Effect of nebulized lidocaine and Intravenous lidocaine on hemodynamic responses of laryngoscopy and endotracheal intubation

Abstract

Laryngoscopy and endotracheal intubation form one of the main steps in general anesthesia. This process elicit a significant sympatho-adrenal responses. So abolishing such responses is a necessary step in the safe induction of general anesthesia. In patients with cardiac or cerebrovascular disease, this response often cause serious complications. This has necessitated the use of various adjuvants such as opioids, beta-blockers, nitroglycerine, lidocaine, and magnesium sulfate, with varying degrees of effectiveness. And in this study the focus will be on lidocaine in two ways of administration for this purpose.

Aim of study: To find the most effective way of lidocaine administration in attenuation of hemodynamic response to laryngoscopy and endotracheal intubation.

Patients and method : A 78 patients categorized into 3 groups, control (C) group of 26 patients received 5 ml of IV normal saline with the induction drugs, intravenous lidocaine (IVL) group of 26 cases received 1.5 mg/kg 2% IV lidocaine 2 minutes prior to laryngoscopy and intubation while nebulized lidocaine (NL) group 0f 26 cases received a 4 ml of 2% lidocaine nebulized by cirrus nebulizer with 5 L/min oxygen flow which usually takes from 10 to 15 minutes then induction immediately started.

Results : Among the 3 groups, demographic data shows no significant difference.

Comparing the C and NL group there is significant difference between them in advantage of lidocaine nebulizer for hemodynamic response attenuation, in C and IVL group comparison there is significant difference in some readings which reflects incomplete blunting effect. So lidocaine nebulizer shows a better results of cardiovascular stability.

Conclusion: Nebulized lidocaine found to be significantly effective in attenuation of hemodynamic changes that accompany direct laryngoscopy and endotracheal intubation.

Keywords: Nebulized lidocaine, Intravenous lidocaine, Hemodynamic responses, laryngoscopy and endotracheal intubation.

Introduction

Direct laryngoscopy :

Direct Laryngoscopy is considered as The most commonly used technique for endotracheal intubation, as it facilitate direct visualization of the vocal cords.[1]

Direct laryngoscopy was pioneered by Kirstein, Killian & Jackson in the late 1800s and early 1900s, and is now this is the most common technique used for endotracheal intubation.[2]

Preparation for direct laryngoscopy comprise a proper patient positioning, preoxygenation and checking of the needed equipment for a proper function. A skilled assistant is one of the crucial requirement for a better outcome. A good and precise preparation is of a superior importance, as the primary attempt of any airway securing or instrumentation should be the best. For direct laryngoscopy to be successful, from mouth to the larynx should be a one line of sight. and this involves the alignment of four anatomical axes, which are oral, oropharyngeal, hypopharyngeal and laryngeal. Patient Positioning in the sniffing position approximates this alignment. And for an optimal head elevation a straight horizontal line from external auditory meatus to sternal notch is useful.[1]

Laryngoscope :

The laryngoscope is a handheld instrument consisting of a blade attached to a handle comes with a light source. The laryngoscope blades are of two types, the curved one (Macintosh as the most popular) and the straight one (Miller as the most popular). Each type is associated with its own technique for use and each type comes with a special advantage and disadvantage.[1]

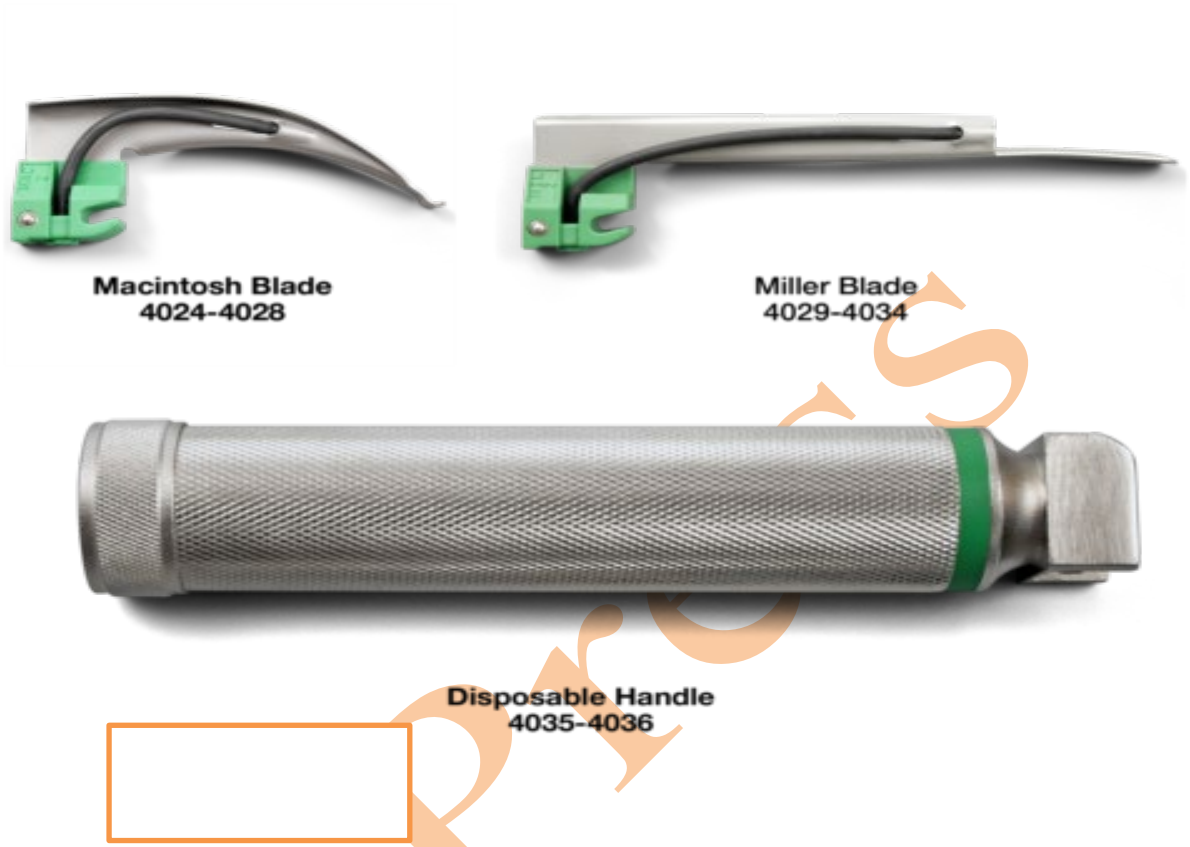


figure (1) Laryngoscope (handle and two types of blades).

