

A Prospective Randomised Study of Intravenous Esmolol , Lignocaine And Combination of Esmolol And Lignocaine for Attenuating Cardiovascular Response Durig Laryngoscopy and Tracheal Intubation

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Abstract :

Background: Primary objective to study efficacy of Esmolol , lignocaine and combination of esmolol and lignocaine with respect to heart rate and blood pressure during laryngoscopy and intubation

Materials and Methods: We conducted this study as a prospective randomized study. A total of 183 adult patients were randomly selected who fulfilled the inclusion criteria. They were divided into three groups and study was conducted.

Conclusion: Combination was found to be more effective than individual Esmolol or lignocaine in attenuating the sympathetic response to laryngoscopy and endotracheal intubation.

Keywords:- lignocaine, esmolol

I. Introduction

Intubation has become an integral part of anaesthetic and critical care of the patient..It has been used since its description by Rowaorrom AND MAGILL in1921.

Direct laryngoscopy and endotracheal intubation is almost always associated with haemodynamic changes due to reflex sympathetic discharge, caused by oropharyngeal and laryngopharyngeal stimulation. This increase in sympathetic activity results in hypertension tachycardia and arrhythmias. This increase in blood pressure and heart rate are usually transitory, variable and unpredictable. Hypertensive patients are more prone to have significant increase in BP whether they have been treated before hand or not for Transitory hypertension and tachycardia may be hazardous to those with hypertension myocardial insufficiency and cerebrovascular diseases

The laryngoscopic reactions in such individuals may predispose to pulmonary edema, myocardial insufficiency and cerebrovascular accidents. Many pharmacological methods have been devised to reduce the extent of haemodynamic events with high dose of opioids, anaesthetics like lignocaine, alpha and beta and vasodilator drugs like nitroglycerine.

Intravenous lignocaine with its well established sympathetic drive suppressant and antiarrhythmic effect was found to be more stable alternative methods to minimize pressor response. Recommendations for attenuation of reflex hypertension and tachycardia are therefore the cardiovascular response to anesthesia for patients at risk must satisfy the following requirements. It must be applicable regardless of patient cooperation, prevent impairment of cerebral blood flow, avoid arousal of patients

IV lignocaine and esmolol appear to fulfil the above criteria . The present study is undertaken to determine the efficacy of IV lignocaine 1.5mg/kg, IV esmolol 0.5 mcg / kg, and IV lignocaine 1.5 mg/kg and IV esmolol 0.5mcg/kg and IV lignocaine 1.5mg/kg and IV esmolol 0.5mg/kg combination in attenuating the sympathetic response to laryngoscopy and intubation.

II. Aims and Objectives

The objective of the present study are Primary objective is to study efficacy of Esmolol , lignocaine and combination of esmolol and lignocaine with respect to heart rate and blood pressure during laryngoscopy and intubation Secondary objective is to study the safety of Esmolol , lignocaine and combination with respect to changes in ECG and adverse effects.

III. Material and methods

Procedure: after taking the patient to the Operation theater

1. Peripheral venous cannulation was done
 2. Monitors , pulse oximeter, ECG, Sphygmomanometer/NIBP were attached to the patient and heart rate, ECG, oxygensaturation and BP were monitored
 3. Pre-oxygenation was done for 3 mins
 - 4 Sedation was given with injection Midazolam 0.03mg/kg i.v
 - 5.Induction was done with injection Thiopentone 5mg/kg i.v.
 6. Muscle relaxant was given with injection Vecuronium 0.15mg/kg i
 - 7, Group A received injection Esomolol 0.5 mg/kg. Lv. 90sec prior to laryngoscopy. Group B received injection Lignocaine 1.5mg/kg i.v. 3 mins Prior to laryngoscopy . and injection Lignocaine 1.5mg/kg i.v. 3 90 secs prior to laryngoscopy
 8. Laryngoscopy and tracheal intubation (average duration less than 15 secs) was performed and anesthesia will be maintained with N2O: O2=50:50
 - 9 Head rate, SBP and DBP, ECG were recorded prior to giving drugs, at the time of mtubation 15 Secs 45 Sec , 1 min, 2 min and 5 min and 15mm after laryngoscopy and intubation.
- Throat packing , positioning , surgical incision was withheld till completion of recording
After completion of surgery reversal was done wherein neostigmine 0.05mg/kg and glycopyrrrolnte 8 mcg/kg
IV, an observation was made related to adverse effects of drugs and anaesthesia related problems and were attended appropriately.

IV. Statistical - analysis:

For Comparison of mean change in SBP from base limit across three groups i.e Esomolol, lignocaine and combination of Esomolol and Lignocaine accepting of 5 % and 8 of 20% 396 anticipated difference of 6mm of Hg with standard deviation of 10 mm of HG, the sample size is 61 per group. Hence the total sample size comes to 183 patients.

Repeated measures of ANOVA was used for comparison of numerical data at different time points within the group . For comparison of numerical data between groups, ANOVA was performed. Categorical data were compared using Chi-Square test

V. Observation and results

Group	N	Me	Std.Dev.	Median	IQR	Minium	maximum	Oneway ANOVA test	
								FValue	P Value
Lignocaine	61	39.43	11.10	40.00	18.00	22.00	60.00		
Esomolol	61	38.84	11.84	40.00	20.00	22.00	60.00	0.019	0.981
Combination	61	39.84	12.06	42.00	24.00	22.00	60.00		

Table 1 : Age Distribution

Table 1 shows age distribution among the three groups . Age ranged between 18-60 years. The mean values of age with standard deviation is 39.43 for lignocaine group, 38.84 for esmolol group and 39.8 for combination group. There is no statically significant difference among the three groups (p value=0.98)

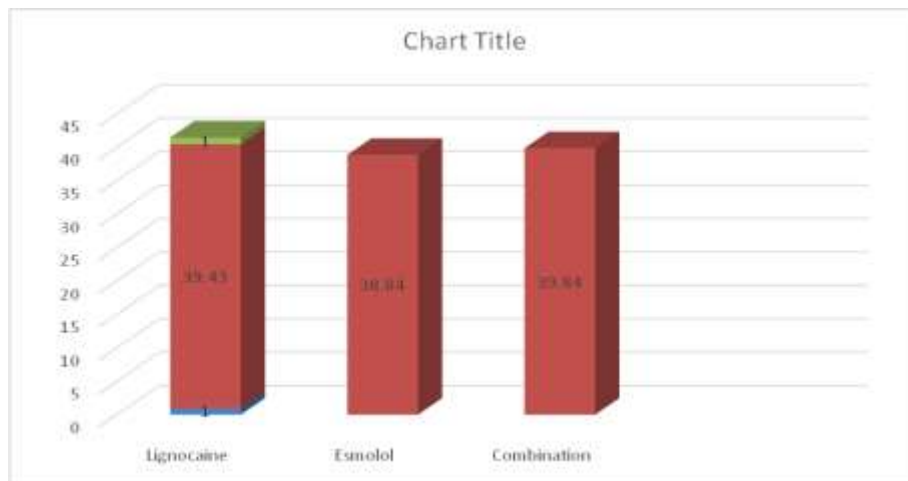
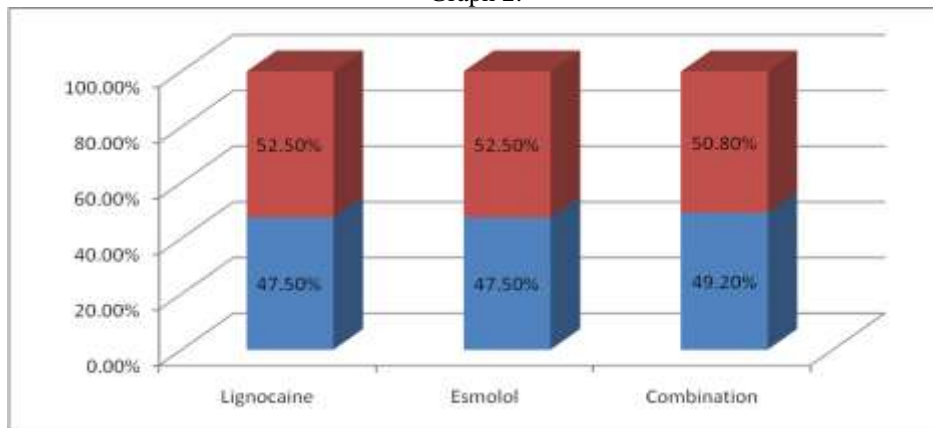


Table: 2 Sex Distreibution

Study Group		Sex		total
		Female	Male	
Lignocaine	Count	29	32	61
	Percent	47.5%	52.5%	100%
Esmolol	Count	29	32	61
	Percent	47.5%	52.5%	100%
Combination	Count	30	31	61
	Percent	49.2%	50.8%	100%
Total	Count	88	95	183
	Percent	48.1%	51.9%	100.0%
Chi-squre Tests	Value	Df	P Value	Association is
Pearson Chi-Square	0.044	2	0.978	Not significant

Table 2 shows distribution of sex among the three groups .It is not statically significant (p value= 0.978)

Graph 2:



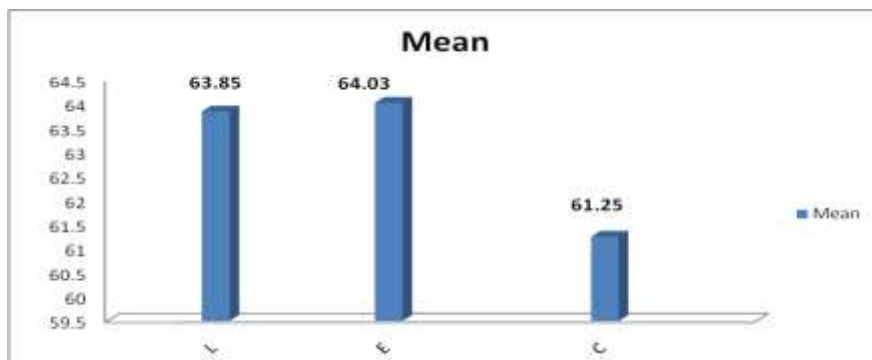
Graph 2 shows percentage of male and female among the three groups

Table 3 : Weight Distribution

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA test	
								F Value	P value
Lignocaine	61	63.85	9.83	64.0	14.00	43.00	86.00	1.490	0.228
Esmolol	61	64.03	10.24	65.00	14.00	34.00	82.00		
Combination	61	61.25	9.86	59.00	13.00	46.00	85.00		

Table 3 shows weight distribution among the three groups. The mean values of weight with standard deviation was 63.85 for lignocaine 64.03 for esmolol and 61.25 for combination weight distribution is not statistically among the three groups (p value =0.22)

Graph 3



Graph 3 Shows mean weight among the three groups.

