"Attenuation of haemodynamic changes during laryngoscopy and endotracheal intubation using IV lidocaine versus IV cloridine"

Rama Krishna Reddy Mudiganti[1,*], Rishita Reddy Magam[2], Rambabu T[3]

[1]Associate Professor, [2]Senior Resident, [3]Professor, Dept. of Anaesthesia, MediCiti Institute of Medical Sciences, Hyderabad

***Corresponding Author:**
Email: drrk_2003@yahoo.com

Abstract

Background: Haemodynamic changes such as hypertension and tachycardia due to laryngoscopy and endotracheal intubation are well known, which are not tolerated by some patients with history of Hypertension, CAD. To attenuate these responses many drugs have been tried.

Aim: To compare the efficacy of IV cloridine in attenuating of haemodynamic responses during laryngoscopy & endotracheal intubation in comparison with IV plain lidocaine.

Design: Randomised controlled study.

Material & Method: The study includes 100 patients, randomly divided into 2 groups. Group L (50 patients) were given IV Lignocaine and Group C (50 patients) IV Cloridine was given.

Statistical Analysis: Descriptive statistics and independent & paired sample 't' tests.

Results & Conclusion: Cloridine in the dose of 3µg/kg IV, given 15 minutes before laryngoscopy and intubation can be a better alternative than IV lidocaine 1.5mg/kg 3 minutes before laryngoscopy and intubation, in attenuating the haemodynamic responses to laryngoscopy and intubation without any side effects. In addition Cloridine also has other advantages such as decrease in the requirement of inhalational agents, desirable sedation etc.

Keyword: IV lidocaine versus IV Cloridine Haemodynamic changes, Layngoscopy, Intubation, Cloridine Lidocaine

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-4994.2016.00042.1

Introduction

Haemodynamic changes like hypertension and tachycardia in response to the sympathetic stimulation due to direct laryngoscopy and endotracheal intubation have been reported as early as 1950 when intubation under light anaesthesia was attempted. However the rise in the pulse rate and blood pressure is usually transient, variable and unpredictable. Usually these changes are well tolerated by healthy individuals. However, these changes may be fatal in patients with hypertension, coronary artery disease or intracranial hypertension. This is mainly due to reflex sympathetic discharge in response to laryngo-tracheal stimulation which in turn leads to increase in plasma catecholamine concentration.

Pressor response is exaggerated in hypertensive patients even though rendered normotensive pre-operatively by antihypertensive medication Pressor response may result in intra-operative myocardial infarction, acute L.V.F, dysrrythmias and intracranial bleed in individuals with end organ decompensation.

Intravenous anaesthetic induction agents alone do not adequately suppress the circulatory responses evolved by endotracheal intubation therefore prior to initiating laryngoscopy and endotracheal intubation additional pharmacological measures should be taken. Various methods include as follows:

- Premedication
- Topical and systemic lidocaine
- Alpha 2 agonists e.g. Cloridine
- Adrenergic Blockers
- Angiotensin- converting enzyme inhibitors
- Opioids e.g. Fentanyl, Alfentanyl, Remifentanyl
- Vasodilators e.g. Isosorbide dinitrate, Nitroglycerine and Sodium nitroprusside
- Inhaled Anaesthetic agents
- Thoracic epidural block

Cloridine, a central alpha–2 agonist which has sedative, hypnotic and antihypertensive action in addition to reducing the anesthetic drugs requirement might be helpful in attenuation of haemodynamic responses to laryngeal stimulation.

Cloridine is available in India as both oral and parenteral forms(as 150µg/ml, 1ml ampoules) and can be used through intravenous route for attenuation of sympathetic response to laryngoscopy and intubation.

Lignocaine belongs to the amide group of local anaesthetics. It also has antiarrhythmic properties & the preservative free form can be used for attenuation of hemodynamic changes during laryngoscopy & endotracheal intubation.

Hence the present study has been undertaken to compare the efficacy of intravenous bolus of cloridine versus intravenous bolus of lidocaine for attenuating the haemodynamic responses to direct laryngoscopy and endotracheal intubation.

Aims and Objectives

- To compare the efficacy of IV cloridine in attenuating of haemodynamic responses during laryngoscopy & endotracheal intubation in comparison with IV plain lidocaine.
- Parameters measured:

Heart rate,
Systolic blood pressure,
Diastolic blood pressure,
Mean blood pressure.