The process of laryngoscopy composes of inserting the blade through mouth and lifting tongue, then proper placing of the balde tip with a lifting force to expose the glottis area and insert the endotracheal tube through vocal cords into the trachea.[1]

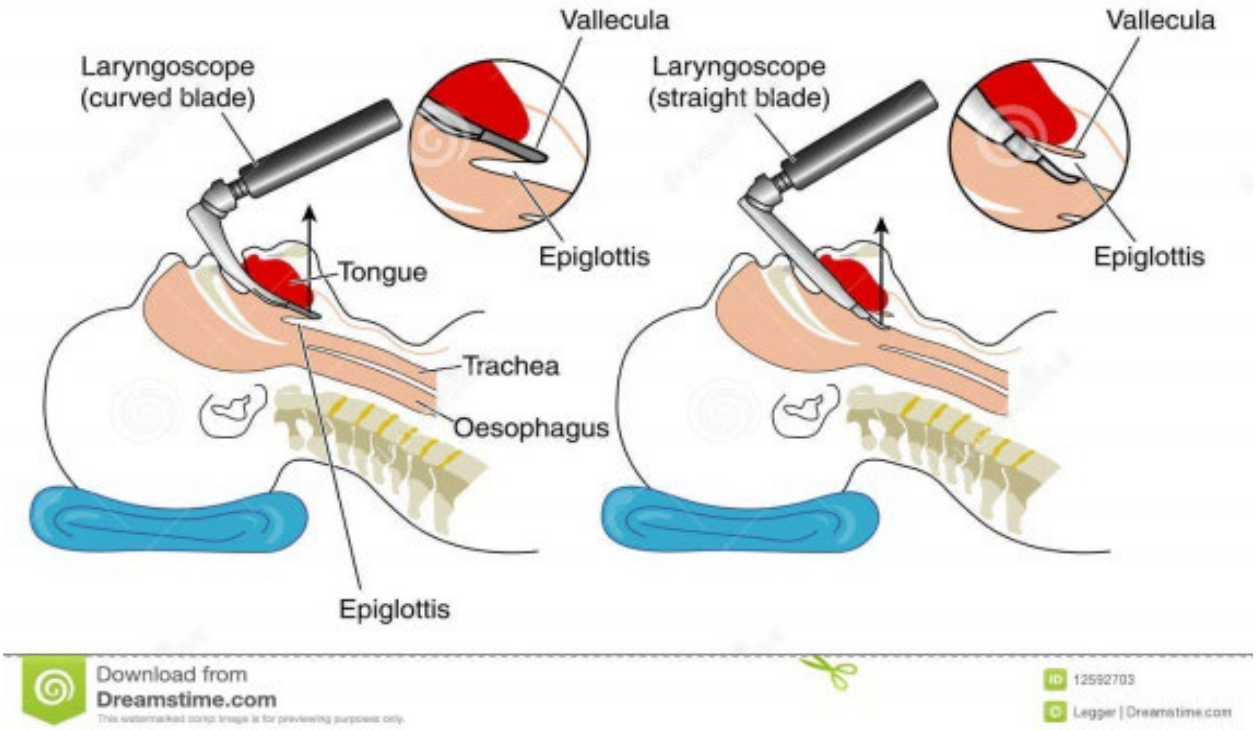


Figure (2) The process of laryngoscopy with Macintosh and Miller blades.

Endotracheal intubation :

Endotracheal intubation is the gold standard procedure for airway management, It is usually facilitated and completed by the aid of laryngoscope by which we can establish a definitive airway, provide a maximum airway protection against gastric acid aspiration and facilitate a positive pressure ventilation with higher airway pressures than supraglottic airway or face mask.[1]

The Endotracheal Tube is inserted through the vocal cords into the trachea under continuous visualization.[1]

Tracheal intubation was initially described for resuscitation (by Kite in 1788) and for laryngeal obstruction. Macewen was the first to advocate tracheal intubation instead of tracheostomy for anaesthesia for head and neck surgery, in 1880. An intubating tube was described by O'Dwyer in 1885. Modern endotracheal anesthesia was developed by Magill and Rowbotham after World War I.[2]

Endotracheal tube, The modern, standard tube is a disposable, single use, cuffed, plastic tube that is designed to be inserted through the nose or mouth and sit with its distal end in the mid-trachea, providing a patent airway to allow for ventilation of the lungs. A diverse endotracheal tubes are available for use in different specialized situations. Many features among the styles are useful in different situations, however, including a universal 15-mm adapter that allows the attachment of the proximal end to different ventilating circuits and devices; a high-volume, low-pressure cuff; a beveled tip to facilitate passage through the vocal cords; and an additional distal opening in the side wall of the endotracheal tube known as a Murphy eye, which serves to provide an additional port for ventilation if the distal end of the tube become obstructed by either secretions or soft tissue.[1]

In most patients, endotracheal intubation is routinely done by Cuffed endotracheal tube; while in neonates and infant cuffless tube could be used. This low-pressure, high-volume cuff is inflated by air to ensure that the tidal volume ventilates the lungs without escaping upward into the upper airways, and to prevent lung aspiration by gastric contents.[1]

Hemodynamic responses :

Airway securing process with intubation induce hemodynamic responses that include tachycardia, hypertension, and dysrhythmias which result from sympatho-adrenal stimulation. Such responses are more serious and pronounced in hypertensive than normotensive patients.[3]