Table 4: Preoperative Heartrate

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA Test	
Lignocaine	61	80.05	6.57	82.00	8.00	66.00	94.00	F Value	P value
Esmolol	61	80.61	7.29	78.00	10.00	64.00	98.00	1.060	0.348
Combination	61	78.39	7.83	78.00	8.0	62.00	98.00		

Table 4 shows preoperative heart rate among the three groups. The mean values of preoperative heartrate with standard deviation is 80.05 for lignocaine 80.61 for esmolol and 78.39 for combination. The preoperative heart rate is not statistically significant among the three groups(p value =0.34)

Graph 4:

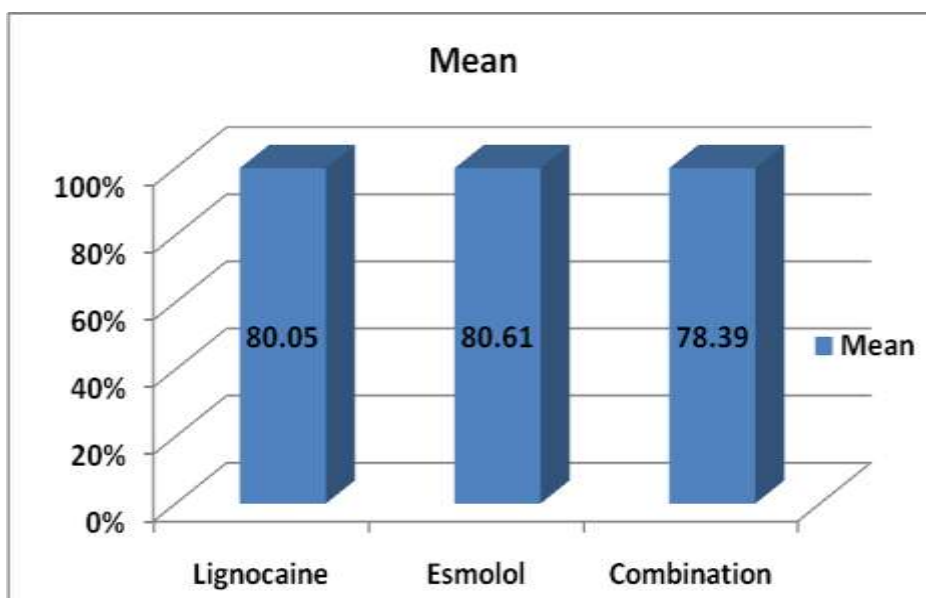


Table 5 : Heart Rate At Intubation

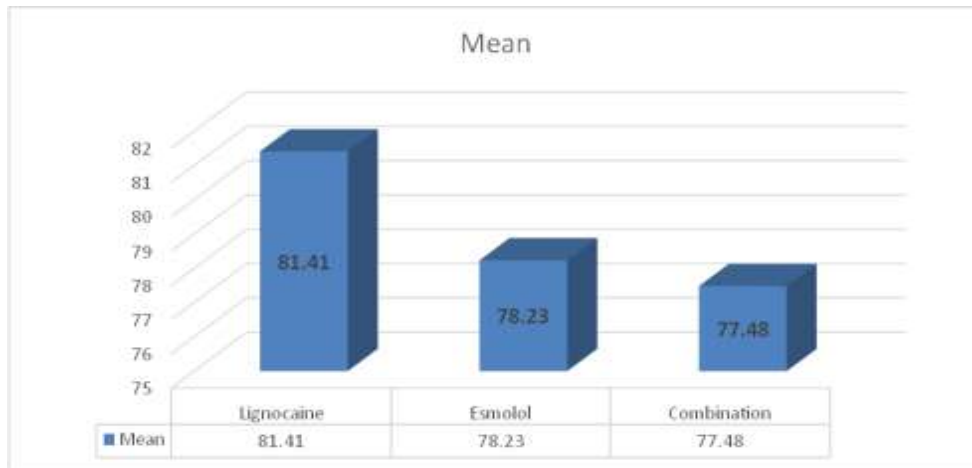
Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA test	
Lignocaine	61	83.18	6.54	85.00	10.00	70.0	98.00	F Value	P value
Esmolol	61	84.07	6.48	86.00	6.00	68.00	98.00	34.266	0.000
Combination	61	72.20	12.27	70.00	18.00	48.00	98.00	Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	
Esmolol vs Combination	yes	

Table 5 shows comparison of heart rate among the three groups the time intubation.

The mean values of heart rate with standard deviation is 83.1 for lignocaine 84.07 for esmolol and 72.2 for combination . This is statistically significant (p values <0.001) Combination when compared with compared with either lignocaine or esmolol the difference in heart rate the time of intubation is statistically significant (p value <0.05)

Graph 5 :



Graph 5 shows mean heart rate at the time of intubation among the three groups.

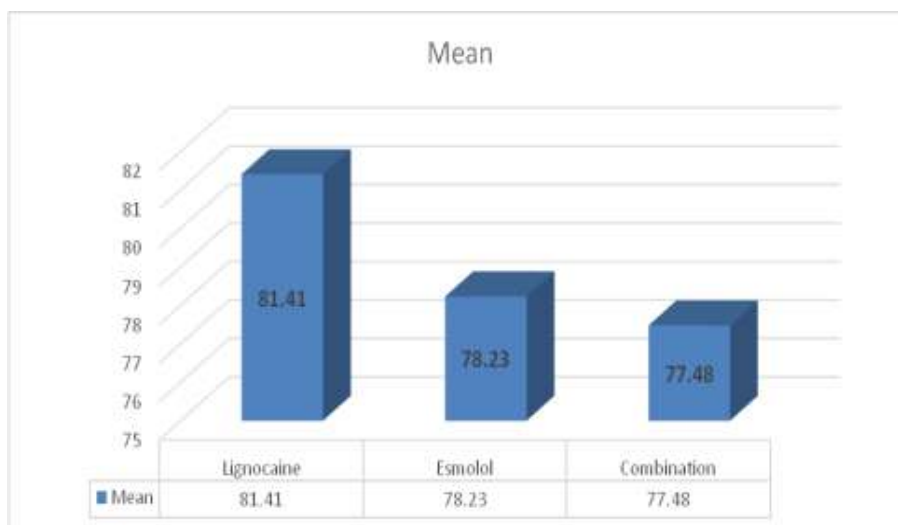
Table 6 Herat Rate At 15 Sec

Group	N	Mean	Std Dev	Med Ian	IQR	Min Imum	Ma Ximum	Oneway ANOVA test	
Lignocaine	61	84.97	7.10	86.00	10.00	68.00	97.00	F Value	P value
Esmolol	61	85.36	6.59	86.00	7.00	68.00	98.00	37.673	0.000
Combination	61	74.13	10.17	75.00	14.00	54.00	97.00	Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		This Gr diff is significant
Comparison	P<0.050	
Esmolol vs Combination	Yes	
Lignocaine vs Combination	Yes	

Table 6 shows the comparison of heart rate at 15 seconds after intubation. The mean values for heart rate with standard deviation is 84.97 for Lignocaine 85.36 for esmolol and 74.13 for combination. When compared with either esmolol or lignocaine at the same stage the difference in heart rate is statistically significant. (p value<0.05)

Graph 6:



Graph 6 shows the mean heart rate at 15 seconds after intubation among the three groups.

Table 7 : Heart Rate At 45 Seconds

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA test	
Lignocaine	61	88.13	7.49	88.00	10.00	66.00	100.00	F Value	P value
Esmolol	61	86.97	6.98	88.00	8.00	66.00	100.	34.324	0.000
Combination	61	76.98	9.77	76.00	11.00	56.00	00	Difference is not significant	

All pair wise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine vs Combination	yes	

Table 7 shows the comparison of heart rate at 45 seconds after intubation . The mean values for heart rate with standard deviation is 83.13 for Lignocaine 86.97 for esmolol and 76.98 The difference is statistically significant (p value<0.05) Combination When compared with either esmolol or lignocaine at the same stage the difference in heart rate is statistically significant. (p value<0.05)

Graph 7:

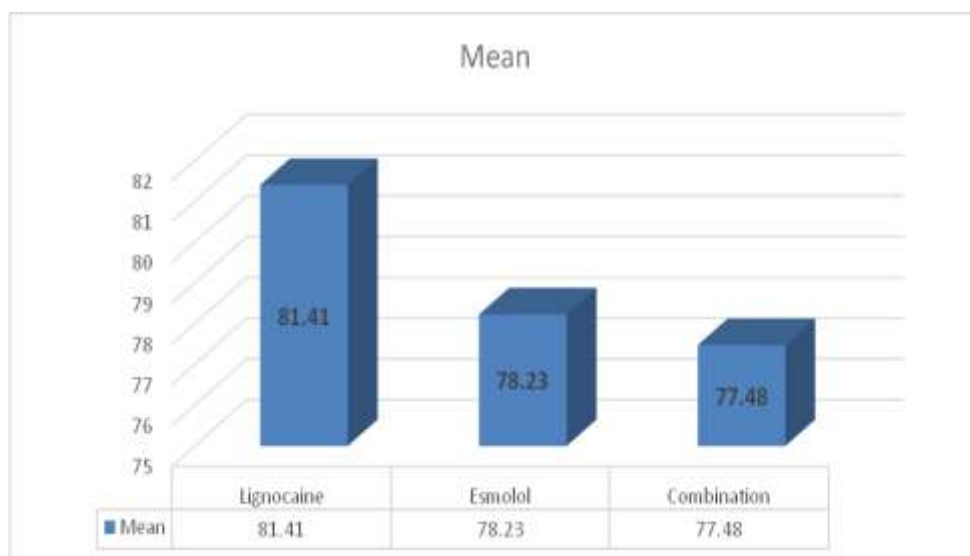
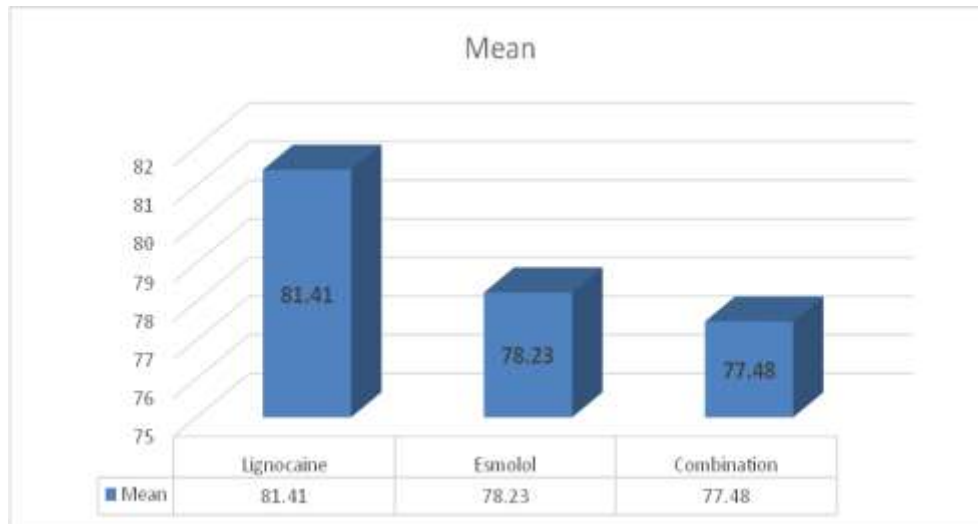


Table 8: Heart Rate At 1 Minute

Group	N	Mean	Std Dev	Median	I Q R	Minimum	Maximum	Oneway ANOVA Test	
Lignocaine	61	90.08	6.73	90.00	9.00	75.00	102.00	F Value	P value
Esmolol	61	86.28	6.15	86.00	6.00	76.00	102.00	25.667	0.000
Combination	61	80.03	10.02	80.00	13.00	58.00	102.00	Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine vs Combination	Yes	

Table 8 shows the comparison of heart rate at 1 minute after intubation . The mean values for heart rate with standard deviation is 90.08 for Lignocaine 86.97 for esmolol and 86.28 for combination The difference is statistically significant (p value<0.05) Esmolol When compared with either 1 lignocaine or combination at the same stage the difference in heart rate is statistically significant. (p value<0.05)



Graph 8 shows the mean hear rate at 1 minute after intubationAmong the three groups.

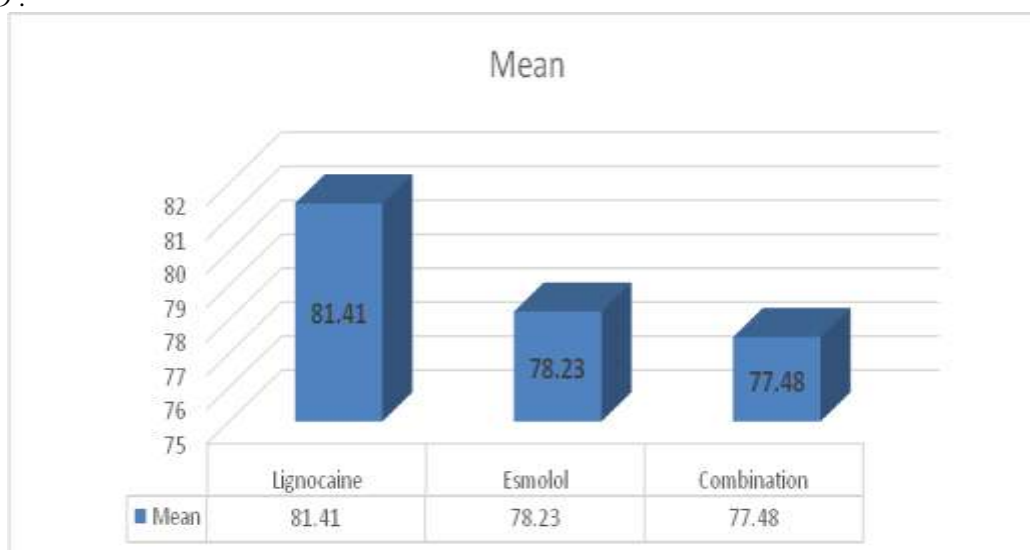
Table 9: Heart Rate At 2 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA test	
Lignocaine	61	89.70	7.40	90.00	7.00	73.00	100.00	F Value	P value
Esmolol	61	83.79	6.40	84.00	8.00	68.00	100.00	17.893	0.000
Combination	61	81.62	9.13	82.00	13.00	62.00		Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	
Esmolol vs Combination	yes	

Table 9 shows the comparison of heart rate at 2 minute after intubation . The mean values for heart rate with standard deviation is 89.7 for Lignocaine 83.79 for esmolol and 81.62 for combination The difference in herat rate is statistically significant(p value<0.05) Combination When compared ignocainel at the same stage the difference in heart rate is statistically significant. (p value<0.05) esmolol when compared to lignocaine at the same shage the difference in heart rate is significant (p vlue <0.05)

Graph 9 :



Graph 9 shows the mean heart rate at 2 minutes after intubation among the three groups.

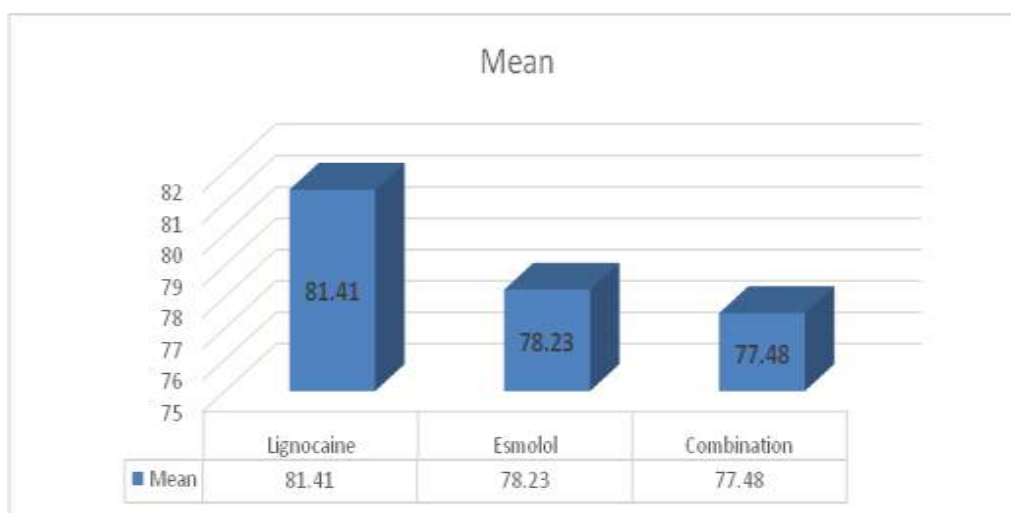
Table 10: Heart Rate At 5 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA test	
Lignocaine	61	86.56	7.13	88.00	7.00	70.00	97.00	F Value	P value
Esmolol	61	81.43	5.63	82.00	5.00	70.00	96.00	16.504	0.000
Combination	61	79.18	8.81	80.00	12.00	60.00	96.00	Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	
Esmolol vs Combination	yes	

Table 10 shows the comparison of heart rate at 5 minute after intubation among the group . The mean values for heart rate with standard deviation is 86.56 for Lignocaine 81.43 for esmolol and 79.18 for combination The difference in heart rate is statistically significant(p value<0.05) Combination When compared lignocaine at the same stage the difference in heart rate is statistically significant. (p value<0.05) the difference in heart rate is significant (p vlue <0.05) between esmolol and lignocaine.

Graph 10 :



Graph 10 shows mean heart rate at 5 minutes after intubation among the three groups.

