DOI: 10.5958/j.2319-5886.2.3.098

International Journal of Medical Research & Health Sciences

www.ijmrhs.com Volume 2 Issue 3 July - Sep Coden: IJMRHS Copyright @2013 ISSN: 2319-5886

Received: 6th Jun 2013 Revised: 3rd Jul 2013 Accepted: 5th Jul 2013

Research Article

ATTENUATION OF CARDIOVASCULAR RESPONSES TO LARYNGOSCOPY AND INTUBATION BY DILTIAZEM AND LIGNOCAINE: A COMPARATIVE STUDY

*Mohan K[1], Mohana Rupa L[2]

[1]Department of Anaesthesia, [2]Department of Pharmacology, Sri Sathya Sai Medical College & Research Institute, Tiruporur, Guduvancherry, Ammapettai, Sembakkam, Tamilnadu, India.

*Corresponding author email: koyeedoctor@gmail.com

ABSTRACT

The study has been designed to investigate the attenuation of cardiovascular responses to laryngoscopy and intubation by diltiazem and lignocaine. Endotracheal intubation is often associated with a hypertension and tachycardia. This response is primarily because of sympatho-adrenal stimulation, associated with laryngoscopy and endotracheal intubation. The rise in the heart rate (HR) and blood pressure increases the myocardial oxygen demand. This increase is tolerated well by normal healthy individuals. However, in patients with Ischemic heart disease (IHD), Hypertensive heart disease and cerebrovascular disease, this sudden rise of heart rate and blood pressure can produce deleterious effects, in the form of myocardial ischemia, pulmonary oedema and cerebral haemorrhage. Many methods, like beta-blockers, deep inhalational anaesthesia, intravenous lignocaine, calcium channel blockers and direct acting vasodilators, have been tried to blunt these harmful pressor responses associated with laryngoscopy and endotracheal intubation. Intravenous lignocaine is a popular method of blunting this response, because of its ability to depress the myocardium and membrane stabilization effect. Diltiazem, a calcium channel blocker can blunt these responses because of its direct acting vasodilating properties and negative chronotropic effect. In view of it, the present study was undertaken to compare the effects of 1.5 mg/kg lignocaine IV given 3 minutes before laryngoscopy and intubation, Diltiazem 0.2 mg/kg IV given 60 seconds before laryngoscopy and intubation and combination of 0.2 mg/kg of diltiazem IV and 1.5 mg/kg of lignocaine IV given 60 seconds before laryngoscope and intubation on laryngoscopic reactions. It was noted that,both lignocaine and diltiazem attenuated the pressor response to laryngoscopy and endotracheal intubation compared to control group. However, the combination of lignocaine and diltiazem gave better protection against the laryngoscopic reaction than when either of the drugs was given alone.

Keywords: Laryngoscopy, tracheal intubation, cardiovascular response, Lignocaine, Diltiazem

INTRODUCTION

Direct laryngoscopy and endotracheal intubation following induction of anaesthesia is always associated with hemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation.[1] This increased sympatho-adrenal activity may result in hypertension, tachycardia and arrhythmias. [2, 3] This increase in blood pressure and heart rate are usually transitory, variable and unpredictable. Hypertensive patients are more prone to have significant increases in blood pressure, whether they have been treated before hand or not. [4] Transitory hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases. This laryngoscopic reaction in such individuals may predispose to development of pulmonary oedema, [5] myocardial insufficiency [6] and cerebrovascular accident. [7] At least in such individuals there is a necessity to blunt these harmful laryngoscopic reactions.

