MRIMS Journal of Health Sciences 2018;6(1) pISSN: 2321-7006, eISSN: 2321-7294
http://www.mrimsjournal.com/

Original Article

Attenuation of hemodynamic response to laryngoscopy and intubation-The Effect of Diltiazem, A randomized controlled study

Swathi Appagalla[1], Manjula V Ramsali[2], Sarada Devi Vankayalapati[3], Surender Pasupuleti [4]

[1]Assistant professor, [2]Assistant professor, [3]Assistant professor, [4] Professor and HOD, Department of Anesthesia, Malla Reddy Medical college for women, Hyderabad

Corresponding Author

Email: manjularamsali@gmail.com

Abstract:

Background: Direct laryngoscopy and tracheal intubation following induction of anesthesia is almost always associated with hemodynamic changes due to reflex sympatho-adrenal activity which may result in hypertension, tachycardia and arrhythmias. Various agents like lidocaine, opioids, esmolol, magnesium sulphate, alpha 2 agonists and propofol have been shown to attenuate these responses, but they have limitations and side effects. Recently several studies have shown that calcium channel antagonist Diltiazem with its direct vasodilation, direct negative chronotropic and dromotropic properties is effective. Our study was designed to determine the efficacy of diltiazem 0.3mg/kg in attenuating the hemodynamic response to laryngoscopy and intubation in ASA I & II patients.

Objectives: The prospective randomized study was done to evaluate the efficacy of Diltiazem in attenuation of hemodynamic response to laryngoscopy and intubation.

Methods: 50 patients aged between 22-55 yrs of either sex of ASA Grade I and II scheduled for elective surgeries were studied after randomization into two groups, Control and Study (Diltiazem) groups. The anesthesia technique was standardized for both the groups. All the patients were given either saline 2ml or diltiazem 0.3 mg/kg in 2ml 60 seconds before laryngoscopy and intubation. The parameters like HR, SBP, DBP, and MAP were recorded at pre-induction, at induction, during laryngoscopy and intubation and at 1min, 2min, 3min, and 5min after intubation. Patients were also observed for side effects like hypotension, bradycardia and bronchospasm.

Results: There was increase in the HR, SBP, DBP and MAP after induction and immediately after laryngoscopy and intubation in the control group but there was a fall in SBP, DBP and MAP in study group. There was no significant change in HR in the study group.

Conclusion: Our study concludes that diltiazem 0.3 mg/kg given IV 60 seconds before laryngoscopy and intubation can be safely employed to attenuate hemodynamic responses without any side effects.

Key words: Cardiovascular response, endotracheal intubation, diltiazem, laryngoscopy

Introduction:

Direct laryngoscopy and endotracheal intubation following induction of anesthesia is almost always associated with hemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. [1, 2] This increased sympatho-adrenal activity may result in hypertension, tachycardia and arrhythmias. [3, 4] These changes are the result of increase in catecholamine activity and are usually transitory, variable and unpredictable. Hypertensive patients are more prone to have significant increases in blood pressure whether they have been treated beforehand or not. [5] 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 edema, [6] myocardial insufficiency[7] and cerebrovascular accident. [7-8]

Many pharmacological and non-pharmacological methods have been devised to reduce the extent of hemodynamic events like high dose of opioids, [9] local anesthetics (lignocaine), [10] alpha and beta adrenergic blockers, [11] vasodilators (nitroglycerine) and minimizing the duration of laryngoscopy to less than 15 seconds. [12] Lignocaine is used in many ways but very popular is application of the drug topically to the larynx and trachea. [13] Intravenous lignocaine has central depressant and anti-arrhythmic effect and was found to be a more suitable alternate method to minimize this pressor response. [14, 15] Several studies have shown that calcium channel antagonist Diltiazem has direct vasodilation and direct negative chronotropic and dromotropic properties so effective in reducing the pressor response. [5, 16]

The present study was undertaken to determine the effect of IV Diltiazem 0.3mg/kg in attenuating the hemodynamic response to laryngoscopy and intubation in ASA I and II patients coming for elective surgeries.