The force applied by the laryngoscope to lift epiglottis during endotracheal intubation and the irritation by the tube Entering the trachea and then cuff expansion can all lead to cardiovascular response and this may cause rupture aneurysm or intracranial hemorrhage in patients who have history of cerebral vascular diseases.[4,5]

The force of lifting by laryngoscope is measured in units of force and it approximately equals to 40N and this cause a remarkable irritation yet not as irritant as the tube entrance into the trachea which have the greatest effect on hemodynamic changes.[6]

Shribmn et.al. found that a 10 seconds laryngoscopy were only similar to laryngoscopy followed by tracheal intubation as the plasma catecholamine levels and circulatory hemodynamic stress responses were almost the same.[5] However, Bucx et al reported that if laryngoscopy takes only 3 seconds, it would cause a less hemodynamic changes than the laryngoscopy followed by endotracheal intubation.[7]

These responses start within 5 seconds reaches a peak in 1–2 minutes and returns back to baseline within 5 minutes.[8]

The heart rate and blood pressure rise is usually transient, unpredictable and variable. Heart rate Average increase has been reported to be 23 beats and blood pressure average increase by 53/54 mmHg.[9,10]

To prevent excessive hyperdynamic responses to endotracheal intubation, Many anesthesiologists agree that a skilled anesthesiologist would try to apply only as low as possible force to patient's larynx when using a laryngoscope.[5,11,12]

The underlying mechanisms of the hemodynamic responses are not fully understood, although they have been attributed to a reflex sympathetic discharge caused by stimulation of the upper respiratory tract, This opinion is supported by the previous observation that hemodynamic responses to endotracheal intubation are associated with an increase in plasma catecholamine concentrations.[5,13] T1 to T4 is the Sympathetic innervation of the heart that originates from the spinal cord, while the innervation of the vascular system originates from T1 to L2, and the adrenal medulla sympathetic innervation is between T3 and L3.[14,15] the cardiovascular response to intubation in patients undergoing total thoracolumbar anesthesia is abolished. In contrast, the sympathetic outflow blockade by epidural anesthesia, either cervico-thoracic anesthesia without blocking the adrenal gland or lumbar epidural anesthesia without blocking the heart, did not affect the cardiovascular response to tracheal intubation.[16,17]

There is a confirmed correlation between the increment of mean arterial pressure following intubation and the increased level of plasma norepinephrine.[13] The increase in plasma norepinephrine concentrations likely reflects the extent of norepinephrine release from the adrenal gland and adrenergic nerve endings (especially from the latter) in response to such sympathetic stimulation.[18]

With hypertensive patients, Increased level of catecholamines and the increased sensitivity of peripheral vessels to catecholamines make them have an exaggerated hemodynamic response in comparison with normotensive patients.[19,20,21,22]

Over the years, many researchers have adopted a various methods for attenuating the pressor response caused by laryngoscopy and tracheal intubation.[23]

Methods to attenuate the response :[2]

- Antihypertensive drugs, e.g. β-blockers, hydralazine, nitroglycerine, sodium nitroprusside. Some may be effective given orally, preoperatively (e.g. β-blockers) but bradycardia may occur.
- Benzodiazepines.
- Deep inhalational anesthesia.
- IV lidocaine 1–2 mg/kg.
- Fentanyl (6–8 μg/kg), alfentanil (30–50 μg/kg) or sufentanil (0.5–1.0 μg/kg) obtund the response if given 1–2 min before intubation.

Insertion of a laryngeal mask airway is typically associated with less hemodynamic changes.[24]

If not blunted or attenuated, The hemodynamic response in patients with hypertension, ischemic heart disease, aneurysmal vascular disease and raised intracranial pressure.[25] may lead to disastrous consequences like myocardial ischemia and infarction, stroke or rupture aneurysm.[26] cardiac arrhythmia especially ventricular bigeminy sometimes occur and may indicate light anesthesia.[2]

Lidocaine :

Lidocaine hydrochloride is an Amide type local anesthetic agent, introduced in 1947 (revolution of regional anesthesia as this agent provides higher safety to the previous agents) and it becomes a standard drug, which other local anesthetics compared with. the injected dose with percentage of 95% undergoes hepatic metabolism with renal excretion. by all routes the onset is rapid duration of action for 1% prepared solution is usually about 1 hour, and increased to about 1.5-2 hours if solution is mixed with adrenaline.[2]

The lidocaine site of action is at the sodium ion channels specifically on the internal surface of nerve cell membranes. Diffusion of the uncharged form through neural sheaths into the axoplasm before ionizing by combining with hydrogen ions. The resulting cation binds reversibly to sodium channels from the inside, locking them in the open state and preventing nerve depolarization. While lidocaine is a weak base agent with a dissociation constant (pKa) equals to 7.7, this results in approximately 25% of molecules being in un-ionized form at a physiological pH of 7.35-7.45 and will be available in crossing through to the inside the nerve cells, meaning that lidocaine with higher pKa values has a more rapid onset of action than other local anesthetics.[27]