- Any associated side effects

Patients and Methods

This study was conducted at MediCiti Institute of Medical Sciences after an approval from the hospital ethical committee. A written informed consent was taken from the patients. 100 patients posted for elective surgeries such as various Orthopaedic, ENT, and General surgical procedures. General anaesthesia was provided with endotracheal intubation for all the patients. The study population was randomly divided into two groups with 50 patients in each group. **Group-L – Lidocaine group (n=50)** – received inj Lidocaine 2% 1.5mg/kg body weight I.V. bolus 3minutes before laryngoscopy

Group-C - Cloridine group (n=50) - received injection Cloridine 3µg/kg (Cloneon, Neon laboratories ltd. 150µg/ml, 1ml ampoules) diluted to 100 ml normal saline intravenously over 5 mins, 15 minutes prior to laryngoscopy and intubation. A thorough preanaesthetic evaluation was done one day before surgery.

Inclusion criteria:

- Age range 18-65 of both sex
- ASA grade I & II
- Mallampatti class I &II.

Exclusion criteria:

- Unwilling Patients
- Age less than 18 or more than 65.
- ASA grade III & IV.
- Mallampatti class III & IV.
- Presence of 1st, 2nd or 3rd degree heart block
- Nasogastric Tube insertion.
- Patients on drugs effecting autonomic nervous system.

Method

All patients included in the study were premedicated with tab alprazolam 0.5 mg and tab ranitidine 150 mg orally at bed time the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night.

On the day of surgery, an 18-gauge intravenous cannula was inserted and an infusion of Ringer lactate was started. The patients were connected to multichannel monitor which records Heart rate, non-invasive measurements of SBP, DBP, MAP, EtCO2 and continuous ECG monitoring and oxygen saturation. The baseline systolic, diastolic blood pressure, mean arterial pressure and heart rate were recorded. The cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II.

All the patients were premedicated with injection glycopyrrolate 0.2mg, injection midazolam 1mg and injection Fentanyl 50ug IV before preoxygenation. Then patients were preoxygenated for 3 minutes via a face mask with Bains circuit. Anaesthesia was induced with thiopentone 5mg/kg as a 2.5% solution. Endotracheal intubation was facilitated with inj Suxamethonium 1.5mg/kg. Laryngoscopy was done using rigid laryngoscope with standard Macintosh blade. Intubation was done with appropriate sized, disposable, high volume low pressure cuffed endotracheal tube and after confirmation of bilateral equal air entry, the endotracheal tube was fixed Laryngoscopy and intubation was done within 15 seconds.

Heart rate, systolic and diastolic blood pressure were recorded at 1,3,5,7 and 10 minute intervals from the onset of laryngoscopy.

In group-L, IV 2% Lidocaine 1.5mg/kg was administered 3 minutes before laryngoscopy and intubation.

In group-C, IV Cloridine 3 µgm/ kg was administered 15 minutes before laryngoscopy and intubation.

Monitoring and Observations

The following cardiovascular parameters were recorded in all patients.

Heart rate [HR] in beats per minute, Systolic blood pressure [SBP] in mm of Hg, Diastolic blood pressure [DBP] in mm of Hg, Mean arterial pressure [MAP] in mm of Hg.

The above cardiovascular parameters were monitored in the following time interval–

1. Pre induction: after giving premedication
2. Post Induction: after induction
3. One minute after laryngoscopy and intubation
4. Three minutes after laryngoscopy and intubation
5. Five minutes after laryngoscopy and intubation
6. Seven minutes after laryngoscopy and intubation
7. Ten minutes after laryngoscopy and intubation

An observation was made related to adverse effects of drugs and anaesthesia related problems and were attended to appropriately.

Incidences of side effects such as Hypertension, Hypotension, Tachycardia, Bradycardia Sedation and any dysrrhythmia like any ventricular or

supraventricular beat or any other rhythm other than sinus were recorded in both groups.

Statistical methods employed

- Descriptive statistics (to measure mean, standard deviation)
- Independent sample 't' test (to measure difference between two groups i.e. intergroup comparison)
- Paired sample 't' test (to measure difference within the group i.e. intragroup comparison)
- Repeated measure ANOVA (groups Vs sessions together)
- Contingency table analysis (for association between the rows and columns)

$p<0.05$ was considered as significant and $p<0.01$ was considered as highly significant.

