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Original Research Article

Evaluation of efficacy of intravenous Diltiazem, Lignocaine and combination of both in attenuating the cardiovascular responses to laryngoscopy and endotracheal intubation in normotensive patients

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Abstract: To find out the efficacy of intravenous diltiazem, lignocaine and combination of both in reducing the effect on cardiovascular system to laryngoscopy and endotracheal intubation in healthy, ASA PS I and normotensive ASA PS II patients. In this Prospective randomized control study, Patients who are scheduled for total abdominal Hysterectomy, vaginal hysterectomy, laparoscopic Appendectomy, tubectomy and cholecystectomy were divided into four groups, Group 1 received normal saline, Group II received lignocaine 1.5mg/kg, Group III received diltiazem 0.3mg/kg, and Group IV received combination diltiazem 0.3mg/kg and lignocaine 1.5mg/kg. Hemodynamic parameters such as heart rate, systolic and diastolic blood pressure and rate pressure product products are recorded at regular intervals. The data analysis is performed by univariate analysis. The hypothesis is validated by various statistical methods by using statistical packages for social sciences (SPSS 17.0 version). Total 100 patients within age group of 20-50 years were selected for study, 25 in each group, the mean weight in Group I was 53.40±6.17Kgs, in Group II it was 53.40±6.73Kgs, in Group III 52.64±8.164 Kgs and Group IV was 52.96±8.97kgs suggesting mean weight in four groups were comparable. In present study with respect to heart rate, systolic and diastolic blood pressure, mean arterial pressure and rate pressure product there was attenuation all these parameters in all groups but the attenuation was maximum in Group IV followed by Group II and Group III respectively. The data from our study suggests that with combination of both diltiazem and lignocaine is significantly more effective than anyone alone for attenuating hemodynamic changes to laryngoscopy and tracheal intubation in normotensive patients.
Keywords: Diltiazem, lignocaine, cardiovascular responses

INTRODUCTION

Endotracheal intubation and Aneasthesia have become an integral part of the Anaesthesiologist's contribution to patient care. Endotracheal intubation is Trans-laryngeal placement of endotracheal tube into trachea via nose or mouth. General anaesthesia procedure involves many stressful events at various stages. The most stressful situations are seen during period of induction, intubation and extubation [1-3]. One of the commonest responses that occur during laryngoscopy and intubation is reflex sympathetic responses like tachycardia, hypertension and cardiac arrhythmias. The CVS response to intubation is exaggerated in hypertensive patients. CVS response to intubation is of a serious concern in patients with hypertension, raised intracranial pressure (ICP), diseased cerebral vasculature or with Ischemic heart disease [4]. Complications that might arise because of CVS responses to laryngoscopy and intubation are acute left ventricular failure, Arrhythmias, Intracranial hemorrhage and pulmonary edema. Present study is undertaken to evaluate efficacy of IV diltiazem, lignocaine and combination of both on cardiovascular responses to endotracheal intubation in healthy, ASA PS I and normotensive ASA PS II patients.

MATERIALS AND METHODS:

In this hospital based randomized prospective study, 100 patients who are scheduled for total abdominal hysterectomy, vaginal hysterectomy, laparoscopic appendectomy, tubectomy and cholecystectomy during the time from June 2015 to June 2016 were divided randomly into 4 groups, 25 in each group by computerized method. GROUP I received 20ml normal saline in 2 syringes of 10 ml each, GROUP II received lignocaine 1.5mg/kg diluted to 10 ml and 10ml of normal saline, GROUP III received diltiazem 0.3mg/kg diluted to 10 ml and 10ml of normal saline, GROUP IV received diltiazem 0.3mg/kg made to a total volume of 10 ml and lignocaine 1.5mg/kg diluted to 10ml. The inclusion criteria were ASA PS grade I & II patients, age group of 20 to 50 years of either gender, mallampati class I patients and exclusion criteria includes ASA PS grade III&IV, history of angina, palpitations, syncopal attacks, treatment with beta blockers or calcium channel blockers, regurgitation prone conditions, history of respiratory problems, duration of endotracheal intubation more than 15 seconds, mallampati class II, and more. After preanaesthetic evaluation, informed, valid, written consent obtained from patients for study, anaesthesia and surgery, baseline hemodynamic parameters recorded and patient premedicated with injection glycopyrrolate 0.2mg and injection midazolam 0.02mg/kg IV. Patient shifted to operative room, multiparameter monitor attached, pre oxygenated and received test drug intravenously 60sec prior to induction. Induction done with thiopentone sodium 2.5% solution 5mg/kg IV slowly. Intubation facilitated by vecuronium 0.1mg/kg IV, lungs ventilated with 100% oxygen, intubation carried out with the aid of Macintosh laryngoscope, oral cuffed endotracheal tube of appropriate size used, After tracheal intubation anaesthesia will be maintained with nitrous oxide, oxygen and propofol infusion, vecuronium as muscle relaxant, fentanyl 0.02mg/kg and diclofenac 75mg in infusion will be used as analgesic. Parameters such as systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate are recorded at Pre-induction, after induction, during laryngoscope and intubation, 1min after intubation, 2min after intubation, 3min after intubation, and 5min after intubation. Watch for any adverse effects in perioperative period.

