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Original Research Article

Attenuation of Haemodynamic Stress Response to Laryngoscopy and Intubation with two Doses of Esmolol Hydrochloride

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ABSTRACT
Direct laryngoscopy and endotracheal intubation is associated with reflex cardiovascular responses mediated by the sympathetic nervous system. Various drugs have been used to attenuate these haemodynamic responses. Esmolol, an ultra short acting β blocker with rapid onset of action is suitable for attenuation of hemodynamic response to laryngoscopy and intubation. A prospective observational study was done with 3 groups of 30 patients each presenting for elective surgery. For attenuation of stress response to intubation, Group A received no drug, Group B received intravenous esmolol 1mg/kg, 1 minute before induction and Group C received intravenous esmolol 2mg/kg 1minute before induction. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were recorded before induction,1minute, 3minute, 5minute, 7minute and 10 minute intervals after induction. It was found that there is a significant hemodynamic response to laryngoscopy and intubation in those who did not receive any drug for hemodynamic response attenuation. Esmolol in a bolus dose of 1mg/kg(B) and 2mg/kg(C) given 1minute before induction effectively attenuated the hemodynamic response to laryngoscopy and intubation. Group C was often associated with systolic blood pressure lesser than the pre-induction values. Esmolol in a bolus dose of 1mg/kg given 1minute before induction is therefore the recommended dose for attenuation of hemodynamic response to laryngoscopy and intubation.
Keywords: *Laryngoscopy, Stress response, Esmolol.*

INTRODUCTION

Of all general anaesthetic techniques of present day, the most popular one is endotracheal intubation after giving inducing agents and muscle relaxant. This technique was first introduced by Sir William Macewan, a Scottish surgeon in 1880. Kirstein used laryngoscope for this purpose in 1895. In man, this method of endotracheal intubation produces reflex cardiovascular responses – tachycardia, hypertension, an increase in cardiac output and a transient rise in central venous pressure. These reflex responses are mediated by increased sympathetic nervous system activity. Later this was confirmed by catecholamine level assays. Even though these transient haemodynamic responses were of little significance to normal healthy patients, this could be life threatening to certain patients; especially

hypertensive patients with impending cardiac failure, patients with ischaemic heart disease, aortic or cerebral aneurysm or raised intra cranial pressures.

Various attempts were made to attenuate these haemodynamic responses to intubation. The agents used include lignocaine, opioids, calcium channel blockers, inhalational agents, nitroglycerine, captopril, adenosine, magnesium sulphate, gabapentin, labetalol and β blockers. β adrenergic blockers are among the most desirable agents to attenuate cardiac responses to laryngeal stimulation. Of the various β adrenergic blockers, esmolol is an attractive option due to its β_1 (cardioselective) blocking properties and its ultra-short duration of action. It has been used for attenuating the pressor response to laryngoscopy and intubation using different bolus and infusion dosage schedules. This study was devised to assess the efficacy of single bolus dose of esmolol in attenuating the pressor response and to compare the efficacy of two different bolus doses of esmolol for the same.

OBJECTIVES

- To assess the efficacy of Esmolol in controlling the pressor response to laryngoscopy and intubation.
- To compare the efficacy of two different bolus doses of esmolol [1mg/kg and 2mg/kg] in controlling the pressor response to laryngoscopy and intubation.

MATERIAL AND METHODS

A prospective observational study involving ninety patients was done in tertiary care teaching hospital after approval by ethics committee of the institution.

Inclusion criteria: a) Age group between 20-40 years b) ASA Grade 1& 2 and normotensive c) Elective surgery only.

Exclusion criteria: a) ASA Grade more than 2 b)Any cardiovascular disease c) Anticipated difficult intubation d) Patients on drugs which may interfere with the study.

Written informed consent was taken from all patients.

The patients were randomly divided into three groups of 30 patients each.

- Group A - received 15ml 5% dextrose and served as control.
- Group B- received i.v. Esmolol hydro-chloride 1mg/kg in 15ml 5% dextrose.
- Group C- received i.v. Esmolol hydro-chloride 2mg/kg in 15ml 5% dextrose.

All patients received premedication of injection Pethidine 1mg/kg intramuscularly and Ondansetron 4mg i.v forty-five minutes before induction. Pulse rate and blood pressure of all the patients were recorded at this time.

For all patients, an intravenous line was established on the forearm with an 18 gauge cannula and Ringer lactate was started at 16 drops per minute. Blood pressure cuff was fixed on the upper arm. ECG leads were attached to all the patients prior to induction and the heart rate and blood pressure were noted. Induction technique was similar for all the groups. All patients received midazolam 0.02mg/kg and glycopyrrolate 0.004mg/kg intravenously 2 minutes before induction. All patients were preoxygenated for three minutes. Induction was with 1-2mg/kg of propofol, followed by 1.5mg/kg of succinyl choline and the patient was ventilated with 100% oxygen. Laryngoscopy was performed with a Macintosh curved blade laryngoscope. The patients were intubated with appropriate sized endotracheal tubes within 15 seconds of laryngoscopy. All the intubations were done by the same person. Patients were then ventilated manually with nitrous oxide and oxygen.

Heart rate and blood pressure (systolic and diastolic) were recorded at 1 minute, 3 minutes (during laryngoscopy and intubation), 5 minutes, 7 minutes & 10 minutes after induction. Blood pressure (systolic and diastolic) and heart rate was recorded from the monitor. Mean arterial pressure and rate pressure product were calculated. Presence of any arrhythmias was also noted. During these ten minutes of monitoring, patients

were not manipulated or subjected to any surgical stimulation. All the patients were given 0.1mg/kg of vecuronium bromide & intermittent positive pressure ventilation was continued throughout the surgery. After the initial 10 minutes, anaesthesia was maintained with maintenance doses of vecuronium, volatile agents & analgesics as needed. Blood pressure and heart rate were recorded every 15 minutes. At the end of surgery, patients were reversed with 0.05 mg/ kg of neostigmine & 0.02 mg/kg of atropine. Adequate recovery was ensured in the recovery room & patients were transferred to the post-operative ward.

Method of attenuating the pressor response

- Group A: Received no drug for attenuating pressor response, but only 15ml 5% dextrose slow i.v. over 15-20 seconds 1 minute before induction.
- Group B: Received 1mg/kg of esmolol hydrochloride in 15ml 5% dextrose slow i.v. over 15-20 seconds 1 minute before induction.
- Group C: Received 2 mg/kg of esmolol hydrochloride in 15ml 5% dextrose slow i.v. over 15-20 seconds 1 minute before induction.

OBSERVATIONS AND RESULTS

Age distribution in the study population

Table 1.