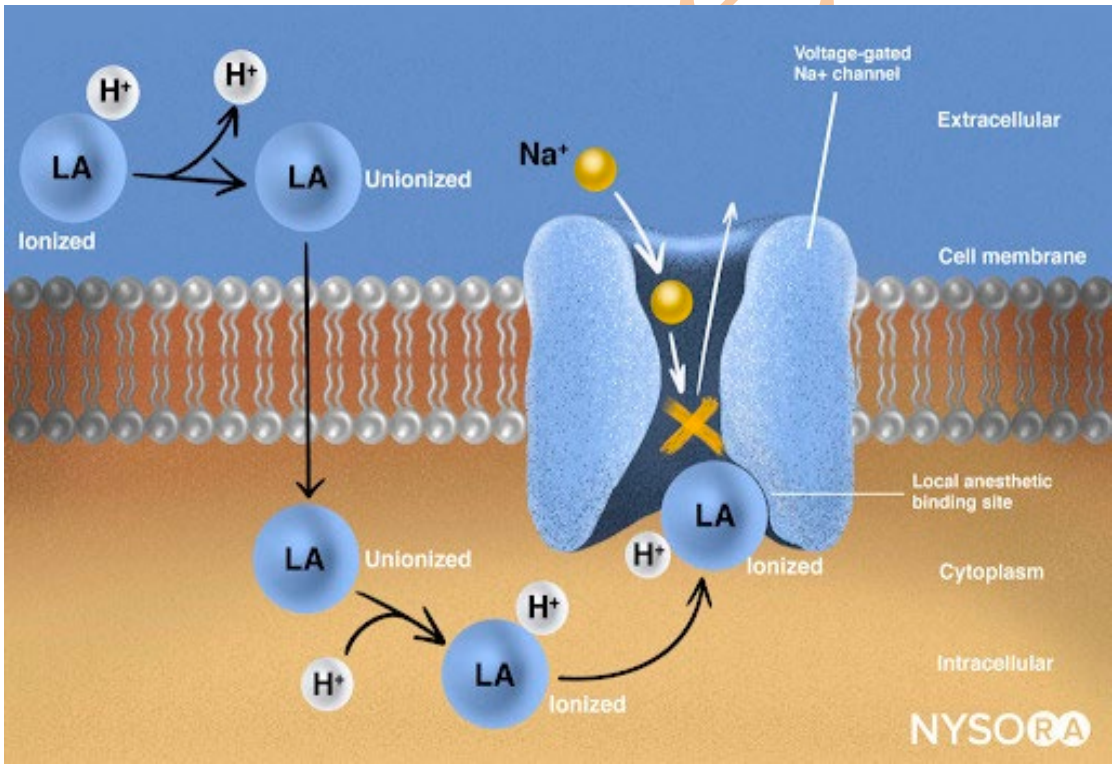


Figure (3) Lidocaine mechanism of action on sodium ion channel.

• **Uses :**[2]

- as a local anesthetic: Usually mixed with adrenaline, because lidocaine tends to induce local vasodilatation.
- IV administration :
  * laryngeal and tracheal reflexes depression (during tracheal intubation or extubation).
  * used to diminish the increment of intracranial pressure associated with laryngoscopy.
  * To reduce potassium increase and muscular pain after succinylcholine.
  * It has been used to produce analgesia (even if it has a low therapeutic ratio).

* in ventricular tachyarrhythmias as it is a class I antiarrhythmic drug.
* sometimes useful in neuropathic pain.

• **Preparations :**[2]

- 0.25%–0.5% solutions in intravenous regional and infiltration anesthesia.
- 1%–2% solutions in epidural anesthesia and nerve blocks.
- 4% solution in topical anaesthesia (mucosa of the respiratory tract, pharynx and mouth).
- 1%–2% gel for urethral instillation, and 5% ointment for skin, rectum and other mucous membranes.

• **Dosage :**[2]

- 1–2 mg/kg IV 2–5 min before intubation or extubation.
- 1 mg/kg IV initially for ventricular arrhythmias then 4 mg/kg/min for 30 min, 2 mg/kg/min for 2 h and 1 mg/kg/min thereafter.

Maximal recommended dose: 3 mg/ kg without adrenaline, 7 mg/kg with adrenaline. Toxic plasma levels: >10 µg/ml.

• **Adverse effects :**[2]

Lidocaine is thought to be directly neurotoxic more than the other local anaesthetics, as following spinal injection there is increased incidence of transient radicular irritation syndrome compared with other drugs.

Lidocaine is contraindicated in patients with a known severe adverse reaction. it considered rare but Anaphylactic reaction to lidocaine is possible, Methemoglobinemia can occur due to lidocaine metabolism to O-toluidine.[6]

Lidocaine has been used in topical and intravenous way for the attenuation of hemodynamic response to laryngoscopy and endotracheal intubation, While Intravenous lidocaine with its well established anti-arrhythmic and centrally depressant effect was found to be a suitable way of minimizing the hemodynamic response; topical lidocaine effect has been controversial.[29,30,31]

The pharyngeal nerves can be anesthetized by inhaling nebulized lidocaine. The glossopharyngeal nerve innervates the oropharynx, soft palate, posterior portion of the tongue, and the pharyngeal surface of the epiglottis.[32]

Lidocaine topically applied to the larynx and trachea in a different ways remains a popular method used alone or in combination with other techniques.[31] but its rate and extent of absorption following topical application is being dependent on concentration of dose administered, action site and time of exposure.[29]

Lidocaine inhalation led to a peak mean plasma concentration of only 1.1 ± 0.5 µg/ml. This concentration is far below the presumed toxic threshold of 5 µg/ml.[33-36] Lidocaine nebulizer as a type of administration routes appears to be a safe way as it produces a low serum level and a reduced occurance of adverse effects in comparison with spray or gel formulations,[37] however, after nebulization of lidocaine Convulsions have been reported as a symptom of local anesthetic toxicity.[38,39] Systemic absorption may be rapid and the maximal safe doses should not be exceeded.[2]

At plasma levels greater than (5 µg/mL), Signs and symptoms of mild toxicity become apparent starting with slurred speech, tinnitus, circumoral paresthesia, and feeling faint. Above (10 µg/mL), seizures or loss of consciousness may happen. at (15 µg/mL), the myocardium and central nervous system are further depressed. above (20 µg/mL) cardiac arrhythmia, respiratory arrest and cardiac arrest can happen.[40]

Aim of study

The primary aim was to evaluate and compare the effect of nebulized and intravenous lidocaine on the hemodynamic changes that usually accompany laryngoscopy and endotracheal intubation and then finding the most adequate way of preventing the complications that may results.

Patients and method

Study location and duration :

This study is accomplished at the Emergency department of Al-Sadder teaching hospital of Al-Najaf province_Iraq from April to September 2022.

Approval :

After the local ethical committee approval, patient informed consent has been taken before the operation.

Study type and patient criteria :

The age group targeted is 18-50 years old of both sexes who admitted for emergency open appendectomy .

It's a randomized clinical trial of 7٨ patients who belong to the physical status I and II of the American society of Anesthesiologists .