Many pharmacological methods have been devised to reduce the extent of hemodynamic events including high dose of opioids, [8] local anaesthetics like lignocaine, [9] alpha and beta adrenergic blockers [10, 11] and vasodilatation drugs like nitroglycerine. [12] Topical anaesthesia with lignocaine applied to the larynx and trachea in a variety of ways remains a popular method used alone or in combination with other techniques. [13] Intravenous lignocaine with its well established centrally depressant and anti-arrhythmic effect was found to be a more suitable alternate method to minimize this pressor response. [14, 15] Recently several studies have shown that calcium channel antagonist like diltiazem, with its direct vasodilation and direct negative chronotropic and dromotropic properties are also effective. [4, 16]

Hence the present study was undertaken to compare the effect of Intravenous lignocaine and intravenous diltiazem on blunting the haemodynamic responses to endotracheal intubation. An attempt is also made to study the effect of combination of these two drugs on haemodynamic response to endotracheal intubation. The advantage of combining diltiazem and lignocaine are considered to be based on their different mechanism of activity and their efficacy when used alone. [4]

Objectives of the study: The main objectives of the present study are:

1. To study the effect of laryngoscopy and intubation on changes in the heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial blood pressure (MAP) and Rate pressure product (RPP)
2. To study the effect of diltiazem 0.2 mg/kg, lignocaine 1.5 mg/kg and combination of diltiazem 0.2 mg/kg i.v. and lignocaine 1.5 mg/kg i.v, on hemodynamic responses to laryngoscopy and endotracheal intubation.

METERIALS AND METHODS

A study was undertaken in Sri Sathya sai medical college & research institute during the year February 2011 to January 2012. The study design was approved by the Institutional ethics committee and informed consent obtained from all the patients prior to the experiment. One hundred and twenty (120) patients were included in the study. The patients were normotensive with age varied from 18 to 60 years with both sex. The patients were selected at random. Patients having any significant systemic disorders, IHD, Hypertensive heart disease, Diabetes Mellitus, Bronchial asthma, patients with previous Myocardial infarction and patients with cerebrovascular insufficiency or associated with any co-morbid diseases were excluded from the study. The study populations were divided into four (4) sub groups with 30 patients in each group.

Control Group: Received normal saline as a placebo and served as control (n=30).

Group I: Received 0.2 mg/kg of Diltiazem i.v. 60 seconds before laryngoscope & intubation (n=30)
Group II: Received 1.5 mg/kg of Lignocaine i.v. 3 minutes before laryngoscopy & intubation (n=30)
Group III: Received combination of 0.2 mg/kg of Diltiazem and 1.5 mg/kg of Lignocaine i.v. 60 seconds before laryngoscopy and intubation (n =30).

Pre-an aesthetically the following investigations were done in all patients; Hemoglobin estimation, Urine examination for albumin, sugar and microscopy, Standard 12- lead electrocardiogram, X-ray chest/ Screening of chest , Blood sugar, FBS/PPBS, Blood urea and hypersensitivity reaction to local anaesthetics.

All the patients included in the study were premedicated with Tab. Alprazolam 0.5 mg, Tab. Ranitidine 150 mg orally at bed time the previous day and Inj. Midazolam 1 mg iv and inj. Pentazocine 15 mg i.v given to all the patients before induction of anesthesia as premedication.

On the arrival of the patient in the operating room, an 18-gauge/20-gauge intravenous cannula was inserted and an infusion of Dextrose with normal saline was started. The patients were connected to Siemens SC-7000, multichannel monitor which records Heart rate, non-invasive blood pressure (NIBP), end-tidal carbon dioxide concentration, and continuous ECG monitoring, MAP and oxygen saturation. The baseline blood pressure and heart rate were recorded from the same non-invasive multichannel monitor and cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II.

Induction of Anaesthesia : Anaesthesia was induced with inj. Thiopentone 5 mg/kg as 2.5% solution and endotracheal intubation was facilitated with Succinylcholine 1.5 mg/kg administered one minute prior to laryngoscopy and intubation. The patients were intubated using appropriate sized cuffed endotracheal tubes. After confirming bilateral equal air entry, the endotracheal tube was secured.