Age (years)	Group A	Group B	Group C
20 – 24	9 30.00%	10 33.30%	11 36.70%
25 – 29	7 23.30%	12 40.00%	5 16.70%
30 – 34	5 16.70%	3 10.00%	10 33.30%
≥ 35	9 30.00%	5 16.70%	4 13.30%

Chi square: 10.117; p >0.05

Gender distribution in the study population

Table 2

Gender	Group A	Group B	Group C
Male	12 40.00%	16 53.30%	14 46.70%
Female	18 60.00%	14 46.70%	16 53.30%

Chi square: 1.071; p >0.05

Analysis of variance (One Way ANOVA) of heart rate at different observations comparing three groups

Table 3

Heart rate	Group	Mean	± SD	F value	p value
Before Induction	A	78.53[a]	9.58	11.637	< 0.001
	B	88.70[b]	11.44		
	C	93.77[b]	15.59		
1 min after Induction	A	85.40[b]	9.02	3.374	< 0.05
	B	79.07[a]	10.05		
	C	79.17[a]	12.99		
3 min after Induction	A	106.43[b]	8.01	44.722	< 0.001
	B	83.70[a]	12.22		
	C	81.53[a]	13.02		
5 min after Induction	A	103.43[b]	8.88	22.4	< 0.001
	B	85.93[a]	12.84		
	C	85.37[a]	13.42		
7 min after Induction	A	95.13[b]	8.70	6.536	< 0.01
	B	85.43[a]	11.36		
	C	87.63[a]	12.30		
10 min after Induction	A	91.17[b]	7.76	2.948	> 0.05
	B	84.70[a]	11.27		
	C	88.53[ab]	11.64		

(a, b, c – Means with same superscript do not differ each other – Duncan's Multiple Range Test)

Chart 3

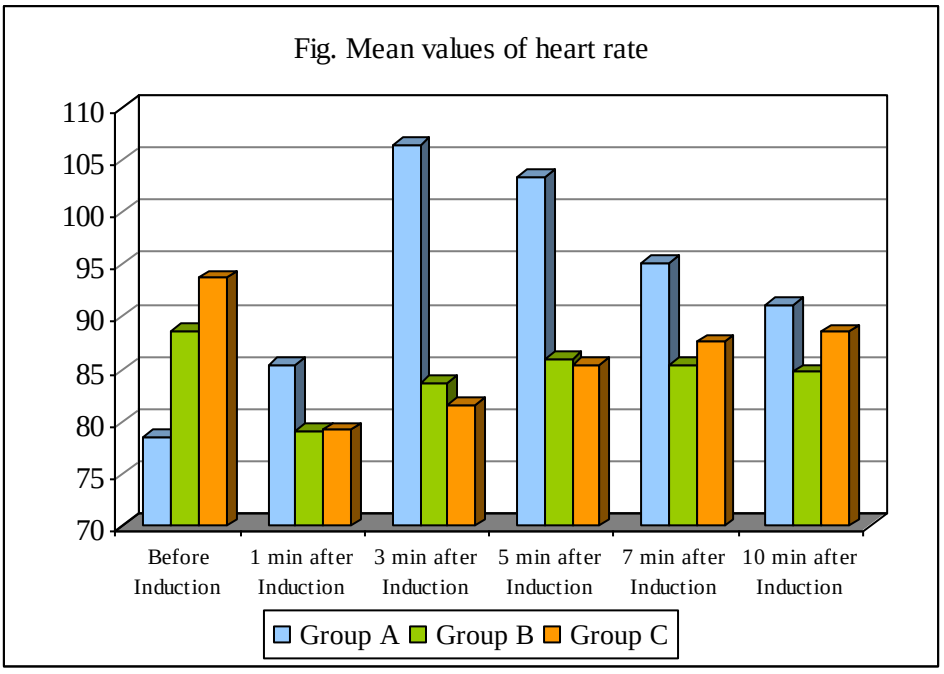
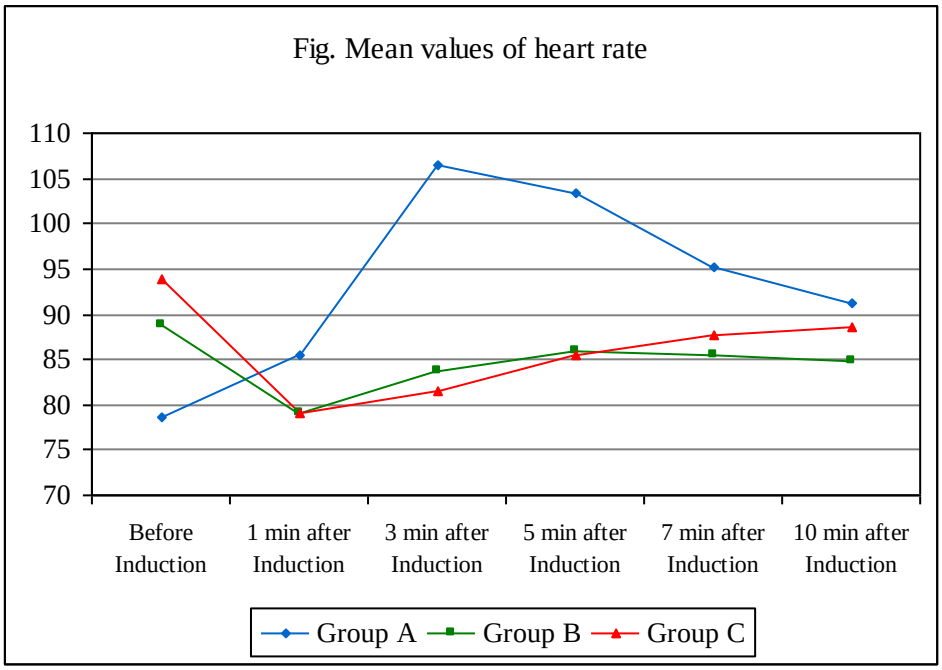


Chart 4



Analysis of variance (One Way ANOVA) of systolic BP at different observations comparing three groups

Table 4

Systolic BP	Group	Mean	± SD	F value	p value
Before Induction	A	120.57[a]	9.33	0.319	> 0.05
	B	122.20[a]	8.69		
	C	122.17[a]	9.12		
1 min after Induction	A	114.40[a]	10.58	1.497	> 0.05
	B	116.63[a]	8.40		
	C	112.13[a]	11.04		
3 min after Induction	A	140.47[c]	12.68	42.348	< 0.001
	B	120.40[b]	11.20		
	C	114.23[a]	10.66		
5 min after Induction	A	134.77[c]	10.80	25.377	< 0.001
	B	123.53[b]	7.82		
	C	117.33[a]	9.96		
7 min after Induction	A	128.07[b]	10.26	3.081	> 0.05
	B	122.27[a]	11.74		
	C	121.60[a]	11.24		
10 min after Induction	A	124.00[a]	8.76	0.013	> 0.05
	B	123.60[a]	12.46		
	C	123.97[a]	10.53		