Material and Methods:

After the Institutional Ethics Committee approval and written informed consent, the present study was carried out on fifty adult patients of either sex, aged between 20 – 65 years, scheduled for various procedures undergoing elective surgery under general anesthesia in ASA grade I/II physical status in the department of anesthesia at MRMCW, Hyderabad from March 2015 to December 2016

Patients suffering from cardiovascular, Respiratory, Cerebrovascular diseases, Diabetes, Hypertension and predicted difficult intubation were excluded from the study. Pre-anesthetic check up was conducted and a complete physical examination was done. Routine investigations like CBP, blood group & typing, Blood Urea, Serum creatinine, BT, CT, Blood sugar, ECG and CXR were done. Patients were randomly divided into two groups of 25 each. Randomization was done by computer generated table.

Group I- Control Group—received 2 ml of Normal Saline IV 60 sec before laryngoscopy & intubation.

Group II- Diltiazem Group—received 0.3 mg/kg of Diltiazem IV 60 sec before laryngoscopy & intubation.

The premedication, induction agent & muscle relaxant agents used for anesthesia technique were standardized for both the groups. In the OR, patients were connected to the standard monitoring like ECG, NIBP & Spo2 prior to induction of anesthesia. After securing wide bore IV line, patients were given glycopyrrolate 0.2mg, ondan 4mg, midazolam 1mg and fentanyl 2µg/kg. Preoxygenated with 100 % O_2 for 3 min induced with Propofol 2mg /kg, vecuronium 0.1mg/kg and lungs were ventilated with O_2 & N_2O for 3 min. Patients received either NS or Diltiazem (0.3mg/kg) 60 sec before laryngoscopy and intubation. Intubation was achieved with an appropriate sized oral cuffed portex endotracheal tube by the aid of macintosh laryngoscope blade. Anesthesia was maintained with O_2 & N_2O, isoflurane and vecuronium with controlled ventilation. At the end of surgery neuromuscular blocked was reversed with neostigmine 2.5 mg & glycopyrrolate 0.4 mg IV. All the patients were followed up in the post operative period and observed for any adverse effects. The anesthesiologist performing the study was blinded to the study drugs. The drug preparation and administration was done by senior anesthesiologist and observations are done by another anesthesiologist who is unaware of the drug administered.

HR, SBP, DBP, MAP, ECG and SpO_2 were monitored continuously. Blood pressure (SBP, DBP, MAP) & Heart Rate (HR) parameters were recorded at pre-induction, after induction, during laryngoscopy and intubation and at 1min, 2min, 3 min and 5 min after intubation. We also observed for any side effects like hypotension, bradycardia, bronchospasm etc.

The parameters were recorded and data were entered into statistical package for social sciences (SPSS-20). Statistical analysis were done using unpaired t test between two groups and paired t test for inter group comparison through graph pad software with quick cals.

Results:

Table 1: Demographic profile

Description	Control group mean±SD	Study group mean±SD
Age in years	36.64±6.87	35.92±9.53
Weight in KG	58±5	55±5.8
Male : Female	12:13	9:16
ASA grade I/II	17/8	18/7
MP grade 1/II	19/6	20/5