Table 11 : Heart Rate At 10 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA test	
Lignocaine	61	83.59	7.09	85.00	8.00	66.0	96.00	F Value	P value
Esmolol	61	79.41	6.20	78.00	8.00	64.0	90.00	12.473	0.000
Combination	61	76.93	8.87	80.00	14.00	58.0	92.00	Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	
Esmolol vs lignocaine	yes	

Table 11 shows the comparison of heart rate at 10 minute after intubation among the group . The mean values for heart rate with standard deviation is 83.59 for Lignocaine 79.41 for esmolol and 76.93 for combination (p value <0.05) lignocaine when compared to combination at the same stage The difference in herat rate is statistically significant(p value<0.01) esmolol When compared lignocainel the difference in heart rate is statistically significant. (p value<0.05)

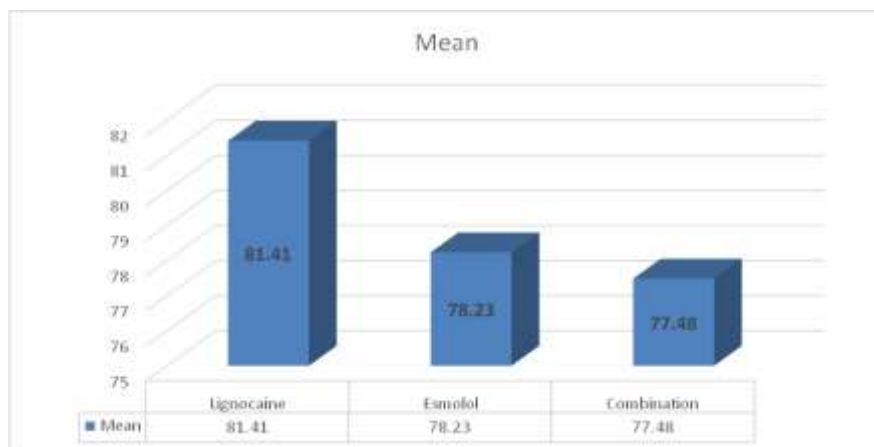


Table 12: Heart Rate At 15 Minutes

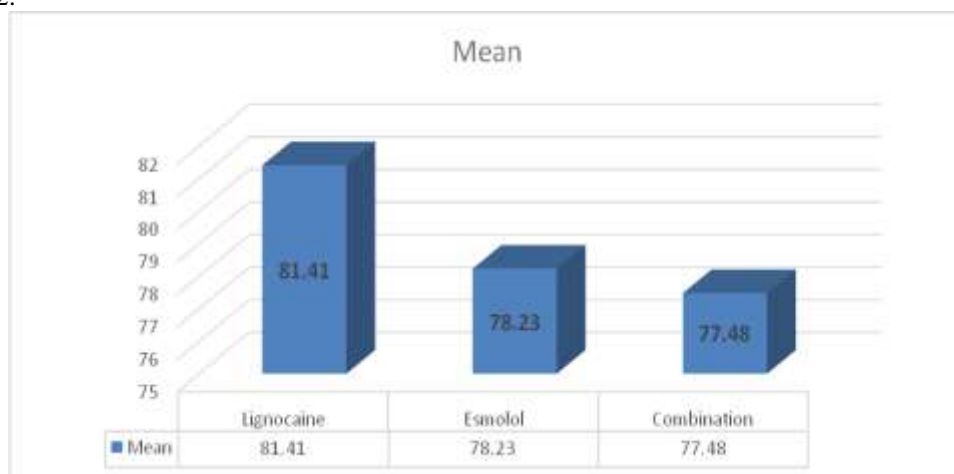
Group	N	Mean	Std Dev	Median	I Q R	Min Imum	Ma Ximum	Oneway ANOVA test	
Lignocaine	61	80.90	5.94	82.00	8.00	68.00	90.00	F Value	P value
Esmolol	61	77.72	6.43	76.00	8.00	66.0	90.00	14.463	0.000
Combination	61	74.00	8.61	76.00	12.00	56.00	90.00	Difference is not significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)			
Comparison	P<0.050	This Gr diff is significant	
Esmolol vs Combination	Yes		
Esmolol vs lignocaine	yes		
Lignocaine VS Combination	yes		

Table 12 shows the comparison of heart rate at 15 minute after intubation among the three group . The mean values for heart rate with standreed deviation is 80.9 for Lignocaine 77.72 for esmolol and 74.0 for combination (p value <0.05)

Esmolol when compared either to combination or lignocaine the difference in heart rate at the same stage The difference in herat rate is statistically significant(p value<0.05) lignociane When compared combination the difference in heart rate is statistically significant. (p value<0.05)

GRAPH 12:



Graph 12 shows the mean heart rate at 15 minutes after intubationAmong the three groups.

Table 13: Preoperative Sbp

Group	N	Mean	Std Dev	Median	IQR	Min Imum	Ma Ximum	Oneway ANOVA Test	
Lignocaine	61	132.69	14.05	132.00	20.00	104.00	168.0	F Value	P value

Esmolol	61	133.61	17.28	130.00	26.00	110.00	170.00	0.061	0.940
Combination	61	133.64	17.88	132.00	26.00	106.00	176.00		

Table 13 shows the distribution of preoperative SBP among the three groups . The mean value of SBP with standard deviation is 132.69 for lignocaine, 133.61 for esmolol and 133.64 for combination . This difference is not statistically (p value>0.05)

Table 14 Sbp At Intubation

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA Test	
Lignocaine	61	136.79	13.84	140.00	20.00	108.00	170.00	F Value	P value
Esmolol	61	135.64	17.36	136.00	26.00	100.00	172.00	8.991	0.00018
Combination	61	124.95	19.68	124.00	28.00	80.00	172.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combination	yes	

Table 14 shows the distribution of preoperative SBP at the time of intubation among the three groups. The mean value of SBP with standard deviation is 136.79 for lignocaine, 135.64 for esmolol and 124.95 for combination . This difference is statistically (p value>0.05) The difference in SBP is also statistically significant when esmolol is compared with combination and lignocaine is compared with combination.(p value>0.05)

Table 15: Sbp At 15 Seconds

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA Test	
Lignocaine	61	138.66	12.68	138.00	20.00		170.00	F Value	P value
Esmolol	61	136.16	17.40	134.00	22.00		172.00	8.991	0.00018
Combination	61	127.38	19.06	128.00	22.00		172.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combination	yes	

Table 15 shows the distribution of preoperative SBP at 15 seconds after intubation among the three groups . The mean value of SBP with standard deviation is 138.66 for lignocaine, 136.16 for esmolol and 127.38 for combination . This difference is statistically (p value>0.05) The difference in SBP is also statistically significant when esmolol is compared with combination and lignocaine is compared with combination.(p value>0.05)

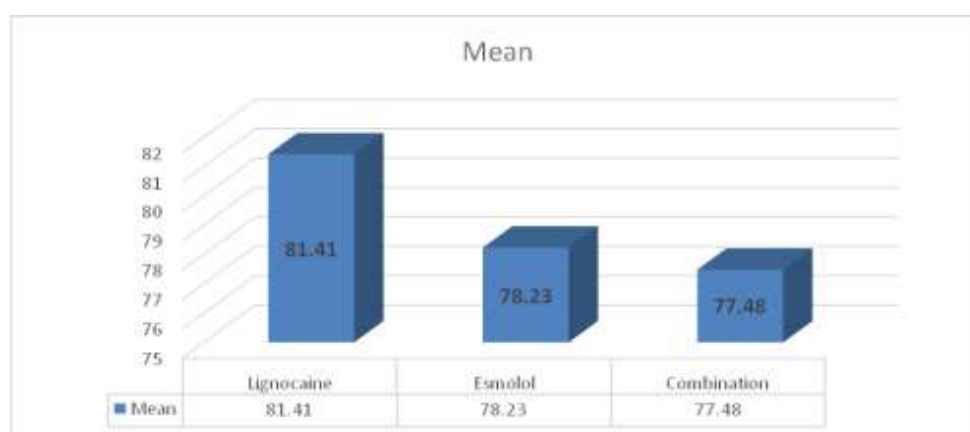


Table 16: Sbp At 45 Seconds

Group	N	Mean	Std Dev	Median	IQR	Min Imum	Ma Ximum	Oneway ANOVA test	
Lignocaine	61	141.33	12.57	144.00	16.00	112.00	168.00	F Value	P value
Esmolol	61	136.36	17.33	136.00	26.00	100.00	170.00	7.110	0.001
Combination	61	130.03	18.78	130.00	22.00	88.00	168.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combination	yes	

Table 16 shows the distribution of preoperative SBP at 45 seconds after intubation among the three groups. The mean value of SBP with standard deviation is 141.33 for lignocaine, 136.36 for esmolol and 130.13 for combination. This difference is statistically significant (p value > 0.001). The difference in SBP is also statistically significant when esmolol is compared with combination and lignocaine is compared with combination (p value > 0.05).

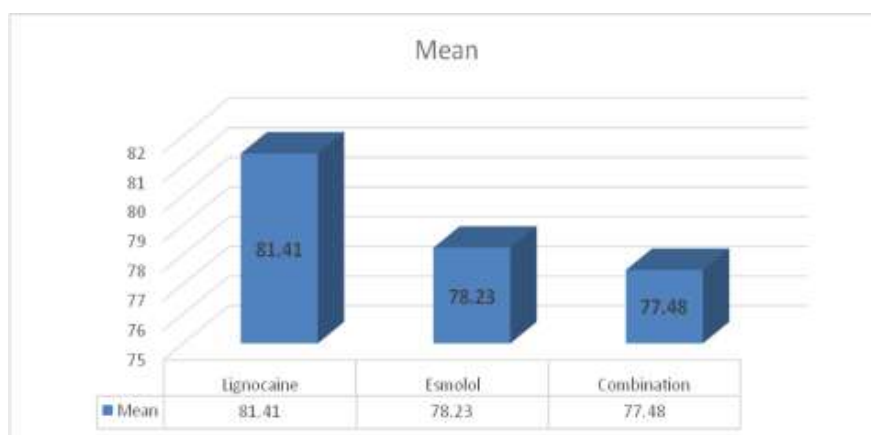


Table 17: Sbp At 1 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min Imum	Ma Ximum	Oneway ANOVA test	
Lignocaine	61	143.21	13.51	144.00	16.00	110.00	170.00	F Value	P value
Esmolol	61	134.46	17.7	134.00	28.00	102.00	170.00	7.380	0.001
Combination	61	131.93	19.21	132.00	20.00	82.00	170.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	
Lignocaine VS Esmolol	yes	

Table 17 shows comparison SBP at 1 minute after intubation among the three groups. The mean value of SBP with standard deviation is 143.21 for lignocaine, 134.46 for esmolol and 131.93 for combination. This difference is statistically significant (p value > 0.05). The difference in SBP is also statistically significant when esmolol is compared with combination and lignocaine is compared with combination (p value > 0.05).