(a, b, c – Means with same superscript do not differ each other – Duncan's Multiple Range Test)

Chart 5

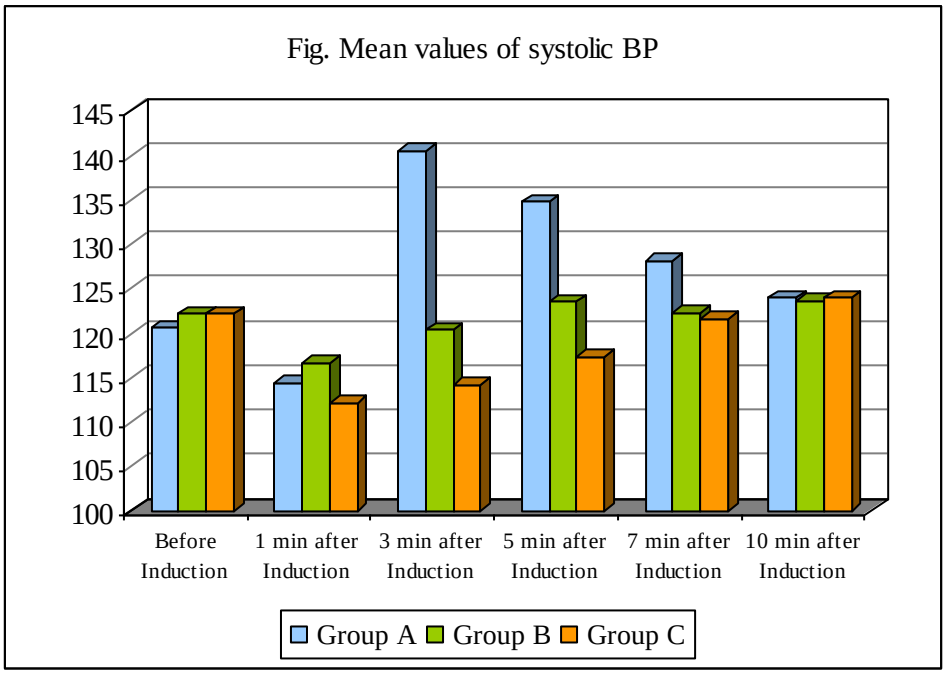
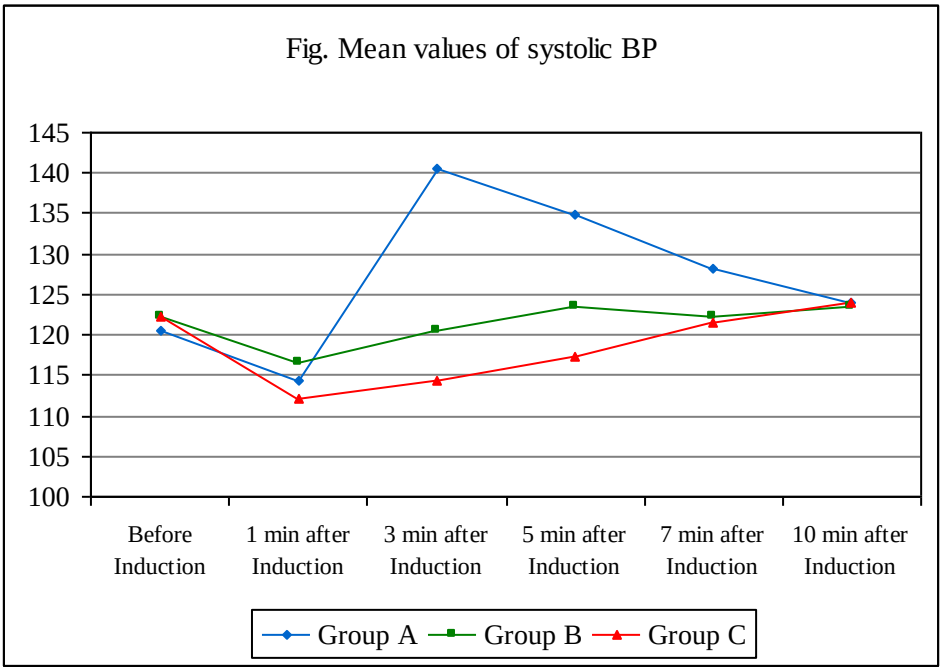


Chart 6



Analysis of variance (One Way ANOVA) of diastolic BP at different observations comparing three groups

Table 5

Diastolic BP	Group	Mean	± SD	F value	p value
Before Induction	A	76.30[a]	5.80	2.08	> 0.05
	B	74.67[a]	6.78		
	C	78.03[a]	6.56		
1 min after Induction	A	73.67[a]	5.37	0.755	> 0.05
	B	71.80[a]	6.45		
	C	73.50[a]	7.54		
3 min after Induction	A	92.93[b]	8.37	45.865	< 0.001
	B	76.43[a]	7.94		
	C	75.80[a]	7.22		
5 min after Induction	A	88.17[b]	7.80	23.111	< 0.001
	B	76.97[a]	7.65		
	C	76.10[a]	7.55		
7 min after Induction	A	84.50[b]	7.92	8.187	< 0.01
	B	76.17[a]	10.55		
	C	76.93[a]	7.69		
10 min after Induction	A	81.53[b]	5.98	2.982	> 0.05
	B	76.57[a]	10.51		
	C	78.33[ab]	6.71		

(a, b, c – Means with same superscript do not differ each other – Duncan's Multiple Range Test)