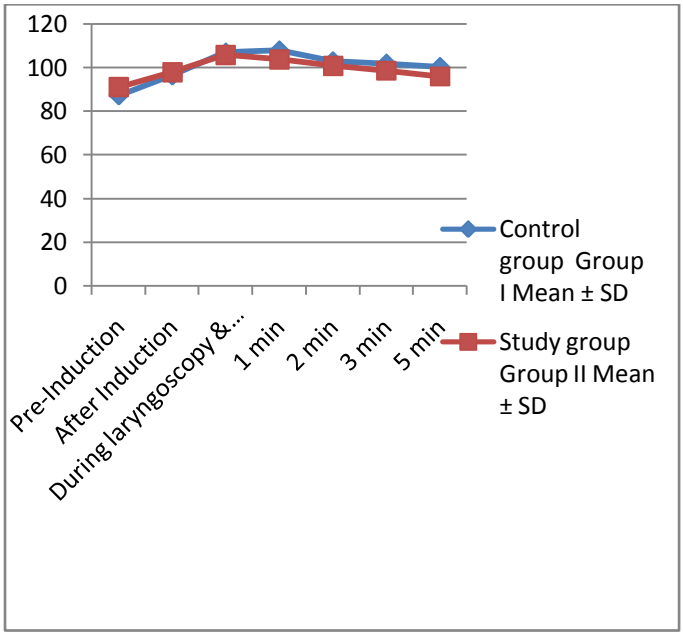
Patients in both the groups were comparable for age, weight, sex ratio and ASA physical status and were not statistically significant. (Table 1)

Table 2: Heart rate Comparison

Time interval	Control group mean±SD	Study group mean±SD	P value	Remarks
Pre-Induction	87.36±9.89	91.1±10.8	0.2059	NS
After Induction	96.52±8.95	98±13.1	0.6433	NS
During laryngoscopy & intubation	107±10.80	106±10.80	0.7448	NS
1 min	108±9.18	104±11	0.1694	NS
2 min	103.52±7.48	101±10.1	0.3612	NS
3 min	101.92±8.33	98.7±9.95	0.2676	NS
5 min	100.40±8.73	96±9.56	0.0959	NS

The above table (table 2) shows the comparison of HR in both the groups. The parameters indicate that the difference between the groups are not statistically significant ($p>0.05$). Pre-induction values are taken as basal values.

Graph 1: HR comparisons



Graph 2: SBP comparisons

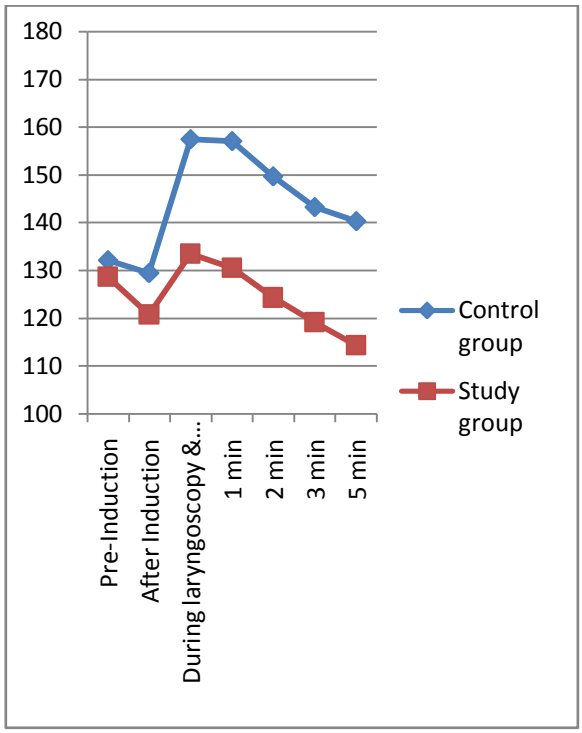


Table 3: SBP Comparison

Time interval	Controlgroup mean±SD	Study group mean±SD	P value	Remarks
Pre-Induction	132.12±9.48	128.68±10.953	0.241	NS
After Induction	129.52±10.48	120.80±15.861	0.027	SS
During laryngoscopy & intubation	157.40±12.055	133.44±9.70	0.0001	ESS
1 min	157.08±11.56	130.52±12.248	0.0001	ESS
2 min	149.68±8.325	124.32±10.024	0.0001	ESS
3 min	143.28±10.710	119.2±9.552	0.0001	ESS
5 min	140.32±11.393	114.32±8.934	0.0001	ESS