Inclusion criteria :

- Age (≥ 18 - ≤ 50 years) .
- Any gender (male & female).
- Patients ASA physical status I & II.
- Operations under general anaesthesia with endotracheal intubation.

Exclusion criteria :

- Patient refusal .
- Patients with known allergy to the study drug or to any of the administered drugs.
- anticipated difficult airway.
- Patients with difficult intubation & which intubation's time takes 15 seconds or more.
- Patients with preexisting hypertension.
- Patients on Beta blockers.

Patient data collection forum :

Demographic data :

Name, Age, Gender, Weight, Medical history, History of previous surgery, History of smoking, History of drug allergy and ASA physical status, Blood pressure, Pulse rate & Spo2 %

Method and data collection :

Patients admitted for emergency open appendectomy requiring general anesthesia with endotracheal intubation. after applying inclusion & exclusion criteria, 78 patients were included and categorized into 3 group, each of 26 patients.

All included patients underwent a detailed pre anesthesia checking (history was taken from each patient, clinical examination was performed by general examination & vital signs measurement). All patients fasted for at least 8 hours.

Anaesthetic & surgical team prepared the operative room, equipments & medications , then let the patient sit on operative table. Intravenous line ,pulse oximetry probe, non-invasive blood pressure cuff; all placed & secured, a baseline heart rate (HR) and blood pressure including SBP, DBP & MAP were measured.

Then The patients were categorized into 3 groups :

- The 1ˢ group (C group)

  Received 5 ml of normal saline IV with the induction drugs of anesthesia.

- The 2nd group (IVL group)

  Received 1.5 mg/kg of 2% IV lidocaine 2 minutes prior to intubation.

- The 3rd group (NL group)

  Received 4 ml of nebulized Lidocaine by a cirrus nebulizer through a face mask with O_2 flow rate of 5 L/min. Nebulization was continued till utilization of the drug is completed (take about 10–15 min.) and then induction of anesthesia immediately started after.

Rapid sequence induction of anesthesia was by IV ketamine (1 mg/kg), IV propofol (2 mg/kg) and rocuronium (0.9 mg/kg). volume controlled ventilation with (6 L/min) O2 flow rate was used after apnea is noticed. Then intubation was done by direct laryngoscopy using appropriate size cuffed endotracheal tube. The duration of this whole procedure regarding airway instrumentation should take less than 15 seconds. (SBP, DBP, MAP & HR) were measured before and immediately after induction and 1, 3, 5, & 7 minutes after intubation.

Maintenance of anesthesia was by isoflurane 1.2% MAC in O2. Setting of ventilator was tidal volume=8-10 ml/kg, frequency=12 breath/minute, peep=5 cmH2O and I:E ratio=1:2.

Statistical analysis :

Data were analyzed using SPSS version 26. Numerical variables presented as mean +/- SD, while categorical variables presented as frequency and percentage. ANOVA test with post hoc LSD test used for multiple comparison. Linear graph used for comparison of mean across study times. P value equal or less than 0.05 was considered significant.

Data analysis

The demographic data including age, gender and ASA physical status of the studied cases haven't shown any significant difference among the 3 groups. (table.1)

		Intervention			Total	P value
		Control (n=26) No.(%)	IV lidocaine (n=26) No.(%)	Nebulized lidocaine (n=26) No.(%)		
Age group	< 20	4 (21.1%)	9 (47.4%)	6 (31.6%)	19	0.5
	21-29	13 (39.3%)	9 (27.2%)	11 (33.3%)	33	
	30-39	5 (27.8%)	7 (38.9%)	6 (33.3%)	18	
	40-50	4 (50.0%)	1 (12.5%)	3 (37.5%)	8	
Mean age±SD		27.6±7.8	25±7.6	27.1±8.5		0.4
Gender	Female	15(34.8%)	14 (32.5%)	14 (32.5%)	43	0.9
	Male	11 (31.4%)	12 (34.3%)	12 (34.3%)	35	
ASA	1	19 (33.3%)	22 (38.5%)	16 (28.0%)	57	0.2
	2	7 (33.3%)	4 (19%)	10 (47.6%)	21	

(Table.1: Demographic data.)

First, the discussion will be about the heart rate changes in the 3 different groups:

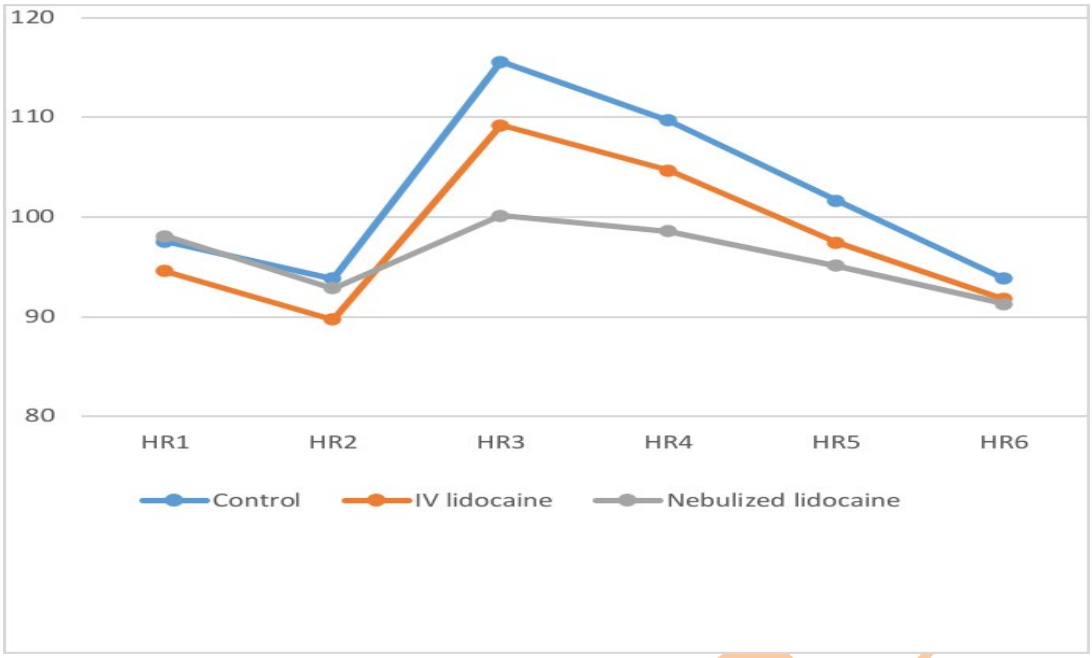
The maximum increase of HR was in the C group followed by IVL group and then the NL which shows a little increase post intubation and the 1st comparison between C & IVL group shows a significant difference (P=0.04) only at 1 minute after intubation & if we compare the C and NL groups there is a significant difference at the 1 & 3 minutes (p=0.0001, p=0.001 respectively) after intubation.(table.2) which means that NL have the advantage of decreasing heart rate over the C and IVL group in response to laryngoscopy and endotracheal intubation.(fig.4)