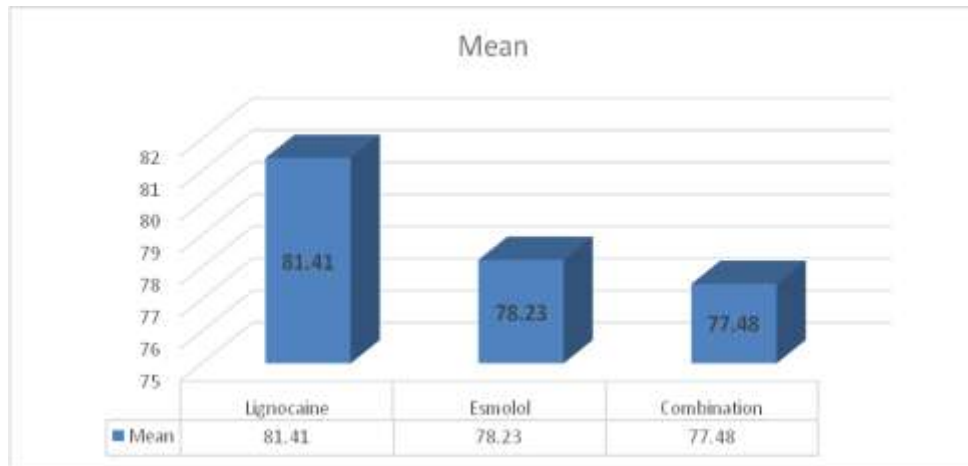


Table 18: Sbp At 2 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA test	P value
Lignocaine	61	140.98	13.62	144.00	16.00	112.00	168.00	F Value	0.011
Esmolol	61	134.46	16.33	132.00	20.00	104.00	172.00	4.589	
Combination	61	132.62	18.01	134.00	22.00	90.00	170.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	This Gr diff is significant
Lignocaine VS Esmolol	yes	

Table 18 shows comparison SBP at 2 minutes after intubation among the three groups. The mean value of SBP with standard deviation is 140.98 for lignocaine, 134.46 for esmolol, and 132.62 for combination. This difference is statistically significant (p value < 0.05). The difference in SBP is also statistically significant when esmolol is compared with combination and lignocaine is compared with combination (p value < 0.05).

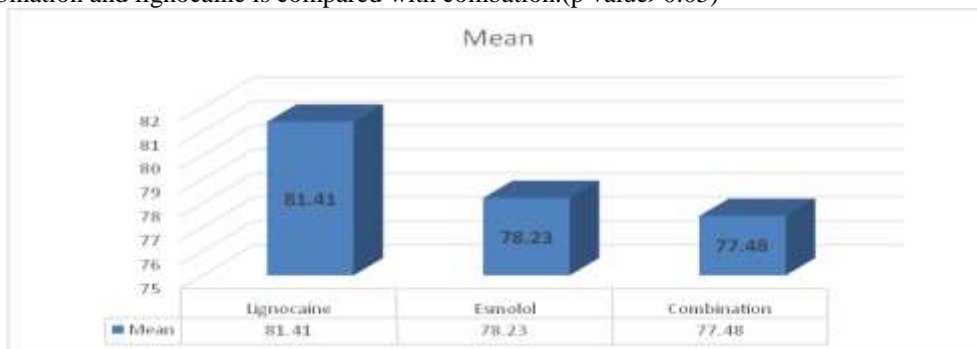


Table 19 : Sbp At 5 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA test	P value
Lignocaine	61	137.84	12.64	138.00	14.00	108.00	162.00	F Value	0.011
Esmolol	61	133.84	15.04	132.00	24.00	106.00	166.00	4.623	
Combination	61	129.51	17.33	130.00	20.00	92.00	168.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	This Gr diff is significant
Lignocaine VS Esmolol	yes	

Table 19 shows comparison SBP at 5 minutes after intubation among the three groups . The mean value if SBP with standred deviation is 137.84 for lignocaine 133.84 for esmolol and 129.51 for combination . This difference is statiscally (p value>0.05) The difference SBP is also statistically whenlognocaine is compared with combination.(p value>0.05)

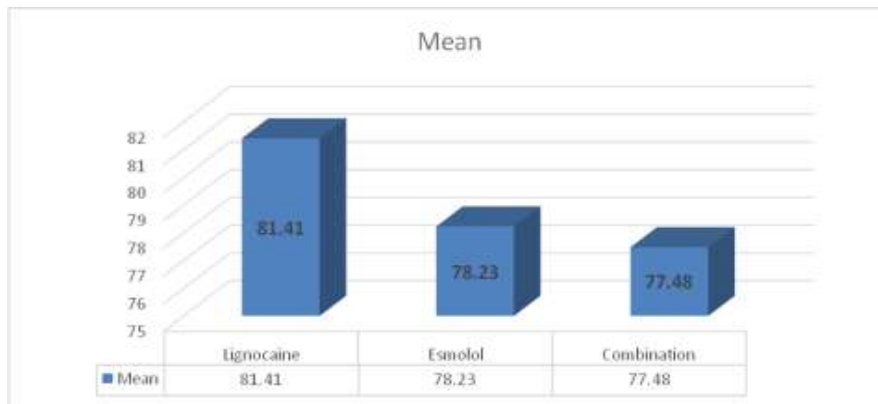


Table 20: Sbp At 10 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min Imum	Ma Ximum	Oneway ANOVA test	
Lignocaine	61	134.89	12.49	138.00	14.00	106.00	162.00	F Value	P value
Esmolol	61	131.67	15388	132.00	22.00	100.00	168.00	3.933	0.021
Combination	61	127.11	17.32	128.00	24.000	90.0	168.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	

Table 20 shows comparison SBP at 10 minutes after intubation among the three groups . The mean value if SBP with standred deviation is 134.89 for lignocaine 131.67 for esmolol and 127.113 for combination . This difference is statiscally (p value>0.05) The difference SBP is also statistically when lognocaine is compared with combination.(p value>0.05)

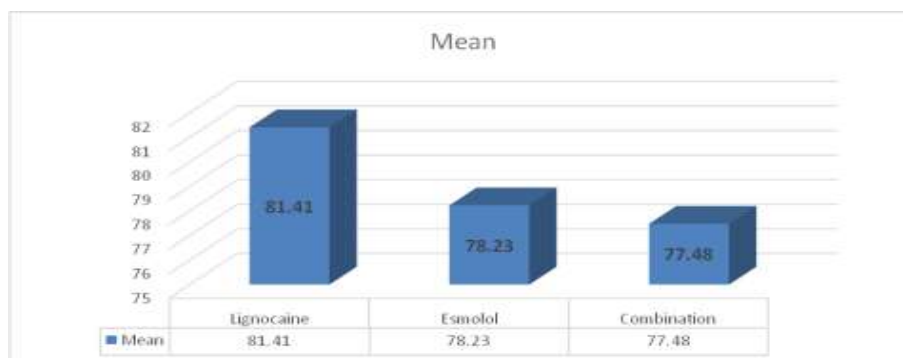


Table 21: Sbp At 15 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min Imum	Ma Ximum	Oneway ANOVA test	
Lignocaine	61	132.26	12.82	134.00	14.00	164.00	164.000	F Value	P value
Esmolol	61	130.46	15.66	130.00	18.00	104.00	170.00	4.340	0.014
Combination	61	124.46	16.98	124.00	24.00	90.	170.0	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Lignocaine vs Combination	Yes	

Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combination	yes	

Table 21 shows comparison SBP at 15 minutes after intubation among the three groups . The mean value if SBP with standred deviation is 132.26 for lignocaine 130.46 for esmolol and 124.46 for combination . This difference is statically (p value>0.05) The difference SBP is also statistically when Esmolol is compared with combination. And Lignocaine compared with combination.(p value>0.05)

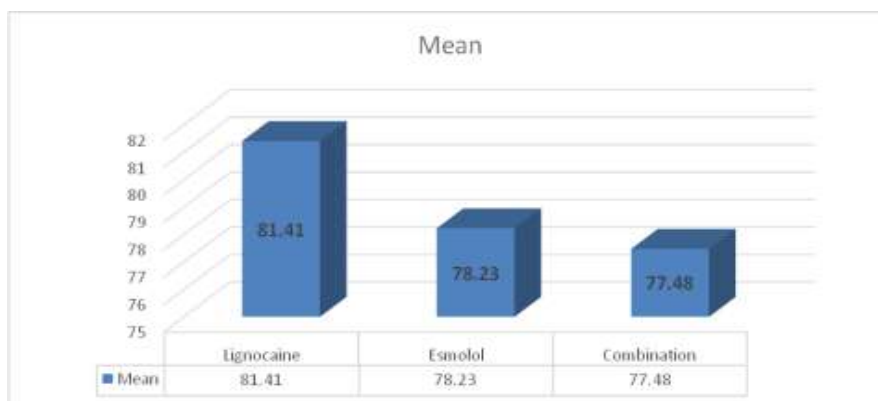


Table 22: Preoperative Dbp

Group	N	Mean	Std Dev	Med ian	IQR	Min Imum	Maimum	Oneway Anovatest	
Lignocaine	61	80.66	5.19	80.00	6.00	70.00	90.00	F Value	P value
Esmolol	61	81.21	7.90	80.00	10.00	70.00	100.00	2.902	0.058
Combination	61	83.57	7.87	82.00	10.00	70.00	100.00	This Gr diff is significant	