Observations and Results

Table 1: Showing the age distribution

Age in Years	Group-L (Lidocaine)		Group-C (Cloridine)	
	Number of Patients	Percent	Number of Patients	Percent
20-24	14	28	15	30
25-29	12	24	04	08
30-34	02	04	08	16
35-39	07	14	05	10
40-44	06	12	06	12
45-50	09	18	12	24
Total	50	100	50	100
Mean±SD	32.36±9.4		33.9±9.9	
Minimum	20		20	
Maximum	50		50	

There was no significant difference in the age of patients between the Group L and Group C. Both groups were similar with respect to age distribution ($p>0.05$).

Table 2: Showing the Body Weight Distribution

Body weight (kg)	Group L (Lidocaine)		Group C (Cloridine)	
	Number of Patients	Percent	Number of Patients	Percent
40 – 44	06	12	05	10
45 – 49	08	16	13	26
50 – 54	15	30	18	36
55 -59	11	22	04	08
60 – 64	10	20	04	08
65 – 70	00	00	05	10
Total	50	100	50	100
Mean±SD	53.1±6.34		51.36±8.53	
Minimum	40		40	
Maximum	65		70	

There was no significant difference in the body weight of patients between the Group L and Group C group ($p>0.05$).

Table 3: Sex Distribution between Group L and Group C

Sex	Group L (Lidocaine)		Group C (Cloridine)	
	Number of Patients	Percent	Number of Patients	Percent
Male	26	52	24	48
Female	24	48	26	52
Total	50	100	50	100

No significant difference was observed in sex wise distribution of the cases between two groups ($P>0.05$).

Table 4: Showing type of surgical procedures

Type of surgery	Number of Patients	
	Group L (Lidocaine)	Group C (Cloridine)
General surgeries	22	07
Orthopedic surgeries	13	22
ENT surgeries	11	19
Miscellaneous surgeries	0 4	02

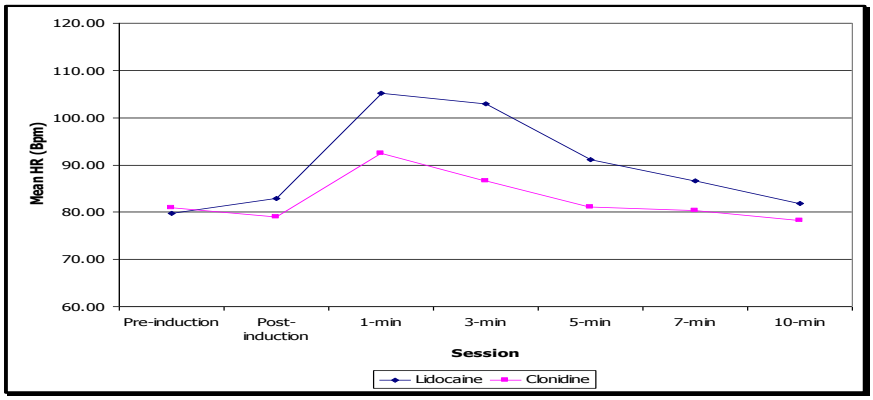


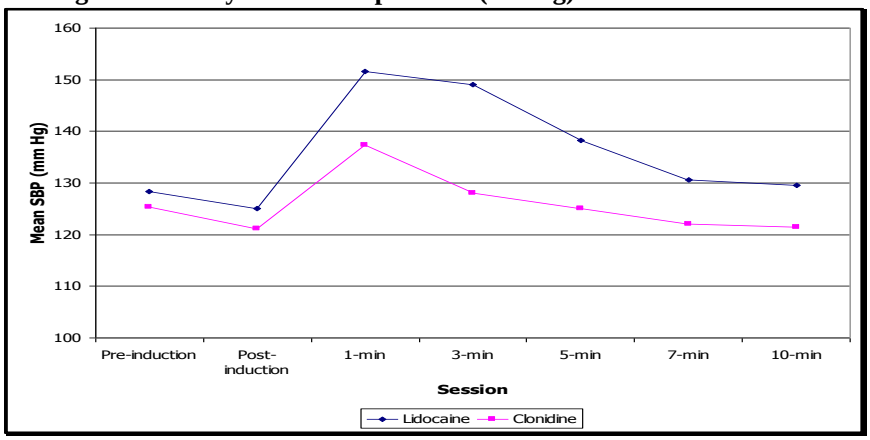
Fig. showing changes in mean Heart rate at various time intervals