And in the comparison between IVL and NL groups, the p value at 1 minute after intubation was the only significant value in the advantage of NL over IVL for the diminishing of heart rate response. (table.2)

(Fig.4) shows that the increase in heart rate was at 1 minute with the highest reading belong to the C group, the lowest to the NL group while the IVL group comes in between. And when it comes to the return to baseline reading, the NL group returns at 5 minutes, the C & IVL groups returns at the 7 minutes after airway instrumentation.

	Control (mean±SD)	IVL (mean±SD)	NL (mean±SD)	P value C vs IVL group	P value C vs NL group	P value IVL vs NL group
HR1	97.6±13.7	94.6±19.2	98.1±12.7	0.5	0.9	0.4
HR2	93.9±12.2	89.7±15.03	92.9±9.7	0.2	0.8	0.4
HR3	115.6±12.6	109.2±12.4	100.2±7.6	**0.04***	**0.0001***	**0.004***
HR4	109.7±12.9	104.7±12.6	98.6±8.1	0.1	**0.001***	0.06
HR5	101.6±13.8	97.4±15.5	95.1±8.4	0.2	0.07	0.5
HR6	93.8±11.9	91.8±13.3	91.5±7.8	0.5	0.4	0.9

HR1:before induction, HR2:after induction, HR3:1st minute after intubation, HR4:3rd minute after intubation, HR5:5th minute after intubation & HR6:7th minute after intubation.
(Table2: comparison of mean heart rate readings among study groups at different times.)



(Fig.4: comparison of mean heart rate readings among study groups at different times.)

Regarding the 2nd parameter (SBP) , C group in comparison with the IVL group shows a significant difference at 1 & 3 minutes post intubation, while in the C and NL group there is a significant difference at 1,3,5&7 minutes after intubation with the advantage of lidocaine nebulizer in the attenuation of SBP.(table.3)(fig.5)

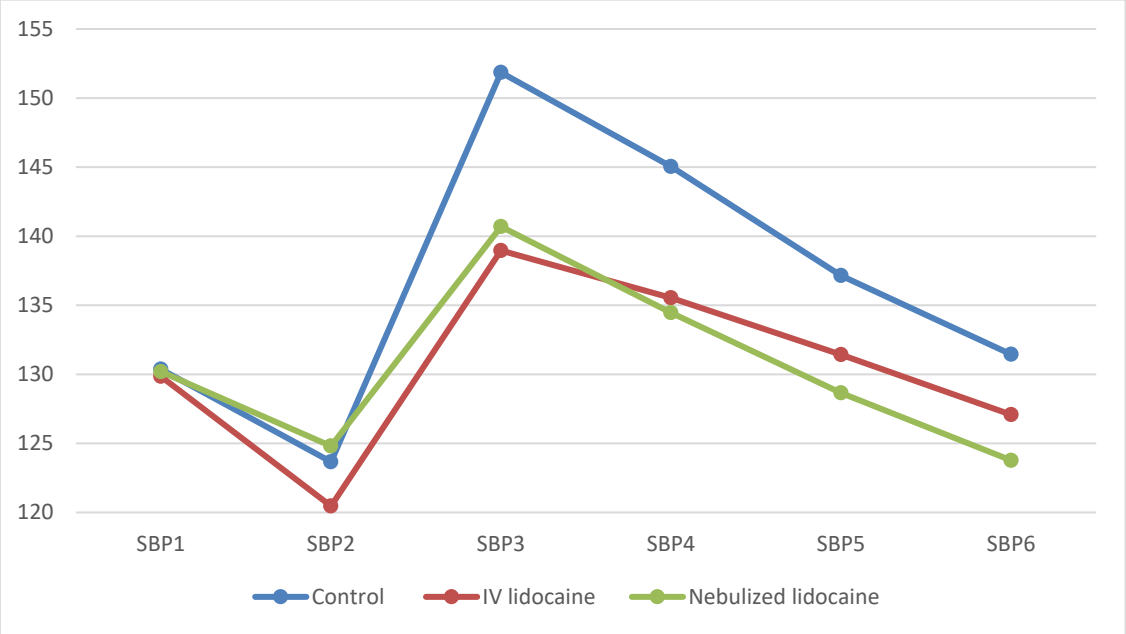
But if the focus was on the IVL and NL groups we would find that there is no significant difference in all the readings which means both of the strategies were effective for the SBP increment.(table.3)(fig.5)

The return to baseline was at minute 7 for C group, and at minute 5 for IVL and NL group post intubation.(fig.5)

	Control (mean±SD)	IVL (mean±SD)	NL (mean±SD)	P value C vs IVL group	P value C vs NL group	P value IVL vs NL group
SBP1	130.4±14.3	129.8±14.5	130.2±18.2	0.9	0.9	0.9
SBP2	123.7±13.3	120.5±16.1	124.8±13.2	0.4	0.7	0.3
SBP3	151.9±12.4	138.96±19.2	140.7±15.3	**0.004***	**0.01***	0.7
SBP4	145.04±16.8	135.5±18.6	134.5±14.02	**0.04***	**0.02***	0.8

SBP5	137.1±17.	131.4±13.4	128.7±11.96	0.2	**0.04***	0.4
SBP6	131.4±13.1	127.1±12.8	123.8±10.7	0.2	**0.03***	0.3

SBP1:before induction, SBP2:after induction, SBP3:1st minute after intubation, SBP4:3rd minute after intubation, SBP5:5th minute after intubation & SBP6:7th minute after intubation.
(Table3: comparison of mean systolic blood pressure readings among study groups at different times.)