Anaesthesia was maintained using 66% nitrous oxide and 33% of oxygen. After the patients recovered from Succinylcholine further neuromuscular blockade was maintained with non-depolarizing muscle relaxants. At the end of the procedure patients were reversed with neostigmine 0.05 mg/kg IV and atropine 0.02 mg/kg IV.

Monitoring : The following cardiovascular parameters were recorded in all the patients

- Heart rate (HR) in beats per minutes (bpm)
- Systolic blood pressure (SBP) in mm Hg
- Diastolic blood pressure (DBP) in mm Hg
- Mean arterial pressure (MAP) in mm Hg
- Rate Pressure Product (RPP) calculated by multiplying the SBP and HR

The above cardiovascular parameters were noted as below one, three, five minute after laryngoscopy and intubation

The data were expressed as Mean ± SEM and analyzed by using student‘t’ test comparing between the groups and within the group. P – Value < 0. 05 were considered as significant.

RESULTS

Table.1: Table showing changes in mean heart rate(bpm)

Groups	**Control**	**Group I**	**Group II**	**Group III**
Basal	83.00 ± 5.86	81.63 ± 9.38	77.20 ± 8.10	77.97 ± 10.42
Pre-Induction	90.73 ± 7.62	87.33 ± 11.60	80.70 ± 7.66	78.53 ± 10.32
Intubation: 1 Min	118.53 ± 6.89	94.47± 11.90*	96.17 ± 8.61*	85.43± 11.08*
3 Min	114.40 ± 9.72	92.30± 11.38*	90.50 ± 9.38*	77.37± 10.57*
5 Min	99.03 ± 5.40	89.37 ± 9.34*	83.93 ± 7.60*	76.07± 10.43*

Data were expressed as Mean ± SEM, *P – Value < 0. 05 significant

Table.2: Table showing changes in mean systolic blood pressure (mmHg)

	Control	Group I	Group II	Group III
Basal	120.40 ± 9.36	132.90 ± 14.91	132.73 ± 12.97	138.13 ± 15.04
Pre-Induction	117.57 ± 10.41	135.87 ± 13.90	132.70 ± 13.85	130.47 ± 14.65
Intubaion 1 Min	164.47 ± 10.41	138.43 ± 19.22*	147.40± 11.33*	140.27± 18.31*
3 Min	150.83 ± 13.34	136.40 ± 17.50*	141.63± 10.89*	129.57± 17.31*
5 Min	134.70 ± 11.62	132.40 ± 12.93*	137.60± 11.18*	122.53± 17.05*

Data were expressed as Mean ± SEM, *P – Value < 0. 05 significant

Table .3: : Table showing changes in mean diastolic blood pressure (mmHg)

	Control	Group I	Group II	Group III
Basal	73.57 ± 6.69	80.83 ± 6.75	79.63 ± 9.37	78.23 ± 8.60
Pre-Induction	73.43 ± 6.30	81.63 ± 8.70	78.97 ± 8.42	75.73 ± 8.11
Intubation: 1 Min	90.23 ± 4.71	83.60 ± 9.12*	85.57 ± 8.75*	81.07 ± 4.89*
3 Min	88.03 ± 5.01	83.57 ± 10.88*	81.57 ± 8.61*	75.90 ± 8.39*
5 Min	82.37 ± 3.96	83.73 ± 9.92*	77.43 ± 8.46*	74.90 ± 7.25*

Data were expressed as Mean ± SEM, *P – Value < 0. 05 significant

Table.4:Table showing changes in the mean arterial pressure (mmHg)

	Control	Group I	Group II	Group III
Basal	88.93 ± 6.64	98.07 ± 9.01	99.70 ± 12.29	97.10 ± 10.68
Pre-Induction	87.77 ± 6.80	99.43 ± 10.32	99.10 ± 12.54	93.50 ± 10.22
Intubation: 1 Min	114.77 ± 5.88	101.27 ± 13.41*	104.33 ± 13.32*	100.63 ± 8.44*
3 Min	108.57 ± 7.05	100.83 ± 13.13*	98.47 ± 11.94*	92.03 ± 9.55*
5 Min	99.37 ± 5.50	101.10 ± 10,07*	97.97 ± 9.60*	92.77 ± 9.66*

