

# A study of the efficacy of cardiac antidysrhythmic drugs in attenuating haemodynamic responses to laryngoscopy and endotracheal intubation in the Black population

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**Abstract:** Background: Laryngeal, tracheal and bronchial receptors are stimulated by mechanical and chemical irritants during laryngoscopy and endotracheal intubation. That almost always triggers powerful cardiovascular responses. Various attempts have been made to attenuate these responses. The aim of this study was to compare the efficacy and safety of cardiac antidysrhythmic drugs lidocaine, diltiazem and esmolol in the attenuation of cardiovascular responses to endotracheal intubation in the Black normotensive population. Patients and Methods: A randomized controlled trial was conducted in 160 adult patients of ASA physical status I or II undergoing various elective surgeries. The patients were randomly divided into four groups of 40 patients in each group - C, L, D, and E. Group - "C" received no drug (control) as placebo, group - "L" received 1.5 mg kg<sup>-1</sup> preservative free lidocaine, group - "D" received 0.2 mg kg<sup>-1</sup> diltiazem, and group - "E" received 2mg kg<sup>-1</sup> esmolol IV. Group "C", "D" and "E", "L" one and two minutes before intubation. Changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were measured and then compared within and between groups. Rate pressure product (RPP) was calculated and evaluated as well. Patients were also observed for any complications. Result: There was a significant increase in SBP, DBP, HR, MAP and RPP from the base line in control group "C" at 1 minute with onward decreases at 3 and 5 minutes respectively after intubation. Percentage change in haemodynamic variables in groups C, L, D and E at 1 minute are as follows: SBP= 23.58%, 11.84%, 9.64% and 9.9%, DBP= 18.73%, 18.89%, 11.93% and 10.40%, HR= 30.45%, 26.00%, 7.01% and 1.50%; MAP= 20.80%, 15.89%, 10.90 and 10.20%; RPP= 61.44%, 40.86%, 17.26% and 11.68% respectively. Only patients receiving placebo had increased SBP, DBP, HR, MAP and RPP values after intubation compared with baseline values (p < 0.05). Conclusions: Given the difference in the pharmacological mechanisms of these drugs, the prophylactic therapy with 2mg kg<sup>-1</sup> esmolol is significantly more effective and safe for attenuating haemodynamic changes to laryngoscopy and tracheal intubation, without producing increased risk of hypertension in the Black population.

**Keywords:** Blood Pressure, Diltiazem, Esmolol, Heart Rate, Intubation, Laryngoscopy, Lidocaine,  
(Source: MeSH, NLM)

## 1. Introduction

Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation<sup>[1]</sup>. This increase in blood pressure

and heart rate are usually transitory, variable and unpredictable lasting for less than 10 minutes<sup>[2]</sup>. It may be well tolerated in healthy people, but may be hazardous in patients with tachycardia, hypertension, myocardial infarction, cerebrovascular disease and other complications<sup>[3-4]</sup>. Various pharmacological approaches have been used to attenuate the pressure responses to laryngoscopy and

tracheal intubation [4-7].

Hypertension is known to occur more frequently in the Black population and is associated with a higher incidence of cerebrovascular and renal complications. According to Gibbs *et al.* Strokes have been found to be more common in the Black hypertensives and hypertension associated end-stage renal failure occurs up to 20 times more commonly in the Black patients compared to non-Blacks [8].

Various pharmacological approaches considered to attenuate haemodynamic changes in Caucasians during endotracheal intubation as it reduces heart rate as well as blood pressure. Specific racial differences need to be considered before treatment in view of a report that African-Americans respond much less to beta adrenergic receptor blocking drugs than Caucasians [9]. Beta-blockers tend to be less effective in the Black hypertensives as a result of the tendency towards a low-renin state and increased peripheral resistance and thus higher doses are required to achieve target blood pressure [8].

Several studies have looked at the efficacy of intravenous diltiazem, esmolol, lidocaine and their combination as an agent to blunt the haemodynamic response to laryngoscopy and intubation in Caucasians with different opinions [6-8], but no study available in Ghanaian population. Efforts are being made to practice safe anaesthesia in Ghana in an attempt to reduce intraoperative complications and mortality during anaesthesia. The purpose of this study was, therefore, to determine the efficacy and safety of intravenous diltiazem, esmolol and lidocaine in attenuating haemodynamic response to laryngoscopy and intubation in the Black population.