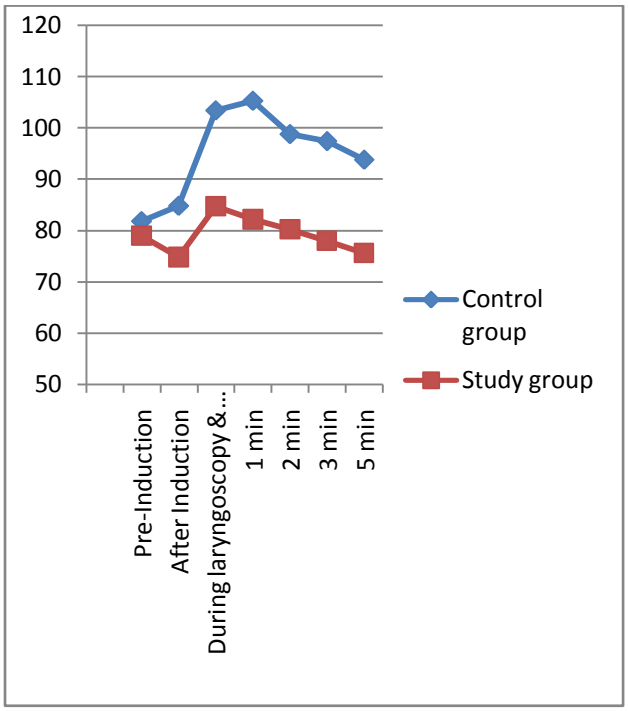
The parameters within the group indicate that there was statistically significant rise in SBP in the control group as compared to basal value at the all times. Where as in study group there was transient rise in SBP only during and after 1 min of laryngoscopy and intubation which was not significant

When compared between the groups the rise in SBP in control group is statistically significant($p<0.05$) during laryngoscopy, 1min, 2min, 3 min & 5min after laryngoscopy and intubation when compared to study group. Pre-induction values are taken as basal values which are not statistically significant ($p>0.05$).

Table 4: DBP Comparison

Time interval	Control group mean±SD	Study group mean±SD	P value	Remarks
Pre-Induction	81.84±8.350	79.00±8.216	0.0730	NS
After Induction	84.84±9.294	74.80±10.124	0.0027	VSS
During laryngoscopy & intubation	103.44±8.471	84.76±9.718	0.0001	ESS
1 min	105.36±9.214	82.16±11.025	0.0001	ESS
2 min	98.88±8.388	80.20±8.365	0.0001	ESS
3 min	97.48±7.912	78±6.93	0.0001	ESS
5 min	93.88±7.190	75.56±7.654	0.0001	ESS

Graph 3: DBP comparison



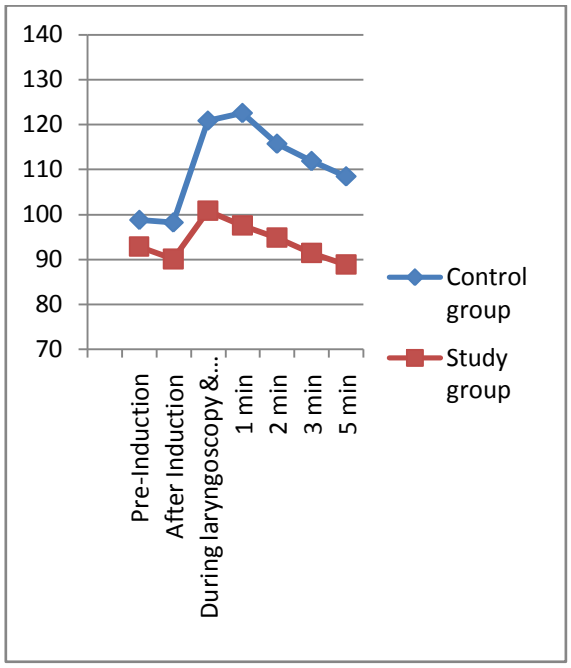
There is a statistically significant rise in DBP in the control group as compared to basal value at the all times. Where as in study group there was transient rise in DBP only during laryngoscopy and after 1 & 2 min of laryngoscopy and intubation but was not significant. Pre-induction values are taken as basal values which are not statistically significant ($p > 0.05$).