In the Group L, the preinduction mean HR was 79.7±6.1 bpm. The mean heart rate after induction was 82.9±6.13, one minute after intubation it was 105.2±7.87 bpm representing a rise of 25.5 bpm from the preinduction heart rate. By 3, 5, 7 and 10 minutes mean HR were 103±7.9 bpm, 91.1±5.53 bpm, 86.6±5.78 and 81.9±5.43 bpm respectively. The mean heart rate did not come to the preinduction levels even by 10th minute. The increase in mean HR at 1, 3, 5 and 7 min minutes after intubation compared to basal HR was statistically highly significant ($p<0.01$).

In Group C (cloridine), the preinduction mean HR was 81±6.63 bpm. The mean heart rate after induction was 79±8.01, and one minute after intubation it was 92.4±8.2 bpm representing a rise of 11.4 bpm. By 3, 5, 7 and 10 minutes the mean HR values were 86.7±6.4 bpm, 81.8±8.39, 80.4±6.7 bpm and 78.2±5.9 respectively. The increase in the mean HR at 1and 3 minute after intubation compared to basal value was statistically significant ($p<0.05$) and the mean heart rate returned to the preinduction level in 5 minutes.

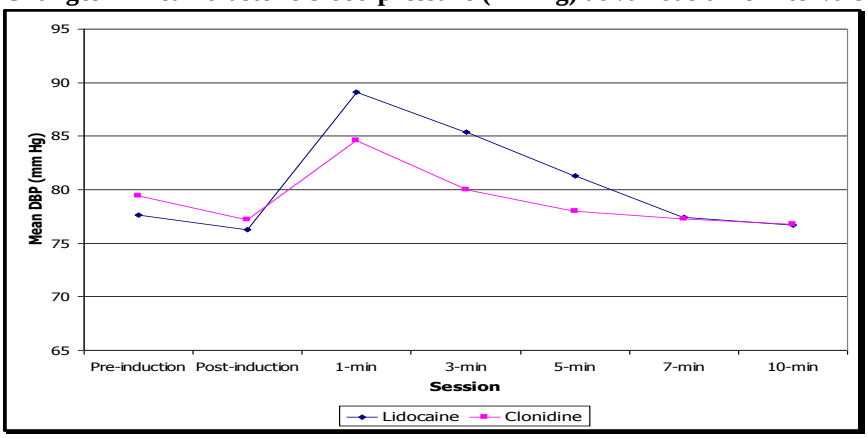
Statistical evaluation between the groups showed that the increase in mean HR observed in group L was statistically highly significant when compared to increase in mean HR in the group C ($p<0.01$) at intubation and 1, 3, 5, 7 and10 minutes following intubation.

Changes in mean systolic blood pressure (mmHg) at various time intervals



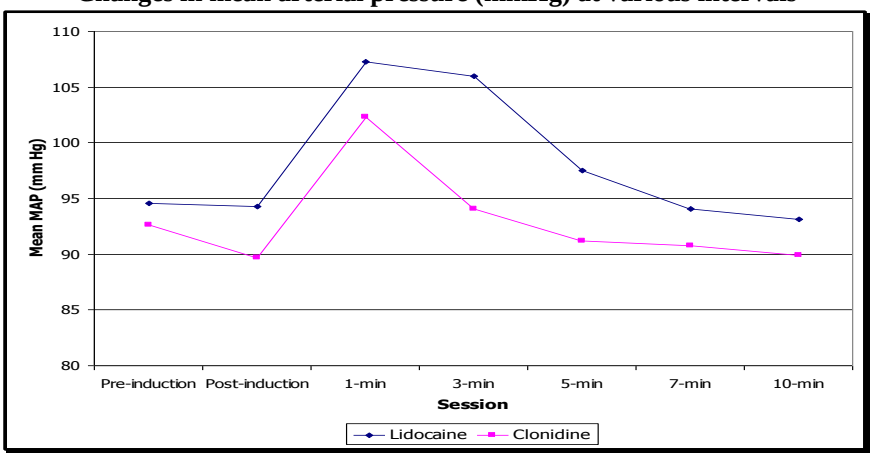
Statistical evaluation between the groups showed that the increase in mean SBP observed in group L was statistically highly significant when compared to increase in mean SBP in the group C ($p <0.01$) at 1, 3, 5, 7 and 10 minutes following intubation.