Chart 7

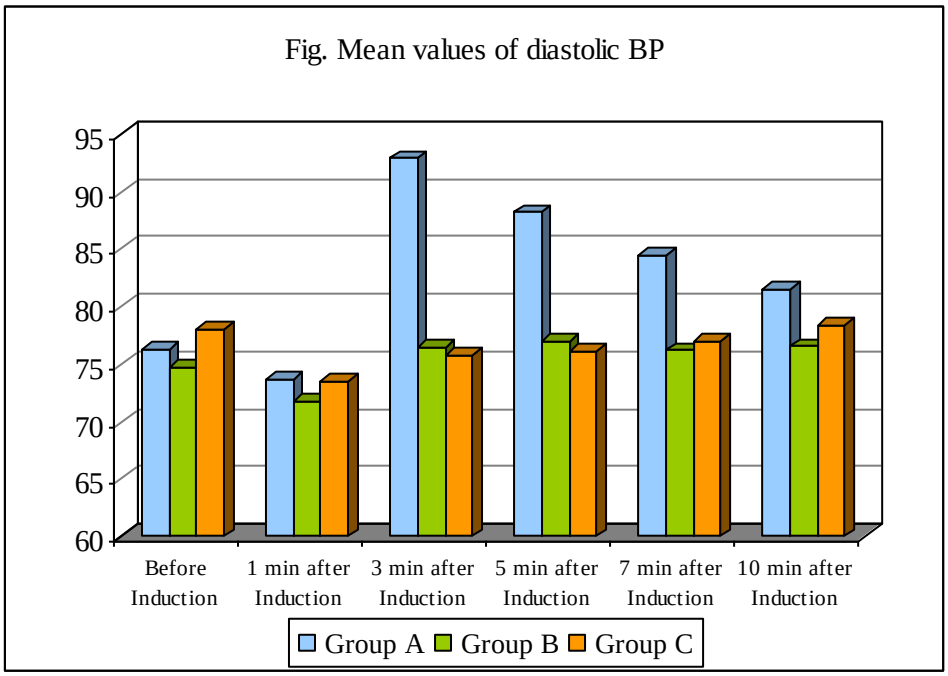
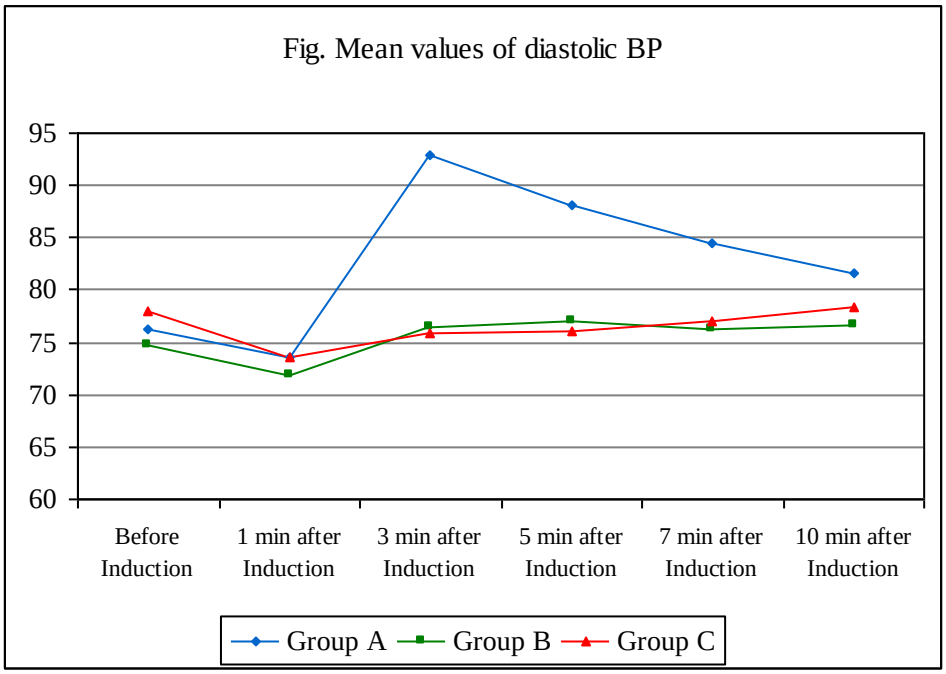


Chart 8



Analysis of variance (One Way ANOVA) of MAP at different observations comparing three groups

Table 6

Mean Arterial Pressure	Group	Mean	± SD	F value	p value
Before Induction	A	91.06[a]	6.56	0.884	> 0.05
	B	90.51[a]	6.75		
	C	92.75[a]	7.05		
1 min after Induction	A	87.24[a]	6.14	0.115	> 0.05
	B	86.75[a]	6.48		
	C	86.38[a]	8.22		
3 min after Induction	A	108.78[b]	8.89	52.104	< 0.001
	B	91.09[a]	8.25		
	C	88.61[a]	7.86		
5 min after Induction	A	103.70[b]	8.32	26.321	< 0.001
	B	92.49[a]	7.17		
	C	89.84[a]	8.02		
7 min after Induction	A	99.02[b]	8.27	6.413	< 0.01
	B	91.53[a]	10.55		
	C	91.82[a]	8.53		
10 min after Induction	A	95.69[a]	6.29	1.279	> 0.05
	B	92.24[a]	10.84		
	C	93.54[a]	7.47		

(a, b, c – Means with same superscript do not differ each other – Duncan's Multiple Range Test)

Chart 9

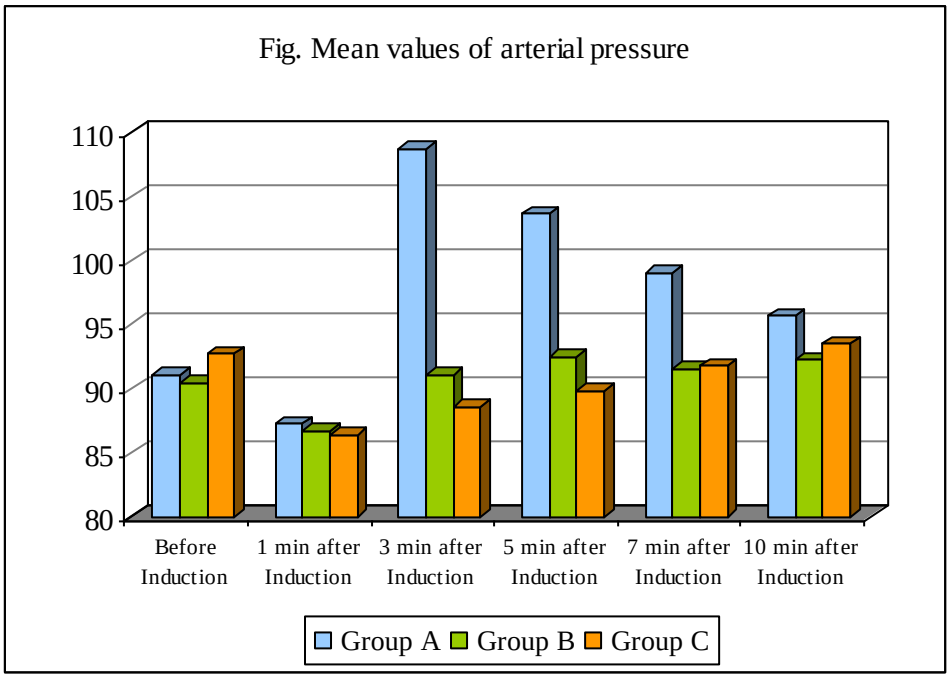
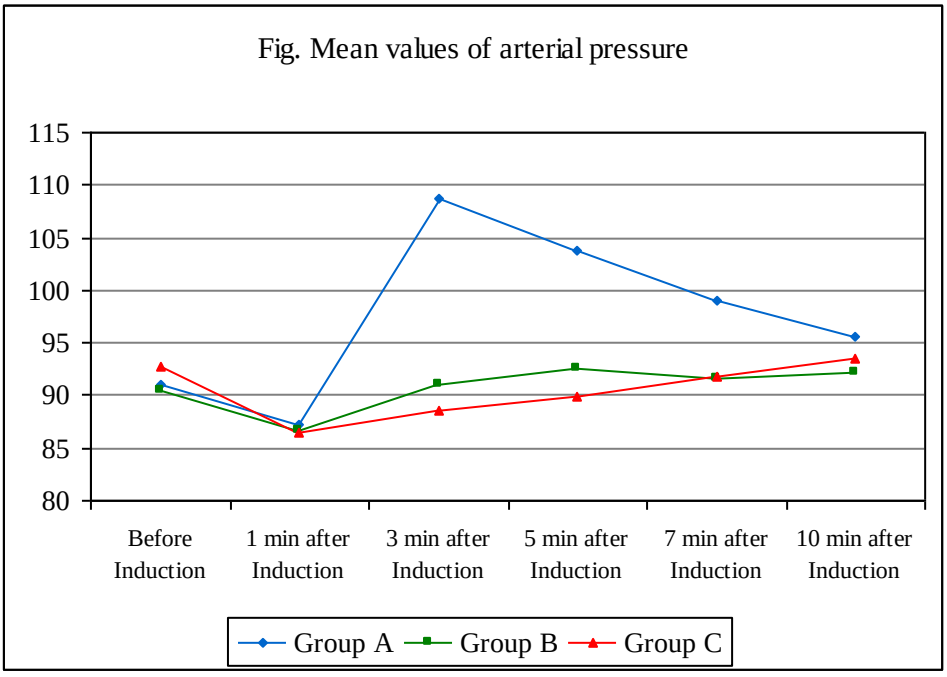