Table 22 shows comparison dbp among the three group The mean value for DBP with standred deviation I 80.66 for lignocaine ,81.21 for esmolol and 83.57 for combination . This difference in DBP is not statistically significant (p value>0.05)

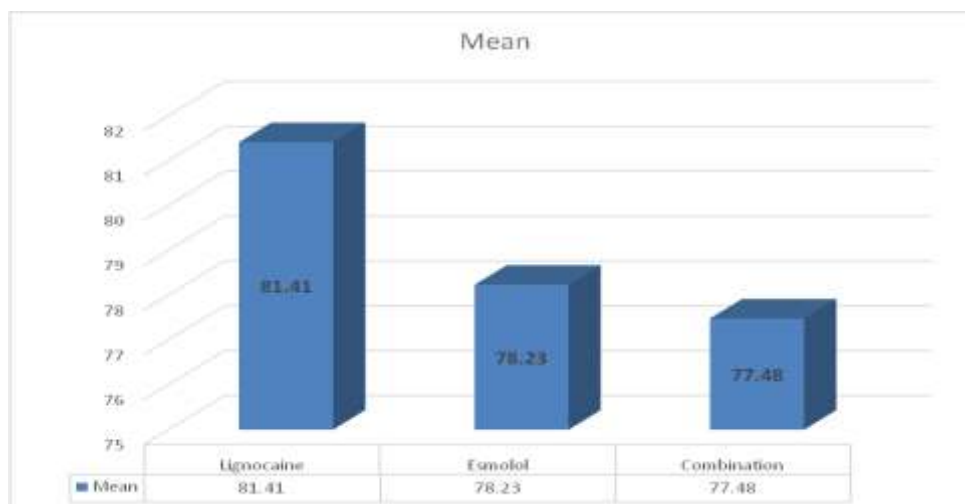


Table 23: Dbp At Intubation

Group	N	Mean	Std Dev	Med ian	IQR	Min Imum	Ma Ximum	Oneway ANOVA Test	
Lignocaine	61	83.66	4.68	82.00	6.00	72.00	94.0	F Value	P value
Esmolol	61	82.13	5.98	82.00	8.00	72.00	94.0	12.237	0.00001
Combination	61	77.90	8.09	78.00	12.00	56.00	92.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combinationl	yes	

Table 23 shows comparison DBP at the time of intubation among the three group The mean value for DBP with standred deviation I 83.38 for lignocaine 82.13 for esmolol and 77.9 for combination .This is statically significant (p value<0.05). This difference in DBP is Between lignocaine and combination is also ststistically significant (p value<0.05)

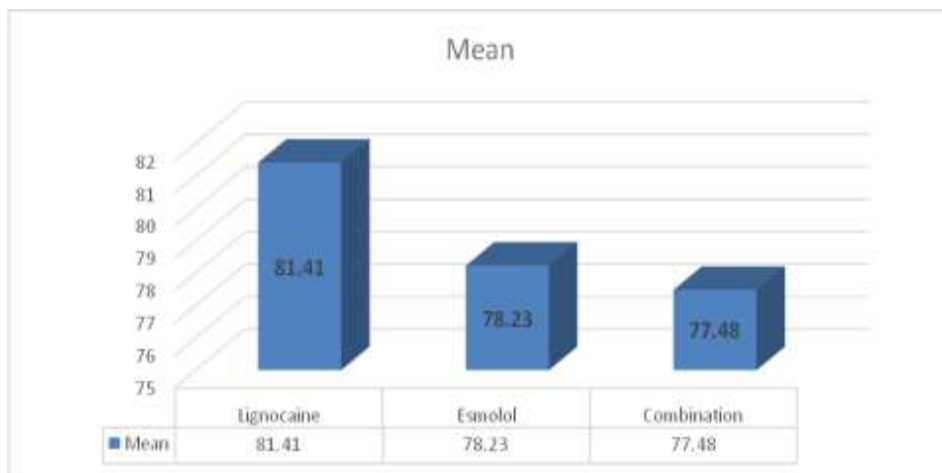


Table 24: Dbp At 15 Seconds

Group	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA Test	
Lignocaine	61	84.85	5.05	86.00	8.00	76.00	94.00	F Value	P value
Esmolol	61	82.89	5.48	82.00	6.00	68.00	90.00	12.237	0.00001
Combination	61	79.77	7.34	80.00	10.00	60.00	94.00	This Gr diff is significant	

All pair wise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combinationl	yes	

Table 24 shows comparison DBP at the 15 seconds afr intubation among the three group The mean value for DBP with standred deviation 84.85 for lignocaine ,82.89 for esmolol and 79.77 for combination . This difference in DBP is not statistically significant (p value>0.05) The difference in DBP between esmolol and combination abd between lignocaine and combination is also statistically significant.

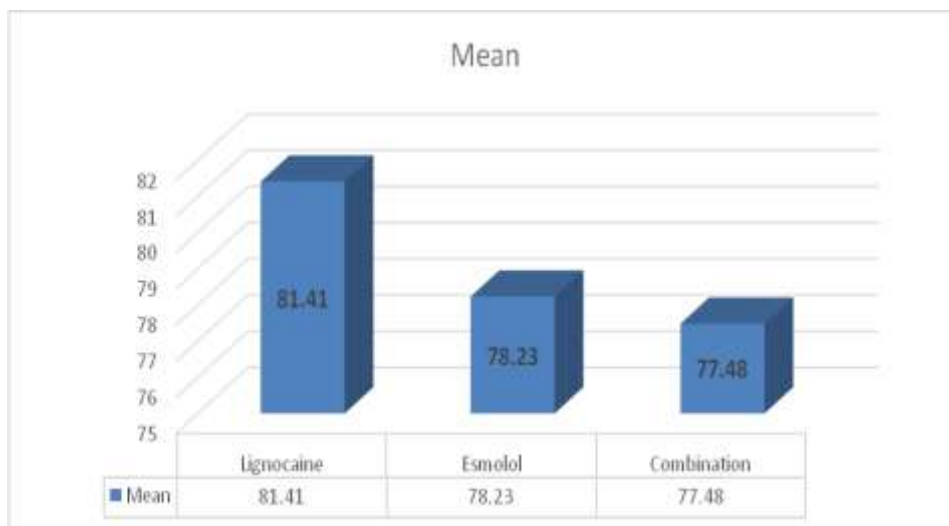


Table 25: Dbp At 45 Seconds

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA test	
								F Value	P value
Lignocaine	61	87.54	5.19	88.00	8.00	74.00	98.00		
Esmolol	61	83.31	7.29	84.00	10.00	64.00	98.00	10.430	0.00005
Combination	61	82.20	7.70	82.00	10.00	60.00	96.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combination	yes	

Table 25 shows comparison DBP at the 45 seconds after intubation among the three groups. The mean value for DBP with standard deviation 87.54 for lignocaine, 83.31 for esmolol and 82.20 for combination. This DBP is statistically significant (p value > 0.05). The difference in DBP between esmolol and combination and between lignocaine and combination is also statistically significant (p value < 0.05).

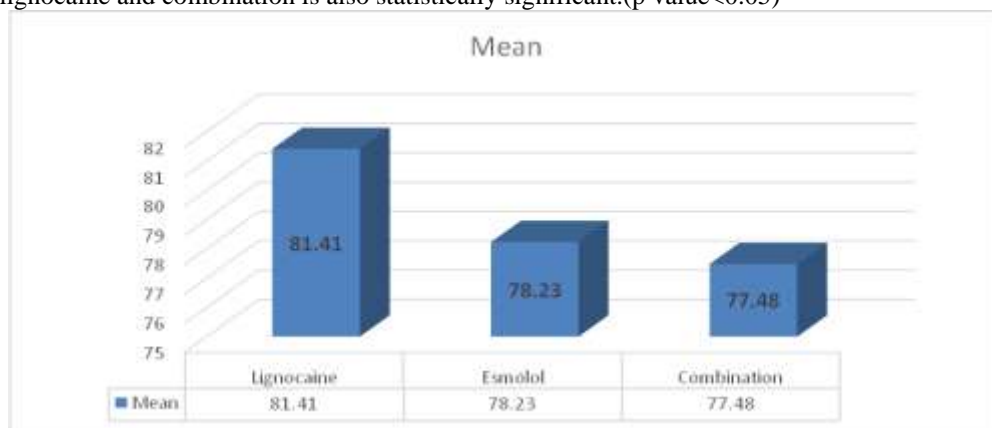


Table 26: Dbp At 1 Minutes

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA Test	
								F Value	P value
Lignocaine	61	88.26	6.45	90.00	8.00	68.00	98.00		
Esmolol	61	80.85	7.34	82.00	8.00	66.00	96.00	16.128	0.00
Combination	61	83.61	7.97	84.00	10.00	62.00	98.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	

Lignocaine VS Combination	yes
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Table 26 shows comparison DBP at the 1 minutes after intubation among the three group The mean value for DBP with standard deviation 88.26 for lignocaine ,80.85 for esmolol and 83.61 for combination . This DBP is statistically significant (p value>0.05) The difference in DBP between esmolol and combination and between lignocaine and combination is also statistically significant.(p value<0.05)