Changes in mean diastolic blood pressure (mmHg) at various time Intervals



Statistical evaluation between the groups showed that the increase in mean DBP observed in group L was statistically highly significant when compared to increase in mean DBP in the group C ($p < 0.01$) at 1min, 3min 5min 7 and 10 min following intubation.

Changes in mean arterial pressure (mmHg) at various intervals



Statistical evaluation between the groups showed that the increase in MAP observed in group L was statistically highly significant when compared to increase in MAP in the group C ($p<0.01$) at 1min, 3min and 5min 7min and 10min following intubation.

Discussion

Laryngoscopy and endotracheal intubation are considered as one of the most critical events during general anaesthesia. They provoke a transient, but marked sympathetic and sympathoadrenal response manifesting as hypertension and tachycardia. These responses are transitory, variable and may not be significant in otherwise normal individuals. But in patients with cardiovascular compromise like hypertension, Ischemic heart disease, Cerebrovascular disease and in patients with intracranial aneurysms even these transient changes in haemodynamics can result in potentially harmful effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral haemorrhage.

Therefore many methods have been tried for attenuation of haemodynamic responses to laryngoscopy and tracheal intubation like, use of inhalational anaesthetic agents **Bedford RF et al**[1], opioids **William M et al 2, Crawford DC et al 3** direct acting vasodilators, **Robert RK Stoelting 4, Dich J Nielson et al 5** calcium channel blockers, **Mikawa K et al**[6] β-blockers **Chung KS et al**[7] and lidocaine **Mounir-Abou-Madi et al**[8] have been tried by various authors for blunting haemodynamic responses to laryngoscopy and intubation. But all such maneuvers had their own limitations. For example, with opioids respiratory depression and non-availability leads to other alternatives, use of halothane was associated with dysrrhythmias, calcium channel blockers produced reflex tachycardia, direct acting vasodilators needed invasive haemodynamic monitoring and lidocaine did not give consistent results in blunting the haemodynamic responses to laryngoscopy and intubation.

Hence a drug which can blunt both the heart rate response and blood pressure response of laryngoscopy and intubation, without having any adverse effects like

respiratory depression and post operative nausea and vomiting, was required for the purpose.

Cloridine, an α-2 agonist, has been found by various authors **Carabine U.A., et al[9]**, **Zalunardo MP et al[10]** to blunt the haemodynamic response for laryngoscopy and intubation. Hence the effects of cloridine for suppression of haemodynamic response to laryngoscopy and intubation was taken up as the study topic.

The present study is undertaken to compare the efficacy of intravenous bolus of cloridine versus intravenous bolus of lidocaine for attenuating the haemodynamic responses to direct laryngoscopy and endotracheal intubation. A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 100 patients posted for elective surgeries selected randomly. General anaesthesia was provided with endotracheal intubation for all the patients. Using Cloridine 3 μgms/ kg body weight single bolus intravenously versus Plain Lidocaine 2% 1.5 mg/kg body weight single bolus intravenously.

This study was conducted at MediCiti Institute OF Medical Sciences, Ghanpur Medchal between December 2012 and June 2014.

Both the groups were comparable with regards to mean age, weight and sex. Both the groups received inj glycopyrrolate 0.2mg, inj midazolam 1mg and inj tramadol 50mg as premedication before induction.

Dosages of the drugs selected

Lignocaine has been employed in various doses for blunting the cardiovascular response to laryngoscopy and intubation.

Intravenous lignocaine 1.5 mg/kg was employed by **Mounir- Abou Madi et al,[11] Stanley Tam et al[12], and Reema Goel et al.[13]**

Intravenous lignocaine 2 mg/kg was employed by **Robert K Stoelting[14]**

Mounir Abou-Madi et al[11]. conducted a study on cardiovascular response to laryngoscopy and intubation following small (0.75 mg/kg) and large (1.5 mg/kg) dose of intravenous lignocaine. They noted 1.5 mg/kg of lignocaine 2% provided better attenuation of responses to intubation than 0.75 mg/kg of intravenous lignocaine.

In view of this in the present study we employed 1.5 mg/kg of lignocaine i.v.

