutes before laryngoscopy, may be because they anesthetize their patients by thiopentone and suxamethonium and they used 1.5 mg/kg IV lidocaine to only 45 Chinese patients, while in our study we used propofol and rocuronium for induction and giving 1mg/kg IV lidocaine to 50 patients 3 minutes before laryngoscopy and intubation²⁵.

Perhaps the time of administration of lidocaine is equally important. Tam et al. in their article “Intravenous lidocaine: optimal time of injection before tracheal intubation”, showed that, when given intravenously 3 minutes before intubation, esmolol and lidocaine appear to have similar efficacies to attenuate moderate hemodynamic changes secondary to emergency intubation in patients with an isolated blunt head injury²⁶.

Wilson et al. showed that irrespective of the timing of administration of injection of lignocaine 2, 3 or 4 minutes before tracheal intubation, there was a significant increase in heart rate of 21-26% in all groups, but no increase in mean arterial pressure (MAP) in response to intubation in any group of patients, but in the placebo group, MAP increased by 19% compared to baseline values²⁷.

In our study, there was a significant rise in HR 3 minutes after intubation in lidocaine group. We injected lidocaine 3

minutes before intubation.

Besides minimizing the cardiovascular response, anesthesia induction for patients at risk must also satisfy the following requirements: it must be applicable regardless of patient group, prevent impairment of cerebral blood flow, and avoid arousal of the patient; it should neither be time-consuming nor affect the duration or modality of the ensuing anesthesia. Among the recommended procedures, intravenous lignocaine or fentanyl appears to best fulfill the criteria. We used fentanyl dose of 1 µg/kg, as this dose is the least dose and found to be effective in attenuating the pressor response, in quite a few studies; moreover, higher doses would lead to undue bradycardia and hypotension.

Our study was designed as single-blind, randomized, prospective, comparative study. We considered factors that could possibly have affected our results. We restricted our study period to 9 minutes because after the commencement of surgery multiple factors like various surgical stimuli play role in hemodynamic response, as compared to laryngoscopy and endotracheal intubation are the only two factors playing role in the pressor response. Nevertheless, our results were possibly limited by the fact that we did not monitor the depth of anesthesia. Doses that are entirely based on mcg/kg or mg/kg probably produce different depths of anesthesia in a given population, which may have affected our results. In addition, we firmly declare, that a more profound induction of anesthesia before tracheal tube insertion may also have influenced the results of this study. Fentanyl and lidocaine are effective in decreasing hemodynamic responses to tracheal intubation, however, neither fentanyl nor lidocaine could inhibit all hemodynamic responses, furthermore, fentanyl had a faster effect than lidocaine.

Conclusions

Both fentanyl in a bolus dose of 1 µg/kg and lidocaine in a bolus dose of 1mg/kg before induction of anesthesia is effective in attenuating the hemodynamic responses to laryngoscopy and endotracheal intubation like heart rate and blood pressure.

Fentanyl provided faster and reliable protection against increases in both heart rate and blood pressure accom-

panying laryngoscopy and endotracheal intubation. No evidence of any myocardial insult was seen in any of the patients in any group in our study.

It is advisable and safe to use fentanyl or lidocaine in patients who are prone to have exaggerated responses of the cardiovascular system during laryngoscopy and intubation.

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