Chart 10



Analysis of variance (One Way ANOVA) of RPP at different observations comparing three groups

Table 7

Rate Pressure Product	Group	Mean	± SD	F value	p value
Before Induction	A	9502.97[a]	1631.45	9.326	< 0.001
	B	10840.13[b]	1594.29		
	C	11471.33[b]	2131.83		
1 min after Induction	A	9764.17[b]	1341.48	3.066	> 0.05
	B	9211.17[ab]	1298.50		
	C	8863.50[a]	1603.52		
3 min after Induction	A	14953.47[b]	1805.77	101.031	< 0.001
	B	10070.53[a]	1712.26		
	C	9282.33[a]	1488.16		
5 min after Induction	A	13960.73[b]	1824.29	49.31	< 0.001
	B	10605.93[a]	1636.46		
	C	9981.67[a]	1533.78		
7 min after Induction	A	12182.57[b]	1518.10	12.302	< 0.001
	B	10411.70[a]	1423.15		
	C	10627.30[a]	1581.12		
10 min after Induction	A	11287.87[b]	1099.96	2.454	> 0.05
	B	10460.43[a]	1594.09		
	C	10962.67[ab]	1619.22		

(a, b, c – Means with same superscript do not differ each other – Duncan's Multiple Range Test)

Chart 11

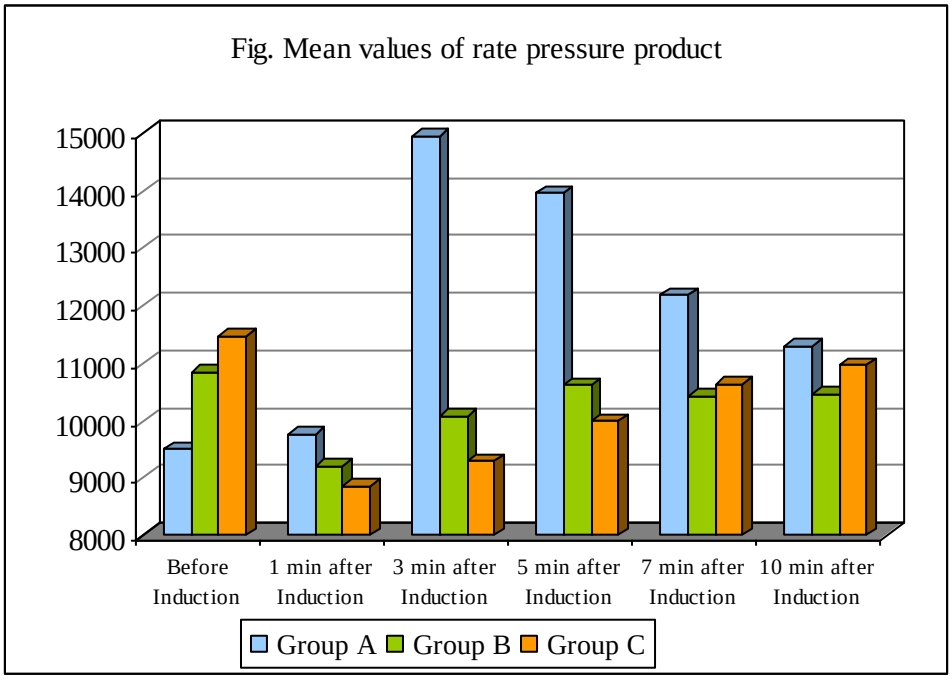
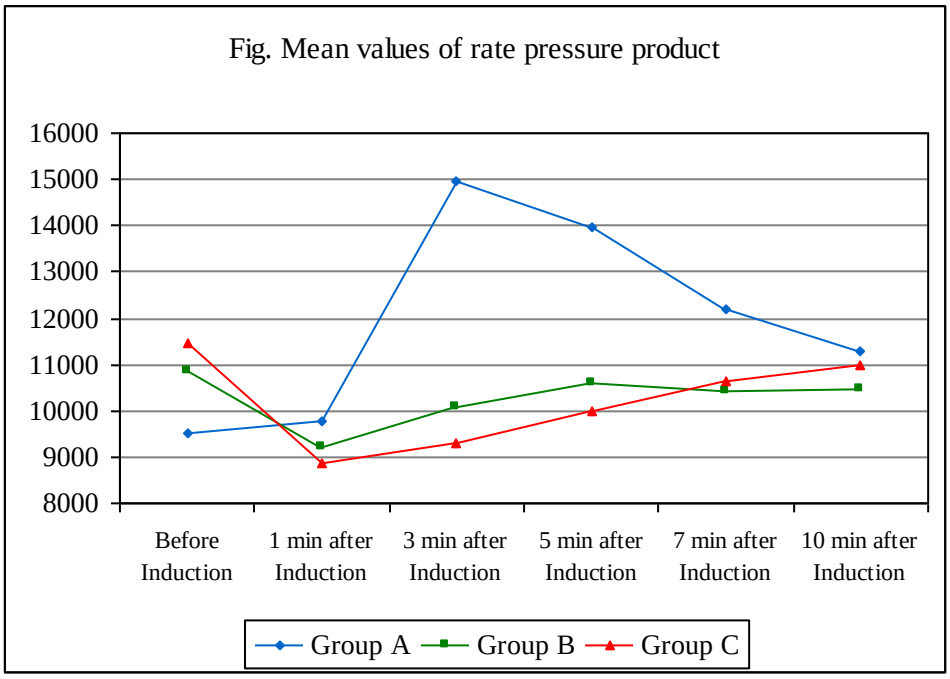