Statistical Analysis:

Analysis carried out using SPSS Version-17 (Statistical Package for Social Science), Univariate analysis of changes in these parameters at baseline, after premedication, on induction, on intubation, and at every minute from 1 to 5 minutes carried out by "Paired t-tests" for within the group comparisons. "Unpaired t-tests" were done for making comparison between the groups. Statistical significance of the differences in the mean values was determined at 5% ($\alpha = 0.05$). Bonferroni correction was used to deal with the effect of multiple testing. Since repeated measurements were made on same subjects in each of the four groups, Anova was carried out to evaluate the "within-group variation" and "between the group variations" due to the effect of the drug being investigated. It was used because four sets of population were compared which were independent and identically distributed with the P value reported at the 95% confidence interval. $P<0.05$ was considered statistically significant. Confidence level corresponds to a Z-score. This is a constant value needed for calculating needed sample size equation. Here are the Z-scores for the most common confidence levels: 90% - Z score = 1.645 95% - Z score = 1.96 99% - Z score = 2.326

Sample size = {(Z-score) 2 X Std Dev X (1-StdDev)} / (margin of error) 2. Based on previous studies - confidence level 95%, standard deviation 0.5, and a margin of error (confidence interval) of +/-5%. Sample size= {(1.96)2 X 0.5(1-0.5)} / (0.05)2 = (3.8416 X 0.25) / 0.0025. = 0.9604 / 0.0025. = 384.16. = 385 Respondents are needed. Due to the limited period of study 100 subjects will be taken for the study.

RESULTS:

In this Prospective randomized control study, A total of 100 patients fulfilled inclusion criteria were taken for study out of which 52% were males and 48% were females in Group I, 60% were males and 40% were females in Group II, 60% were males and 40% were females in Group III, 60% were males and 40% were females in Group IV. Most of the patients (Group I 92%, Group II 80%, Group III 84% and Group IV 76%) in the groups were aged between 21 and 40 years. The mean age in Group I was 32.32±7.02, Group II it was 36.84±9.64, Group III 33.68±8.61 and Group IV was 31.40±9.78 years suggesting all the groups had comparable demographic characteristics. The mean weight in Group I was 53.40±6.17Kgs, in Group II it was 53.40±6.73Kgs, in Group III 52.64±8.164 Kgs and Group IV was 52.96±8.97kgs suggesting mean weight in four groups were comparable.

Table 1: Comparison of heart rate changes in present study at regular intervals.

Time	Present study (N = 100)			
	Normal Saline (N= 25) Mean±SD	Lignocaine (N= 25) Mean±SD	Diltiazem (N= 25) Mean±SD	Ligno + Dilti (N= 25) Mean±SD
Pre induction	84.64±3.30	84±7.3	84.56±3.27	83.32±3.18
After induction	92.68±3.06	73.87±7.9	92.52±3.86	90.72±3.01
During Laryngoscopy	122.80±2.76	84.63±12.6	108.32±3.03	87.36±4.39
After 1 min	122.48±2.99	83.77±15.4	106.48±2.97	84.88±4.38
After 2 min	118.56±0.83	79.27±1.7	03.00±2.65	83.88±4.33
After 3 min	115.92±3.17	74.73±10.5	99.88±2.60	83.72±4.65
After 5 min	114.72±3.63	72.93±12.1	98.72±2.63	83.36±4.43