## 2. Patients and Methods

This study was undertaken after an institutional approval by the Committee on Human Research Publications and Ethics was obtained. The study was conducted from November 2011 to May 2012. Informed consent was obtained from 160 patients. The study population consisted of American Society of Anesthesiologists (ASA) physical status I or II, male and female adults between the ages of 18-65 years scheduled for various elective surgical procedures under general anesthesia.

### 2.1. Study design

This study was a prospective, randomized and double blinded clinical comparison in the Black population. The Sample size for the study was 160 generated using a sample size calculator. The study Participants were randomly divided into four groups by a computer generated randomization table. A study nurse (Person A) who was not involved in the randomisation process prepared the study drugs, all of which were diluted to 10 millilitres. All drugs were coded to enhance blinding. Person B monitored the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) with

respect to time whilst Person C was responsible for intubation of the patients. Person A and C were kept constant throughout the study. Person B, C and the patient were unaware of the drug injected to enable double-blinding.

Inclusion criteria for the study were ASA class I or II, age range 18 - 65, oropharyngeal anatomy of Mallampati class I and any operation other than cardiac surgery performed under general anesthesia with endotracheal intubation.

Exclusion criteria for the study included patients who were morbidly obese, patients with cardiovascular disease, Heart rate <60 beats per minute (bpm), basal SBP <100 mm Hg and other conditions such as bronchial asthma, patients showing stressful features during induction and laryngoscopy (bucking, coughing, vomiting), patients undergoing emergency surgery, diabetes mellitus, pregnant, drug allergies, difficult intubations and intubations in which total duration of laryngoscopy exceeded 15 seconds were excluded from the study.

### 2.2. Pre-surgical Protocol

The day prior to surgery all patients underwent a preanesthetic evaluation with special consideration to elicit a history of hypertension, dyspnoea, chest pain, cough, wheezing, convulsions and diabetes mellitus, as well as previous anesthetic history and drug sensitivity. Information collected included weight, nutritional status, airway assessment by the Mallampatti scoring system, a detailed examination of the respiratory, cardiovascular and central nervous system. A preoperative routine investigations such as haemoglobin, haematocrit, total lymphocyte count, differential lymphocyte count, serum electrolytes, blood group/Rh typing, blood urea nitrogen, serum creatinine, fasting blood sugar, chest radiography and electro-cardiogram in all patients. Patients were advised to fast the night prior to surgery.

### 2.3. Surgical Protocol

After patient identification a short preoperative history was taken, clinical examination and routine investigations were rechecked in all patients. Study objective and procedure were explained to the participants and a written informed consent was obtained from each participant.

Intravenous access was secured and infusion of Ringer's lactate solution started. The patients were premedicated with 0.008 mg kg<sup>-1</sup> glycopyrrolate-bromide intramuscularly 30 minutes prior to surgery. Patients were then shifted to the operating room after which routine non-invasive monitor was applied and vital signs monitored. Midazolam 0.04mg kg<sup>-1</sup> was administered intravenously over 30 seconds as premedication and patients were preoxygenated with four to five breaths of 100% oxygen. The patients were induced with 6mg kg<sup>-1</sup> IV thiopentone sodium in incremental doses until loss of eyelash reflex occurred, 0.12mg kg<sup>-1</sup> IV vecuronium bromide was given over 20

seconds, followed up by administering the study drugs as per study protocol before laryngoscopy and intubation.

The study drug was randomly allocated to patients in a double blinded manner. Patients were ventilated with oxygen and 1% halothane using IPPV with a fresh gas flow of 6 litres  $\text{min}^{-1}$  by Bain circuit until intubation. About 2 minutes after IV vecuronium, laryngoscopy was performed with a Macintosh laryngoscope blade and trachea intubated with an appropriate size cuffed endotracheal (ET) tube. After confirmation of correct placement of ET tube, anaesthesia was then maintained with  $\text{O}_2$  and halothane.

HR, SBP, DBP, MAP, RPP (rate pressure product),  $\text{SpO}_2$  (oxygen saturation) and ECG (electrocardiogram) changes were recorded before induction (Basal) and after tracheal intubation at 1, 3 and 5 minutes for the purpose of this study. No manipulation like painting and draping the area of operation was allowed till 10 minutes after intubation. Injection fentanyl 2 micrograms  $\text{kg}^{-1}$  was given before surgery.