Chart 12



Comparison of different parameters of Group A at different observations with observation before induction

Table 8

Group A

Parameter	Observations	Mean	± SD	t value	p value
Heart Rate	Before Induction	78.53	9.58	-5.083	< 0.001
	1 min after Induction	85.40	9.02		
	Before Induction	78.53	9.58	-20.659	< 0.001
	3 min after Induction	106.43	8.01		
	Before Induction	78.53	9.58	-20.073	< 0.001
	5 min after Induction	103.43	8.88		
	Before Induction	78.53	9.58	-11.802	< 0.001
	7 min after Induction	95.13	8.70		
	Before Induction	78.53	9.58	-9.307	< 0.001
	10 min after Induction	91.17	7.76		
Systolic BP	Before Induction	120.57	9.33	6.26	< 0.001
	1 min after Induction	114.40	10.58		
	Before Induction	120.57	9.33	-15.182	< 0.001
	3 min after Induction	140.47	12.68		
	Before Induction	120.57	9.33	-10.629	< 0.001
	5 min after Induction	134.77	10.80		
	Before Induction	120.57	9.33	-5.341	< 0.001
	7 min after Induction	128.07	10.26		
	Before Induction	120.57	9.33	-3.226	< 0.01
	10 min after Induction	124.00	8.76		
Diastolic BP	Before Induction	76.30	5.80	2.981	< 0.01

1 min after Induction	73.67	5.37		
Before Induction	76.30	5.80	-14.098	< 0.001
3 min after Induction	92.93	8.37		
Before Induction	76.30	5.80	-11.870	< 0.001
5 min after Induction	88.17	7.80		
Before Induction	76.30	5.80	-7.869	< 0.001
7 min after Induction	84.50	7.92		
Before Induction	76.30	5.80	-6.458	< 0.001
10 min after Induction	81.53	5.98		

Comparison of different parameters of Group A at different observations with observation before induction

Table 9.

Parameter	Observations	Mean	± SD	t value	p value
Mean Arterial Pressure	Before Induction	91.06	6.56	4.631	< 0.001
	1 min after Induction	87.24	6.14		
	Before Induction	91.06	6.56	-17.745	< 0.001
	3 min after Induction	108.78	8.89		
	Before Induction	91.06	6.56	-13.421	< 0.001
	5 min after Induction	103.70	8.32		
	Before Induction	91.06	6.56	-7.820	< 0.001
	7 min after Induction	99.02	8.27		
	Before Induction	91.06	6.56	-6.816	< 0.001
	10 min after Induction	95.69	6.29		
Rate Pressure Product	Before Induction	9502.97	1631.45	-1.617	> 0.05
	1 min after Induction	9764.17	1341.48		
	Before Induction	9502.97	1631.45	-23.239	< 0.001
	3 min after Induction	14953.47	1805.77		
	Before Induction	9502.97	1631.45	-19.162	< 0.001
	5 min after Induction	13960.73	1824.29		
	Before Induction	9502.97	1631.45	-11.220	< 0.001
	7 min after Induction	12182.57	1518.10		
	Before Induction	9502.97	1631.45	-9.090	< 0.001
	10 min after Induction	11287.87	1099.96		

Comparison of different parameters of Group B at different observations with observation before induction

Table 10

Group B

Parameter	Observations	Mean	± SD	t value	p value
Heart Rate	Before Induction	88.70	11.44	6.541	< 0.001
	1 min after Induction	79.07	10.05		
	Before Induction	88.70	11.44	2.225	< 0.05
	3 min after Induction	83.70	12.22		
	Before Induction	88.70	11.44	1.375	> 0.05
	5 min after Induction	85.93	12.84		
	Before Induction	88.70	11.44	2.532	< 0.05
	7 min after Induction	85.43	11.36		
	Before Induction	88.70	11.44	3.252	< 0.01
	10 min after Induction	84.70	11.27		
Systolic BP	Before Induction	122.20	8.69	6.524	< 0.001
	1 min after Induction	116.63	8.40		
	Before Induction	122.20	8.69	1.151	> 0.05
	3 min after Induction	120.40	11.20		
	Before Induction	122.20	8.69	-1.106	> 0.05
	5 min after Induction	123.53	7.82		
	Before Induction	122.20	8.69	-0.044	> 0.05
	7 min after Induction	122.27	11.74		
	Before Induction	122.20	8.69	-0.840	> 0.05
	10 min after Induction	123.60	12.46		
Diastolic BP	Before Induction	74.67	6.78	4.687	< 0.001
	1 min after Induction	71.80	6.45		
	Before Induction	74.67	6.78	-1.212	> 0.05
	3 min after Induction	76.43	7.94		
	Before Induction	74.67	6.78	-2.597	< 0.05
	5 min after Induction	76.97	7.65		
	Before Induction	74.67	6.78	-1.144	> 0.05
	7 min after Induction	76.17	10.55		
	Before Induction	74.67	6.78	-1.355	> 0.05
	10 min after Induction	76.57	10.51		

Comparison of different parameters of Group B at different observations with observation before induction

Table 11

Parameter	Observations	Mean	± SD	t value	P value
Mean Arterial Pressure	Before Induction	90.51	6.75	6.425	< 0.001
	1 min after Induction	86.75	6.48		
	Before Induction	90.51	6.75	-0.408	> 0.05
	3 min after Induction	91.09	8.25		
	Before Induction	90.51	6.75	-2.270	< 0.05
	5 min after Induction	92.49	7.17		
	Before Induction	90.51	6.75	-0.807	> 0.05
	7 min after Induction	91.53	10.55		
	Before Induction	90.51	6.75	-1.245	> 0.05
	10 min after Induction	92.24	10.84		
Rate Pressure Product	Before Induction	10840.13	1594.29	7.804	< 0.001
	1 min after Induction	9211.17	1298.50		
	Before Induction	10840.13	1594.29	2.065	< 0.05
	3 min after Induction	10070.53	1712.26		
	Before Induction	10840.13	1594.29	0.753	> 0.05
	5 min after Induction	10605.93	1636.46		
	Before Induction	10840.13	1594.29	1.877	> 0.05
	7 min after Induction	10411.70	1423.15		
	Before Induction	10840.13	1594.29	1.659	> 0.05
	10 min after Induction	10460.43	1594.09		