Intravenous Cloridine 3 μgms/kg was employed by **Zalunardo MP. et al[10], Marinangeli F. et al[15] Zalunardo MP. et al[16]** successfully.

Wright P.M.C. et al[17] showed that cloridine at 1.25 μg/kg is not effective for blunting the hemodynamic response to laryngoscopy and intubation.

Carabine U.A. et al[9] showed that dosage 0.625 and 1.25 μg/kg produces partial attenuation of intubation response.

In view of this in the present study we employed 3 μgms/kg of Cloridine i.v.

Timing of administration

Stanlay Tam et al[12] studied the optimal time of lignocaine injection before tracheal intubation to prevent the pressor response to laryngoscopy and intubation. Lignocaine in the dose of 1.5 mg/kg was given intravenously 1 min, 2 min, 3 min and 5 min before intubation. They noted that, intravenous lignocaine attenuated the increase in Heart rate (HR) and Arterial Blood Pressure (ABP), only when given 3 min, before intubation and did not give any desired protection when given at 1 min, 2 min and 5 min before intubation. In view of it, in the present study we employed lignocaine in the dose of 1.5 mg/kg i.v. and lignocaine was given 3 min before intubation.

Wright PMC et al[17] Carabine UA et al[9] Zolunardo MP et al,[10] Marinangeli F et al[15], have employed cloridine 15 min before intubation.

In view of the above, in the present study cloridine was employed 15 minutes before laryngoscopy and intubation to blunt the haemodynamic response.

Comparison with other studies

The present study is compared to 3 other recent studies done by **Mohan K et al[18]**, Gautam et al and Joshi et al.

Mohan K, et al[18] in 2013 studied the attenuation of cardiovascular responses to laryngoscopy and intubation by Diltiazem and Lignocaine. The study population were divided into 4 groups with 30 patients in each group.

Control group: received normal saline as a placebo and served as control(n=30)

Group I: Received 0.2mg/kg Diltiazem I.V 60 seconds before intubation (n=30).

Group II: Received 1.5mg/kg Lignocaine I.V 3minutes before intubation(n=30).

Group III: Received combination of 0.2mg/kg Diltiazem and 1.5mg/kg Lignocaine 60 seconds before intubation (n=30)

Gautam A et al, 2013 conducted a study to compare the efficacy of oral and IV Cloridine in attenuating hemodynamic responses to laryngoscopy and intubation. Patients were randomly divided into 2 groups of 30 each.

Group I (n=30): received oral cloridine 3ug/kg 90 mins before induction.

Group II (n=30): received IV cloridine 3ug/kg before induction=30).

Joshi et al[19], 2012 conducted a study on attenuation of cardiovascular responses to laryngoscopy and endotracheal intubation, comparative evaluation of oral Cloridine and Lignocaine. 90 patients were randomly divided in 3 groups of 30 each.

Group I (n=30): Patients did not receive anything, control group.

Group II(n=30): patients receiving 1.5mh/kg of preservative free 2% Lignocaine 90 seconds before laryngoscopy.
Group III (n=30): patients receiving Cloridine 0.2mg orally 90 mins prior to induction of anaesthesia.

Present study, comparison of IV lignocaine and IV cloridine in attenuation of hemodynamic responses to largyngoscopy and intubation. 100 patients were randomly divided into 2 groups of 50 each.
Group L (n=50): Received 2% preservative free Lignocaine 1.5mg/kg 3 mins before Intubation.
Group C (n=50): Received 3ug/kg Cloridine over 5 mins as an infusion in 100 ml NS 15 mins before intubation.

Mean heart rate [pre induction – peak rise difference (after 1 min) in percentage]: comparison with other studies

Mohan K et al (2013)[18] showed that heart rate in lignocaine group increased by 19.1% after laryngoscopy and intubation compared to control(30%) and Diltiazem (8.1%).

Gautam A et al (2013)[20] in their study, reported that IV Cloridine group had a rise of 13.2% increase in heart rate after laryngoscopy and intubation against Oral Cloridine which had a 16.4% rise .

Joshi et al (2012) [19] showed that heart rate in Lignocaine group rises by 5% compared to 4% rise in oral Cloridine and 39% in control group .