#### 2.4. Parameters and statistical analysis

Summary statistics of patient demographic and anthropometric characteristics for all the groups were reported as means  $\pm$  standard error of the mean (SEM). HR, SBP, DBP and MAP were recorded before induction (Baseline), after endotracheal intubation at 1, 3 and 5 minutes. From the data RPP was calculated by multiplying heart rate with systolic blood pressure. Patients were also observed for complications like hypotension, hypertension, arrhythmias and hypoxaemia. Statistical analysis was done by unpaired t- test whilst categorical data were compared using Fischer's exact test and p values were calculated. Haemodynamic variables were represented by mean  $\pm$  SEM. ANOVA with repeated measures was used to compare the changes in HR, MAP and RPP values. Bonferroni's multiple comparison test was applied to evaluate intra group comparisons. The statistical package SPSS<sup>®</sup> 17.0 and Graphpad prism 5 was used.  $P < 0.05$   $P < 0.001$  were considered significant and highly significant respectively for the study.

### 3. Results

All the demographic and anthropometric profiles in the control, case and total group were comparable (Tab.1). The male to female ratio of control group-“C” was 1:2.64 whereas lignocaine group-“L”, diltiazem group-“D” and esmolol group “E” were 1:1.22, 1:1.5 and 1:1.5 ( $p=0.25$ ) respectively ( Fig.1). Out of the one hundred and sixty participants enrolled in this study, the average age was  $41.81 \pm 1.08$  years, ranging from a minimum of 18 years to a maximum of 63 years. The ages of the case and controls of this study was matched with no statistical significant difference between their mean ages ( $41.82 \pm 1.27$ ,  $41.78 \pm 2.01$ ,  $p=0.9867$  for case and control respectively). Averagely an individual included in this study weighed  $70.54 \pm 0.75$  kilograms and measured  $163.80 \pm 0.41$

centimetres high. The weight range was found to be a minimum of 48.00 kg to a maximum of 97.00 kg, the shortest participant among the population measured 147 cm, and the tallest 174 cm. The mean weight and height of the cases and controls were statistically comparable ( $p=0.5073$ ,  $0.4698$ , respectively). Averagely the body mass index of the total participants as well as those in the individual groups according to the world health organisation's criteria could be said to be overweight ( $26.26 \pm 0.25$ ,  $26.31 \pm 0.29$  and  $26.11 \pm 0.54$   $\text{Kg/m}^2$  for the total population, the case and control respectively). However though majority of the participants (56.25%) were found to be overweight, 3.75% were classified as underweight, 27.50% as normal weight, and 12.50% as obese. As show no significant difference was found when both the mean body mass indices as well as the component weight classifications were compared among the case and the control participants (Tab.1).

Comparison of haemodynamic variables in the control and study groups at baseline and time (1, 3 and 5 minutes) after intubation (Table 2-8). An increase in SBP, DBP, HR, MAP and RPP from the base line and maximum at 1 minute after intubation were observed in control group-“C”, however in the groups- lidocaine- “L”, diltiazem-“D” and esmolol-“E” there were no significant variation of SBP, DBP, HR, MAP and RPP from the base line 1 minute after laryngoscopy and intubation (Table 6). The maximum increase in SBP and DBP over the baseline values ( $123.9 \pm 1.02$ ,  $125.8 \pm 1.11$ ,  $125.5 \pm 1.15$  and  $125.10 \pm 1.31$ ) and ( $83.70 \pm 1.06$ ,  $82.85 \pm 0.90$ ,  $82.13 \pm 0.80$  and  $81.93 \pm 0.79$ ), in the groups C, L, D and E were recorded at one minute ( $153.10 \pm 2.02$ ,  $140.70 \pm 1.57$ ,  $137.6 \pm 1.37$  and  $137.5 \pm 1.40$ ) and ( $99.38 \pm 0.82$ ,  $98.50 \pm 0.77$ ,  $91.93 \pm 0.81$ , and  $90.43 \pm 0.93$ ) after intubation. The Percentage changes in SBP and DBP from baseline and 1min after intubation were (23.58%, 11.84%, 9.64% and 9.90%) and (18.73%, 18.89%, 18.89% and 10.40%) in groups-C, L, D and E respectively (Fig. 2 SYS1 and DIA1).