(Fig.5: comparison of mean systolic blood pressure readings among study groups at different times)

About the DBP, no significant difference was between C and IVL group as both of them showed increment of DBP post intubation, the significant difference was only between the C and NL groups at 1 & 3 minutes after intubation, with the advantage of NL in reducing the DBP in response to laryngoscopy and intubation.(table.4)

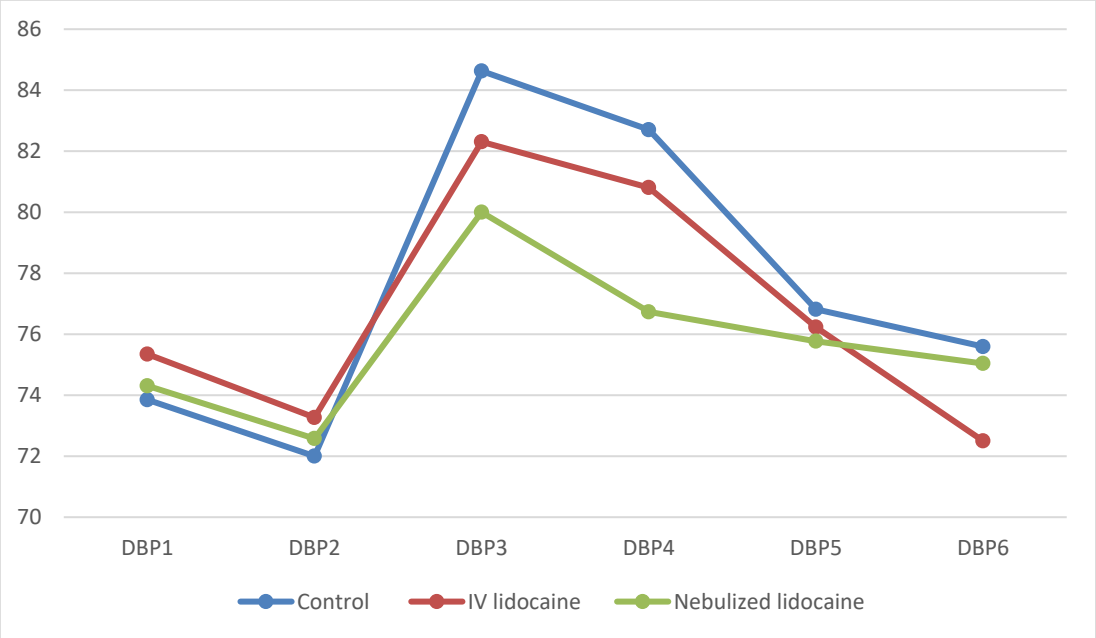
And there was no remarkable difference between the NL and IVL groups.(table.4)

The highest increment of DBP in the 1st minute after intubation belongs to control group, the lowest increment belongs to the NL group while IVL comes in between.(fig.6)

	Control (mean±SD)	IVL (mean±SD)	NL (mean±SD)	P value C vs IVL	P value C vs NL	P value IVL vs NL

				group	group	group
DBP1	73.9±6.5	75.3±8.9	74.3±7.4	0.5	0.8	0.6
DBP2	72±6.7	73.3±9.4	72.6±5.9	0.5	0.8	0.7
DBP3	84.6±10.7	82.3±8.1	80±6.2	0.3	**0.05***	0.3
DBP4	82.7±9.6	80.8±6.8	76.7±6.7	0.4	**0.007***	0.06
DBP5	76.8±10.3	76.2±6.5	75.8±5.98	0.8	0.6	0.8
DBP6	75.6±11.1	72.5±6.5	75.04±7.4	0.2	0.8	0.3

DBP1:before induction, DBP2:after induction, DBP3:1st minute after intubation, DBP4:3rd minute after intubation, DBP5:5th minute after intubation & DBP6:7th minute after intubation.
(Table4: comparison of mean diastolic blood pressure readings among study groups at different times.)



(Fig.6:comparison of mean diastolic blood pressure readings among study groups at different times)

And the last parameter (MAP), at 1 minute after intubation, significant difference is clear between the C and IVL group but the significant difference between the C and NL groups was at the 1 & 3 minutes after intubation and that's give the benefit of using NL on blunting the pressor response of laryngoscopy and intubation.(table.5)(fig.7)

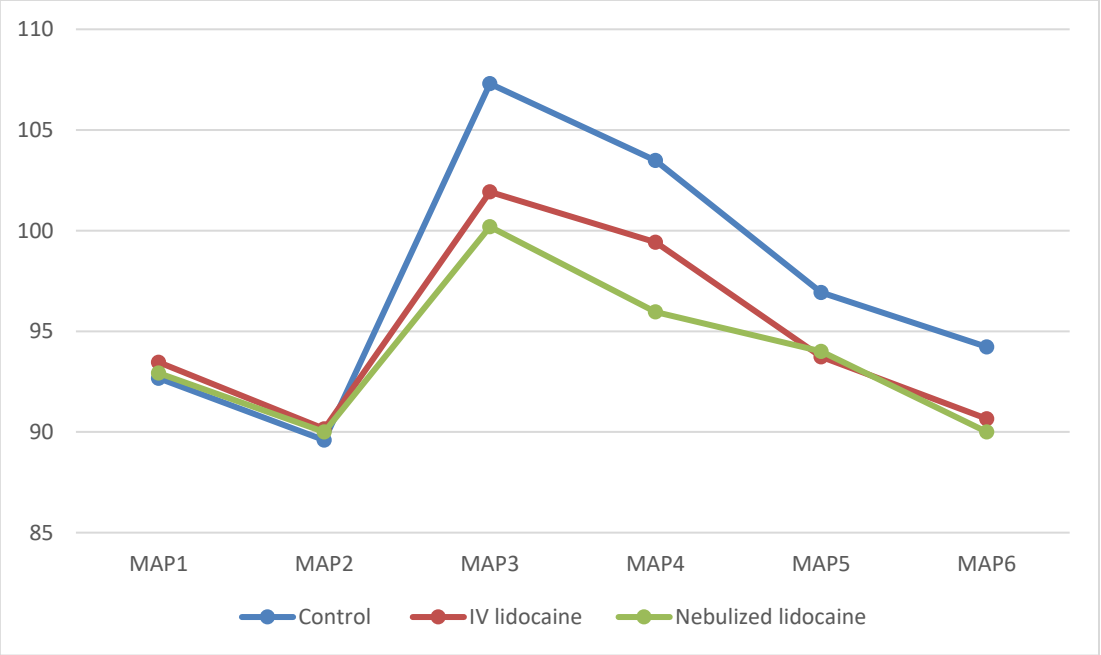
(Fig.7) shows that the MAP maximum reading after airway instrumentation belong to the C group followed by IVL group followed by NL group at the 1 minute.