The inter group comparison of DBP showed rise in DBP in control group at induction, during laryngoscopy and at 1, 2, 3 and 5 min after laryngoscopy and intubation to the control group which was statistically significant($p<0.05$).

Table 5: MAP Comparison

Time interval	Control group mean±SD	Study group mean±SD	P value	Remarks
Pre-Induction	98.80±8.655	92.72±7.586	0.111	NS
After Induction	98.20±9.147	90±9.819	0.0038	VSS
During laryngoscopy & intubation	120.84±9.603	100.72±8.925	0.0001	ESS
1 min	122.60±8.36	97.52±10.199	0.0001	ESS
2 min	115.76±8.04	94.72±8.218	0.0001	ESS
3 min	111.92±8.650	91.36±6.98	0.0001	ESS
5 min	108.48±7.95	88.84±6.938	0.0005	ESS

Graph 4: MAP comparison



There is statistically significant rise in MAP in the control group as compared to basal value at the all times. Where as in study group there was transient rise in MAP only during laryngoscopy, and at 1, 2 min of laryngoscopy and intubation which was not statistically significant

Pre-induction values are taken as basal values which are not statistically significant ($p>0.05$). The rise in MAP in control group is statistically significant ($p<0.05$) at induction, during laryngoscopy and at1, 2, 3, 5 min after laryngoscopy and intubation when compared to study group.

Discussion:

The introduction of general anesthesia made it possible to induce a state of controlled unconsciousness so that a patient is insensitive to pain and unaware of the events occurring during the surgical procedure. Traditional laryngoscopy and tracheal intubation is the mainstay in safeguarding the airway in such patients. Although intubation has its own advantages such as safe secured airway, prevention of aspiration and delivery of anesthetic gases but it is not without complications.

Laryngoscopy and tracheal intubation may provoke a transient but marked sympathetic and sympathoadrenal response manifesting as tachycardia, hypertension and arrhythmias. [3, 4] The haemodynamic changes brought about by laryngoscopy and tracheal intubation was first discovered by Reid and Brace. [18] But later Burstein et al [19] found the pressor response was due to augmented sympathetic response provoked by stimulation of epipharynx and laryngopharynx. These factors were further confirmed by Prys-Roberts. [4]

These pressor responses are transient, variable and may not be of much significance in normal healthy patients. But in patients with co-morbidities, these transient changes can

result in potentially deleterious effects like ventricular dysarrhythmias [4], left ventricular failure, [6] pulmonary edema, [6] myocardial ischemia [7] and cerebral hemorrhage. [8] These responses need to be attenuated as far as possible. Various pharmacological and mechanical modalities have been used to attenuate these responses but have their own limitations. Opioids were found to be effective but caused respiratory depression, chest wall rigidity and prolonged recovery time. Devault et al [20] employed adrenergic blockers and Robert K Stoelting [23] used direct acting vasodilators to attenuate the hemodynamic pressor response to laryngoscopy and tracheal intubation. The disadvantage of using Beta blockers was long duration of action causing intraoperative hypotension whereas vasodilators caused reflex tachycardia and also required the need for invasive arterial BP monitoring.

Diltiazem is a calcium channel blocker with rapid onset and short duration of action. It is effective in attenuating the increase in pulse rate and BP following laryngoscopy and tracheal intubation. This is due to its vasodilatory and negative chronotropic and dromotropic effects.

The present study was under taken to know the severity, duration of hemodynamic responses to laryngoscopy and intubation and to observe the efficacy of Diltiazem in blunting hemodynamic responses.

The study was conducted in 50 patients of two groups of 25 each. Group I served as control group and received normal saline 2 ml IV where as Group II served as study group and received Diltiazem 0.3 mg/kg IV 60 sec before intubation in identical syringe. General anesthesia technique was standardized for both the groups.