In the present study, after laryngoscopy and endotracheal intubation there was a rise in heart rate in both the groups. In lignocaine group, it reached a peak of 105.2±7.87 beats/min after 1 min post intubation which is 31% above the pre induction heart rate (79.7±6.1). In Cloridine group, the peak heart rate was 92.4±8.2 which is 14% above the ore induction heart rate (81±6.63). Heart rate subsequently decline to 81.9±5.13 and 78.2±5.9 in Lignocaine and Cloridine groups respectively at 10 mins.

Heart rate was significantly higher in Lignocaine group as compared to Cloridine group. In Lignocaine group it gradually reduced but did not come to preinduction level even by the end of 10 minutes. In Cloridine group it came to the preinduction level by the end of the 5th minute.

So as per the present study, Cloridine blunts increase in heart rate more effectively as compared to Lignocaine following laryngoscopy and intubation.

Mean systolic blood pressure [pre induction – peak rise difference (after 1 min) in percentage]: comparison with other studies

Table showing comparision of mean systolic blood pressure with other groups

Group	Mohan K *et al*[18] (2013)	Gautam A et al[20] *(2013)*	Joshi *et al*[19] (2012)	Present Study
Lignocaine	11% increase		2% increase	18% increase
IV Cloridine		0.1% decrease		9% increase
	IV Diltiazem: 2% increase	Oral cloridine: 9% increase	Oral cloridine: 1% decrease	
	Control: 40% increase		Control: 23% increase	

Mean diastolic blood pressure [pre induction – peak rise difference (after 1 min) in percentage]: comparison with other studies

Table showing comparison of mean diastolic blood pressure with other groups.

Group	Mohan K *et al*(2013)	Gautam A *et al (2013)*	Joshi *et al (2012)*	Present Study
Lignocaine	8.3% increase		4% Increase	12% increase
IV Cloridine		1.3% increase		7% increase
	IV Diltiazem: 2.4% increase	Oral cloridine: 9.3% increase	Oral Cloridine: 1% decrease	
	Control: 23% increase		Control: 23% increase	

Summary

A clinical comparative study entitled **"Attenuation of hemodynamic changes during laryngoscopy and endotracheal intubation using IV Lignocaine versus IV Cloridine",** was undertaken in MediCiti Institute of Medical Sciences, Medchal, RR District, Telangana

State during the period between December 2012 to June 2014.

Laryngoscopy and intubation frequently induce cardiovascular stress responses characterized by hypertension tachycardia and raised serum concentration of catecholamines, which may culminate in increased perioperative morbidity.

In the present study, IV Cloridine is compared with IV Lignocaine for attenuation of the hemodynamic responses to laryngoscopy and endotracheal intubation.

One hundred patients of either sex belonging to ASA I & II physical status, posted for elective surgeries were selected and were randomly allocated into two groups L (Lignocaine) and C (Cloridine).

Group L patients received Inj Lignocaine 1.5mg/kg three minutes before laryngoscopy and endotracheal intubation and Group C received 3mcg/kg Cloridine 15 minutes before laryngoscopy and endotracheal intubation.

Both the groups were premedicated and intubated under same conditions and hemodynamic variable like heart rate, systolic blood pressure , diastolic blood pressure , mean arterial pressure were measured pre induction, post induction, and at 1, 3, 5, 7, 10 minutes after intubation using standard monitoring equipment.

There was marked increase in HR, SBP, DBP and MAP 1 minute following laryngoscopy and intubation in the lidocaine group. Intravenous cloridine given 15minutes before intubation in the dose of 3µg/kg body weight effectively attenuated the haemodynamic response after laryngoscopy and intubation. However, there was a rise in HR, SBP, DBP, MAP values 1 min following intubation in cloridine group which was clinically not significant though statistically significant.

Conclusion

From the present study it can be concluded that

- In Lidocaine group patients who received 1.5mg/kg, 3 minutes before intubation, there was a significant rise in the mean heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) occurred one minute following laryngoscopy and intubation.
- In cloridine group patients, cloridine in the dose of 3µg /kg IV, given 15 minutes before intubation, effectively attenuated the heart rate response and also arterial pressure response to laryngoscopy and intubation.

Hence it is concluded that cloridine in the dose of 3µg/kg IV, given 15 minutes before laryngoscopy and intubation can be a better alternative than IV lidocaine in attenuating the haemodynamic responses to laryngoscopy and intubation without any side effects. In addition Cloridine also has other advantages such as decrease in the requirement of inhalational agents, desirable sedation etc.

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