In groups C, L, D and E maximum increase in mean heart rate over the baseline values were  $89.00 \pm 1.47$ ,  $87.30 \pm 1.47$ ,  $86.80 \pm 1.39$  and  $90.80 \pm 1.36$  respectively and at one minute were  $116.10 \pm 1.20$ ,  $110.00 \pm 0.78$ ,  $92.88 \pm 0.99$  and  $92.20 \pm 1.54$  after intubation respectively. The Percentage changes in HR from baseline and 1min after intubation were 30.45%, 26.00%, 7.01% and 1.50% in groups-C, L, D and E respectively (Fig. 2 HR1).

The MAP was increased in group-C as compared to groups-L, D, and E following laryngoscopy and endotracheal intubation. The maximum increase in MAP over the baseline values ( $97.08 \pm 0.79$ ,  $97.16 \pm 0.70$ ,  $96.57 \pm 0.62$  and  $96.33 \pm 0.68$ ) in the groups C, L, D and E were recorded at one minute ( $117.3 \pm 0.94$ ,  $112.6 \pm 0.70$ ,  $107.1 \pm 0.77$  and  $106.10 \pm 0.79$ ) after intubation. The Percentage changes in MAP from baseline and 1min after intubation were 20.83%, 15.89%, 10.90% and 10.20% in groups-C, L, D and E respectively (Fig. 2 MAP1).

There was marked elevation of rate pressure product in group-C as compared to groups-L, D, and E after

laryngoscopy and intubation with baseline values  $11010 \pm 189.2$ ,  $10970 \pm 206.2$ ,  $10890 \pm 197.3$  and  $11350 \pm 194.4$  respectively. One minute values of groups-C, L, D and E were  $17780 \pm 304.5$ ,  $15460 \pm 170.1$ ,  $12770 \pm 182.4$  and  $12680 \pm 253.7$ , respectively. The Percentage changes in RPP from baseline and 1min after intubation were 61.49%, 40.93%, 17.26% and 11.68% in groups-C, L, D and E respectively (Fig. 2 RPP1).

In all four groups the vitals remained attenuated for 3 minutes after intubation; however the vitals returned to baseline values after five minutes. Control group patients undergoing laryngoscopy and intubation showed an incidence of 8% ventricular ectopics and 5% dropped beats however no such findings were recorded in the lignocaine, diltiazem and esmolol groups.

**Table 1:** Demographic and Anthropometric characteristics of the study population stratified as case and control

Parameters	Total (n = 160)	Case (n = 120)	Control (n = 40)	P-value
Age(yrs)	41.81 $\pm$ 1.08	41.82 $\pm$ 1.27	41.78 $\pm$ 2.01	0.987
Anthropometric parameters				
Weight (Kg)	70.54 $\pm$ 0.75	70.83 $\pm$ 0.86	69.68 $\pm$ 1.55	0.507
Height (cm)	163.80 $\pm$ 0.41	164.00 $\pm$ 0.49	163.30 $\pm$ 0.73	0.469
BMI(Kg/m <sup>2</sup> )	26.26 $\pm$ 0.25	26.31 $\pm$ 0.29	26.11 $\pm$ 0.54	0.724
BSA (m <sup>2</sup> )	1.79 $\pm$ 0.01	1.79 $\pm$ 0.01	1.77 $\pm$ 0.02	0.444
Underweight	6/160(3.75)	4/120(3.33)	2/40(5.00)	0.640
Normal	44/160(27.50)	30/120(25.00)	14/40(35.00)	0.226
Overweight	90/160(56.25)	71/120(59.17)	19/40(47.50)	0.204
Obese	20/160(12.50)	15/120(12.50)	5/40(12.50)	1.000

Continuous data were presented as mean  $\pm$  SEM; categorical data are presented as proportion with percentages in parenthesis. Continuous data were compared using unpaired t-test whilst categorical data were compared using Fischer's exact test. p is significant at the 0.05 level (2-tailed). Underweight (BMI  $\leq 20$ ), Normal weight (BMI 20–25), overweight (BMI 25–29.9) and obese (BMI  $\geq 30$ )