Both the groups were comparable for demographic data. The pre-induction values were taken as base line values. Our results showed that there was an increase in HR after induction and immediately after laryngoscopy and intubation in both the groups, but these changes were not statistically significant. SBP, DBP and MAP increased during laryngoscopy and at 1, 2, 3, & 5 min after laryngoscopy and intubation in control group, where as in the study group there was minimal increase in SBP, DBP and MAP only during laryngoscopy and 1 min after laryngoscopy and intubation which returned to baseline by 2 min.

Three calcium channel blockers were compared in normotensive patients by Mikawa et al [16] as regard to their effect on pressor response. In their study, verapamil completely blunted the increase in BP due to laryngoscopy and intubation and produced mild hypotension 5min after induction. Nicardipine blunted the BP rise but produced tachycardia, while verapamil could effectively blunt tachycardia. Attempts to attenuate these hemodynamic responses have been partially successful. As IV form of Diltiazem is easily available now days, we studied the hemodynamic responses to laryngoscopy and intubation.

IV Diltiazem was administered 60 sec (1 min) before the start of laryngoscopy in our study and was planned in such a way that the effect of Diltiazem in lowering BP coincided with the hemodynamic responses to laryngoscopy. This fact is essentially based on the study reports of Mikawa et al [21] and Stoelting. [10]

There was a slight increase in HR and decrease in BP (SBP, DBP and MAP) with induction of anesthesia in our study group. This can be explained by the fact that propofol can cause myocardial depressant and peripheral vasodilatation leading to hypotension and tachycardia. The rise in HR was 10.5% in control group and 7.57% in Diltiazem group. This co-relates with the study reports of Millar Forbe et al [9] and Mikawa et al. [21].

HR was increased in both the groups and the difference was not significant statistically. SBP rise was highest in the control group as compared to the study group during laryngoscopy and intubation. These observations were in concurrence with the study reports of Mikawa et al [21] and Hasegawa et al. [22] Similarly Mohan et al [24] and Medha Sangawar et al [25] in their study concluded that Diltiazem was useful in attenuation of blood pressure response but not effective in preventing tachycardia. Mean SBP rise was 19.4% vs. 1.36% during laryngoscopy and intubation and at 1 min following intubation in the control vs. Diltiazem group. This was extremely significant statistically. Values returned to the baseline by 2 min in the study group whereas in control group even at 5 minutes values were high. Same with MAP, the values were 22.3% vs. 8.6% in control vs. Diltiazem group respectively during laryngoscopy and intubation and at 1min following intubation. DBP and MAP values returned to base line in 2 min in the Diltiazem group but in control group the readings were high even at 5 min.

In our study, the side effects and complications were very few. We noticed hypotension in 2 patients in the study group which improved with IV fluids and did not require pharmacological intervention.

Conclusion:

Diltiazem- a calcium channel blocker in the dose of 0.3mg/ kg IV given 60sec before laryngoscopy attenuates the hemodynamic response to laryngoscopy and intubation. The effects of Diltiazem are more significant on the blood pressure changes than heart rate. Hence we conclude that single bolus dose of Diltiazem 0.3 mg/kg IV given 60 sec before laryngoscopy can be safely employed to attenuate hemodynamic responses without any side effects.

References:

1. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine response to laryngoscopy and with or without intubation. Br J Anesth 1986;59:295-9.
2. Goel R, Rani R, Singh OP. Attenuation of cardiovascular responses to laryngoscopy and intubation by various drugs in normotensive patients. Hospital today. 2000; 9.
3. Stoelting RK. Blood pressure and heart rate changes during short duration laryngoscopy for tracheal