Table 2: Comparison of Systolic blood pressure changes in present study at regular intervals

Time	Present study (N= 100)			
	Normal Saline (N= 25) Mean±SD	Lignocaine (N= 25) Mean±SD	Diltiazem (N= 25) Mean±SD	Ligno + Dilti (N= 25) Mean ±SD
Pre induction	123.88±1.69	118.60±2.12	122.80±2.29	122.80±2.29
After induction	120.44±1.62	118.56±1.74	118.12±2.27	118.12±2.27
During laryngoscopy	158.00±3.87	135.68±2.12	132.96±1.91	118.12±2.27
After 1 min	157.44±3.18	131.68±2.26	127.76±1.99	127.76±1.99
After 2 min	150.60±2.08	130.08±2.29	124.92±1.54	124.92±1.54
After 3 min	146.80±2.28	126.56±2.17	122.16±1.78	122.16±1.78
After 5 min	146.08±2.1	117.61±2.29	120.52±1.90	120.52±1.90

In present study with respect to heart rate, systolic and diastolic blood pressure, mean arterial pressure and rate pressure product there was attenuation all these parameters in all groups but the attenuation was maximum in Group IV followed by Group II and Group III respectively.

DISCUSSION:

The reflex hemodynamic response to laryngoscopy and tracheal intubation was known to anesthesiologist since a long time. Anaesthesiologist aim at suppressing sympathetic responses at the time of laryngoscopy and intubation. In 1998, Fugi *et al.;* studied the effect of diltiazem, lignocaine and n diltiazem-lignocaine combination for the attenuation of cardiovascular responses to intubation in hypertensive patients [4]. The study population consists of 60 hypertensive patients divided into three groups with 20 patients in each group. Group I – Received 0.3 mg/kg diltiazem IV 60 seconds before intubation Group II – Received 1.5 mg/kg lignocaine IV 3 minutes before intubation Group III- Received combination of inj. Diltiazem 0.3 mg/kg IV and inj. Lignocaine. They concluded that prophylactic therapy with diltiazem-lignocaine combination is more effective than diltiazem or lignocaine alone for attenuating the cardiovascular changes associated with tracheal intubation in hypertensive patients [4]. In 2012 Gupta *et al.;* undertook a study to compare clinical efficacy of combination of diltiazem and lignocaine in attenuating hemodynamic changes during tracheal intubation and comparing the response when they are used alone [5]. 120 ASA PS grade I&II patients were randomly divided into four groups (using a random sequence generator) of 30 each according to the drug given before intubation to attenuate the hemodynamic response to intubation [5]. The primary outcome of the study was that diltiazem-lignocaine combination is safe and effective in attenuating pressor response to tracheal intubation. We are going to study the efficacy of diltiazem, lignocaine and combination of diltiazem +lignocaine to reduce the pressor response during intubation. Though similar study was done by Fujy *et al.;* in 1998 and Gupta *et al.;* in 2012 but no such study was done in District Hospital

level [4, 5]. For this reason the present study has chosen to evaluate the efficacy of the study drugs as well as to compare the results with the previous studies.

In present study, with respect to Heart rate, systolic blood pressure and diastolic blood pressure there was significant rise in all three parameters in control group when compared with rest three groups, there was attenuation of heart rate, systolic and diastolic blood pressure in all three groups but the attenuation was maximum in dilti+lido group followed by lignocaine group and diltiazem group respectively. The limitation of the study is its use only in ASA PS grade I & normotensive ASA PS II patients.

CONCLUSION:

The data from our study suggests that diltiazem and lignocaine when injected alone can blunt the cardiovascular responses to laryngoscopy and tracheal intubation successfully. However, the primary hypothesis that with combination of these two drugs is significantly more effective than any one alone for attenuating hemodynamic changes to laryngoscopy and tracheal intubation in normotensive patients. The diltiazem and lignocaine combination appears to be very effective and safe and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anaesthesia, laryngoscopy and tracheal intubation. The limitation of the study is its use only in ASA PS grade I & normotensive ASA PS II patients.

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