**Table2:** Change in haemodynamic variables in the study groups at Basal

Parameter	Control	Lidocaine	Diltiazem	Esmolol	p-value
SBP (mmHg)	123.9 $\pm$ 1.02	125.8 $\pm$ 1.11	125.5 $\pm$ 1.15	125.1 $\pm$ 1.31	0.661
DBP (mmHg)	83.70 $\pm$ 1.06	82.85 $\pm$ 0.90	82.13 $\pm$ 0.80	81.93 $\pm$ 0.79	0.489
HR (per min)	89.00 $\pm$ 1.47	87.30 $\pm$ 1.47	86.80 $\pm$ 1.39	90.80 $\pm$ 1.36	0.186
MAP (mmHg)	97.08 $\pm$ 0.79	97.16 $\pm$ 0.70	96.57 $\pm$ 0.62	96.33 $\pm$ 0.68	0.802
RPP	11010 $\pm$ 189.2	10970 $\pm$ 206.2	10890 $\pm$ 197.3	11350 $\pm$ 194.4	0.357

Data are presented as means  $\pm$  SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values.

**Table3:** Change in haemodynamic variables in the study groups at 1min

Parameter	Control	Lidocaine	Diltiazem	Esmolol	p-value
SBP (mmHg)	153.1 $\pm$ 2.025	140.7 $\pm$ 1.575 ***	137.6 $\pm$ 1.37***	137.5 $\pm$ 1.40***	P<0.0001
DBP (mmHg)	99.38 $\pm$ 0.82	98.50 $\pm$ 0.77	91.93 $\pm$ 0.81***	90.43 $\pm$ 0.93***	P<0.0001
HR (per min)	116.1 $\pm$ 1.20	110.0 $\pm$ 0.78***	92.88 $\pm$ 0.99***	92.20 $\pm$ 1.54***	P<0.0001
MAP (mmHg)	117.3 $\pm$ 0.94	112.6 $\pm$ 0.70***	107.1 $\pm$ 0.77***	106.1 $\pm$ 0.79***	P<0.0001
RPP	17780 $\pm$ 304.5	15460 $\pm$ 170.1 ***	12770 $\pm$ 182.4 ***	12680 $\pm$ 253.7 ***	P<0.0001

Data are presented as means  $\pm$  SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values. p is significant at < 0.05\*, < 0.01\*\* and <0.001\*\*\*

**Table4:** Change in haemodynamic variables in the study groups at 3min

Parameter	Control	Lidocaine	Diltiazem	Esmolol	p-value
SBP (mmHg)	145.0 $\pm$ 2.04	136.7 $\pm$ 1.29**	133.1 $\pm$ 1.29***	131.9 $\pm$ 1.39***	P<0.0001
DBP (mmHg)	94.28 $\pm$ 0.802	91.80 $\pm$ 0.88	85.15 $\pm$ 0.85***	82.63 $\pm$ 0.83***	P<0.0001
HR (per min)	109.5 $\pm$ 1.16	101.1 $\pm$ 1.31***	89.90 $\pm$ 1.08***	91.40 $\pm$ 1.19***	P<0.0001
MAP (mmHg)	111.2 $\pm$ 0.88	106.8 $\pm$ 0.70***	101.1 $\pm$ 0.80***	99.04 $\pm$ 0.65***	P<0.0001
RPP	15860 $\pm$ 267.3	13810 $\pm$ 200.5 ***	11980 $\pm$ 205.2 ***	12060 $\pm$ 213.7 ***	P<0.0001

Data are presented as means  $\pm$  SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values. p is significant at < 0.05\*, < 0.01\*\* and <0.001\*\*\*

**Table 5:** Change in haemodynamic variables in the study groups at 5 min

Parameter	Control	Lidocaine	Diltiazem	Esmolol	p-value
SBP (mmHg)	131.6 ± 1.59	131.2 ± 1.79	128.2 ± 1.45	126.3 ± 1.37	0.0478
DBP (mmHg)	87.10 ± 0.87	86.00 ± 0.88	83.50 ± 0.73*	79.03 ± 0.93***	P<0.0001
HR (per min)	98.13 ± 1.47	97.80 ± 1.40	87.70 ± 1.41**	88.20 ± 1.39***	P<0.0001
MAP (mmHg)	101.9 ± 0.75	101.1 ± 0.76	98.38 ± 0.73**	94.77 ± 0.77***	P<0.0001
RPP	12910 ± 248.8	12840 ± 261.7	11270 ± 257.9 ***	11140 ± 221.5 ***	P<0.0001