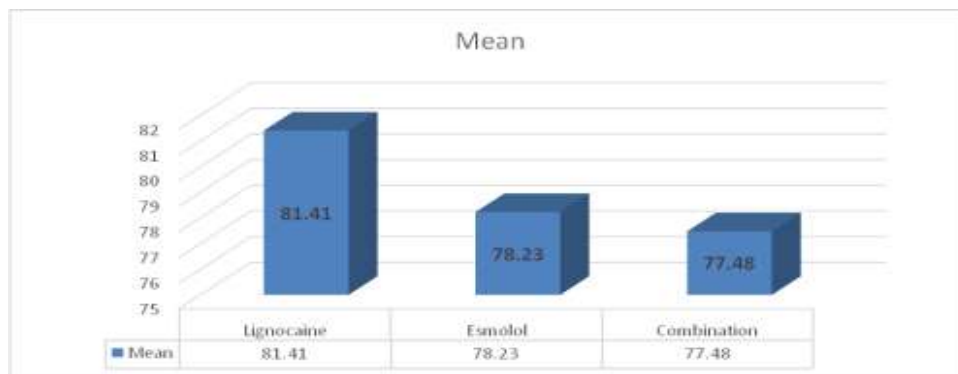


Table 27: Dbp At 2 Minutes

Group	N	Mean	Std Dev	Median	IQR	Minimum	Maximum	Oneway ANOVA Test	
Lignocaine	61	87.25	6.05	88.00	8.00	72.00	98.00	F Value	P value
Esmolol	61	80.46	7.08	80.00	8.00	66.00	98.00	15.694	0.00003
Combination	61	84.03	6.90	84.00	8.00	64.00	98.00	This Gr diff is significant	

All pair wise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Combination	Yes	
Lignocaine VS Combination	yes	
Lignocaine vs Combination	yes	

Table 27 shows comparison DBP at the 2 minutes after intubation among the three group The mean value for DBP with standard deviation 87.25 for lignocaine ,80.46 for esmolol and 84.03 for combination . This DBP is statistically significant (p value>0.05) The difference in DBP between esmolol and Lignocaine and combination and between lignocaine and combination is also statistically significant.(p value<0.05)

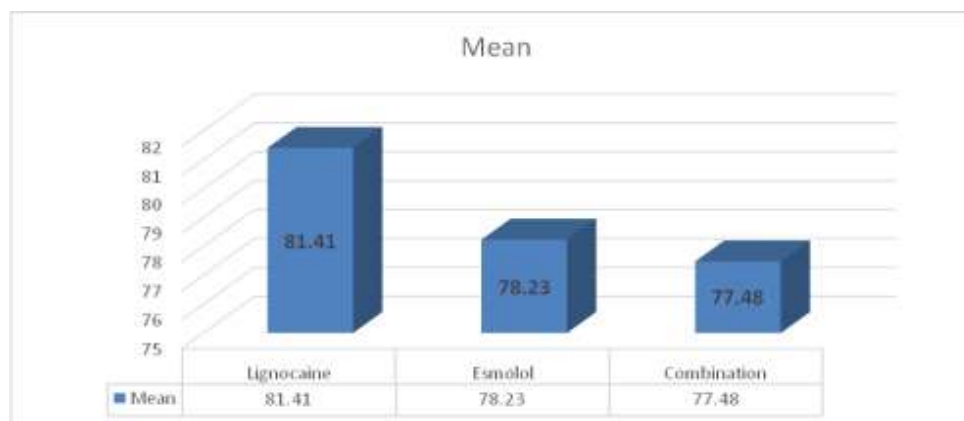


Table 28: Dbp At 5 Minutes

Group	N	Mean	Std	Med	IQR	Min	Ma	Oneway ANOVA
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			Dev	ian	Imum	Ximum	test	
Lignocaine	61	85.48	5.55	88.00	10.00	70.00	96.00	F Value
Esmolol	61	80.59	6.67	80.00	6.00	68.00	96.00	10.155
Combination	61	81.61	6.67	82.00	6.00	66.00	96.00	This Gr diff is significant

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Lignocaine	Yes	
Lignocaine VS Combinationl	yes	

Table 28 shows comparison DBP at the 5 minutes after intubation among the three group. The mean value for DBP with standard deviation 85.48 for lignocaine, 80.59 for esmolol and 81.61 for combination. This DBP is statistically significant (p value>0.05). The difference in DBP between esmolol and Lignocaine and combination and between lignocaine and combination is also statistically significant.(p value<0.05)

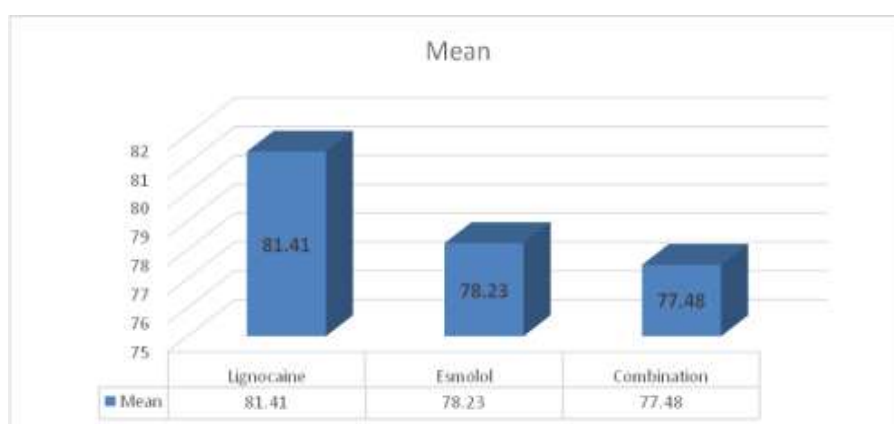


Table 29: Dbp At 10 Minutes

Group	mean	N	Mean	Std Dev	Median	IQR	Min	Maximum	Oneway ANOVA test	
Lignocaine	83.25	61	83.25	5.33	86.00	10.00	72.30	90.00	F Value	P value
Esmolol	79.67	61	79.67	6.28	78.00	6.00	70.00	94.00	7.962	0.00048
Combination	79.41	61	79.41	6.14	78.00	6.00	66.00	94.00	This Gr diff is significant	

All pairwise Multiple Comparison Procedures (Holm-Sidak Method)		
Comparison	P<0.050	This Gr diff is significant
Esmolol vs Lignocaine	Yes	
Lignocaine VS Combinationl	yes	

Table 29 shows comparison DBP at the 10 minutes after intubation among the three group. The mean value for DBP with standard deviation 83.25 for lignocaine, 79.67 for esmolol and 79.41 for combination. This DBP is statistically significant (p value>0.05). The difference in DBP between esmolol and Lignocaine and between lignocaine and combination is also statistically significant.(p value<0.05)

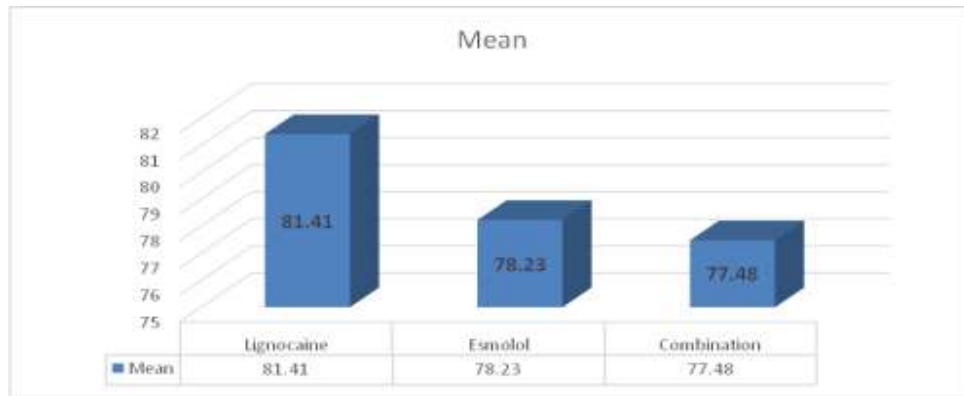
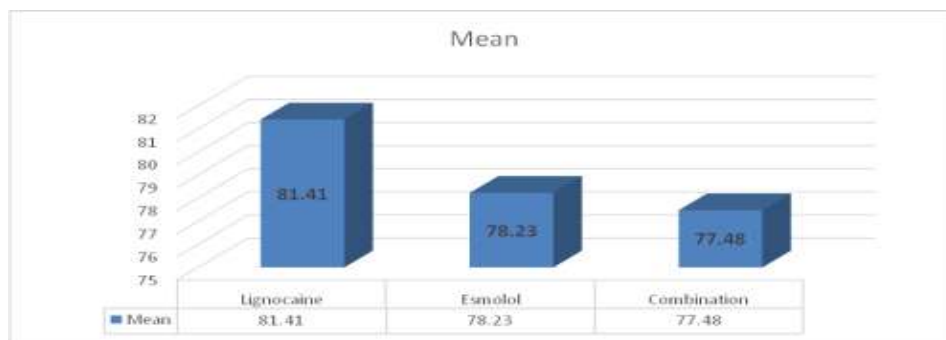


Table 30: Dbp At 15 Minutes

Group	N	Mean	Std Dev	Median	IQR	Min	Max	Oneway ANOVA test	
								F Value	P value
Lignocaine	61	81.41	4.97	82.00	6.00	70.00	90.00	9.361	0.00013
Esmolol	61	78.23	5.39	78.00	8.00	70.00	90.00	This Gr diff is significant	
Combination	61	77.48	5.61	78.00	6.00	64.00	90.00		

Table30 shows comparison DBP at the 15 minutes after intubation among the three group The mean value for DBP with standred deviation 81.41 for lignocaine ,78.23 for esmolol and 77.43 for combination . This DBP is statistically significant (p value>0.05) The difference in DBP between esmolol and Lignocaine and and between lignocaine and combination is also statistically significant.(p value<0.05)