Comparison of different parameters of Group C at different observations with observation before induction

Table 12

Group C

Parameter	Observations	Mean	± SD	t value	p value
Heart Rate	Before Induction	93.77	15.59	12.145	< 0.001
	1 min after Induction	79.17	12.99		
	Before Induction	93.77	15.59	10.579	< 0.001
	3 min after Induction	81.53	13.02		
	Before Induction	93.77	15.59	7.399	< 0.001
	5 min after Induction	85.37	13.42		
	Before Induction	93.77	15.59	5.369	< 0.001
	7 min after Induction	87.63	12.30		
	Before Induction	93.77	15.59	4.019	< 0.001
	10 min after Induction	88.53	11.64		
Systolic BP	Before Induction	122.17	9.12	5.718	< 0.001
	1 min after Induction	112.13	11.04		

	Before Induction	122.17	9.12	4.539	< 0.001
	3 min after Induction	114.23	10.66		
	Before Induction	122.17	9.12	2.66	< 0.05
	5 min after Induction	117.33	9.96		
	Before Induction	122.17	9.12	0.279	> 0.05
	7 min after Induction	121.60	11.24		
	Before Induction	122.17	9.12	-0.914	> 0.05
	10 min after Induction	123.97	10.53		
Diastolic BP	Before Induction	78.03	6.56	3.333	< 0.01
	1 min after Induction	73.50	7.54		
	Before Induction	78.03	6.56	1.707	> 0.05
	3 min after Induction	75.80	7.22		
	Before Induction	78.03	6.56	1.297	> 0.05
	5 min after Induction	76.10	7.55		
	Before Induction	78.03	6.56	0.706	> 0.05
	7 min after Induction	76.93	7.69		
	Before Induction	78.03	6.56	-0.193	> 0.05
	10 min after Induction	78.33	6.71		

Comparison of different parameters of Group C at different observations with observation before induction

Table 13

Parameter	Observations	Mean	± SD	t value	p value
Mean Arterial Pressure	Before Induction	92.75	7.05	4.519	< 0.001
	1 min after Induction	86.38	8.22		
	Before Induction	92.75	7.05	3.095	< 0.01
	3 min after Induction	88.61	7.86		
	Before Induction	92.75	7.05	1.927	> 0.05
	5 min after Induction	89.84	8.02		
	Before Induction	92.75	7.05	0.57	> 0.05
	7 min after Induction	91.82	8.53		
	Before Induction	92.75	7.05	-0.505	> 0.05
	10 min after Induction	93.54	7.47		
Rate Pressure Product	Before Induction	11471.33	2131.83	9.448	< 0.001
	1 min after Induction	8863.50	1603.52		
	Before Induction	11471.33	2131.83	8.586	< 0.001
	3 min after Induction	9282.33	1488.16		
	Before Induction	11471.33	2131.83	5.572	< 0.001
	5 min after Induction	9981.67	1533.78		
	Before Induction	11471.33	2131.83	2.862	< 0.01
	7 min after Induction	10627.30	1581.12		
	Before Induction	11471.33	2131.83	1.709	> 0.05
	10 min after Induction	10962.67	1619.22		

DISCUSSION

There are three groups of 30 patients each in the study. Group A received no drug for attenuation of hemodynamic response to laryngoscopy and intubation. Group B received intravenous esmolol 1mg/kg, 1 minute before induction and Group C received intravenous esmolol 2mg/kg 1minute before induction for attenuation of stress response to intubation. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were recorded before induction,1minute, 3minute, 5minute, 7minute and 10 minute intervals after induction.

The data collected were transformed into a master sheet one for each group. In order to compare the data and to draw conclusions; the mean and standard deviation of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were calculated. The effect of the drugs were compared to the control group by considering the above pressor response variables. Data were analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 10. Data are expressed in its frequency and percentage. To elucidate the associations and comparisons between different parameters, Chi square (χ^2) test was used as nonparametric test. Analysis of variance (One Way ANOVA) were performed as parametric test to compare different variables. Duncan's multiple range (DMR) test was employed for post hoc comparisons. Student's t test was used to compare paired parametric parameters. For all statistical evaluations, a two-tailed probability value, < 0.05 was considered significant.

There was no significant difference in patient variables like age [table 1] and gender [table 2] between the three groups.

HEART RATE

The mean heart rate in the control group [Group A], showed significant increase following laryngoscopy and intubation ($p<0.001$ in 3 & 5 minute intervals and $p<0.01$ at 7 minutes) compared to the two esmolol groups and then decreased [table 3, chart 3, chart 4, table 8]. This is supported by the study by King BD et al., which showed significant increases in heart rate and BP following laryngoscopy and intubation.(1)

Group B and Group C did not show significant increase in heart rate following laryngoscopy and intubation [table 3, chart 3, chart 4]. This proves the efficacy of esmolol in attenuating the pressor response to laryngoscopy and intubation. This is consistant with the Canadian multicentric trial in 1991 carried out by Miller RD et al.(2) Another randomized double blind placebo controlled study by Sharma S et al. conducted at PGI Chandigarh, India(1996 August) also supports this. (3)

The difference in heart rate between the two esmolol groups (1mg/kg group and 2 mg/kg group) was not statistically significant at all time intervals [table 3, chart 3, chart 4]. This is supported by the study done by Kovac AL et al, where the hemodynamic effects with different doses of esmolol were similar. (4) The study by Rathore A et al. conducted in 2002 also showed decrease in heart rate response with all the three doses of esmolol. (5) Thus esmolol 1mg/kg is enough for attenuating the heart rate response to laryngoscopy and intubation. This is supported by the study conducted by Gaubatz CL et al. (6) At 10 minutes after induction, the difference in heart rate between the three groups was not statistically significant ($p>0.05$), probably due to the short duration of action of esmolol [elimination half life – 9 minutes].

SYSTOLIC BLOOD PRESSURE

The mean systolic blood pressure in the control group (Group A) showed significant increase following laryngoscopy and intubation (3, 5 and 7 minute intervals) compared to the two esmolol groups [table 4, chart 5, chart 6, table 8]. This is supported by the study done by King BD et al., which showed significant increases in heart rate and BP following laryngoscopy and intubation.(1)

Group B did not show any significant increase in systolic blood pressure ($p>0.05$) following

laryngoscopy and intubation (3, 5, 7 and 10 minute intervals) [table 10]. Group C did not show significant increase in systolic blood pressure, but showed clinically significant decrease in systolic blood pressure at 3 minute ($p<0.001$) and 5 minute ($p<0.05$) intervals [table 12]. This proves the efficacy of esmolol in attenuating the systolic blood pressure response to laryngoscopy and intubation. This is consistant with the study by Reves JG et al.[7] The study by Liu PL et al. also showed significant ($p<0.05$) attenuation of the systolic blood pressure response to laryngoscopy and intubation.[8] Statistically significant decrease in systolic blood pressure response to laryngo-scopy and intubation was also demonstrated in the study by Zargar JA et al.[9]

Among the two doses of esmolol it was found that 1mg/kg (Group B) was effective in attenuating the systolic blood pressure response to laryngoscopy and intubation. Esmolol in a dose of 2mg/kg (Group C) showed significant decrease in systolic blood pressure compared to the pre-induction values [table 12]. This is consistent with the Canadian multicentre trial by Miller RD et al.[2] At 10 minutes after induction, the difference in systolic blood pressure between the three groups was not statistically significant ($p>0.05$) [table 4], probably due to the short duration of action of esmolol [elimination half life – 9 minutes].