Data were expressed as Mean ± SEM, *P – Value < 0. 05 significant

Table.5: Showing changes in mean rate pressure product (RPP)

	Control	Group I	Group II	Group III
Basal	9,983.93	10,872.27	10,261.10	10,825.43
Pre-Induction	10,670.47	11,900.77	10,733.93	10,249.83
Intubation: 1 Min	19,483.20	13,175.13*	14,195.00*	12,027.87*
3 Min	17,264.80	12,675.27*	12,827.43*	10,037.77*
5 Min	13,325.80	11,874.10*	11,556.17*	9,367.83*

Data were expressed as Mean ± SEM, *P – Value < 0. 05 significant

DISCUSSION

General anaesthesia has almost become synonymous with endotracheal anaesthesia. As a matter of fact, the rapid studies made in the speciality of anaesthesia can directly be attributed to our ability to manage the airway. The hemodynamic responses to laryngoscopy and endotracheal intubation have been a topic of discussion right since 1940. When Reid et, al [17] found that stimulation of upper respiratory tract provoked an increase in vagal activity. A year later Burstein et al [18] totally contradicting Reid's statement, found that the pressor response occurring at laryngoscopy and endotracheal intubation was due to augmented sympathetic

response, provoked by stimulation of epipharynx and laryngopharynx. These factors were further confirmed by Prys-Roberts [3].

These responses are transitory, variable and may not be of much significant in otherwise normal healthy patients. But in patients with cardiovascular compromise like Ischemic heart disease (IHD) and Hypertension, patients with cerebrovascular diseases and in patients with intracranial aneurysms, even these transient changes can result in potentially deleterious effects like left ventricular failure, [5] pulmonary oedema, myocardial ischemia [6] and ventricular dysrhythmias [3] and cerebral haemorrhage.[7]

In early sixties, inhalational anaesthetic agents were used to attenuate the laryngoscopic reactions. But inhalational anaesthetic agents had their own demerits, for example myocardial depression and arrhythmogenicity with halothane, nephrotoxicity with methoxyflurane coronary steal with Isoflurane. Among the pharmacological agents used for blunting the hemodynamic responses, opioids were found to be effective but they caused respiratory depression, chest wall rigidity and prolong the recovery time. [8, 19] Adrenergic blockers were employed by Devault et al., [10] and direct acting vasodilators was employed by Robert K, Stoelting. [20] Both these agents were found to be effective in suppressing hemodynamic responses to laryngoscopy and endotracheal intubation. However, adrenergic blockers had long duration of action which outlasted the transient intubation response and caused intraoperative hypotension. Direct acting vasodilators also had the disadvantage of producing reflex tachycardia. Lignocaine which avoids these problems has been successfully used to blunt the hemodynamic responses to intubation, Hamil et al. [21] studied the effect of lignocaine on endotracheal intubation when given by laryngotracheal route and intravenous route and came to a conclusion that intravenous lignocaine is the preferred route for administering lignocaine prior to endotracheal intubation.

Recently Mikawa et al., [16] have reported that calcium channel antagonists like Nicardipine and Diltiazem are also effective in controlling the hemodynamic responses to laryngoscopy and intubation in normotensive as well as in hypertensive patients. A good correlation has been demonstrated between the cardiovascular responses to intubation and changes in plasma catecholamine concentrations. Calcium ions exert a major role in the release of catecholamines from the adrenal gland and adrenergic nerve endings, which affects plasma concentrations of catecholamines in response of sympathetic stimulation. Animal experiments have shown that calcium channel antagonists inhibited catecholamine release from the sympathetic nerve endings by electrical stimulation. In a study in healthy volunteers, the blocker inhibited the increase in plasma adrenaline induced by exercise. These observations suggest that calcium channel antagonists interfere with catecholamine release after tracheal intubation. Yashitoka Fuji et al [22] noted that between diltiazem and Nicardipine, diltiazem was found to be superior to Nicardipine in attenuating the hemodynamic response to laryngoscopy and intubation. G. Godet et, al., [23] noted that diltiazem prevents intraoperative myocardial ischaemia during non-cardiac surgery.