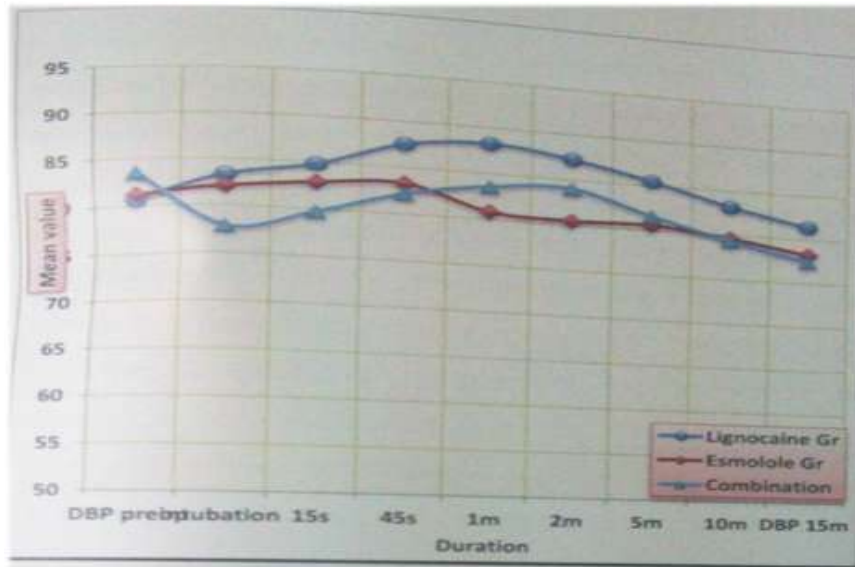


Graph 31:

Graph 31 shows the heart rate at different duration among the three groups

Graph 32:

Graph 33



VI. Discussion

A hemodynamic response of increased HR and BP to manipulation in the area of the larynx, by means of laryngoscopy and intubation, has been well recognized for 60 years. Stimulation of mechanoreceptors in the pharyngeal wall, epiglottis, and vocal cords is thought to be the cause for the haemodynamic response. The receptors are abundant over arytenoid cartilage, vocal cords, epiglottis and hypopharynx. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals, but either one or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases. The transient changes can result in potentially deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia and cerebral hemorrhage [7,30].

Intubation is associated with a cardiovascular response of elevated blood pressure and pulse, occasional dysrhythmias, cough reflexes, increased intracranial pressure, and increased intraocular pressure. If no specific measures are taken to prevent haemodynamic response, the HR can increase from 26%-66% depending on the method of induction [44,45] and SBP can increase from 36%-45% [44,45]. In patients with atherosclerotic heart disease, intracranial lesions, and potential penetrating eye injuries, these responses to intubation are of greater risk. About half the patients with coronary artery disease experience episodes of myocardial ischemia during intubation when no specific prevention is undertaken. Adversity of results exist about protective measures against haemodynamic and catecholamine responses to laryngoscopy and intubation, but no single anaesthetic technique has become generally accepted as being effective in preventing or attenuating these responses [19]. Many techniques have been recommended. The drugs used were either partially effective or had other undesirable effects on the patients [43].

Topical application of local anaesthetics, infiltration or nerve blocks [48], B-blockers, calcium channel blockers, droperidol, Clonidine, sodium nitroprusside, lignocaine, fentanyl etc. are now used. No single drug or technique is satisfactory.

In a study conducted criteria for selection of appropriate drug to prevent sympathetic response were noted. The drug must be applicable regardless of patient collaboration, prevent impairment cerebral blood flow and avoid arousal of the patient. It should neither be time consuming nor affect the duration or modality of the ensuing anaesthesia. Intravenous lignocaine and esmolol appear to best fulfill the above criteria. Various studies have reviewed the effect of lignocaine to blunt these responses. It is tried in various forms like viscous Lignocaine, aerosol, or laryngeal spray before the induction of anaesthesia and inhalation of lignocaine prior to induction of anaesthesia.

Some studies note a response of intravenous lignocaine in blunting rises in pulse, blood pressure, intracranial and intraocular pressure. Yukioka et al [17] showed that cough reflex was suppressed completely by IV lignocaine and also minimizes blood pressure fluctuations after tracheal intubation. Abou-Madi et al [13] have discussed the possible mechanisms to account for these observations with IV lignocaine. These include a direct myocardial depressant effect, a peripheral vasodilation effect and finally an effect on synaptic transmission.

Lev & Rosen [47] wrote a review on "Prophylactic lidocaine use Preintubation". They said that a dose of prophylactic lidocaine of 1.5 mg/kg given intravenously 3 minutes before intubation is optimal. No studies document any harmful effects of Prophylactic lidocaine given preintubation. Recent studies, however, have questioned lignocaine's efficacy. In Singh et al's [47] study IV Lignocaine 1.5mg/kg was ineffective in controlling the acute haemodynamic response following laryngoscopy and intubation. So the need for a better alternative

was initialized. A number of studies on the cardiovascular response to Laryngoscopy and ETI show that adequate depth of anaesthesia and quick smooth laryngoscopy is the mainstay for blunting this response. Ebert et al 17 did a comparative study of attenuation by esmolol (500 mcg/kg/min X 6 minutes, followed by 300mcg/kg/min X 9 minutes), or fentanyl (0.8 mcg/kg/min X 10minutes) Fentanyl decreased the SBP MAP and DBP significantly below the baseline, while these pressures were either retained at or elevated slightly above control in the esmolol group. In these doses, the HR response to laryngoscopy was more effectively blocked by fentanyl, while esmolol better retained perfusion pressure. There were no complications or ischaemic electrocardiographic changes in any patient.

Feng et al 48 found 75% and 45% incidence of tachycardia and 70% and 40% incidence of hypertension with lignocaine (2mg/kg) and fentanyl (3mcg/kg) respectively. However, their definition of tachycardia was HR > 100 per minute. Secondly they intubated their patients 3 minutes after the study drug administration.

Beta-blockers with bradycardiac antihypertensive antiarrhythmia and antiischaemic properties have been advocated. As opposed to lignocaine, these agents are more effective in preventing the changes in heart rate than the pressor response 47. Because of their depressor effect on the myocardium, their place still remains to be defined, especially in the cardiac risk patient.

Previous studies have shown that unique pharmacokinetic behaviour of esmolol makes it well suited for controlling the cardiovascular response to tracheal intubation and laryngoscopy when used as a continuous infusion technique 25. A simple alternative is using bolus doses of esmolol and many studies have investigated this and concluded it to be efficacious in attenuating the cardiovascular response to laryngoscopy and tracheal intubation 49. In studies conducted before, 2mg/kg IV bolus esmolol injected prior to induction has been effective in attenuating cardiovascular response to laryngoscopy and intubation. Optimal time of administration is 3 minutes before laryngoscopy and intubation 24. Esmolol also prevented the Bispectral index during induction of anaesthesia and orotracheal intubation.

Christoph h. Kindler et al 55 found patients receiving iv lignocaine 1.5 mg/kg show statistically nonsignificant increase in heart rate. Esmolol both 1 mg/kg and 2 mg/kg has significant effect on the heart rate. Combination of esmolol and lignocaine has the highest effect in attenuating the heart rate response to intubation, Anila D, Lalde et al 56 found fentanyl 2 mcg/kg causes significantly lesser rise (5.46%) in heart rate compared to lignocaine (16.23%), The rise in heart rate persisted for 2, 5 and 10 minutes both fentanyl and lignocaine group. Christoph h. Kindler et al 55 found patients receiving iv lignocaine 1.5 mg/kg show no significant control on rise of SBP as compared to placebo. Esmolol both 1mg/kg and 2mg/kg do not differ statistically from placebo group. Combination group has a significant lower rise in SBP at 1, 2 and 5 minutes. In our study the rise in heart rate was highest in lignocaine group maximum at 1min after intubation (12-5%) from base line as compared to esmolol and combination group. Heart rate increased maximum till 10 minutes and then came near the baseline at the end of fifteen minutes. Esmolol group also showed significant attenuation of heart rate response to intubation ($p < 0.05$). The maximum increase in heart rate was at 45 seconds after intubation (7.8%). Heart rate increased till 1 minute after intubation and neared baseline by 5 minutes and then decreased by 10 minutes. Combination group was found to significantly attenuate the response ($p < 0.05$), there was a decrease in heart rate just after giving the drug (5.4% at intubation), Maximum increase in heart rate was at 2min after intubation (4.1%). Heart rate neared baseline by 5 minutes and then decreased at 10 minutes after intubation. SBP increased maximum in lignocaine group maximum at 1 minute after intubation (7.9%) as compared to baseline values. A decrease at 15 minutes. Esmolol group significantly attenuated the rise in SBP ($p < 0.05$). Maximum increase in SBP was at 45 seconds (2.05%) after which it decreased till 15 minutes. Combination group showed maximum attenuation in rise of SBP ($p < 0.05$). There was initial decrease in SBP (6.5%) and maximum increase was at 1 minute after which it again decreased till 15 minutes.

DBP increased maximum in lignocaine group maximum at 1 minute after intubation (9.4%) as compared to baseline values. DBP reached near baseline by 15 minutes. Esmolol group significantly attenuated the rise in DBP ($p < 0.05$). Maximum increase in DBP was at 45 seconds (2.5%) after which it decreased till 15 minutes. Combination group showed maximum attenuation in rise of DBP ($p < 0.05$). There was initial decrease in DBP (6.7%) and maximum increase was at 1 minute (0.6%) after which it again decreased till 15 minutes. In the combination group the significant attenuation of the Cardiovascular response can be attributed to the initial decrease in heart rate, SBP and DBP.

None of the group had any arrhythmia in the ecg. There were two instances of bradycardia with HR 48 (3.2%) in the combination group and one episode of hypotension with BP 84/56 (1.1%) which is not statistically significant.

VII. Conclusion

From the present study it can be concluded that

1. The cardiovascular reactions persist for about few minutes after which they return towards baseline values.

2. Combination was found to be more effective than individual Esmolol or lignocaine in attenuating the sympathetic response to laryngoscopy and endotracheal intubation.
3. Esmolol significantly attenuates the sympathetic response.
4. Lignocaine marginally reduces the sympathetic response to laryngoscopy and intubation in comparison to esmolol and Combination.
5. All the three groups were found to be safe to administer.

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