DIASTOLIC BLOOD PRESSURE

The mean diastolic blood pressure in the control group (Group A) showed significant increase ($p<0.001$) following laryngoscopy and intubation (3, 5, 7 and 10 minute intervals) compared to the two esmolol groups [table 5, chart 7, chart 8, table 8]. This is supported by the study done by King BD et al., which showed significant increases in heart rate and BP following laryngoscopy and intubation.[1]

Group B did not show significant increase in diastolic blood pressure ($p>0.05$) following laryngoscopy and intubation (3, 7 and 10 minute intervals) [table 10]. Group C did not show any significant increase in diastolic blood pressure ($p>0.05$) following laryngoscopy and intubation (3, 5, 7 and 10 minute intervals) [table 12]. This proves the efficacy of esmolol in attenuating the diastolic blood pressure response to laryngoscopy and intubation. This is consistant with the studies by Ghaus MS et al.[10], Sharma S et al.[11] and the meta-analysis by Figueredo E et al.[12] which showed effective blunting of the pressor response following laryngoscopy and intubation. The difference in diastolic blood pressure response between the two esmolol groups (1mg/kg group and 2 mg/kg group) was not statistically significant [table 5, chart 7, chart 8].

MEAN ARTERIAL PRESSURE

The mean MAP [mean arterial pressure] in the control group (Group A) showed significant increase ($p<0.001$) following laryngoscopy and intubation (3, 5, 7 and 10 minute intervals) compared to the two esmolol groups [table 6, chart 9, chart 10, table 9]. This is supported by the study done by Murthy VS et al., which showed significant increases in mean arterial pressure following laryngoscopy and intubation.[13]

Group B did not show significant increase in mean arterial pressure response following laryngoscopy and intubation ($p>0.05$ at 3, 7 and 10 minute intervals) [table 11]. Group C also did not show significant increase in mean arterial pressure response following laryngoscopy and intubation ($p>0.05$ at 5, 7 and 10 minute intervals) [table 13]. This proves the efficacy of esmolol in attenuating the mean arterial pressure response to laryngoscopy and intubation. This is consistant with the meta-analysis by Figueredo E et al.[12] and the study by Rathore A et al.[5]

The difference in mean arterial pressure between the two esmolol groups (1mg/kg group and 2 mg/kg group) was not statistically significant [table 6, chart 9, chart 10] showing that a higher dose was unnecessary for attenuating the mean arterial pressure response to laryngoscopy and intubation. This is supported by the study by Kovac AL et al. [4]

RATE PRESSURE PRODUCT

The mean rate pressure product in the control group (Group A) showed significant increase ($p<0.001$) following laryngoscopy and intubation (3, 5, 7 and 10 minute intervals) compared to the two esmolol groups [table 7, chart 11, chart 12, table 9]. This is consistent with studies by Menkhaus PG et al [14], Murthy VS et al [13], Liu PL et al [8], Kovac AL et al [4] and Rathore A et al [5].

Group B showed significant decrease in rate pressure product response following laryngoscopy and intubation at 3 minute interval ($p<0.05$) and no significant difference ($p>0.05$) at 5, 7 and 10 minute intervals [table 11]. Group C also showed significant decrease in rate pressure product response following laryngoscopy and intubation at 3, 5 ($p<0.001$) and 7 minute ($p<0.01$) intervals [table 13]. This proves the efficacy of esmolol in attenuating the rate pressure product response to laryngoscopy and intubation. This is also consistant with the studies by Menkhaus PG et al [14], Murthy VS et al [13], Liu PL et al [8], Kovac AL et al [4] and Rathore A et al [5].

The rate pressure product values were above 12000 at 3, 5 and 7 minute intervals in Group A, but in both Group B and Group C it was below 12000 at all time intervals. The study by Barash PG and Kopriva CJ showed that angina threshold of rate pressure product usually ranges from 15000 to 20000. A high rate pressure product indicates a potential danger of myocardial ischemia, but a normal or low rate pressure product does not rule out ischemia. Patients with tachycardia and hypotension may have normal rate pressure product but both tachycardia [increased O_2 demand and decreased O_2 supply] and hypotension [decreased O_2 supply] may cause myocardial ischemia. The study recommended to keep the rate pressure product less than 12000.[15]

The difference in rate pressure product between the two esmolol groups (1mg/kg group and 2 mg/kg group) was not statistically significant [table 7, chart 11, chart 12] showing that a higher dose was unnecessary for attenuating the rate pressure product response to laryngoscopy and intubation. This is supported by the study by Kovac AL et al. [4]

ARRHYTHMIAS

There were no significant arrhythmias in the three study groups in any of the time intervals. This is supported by the study by Rathore A et al.[5]

SUMMARY AND CONCLUSION

Reflex cardiovascular responses to direct laryngoscopy and endotracheal intubation, mediated by the sympathetic nervous system could lead to serious complications especially in those with cardiac and cerebral disorders. A prospective observational study was done with 3 groups of 30 patients each presenting for elective surgery. For attenuation of stress response to intubation, Group A received no drug, Group B received intravenous esmolol 1mg/kg, 1 minute before induction and Group C received intravenous esmolol 2mg/kg 1minute before induction. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were recorded before induction,1minute, 3minute, 5minute, 7minute and 10 minute intervals after induction. It was found that there is a significant hemodynamic response to laryngoscopy and intubation in those who did not receive any drug for hemodynamic response attenuation as demonstrated by a significant increase in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product. Esmolol, an ultra short acting β blocker with rapid onset of action is suitable for attenuation of hemodynamic response to laryngoscopy and intubation. Esmolol in a bolus dose of 1mg/kg given 1minute before induction effectively attenuated the hemodynamic response to laryngoscopy and intubation. smolol in a bolus dose of 2mg/kg given 1minute before induction also effectively attenuated the hemodynamic response but was often associated with systolic blood pressure lesser than the pre-induction values. Hence it can be concluded that

esmolol in a bolus dose of 1mg/kg given 1minute before induction is the recommended dose for attenuation of hemodynamic response to laryngoscopy and intubation.

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