In view of these advantages of lignocaine and diltiazem the present study was carried out to evaluate the efficacy of these two drugs in blunting the hemodynamic response. An attempt was also made to study the effect of combination of these two drugs on the hemodynamic response to laryngoscopy and intubation.

In the present study also we noticed that though both diltiazem and lignocaine partially attenuated the pressor response to laryngoscopy the results of the combination group were superior to either of the drugs when given alone. This is reflected by RPP changes. In diltiazem group RPP increased by an average of 2302, while in lignocaine group it increased by 3933. However,

in combination group it increased by only 1488. The difference in rise of RPP between the three groups is statistically significant.

Thus overall, from the present study it was seen that pressor response to laryngoscopy without any drugs employed for attenuation results in marked rise of HR, SBP, DBP MAP and RPP. Both diltiazem 0.2mg/kg IV given 60 seconds before intubation and intravenous lignocaine 1.5 mg/kg given 3 minutes before intubation, significantly attenuates the pressor response to laryngoscopy. The results of diltiazem 0.2 mg/kg were superior to intravenous lignocaine 1.5 mg/kg.The combination of diltiazem and intravenous lignocaine given 60 seconds earlier to intubation very significantly attenuates the increase in HR, SBP, DBP, MAP and RPP associated with laryngoscopy and intubation. However, this combination may sometimes in small percentage of patients may produce significant fall of blood pressure. Caution should be taken when using this combination against the development of hypotension. However this hypotension was easily manageable and did not produce any untoward effects on the patients.

CONCLUSION

From the present study it can be concluded that, marked rise in the HR, SBP, DBP, MAP and RPP occur one minute following laryngoscopy and intubation, when no drug is employed to attenuate the pressor response to intubation. This cardiovascular reaction persists for about 5 minutes after which they return towards baseline values. Diltiazem in the dose of 0.2 mg/kg IV given 60 seconds earlier to intubation blunts the cardiovascular response to intubation. The effects of diltiazem are more marked on the blood pressure changes than on the heart rate. Intravenous lignocaine 2 % in the dose of 1.5 mg/kg given 3 minutes before laryngoscopy and intubation is also helpful in attenuating the cardiovascular response to intubation. The effect of lignocaine is also more marked on the blood pressure changes rather than the heart rate changes. Combination of lignocaine 1.5 mg/kg iv and diltiazem 0.2 mg/kg iv given 60 seconds earlier to intubation effectively blunts the HR, SBP, DBP, MAP and RPP associated with intubation. Combination of diltiazem and lignocaine is more effective than diltiazem or lignocaine, when given alone in blunting the pressor response.

REFERENCES

1. Reema Goel, Raka Rani, Singh OP, Deepak Malviya, Arya SK. Attenuation of cardiovascular responses to laryngoscopy and intubation by various drugs in normotensive patients, Hospital Today. 2000; 9.
2. Robert K. Stoelting MD. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation. Influence of viscous or intravenous lidocaine. Anaesthesia Analgesia. 1978; 57: 197-99.
3. Prys-Roberts, Greene LT, Meloche R and Foex P. Studies of anaesthesia in relation to hypertension-II. Haemodynamic consequences of induction and endotracheal intubation. British Journal of Anaesthesia. 1971; 43: 541-47.
4. Yoshitaka Fujii, Yuhji Saitoh, Shinji Takahashi, Hidenori Toyooka. Diltiazem-lidocaine combination for the attenuation of cardiovascular responses to tracheal intubation in hypertensive patients. Canadian Journal of Anaesthesia. 1998; 45: 935-37.
5. Elisabeth J Fox, Garry S Sklar, Constance H Hill, Raymond Villanueva, Benton D King. Complication related to the pressor response to endotracheal intubation. Anaesthesiology. 1977; 47: 524-25.
6. Dalton B and Guiney T. Myocardial ischaemia from tachycardia and hypertension in coronary heart disease – Patient's undergoing anaesthesia. Ann. Mtg. American Society of Anaesthesiologists, Boston. 1972; pp. 201-02.