Data are presented as means ± SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values. p is significant at < 0.05\*, < 0.01\*\* and <0.001\*\*\*

**Table 2 :** Change in haemodynamic variables in the study groups at 1 min with intragroup comparison.

Parameter	Lidocaine	Diltiazem	Esmolol	PI	PII	PIII	PIV
SBP (mmHg)	140.7 ± 1.575	137.6 ± 1.37	137.5 ± 1.40	0.2068	0.1381	0.1301	0.9594
DBP (mmHg)	98.50 ± 0.77	91.93 ± 0.81	90.43 ± 0.93	P<0.0001	P<0.0001	P<0.0001	0.2277
HR (per min)	110.0 ± 0.78	92.88 ± 0.99	92.20 ± 1.54	P<0.0001	P<0.0001	P<0.0001	0.7131
MAP (mmHg)	112.6 ± 0.70	107.1 ± 0.77	106.1 ± 0.79	P<0.0001	P<0.0001	P<0.0001	0.3493
RPP	15460 ± 170.1	12770 ± 182.4	12680 ± 253.7	P<0.0001	P<0.0001	P<0.0001	0.7690

Data are presented as means ± SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values. Bonferroni's multiple comparison tests were used to make intragroup comparisons. Comparison PI- L,D&E, PII- L&D, PIII- L&E, PIV- D&E

**Table 3:** Change in haemodynamic variables in the study groups at 3 min with intragroup comparison.

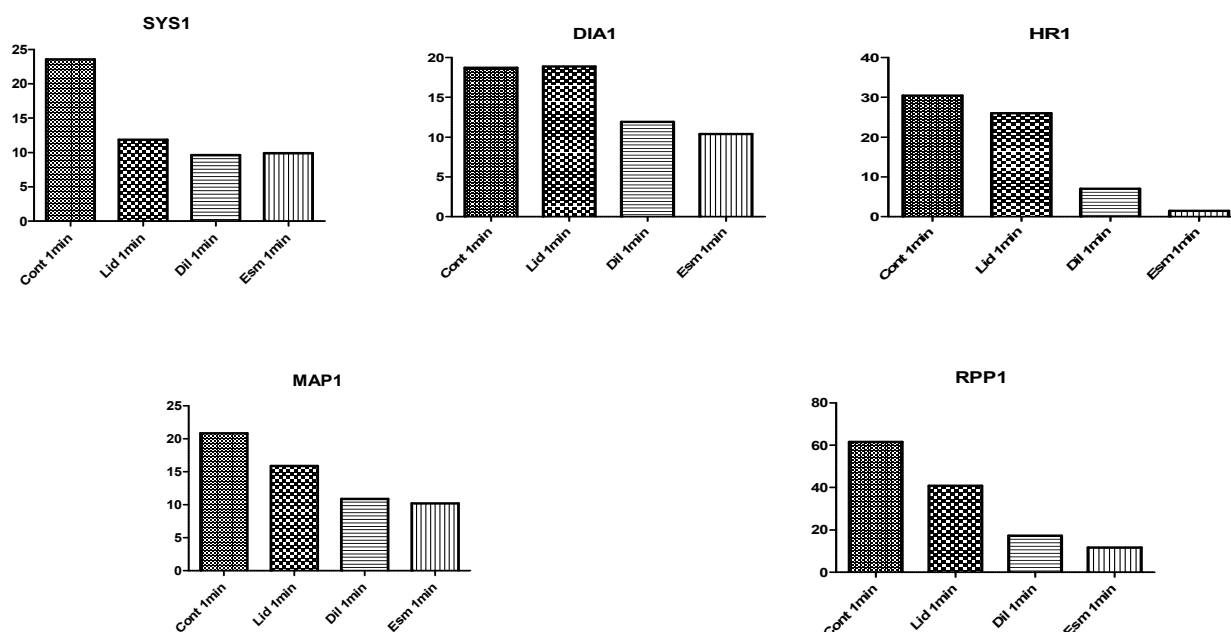
Parameter	Lidocaine	Diltiazem	Esmolol	PI	PII	PIII	PIV
SBP (mmHg)	136.7 ± 1.29	133.1 ± 1.29	131.9 ± 1.39	0.0293	0.0487	0.0125	0.5291
DBP (mmHg)	91.80 ± 0.88	85.15 ± 0.85	82.63 ± 0.83	P<0.0001	P<0.0001	P<0.0001	0.0367
HR (per min)	101.1 ± 1.31	89.90 ± 1.08	91.40 ± 1.19	P<0.0001	P<0.0001	P<0.0001	0.3529
MAP (mmHg)	106.8 ± 0.70	101.1 ± 0.80	99.04 ± 0.65	P<0.0001	P<0.0001	P<0.0001	0.0473
RPP	13810 ± 200.5	11980 ± 205.2	12060 ± 213.7	P<0.0001	P<0.0001	P<0.0001	0.7704