intubation: influence of viscous or intravenous lidocaine. Anesth Analg 1978; 57:197-9.
4. Prys-Roberts, Greene LT, Meloche R, Foex P. studies of Anesthesia in relation to hypertension-II. Haemodynamic consequences of induction and endotracheal intubation. Br J Anesth 1971;43:541-7.
5. Fujii Y, Saitoh Y, Takahashi S, Toyooka H. Diltiazem- lidocaine combination for attenuation of cardiovascular response to tracheal intubation in hypertensive patients. Canadian J Anaesth 1998;45:935-7.
6. Fox EJ, Sklar GS, Hill CH et al. Complications related to the pressor response to endotracheal intubation. Anaesthesiol 1977;47:524-25.
7. Dalton B, Guiney T. Myocardial ischemia from tachycardia and hypertension in coronary heart disease: Patient's undergoing anesthesia. Ann Mtg Am Soc Anestheiologists, Boston. 1972;99:201-2.
8. Donegan MF, Bedford RF. Intravenously administered lignocaine prevents Intracranial hypertension during endotracheal suctioning. Anaesthesiol 1980;52:516-8.
9. Millar Forbes A, Dally FG. Acute hypertension during induction of anesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970;42:618-24.
10. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation with or without prior oropharyngeal viscous lidocaine. Anaesth Analg 1977;56: 618-21.
11. Prys-Roberts C, Foex P. Studies of Anesthesia in relation to hypertension- V. Adrenergic beta-receptor blockade. Br J Anesth 1973;45:671-80.
12. Nielson DJ. The effect of intranasally administered nitroglycerine on the blood pressure to laryngoscopy and intubation in patients undergoing coronary artery bypass graft surgery. Acta Anaesthesiol Scand 1986;30:23-7.
13. Madi MA, Keszler H. A method for prevention of cardiovascular responses to laryngoscopy and intubation. Canadian Anaesth Soc J 1975;22(3):316-29.
14. Tam S, Chung F, Campbell M. Intravenous lignocaine; optimal time for injection before tracheal intubation. Anaesth Analg. 1987; 66:1036-8.
15. Madi MA, Keszler H. Cardiovascular responses to laryngoscopy and tracheal intubation following small and large intravenous dose of lidocaine. Canadian Soc Anaesth J 1977;24(1):12-8.
16. Mikawa K, Nishina K, Maekawa N, Obara H. Comparison of nicardipine, diltiazem and verapamil for controlling the cardiovascular responses to tracheal intubation. Br J Anaesth 1996;76:221-6.
17. Fujii Y, Saitoh Y. Effects of calcium channel blockers on circulatory response to tracheal intubation in hypertensive patients. Canadian J Anaesth 1995;42(9):785-8.
18. Reid LC, Bruce DE. Initiation of respiratory tract reflexes and it effects on heart surgery. Gynecol Obstet 1940;70:157.
19. Burstein CL, Lo Pinto FJ. Electrocardiographic studies during endotracheal intubation, effects during usual routine techniques. Anesthesiol 1950;11:224.
20. Devult M, Greisfenstein FE. Circulatory responses to endotracheal intubation in light general anesthesia; the effect of atropine and pentolamine. Anaesthesiol 1960;21:360-2.
21. Mikawa K, Ikegaki J, Maekawa N. The effect of diltiazem on the cardiovascular response to tracheal intubation. Anaesth 1990;45:289-93.
22. Hasegawa J, Mitsuhata H, Matsumoto S, Enzan K. Attenuation of cardiovascular response to laryngoscopy and tracheal intubation with bolus injection of diltiazem. Masui. 1992;41(3):356-62.
23. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. Anaesth Analg 1979;58:116-9.
24. Mohan. Attenuation of cardiovascular response to laryngoscopy and intubation with Diltiazem and Lignocaine. Int J Med Res Health Sci 2013;2(3): 557-63
25. Sangawar M. Attenuation of Cardiovascular Responses to Endotracheal Intubation with Diltiazem. Res Chronicle Health Sci 2016;2(1):260-5.

Cite this article as: Swathi A, Manjula VR, Sarada Devi V, Surender P. Attenuation of hemodynamic response to laryngoscopy and intubation-The Effect of Diltiazem, A randomized controlled study. MRIMS J Health Sciences 2018;6(1):31-36.

Source of Support: Nil. **Conflict of Interest:** None.