The level of attenuation of HR, SBP, DBP & MAP was found to be greater in the NL group in comparison with the C group at the 1st & 3rd minutes after intubation.

* Arrhythmia of any type was not noted in the studied cases.

	Control (mean±SD)	IVL (mean±SD)	NL (mean±SD)	P value C vs IVL group	P value C vs NL group	P value IVL vs NL group
MAP1	92.7±7.3	93.5±8.5	92.9±9.4	0.7	0.9	0.8
MAP2	89.6±8.3	90.2±8.6	90±7.5	0.8	0.8	0.9
MAP3	107.3±9.3	101.9±8.4	100.2±7.4	**0.02***	**0.003***	0.5
MAP4	103.5±9.9	99.4±7.3	95.9±7.3	0.08	**0.001***	0.1
MAP5	96.9±11.8	93.7±8.5	94±5.9	0.2	0.2	0.9
MAP6	94.2±10.8	90.7±7.2	90±7.1	0.1	0.08	0.8

MAP1:before induction, MAP2:after induction, MAP3:1st minute after intubation, MAP4:3rd minute after intubation, MAP5:5th minute after intubation & MAP6:7th minute after intubation.
(Table5: comparison of mean arterial pressure readings among study groups at different times)



(Fig.7: comparison of mean (mean arterial pressure) readings among study groups at different times)

Discussion

Airway instrumentation by laryngoscope and endotracheal tube insertion elicit a significant sympatho-adrenal response. While a transient response is of confined consequence to healthy people, it could be risky to patient with hypertention as they have a labile cardiovascular system.[20,41] but Forbes and Dally published a case showed changes of acute ischemia in a previously healthy normotensive male patient when his BP reached 190/130 mmHg.[42] So suppressing a hypertensive response to airway manipulation is one of the crucial prerequisites for a proper general anesthesia.

Lidocaine has been used in topical and intravenous approach for blunting the pressor response.

The effect of topical lidocaine in the diminishing of this response to laryngoscopy & endotracheal intubation has been controversial. In this study the effect of NL was significantly beneficial if we compare it with the C group in the attenuation of tachycardia and hypertension. and here is some studies that agrees with the results in this research.

Venus et al. reported that The pressor response and tachycardia observed with airway instrumentation were successfully abolished by (240 mg) lidocaine nebulizer & For a greater cardiovascular stability This technique of anesthetizing upper airways prior to intubation may be considered.[43] And peltons et al. mentioned that as an adjunct to GA, lidocaine topical use on the tracheobronchial mucosa is effective in abolishing laryngeal reflexes.[44]

And not to forget Abd El_Hamid *et al* and Sklar *et al*. as both of them founded that NL is efficient in the attenuation of hemodynamic response to the process of intubation, as Lidocaine nebulizer's attenuating effect seems to be by direct local anesthesia.[45,46]

While kumar et al said that nebulization with lidocaine didn't show any further benefits in the attenuation of hemodynamic response, And we shouldn't use NL alone for this purpose. the cause could be due to the time taken by laryngoscopy with endotracheal intubation as he included a maximum time of less than 30 seconds.[47] but it is ideally should take less than 15 seconds to alleviate the hypertension & tachycardia as Stoelting et al advise in his study.[48]

The systemic absorption of lidocaine after nebulization is unpredictable. so following topical administration and if continuous nebulization used then the estimated loss of NL is likely to be >50%. losing of mist around patients mouth with exhaling and breath holding result in the loss of NL of >50%.[49]

When lidocaine nebulizer was more efficient than intravenous for the purpose of attenuation of hemodynamic response, this result could be explained as the IV use increase the depth of anesthesia. Himes et al.[50] while the local use by nebulization has the effect of as local anesthetic in addition to increasing the depth of anesthesia by systemic absorption through mucosa of airways.[31] this lidocaine absorption depends on the administered dose concentration, the action site and exposure time.[29] plasma lidocaine concentration is about (2.7 µg/ml) after topical aerosol application with a (3 mg/kg).[44]

And when the time of intravenous lidocaine administration before intubation makes a difference on the cardiovascular stability as Tam et al stated that (1.5 mg/kg) IVL administered 3 minutes before intubation offered statistically significant attenuation of hemodynamic changes but IVL given 2 minutes prior to intubation (the same dose and time used in our study) offers no significant protection from hypertension and tachycardia,[30] so time factor can participate in such a difference between the IVL & NL.

Conclusion and Recommendations

Conclusion :

Nebulized lidocaine was more effective than intravenous lidocaine for attenuation of hypertension and tachycardia that accompany the procedure of laryngoscopy and endotracheal intubation.

Recommendations :

. Evaluate the effect of lidocaine nebulizer and bind it with the level of plasma lidocaine.

. Target a hypertensive group of patients required general anesthesia with the same or different dose.

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