Data are presented as means ± SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values. Bonferroni's multiple comparison tests were used to make intragroup comparisons. Comparison PI- L,D&E, PII- L&D, PIII- L&E, PIV- D&E

**Table 4:** Change in haemodynamic variables in the study groups at 5 min with intragroup comparison.

Parameter	Lidocaine	Diltiazem	Esmolol	PI	PII	PIII	PIV
SBP(mmHg)	131.2 ± 1.79	128.2 ± 1.45	126.3 ± 1.37	0.0758	0.1853	0.0302	0.343
DBP(mmHg)	86.00 ± 0.88	83.50 ± 0.73	79.03 ± 0.93	P<0.0001	0.0318	P<0.0001	0.001
HR(per min)	97.80 ± 1.40	87.70 ± 1.41	88.20 ± 1.39	P<0.0001	P<0.0001	P<0.0001	0.801
MAP(mmHg)	101.1 ± 0.76	98.38 ± 0.73	94.77 ± 0.77	P<0.0001	0.0124	P<0.0001	0.001
RPP	12840 ± 261.7	11270 ± 257.9	11140 ± 221.5	P<0.0001	P<0.0001	P<0.0001	0.713

Data are presented as means ± SEM, and p value. ANOVA with repeated measures was used to compare the changes in SBP, DBP, HR, MAP and RPP values. Bonferroni's multiple comparison tests were used to make intragroup comparisons. Comparison PI- L,D&E, PII- L&D, PIII- L&E, PIV- D&E



**Figure 2:** Percentage changes in haemodynamic variables from baseline and one minute after intubation in the study population stratified by treatment

Figure 2. Percentage change was calculated as follows: [(Variable estimate for time after intubation – Basal estimate for variable) / Basal estimate for variable] X 100%, RPP = Rate pressure product

## 4. Discussion

In designing this experiment, our primary objective was to study the efficacy and safety of cardiac antidysrhythmic beta, calcium and sodium channel blockers on haemodynamic changes due to endotracheal intubation in normotensive Black patients. The precise mechanism which leads to the haemodynamic response to laryngoscopy and intubation probably involves intense sympathetic discharges and release of catecholamine<sup>[8]</sup>. As visible in the control group, markedly high cardiovascular changes occurred within few seconds following laryngoscopy and intubation. It was also determined that intravenous administration of lidocaine, considerably attenuated unwanted pressor response to laryngoscopy and tracheal intubation when given two minutes before laryngoscopy. The results of various studies, in the last decade, on the effect of haemodynamic responses to tracheal induction have varied considerably. Many studies have reported beneficial effect<sup>[10-11]</sup>, while others showed no effect in Caucasians<sup>[12-13]</sup>. The difference in the results of various studies involving lidocaine, to some extent, can be explained by differences in study designs including variations in dose and timing of drug administration in relation to intubation<sup>[14]</sup>. Lidocaine attenuate haemodynamic response to laryngoscopy and intubation by one or combination of following mechanisms: lidocaine acts mainly by inhibiting sodium influx in the voltage gated sodium channels. When the influx of sodium is interrupted,

signal conduction is inhibited. It also acts by decreasing the sensitivity to heart muscle to electrical pulses. This will in turn slow down conduction of electrical signals in the heart muscles, and therefore helps to restore a regular heart beat rhythm<sup>[15]</sup>. The beneficial effect of lidocaine on the haemodynamic changes may also due to its direct cardiac depression and peripheral vasodilatation properties, its ability to suppress airway reflexes elicited by irritation of tracheal mucosa, and its analgesic as well as antiarrhythmia properties<sup>[16]</sup>.