7. Donegan MF and Bedford RF. Intravenously administered lignocaine prevents intracranial hypertension during endotracheal suctioning. Anaesthesiology, 1980; 52:516-18.
8. Forbes AM and Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. British Journal of Anaesthesia. 1970; 42: 618-22.
9. Stoelting RK. Circulating responses to laryngoscopy and intubation with or without prior oropharyngeal viscous lidocaine. Anaesthesia Analgesia. 1977; 56: 618-21.
10. Devault M, Greifenstein FE and Harris JR. Circulatory responses to endotracheal intubation in light general anaesthesia; the effect of atropine and phentolamine. Anaesthesiology. 1960; 21: 360-62.
11. Prys-Roberts C, Foex P, Biro GP and Roberts JG. Studies of anaesthesia in relation to hypertension Adrenergic beta-receptor blockade. British Journal of Anaesthesia. 1973; 45: 671-80.
12. Dich J Nielson. The effect of intranasally administered nitroglycerine on the blood pressure response to laryngoscopy and intubation in patients undergoing coronary artery bypass graft surgery. Acta Anaesthesiologica Scandinavia. 1986; 30: 23-27.
13. Mounir-Abou-Madi, Hugo Keszler and Odile Yacoub. A method for prevention of cardiovascular responses to laryngoscopy and intubation. Canadian Anaesthetic Society Journal. 1975; 22(3):316-29.
14. Stanley Tam, Frances Chung and Michael Campbell. Intravenous lignocaine: optimal time for injection before tracheal intubation. Anaesthesia. Analgesia. 1987; 66: 1036-38.
15. Mounir-Abou-Madi, Hugo Keszler and Joseh M Yacoub. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous dose of lidocaine. Canadian Society Anaesthesia Journal. 1977; 24(1):12-18.
16. Mikawa K, Nishina K, Maekawa N and H. Obara. Comparison of nicardipine, diltiazem and verapamil for controlling the cardiovascular responses to tracheal intubation. British Journal of Anaesthesia. 1996; 76: 221-26.
17. Reid LC and Bruce DE. Initiation of respiratory tract reflexes and its effects on heart. Surgy. Gynae. Obstretrics. 1940; 70: 157.
18. Burstein CL, Lo Pinto FJ and Newman W. Electrocardiographic studies during endotracheal intubation 1, effects during usual routine techniques. Anaesthesiology. 1950; 11:224.
19. Bedford RF and Lt Marshal K. Cardiovascular responses to endotracheal intubation during four anaesthetic techniques. Acta Anaesthesiologica Scandinavia. 1984; 28: 563-66.
20. Robert RK Stoelting. Attenuation of blood pressure responses to laryngoscopy and tracheal intubation with sodium nitroprusside. Anaesthesia Analg. 1979; 58(2): 116-19.
21. Churchill-Davidson HC. A practice of anaesthesia, 5th Edition, P.G. Publishing Limited: New Delhi, 1984.
22. Yoshitaka Fujii, Hiroyoshi Tanaka, Yuhji Saitoh, Hidenori Tayooka D. Effects of calcium channel blockers on circulatory response to tracheal intubation in hypertensive patients: Nicardipine versus Diltiazem. Canadian Journal of Anaesthesia. 1995; 42(9): 785-88.
23. Richard S Himes, Cosmo A, Difazio et al. Effects of lidocaine on the anaesthetic requirement for nitrous oxide and halothane. Anaesthesiology. 1977; 47: 437-40.