In our study, 0.2 mg kg<sup>-1</sup> diltiazem given at one minute before intubation sufficiently reduced the circulatory responses in normotensive Black patients. Diltiazem prevents/blocks the release of catecholamines, which reduces sympathetic nervous system reactions<sup>[17]</sup>. By slowing conduction of normal electrical impulse through the AV node, diltiazem increases the time needed for each beat, normally resulting in reduced myocardium oxygen consumption<sup>[18]</sup>. Our results are in agreement with previous reports in Caucasians that diltiazem can, in fact, attenuate hypertension associated with tracheal intubation<sup>[19]</sup>. Surprisingly Lee et al. (2002) found, when diltiazem alone was administered it did not attenuate heart rate<sup>[20]</sup>. This might be explained by dosage differences and timing of administration of drugs. In that study, drug was given 90 seconds before laryngoscopy as opposed to the 60 seconds in the current study. The use of calcium blockers can be best utilized when their peak effects corresponds to that of pressor responses. It has been reported before that, MAP begins to increase about 15 seconds after laryngoscopy and

reaches peak value around 45 seconds, if no treatment is administered to patients <sup>[20]</sup>. That's why, in our study, diltiazem was administered 1 minute before laryngoscopy. Manjunath et al. found diltiazem 0.2mg.kg<sup>-1</sup> one minute before laryngoscopy and intubation blunts unwanted haemodynamic responses in Asian population.

Esmolol significantly reduced the circulatory responses in this cohort of normotensive Black patients.  $\beta$ - blockers minimize the increase in heart rate and blood pressure by attenuating positive chronotropic and inotropic effects of the increase in adrenergic activity. Esmolol possesses several properties which makes it a valuable agent to obtund the cardiovascular response. It is a cardio selective agent, has ultra-short duration of action (9 minutes) and has not been reported to have significant drug interaction with commonly used anaesthetic drugs <sup>[21]</sup>. Bostana and Eroglu reported that IV esmolol in doses of 1 mg kg<sup>-1</sup> before intubation was effective in suppressing heart rate and arterial blood pressure in Caucasians <sup>[22]</sup>. Kumar *et al.* have reported optimal results while using higher doses of esmolol (2 mg kg<sup>-1</sup>) in an Asian population, without any incidence of unplanned hypotension or bradycardia <sup>[23]</sup>. In this normotensive cohort of Black population, esmolol, at a dose of 2 mg kg<sup>-1</sup> effectively decreased HR, SBP, DBP, MAP and RPP without any incidence of hypotension or bradycardia. This study further observed a reduction in DBP less than that in SBP resulting in a better control of the MAP in the study population. Gupta *et al.* there has been no consensus regarding the optimum dose and timing of esmolol delivery in Caucasian population <sup>[2]</sup>.

Studies have shown when intraoperative heart rate is more than 110 beats min<sup>-1</sup> there is increased myocardial oxygen requirement and incidence of Myocardial infarction. In our study none of the patients in study groups showed heart rate >110 beats min<sup>-1</sup>. RPP as calculated by multiplying heart rate with systolic blood pressure. The RPP levels close to 20,000 are normally associated with angina and myocardial ischemia <sup>[1]</sup>. RPP at 1 min after intubation remained less than 20,000 in study drug groups. These finding confirms the cardioprotective effect of study drugs during laryngoscopy and endotracheal intubation.

## 5. Conclusions

Intravenous lidocaine (1.5 mg kg<sup>-1</sup>), diltiazem (0.2 mg kg<sup>-1</sup>) and esmolol (2 mg kg<sup>-1</sup>) are effective agents in suppressing the hemodynamic response to laryngoscopy and intubation without any deleterious effect. Given the difference in the pharmacological mechanisms of these drugs, the prophylactic therapy with 2mg kg<sup>-1</sup> esmolol appears to be significantly more effective and safe for attenuating haemodynamic changes to laryngoscopy and tracheal intubation. Esmolol should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia in the Black populations.

## Comments

Further studies needs to be done in high-risk patients, using longer duration infusions to investigate the safety and efficacy of esmolol in reducing the frequency of myocardial ischaemia after non-cardiac and cardiac surgery in the Black populations.

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