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Original research article

I.V. esmolol hydrochloride and I.V. clonidine: Blood pressure changes in response to laryngoscopy and intubation

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Abstract

Intravenous anaesthetic induction agents alone do not adequately suppress the circulatory responses evolved by endotracheal intubation therefore prior to initiating laryngoscopy and endotracheal intubation additional pharmacological measures should be taken. A clinical comparative single blinded study of attenuation of sympathetic response to laryngoscopy and intubation was done in 90patients posted for elective surgeries selected randomly. Patients undergoing various Orthopaedic, ENT, and General surgical procedures were selected. We observed in our study, in the control group systolic blood pressure increased maximally after 1 minute from onset of laryngoscopy and intubation and then it gradually decreased to preinduction level over 10 minutes. When we compare esmolol, we found statistical significant difference of a higher fall of the systolic blood pressure in clonidine groups.

Keywords: Blood Pressure Changes, Laryngoscopy and Intubation, Esmolol Hydrochloride and I.V. Clonidine

Introduction

Haemodynamic changes like hypertension and tachycardia in response to the sympathetic stimulation due to direct laryngoscopy and endotracheal intubation have been reported as early as 1950 when intubation was under light anaesthesia. However the rise in the pulse rate and blood pressure is usually transient, variable and unpredictable. Usually these changes are well tolerated by healthy individuals. However, these changes may be fatal in patients with hypertension, coronary artery disease or intracranial hypertension. This is mainly due to reflex sympathetic discharge in responses to laryngotracheal stimulation which in turn leads to increased plasma norepinephrine concentration [1].

Pressor response is exaggerated in hypertensive patients even though rendered normotensive pre-operatively by antihypertensive medication Pressor response may result in intra-operative myocardial infarction. Pressor response can cause acute L.V.F (left ventricular failure), dysrrythmias and intracranial bleed in individuals with end organ decompensation [2].

Intravenous anaesthetic induction agents alone do not adequately suppress the circulatory responses evolved by endotracheal intubation therefore prior to initiating laryngoscopy and endotracheal intubation additional pharmacological measures should be taken. Various methods include as follows:

- Premedication
- Topical and systemic lidocaine
- Vasodilators eg Isosorbide dinitrite, NTG and SNP
- Adrenergic Blockers
- Angiotensin- converting enzyme inhibitors
- Opioids eg Fentanyl, Alfentanyl, Remifentanyl
- Alpha 2 agonist eg Clonidine
- Inhaled Anaesthetic agents
- Thoracic epidural block

Recommendations for attenuating reflex tachycardia and hypertension are therefore manifold. The technique besides minimizing Cardiovascular responses to anaesthesia for patient at risk must also satisfy the following requirements [3],

1. It must be applicable regardless of patient's collaboration
2. It should prevent impairement of cerebral blood flow and avoid arousal of the patient.

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3. It should neither be time consuming nor effect the duration or modality of ensuing anaesthesia.

In appropriate doses narcotics like Fentanyl control both HR and BP responses, but requirement of higher doses and sometimes non availability of the drug is the main obstacle in routine use. Inhalational agents also do not have satisfactory effects and may need higher concentrations which may cause serious effects like hypotension bradycardia and delayed recovery [4].

Clonidine, a central alpha–2 agonist which is available now has been tried for blunting haemodynamic responses to laryngoscopy and intubation. Clonidine has sedative, analgesic, antihypertensive actions in addition to reducing the anesthetic drugs requirement which might be helpful in attenuation of haemodynamic responses to laryngeal stimulation [5].

Intially Clonidine was available in India as oral preparation only and as such oral preparation was only being used. Now clonidine has been introduced in parenteral form (Cloneon, Neon laboratory ltd. 150µg/ml, 1ml ampoules) and can be used through intravenous route for attenuation of sympathetic response to laryngoscopy and intubation [4, 6].

Hence the present study has been undertaken to compare the efficacy of intravenous bolus of clonidine versus intravenous bolus of esmolol for attenuating the haemodynamic responses to direct laryngoscopy and endotracheal intubation.

Methodology

A clinical comparative single blinded study of attenuation of sympathetic response to laryngoscopy and intubation was done in 90patients posted for elective surgeries selected randomly. Patients undergoing various Orthopaedic, ENT, and General surgical procedures were selected.

General anaesthesia was provided with endotracheal intubation for all the patients. Using Clonidine 3µgm/ kg body weight single bolus intravenously versus Esmolol 1.5 mg/kg body weight single bolus intravenously and control group.

A thorough pre-operative Anaesthetic checkup was done a day before surgery

Inclusion criteria

1. Age between 18 to 50 years of both sex
2. ASA (American society of anesthesiologists) I and II
3. Elective Surgery

Exclusion criteria

- Anticipated difficult intubation
- Patients in whom laryngoscopy and intubation proved to be prolonged or difficult.
- Patient with Mallampati with Grade III and IV

The study population was randomly divided into three groups with 30 patients in each group by lottery system on day of operation

Group I: Control group (n=30). No drug was administered for attenuating sympathetic response to laryngoscopy and intubation.

Group II: Inj Esmolol (Neotach) (n=30) 1.5mg/kg IV – received 3 minutes before laryngoscopy and intubation.

Group III: Clonidine group (n=30) - received injection Clonidine 3µg/kg (Cloneon, Neon laboratories ltd. 150µg/ml, 1ml ampoules) diluted to 10 ml normal saline intravenously over 120 seconds, 15 minutes prior to laryngoscopy and intubation.

Results

Table 1: Showing the intragroup comparison of mean systolic blood pressure (SBP in mmHg) changes in response to laryngoscopy and intubation

	Group	Mean	Std. Deviation	N
S.B.P. Pi	Control	129.28	9.693	30
	Esmolol	130.52	12.316	30
	Clonidine	128.83	12.157	30
	Total	129.55	11.307	90
S.B.P. Poi	Control	125.96	9.541	30
	Esmolol	128.84	12.040	30
	Clonidine	127.92	12.197	30
	Total	127.57	11.223	90
S.B.P. 1 min	Control	154.32	10.082	30

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	Esmolol	146.36	11.254	30
	Clonidine	137.00	11.085	30
	Total	146.01	12.812	90
S.B.P. 3 min	Control	151.56	10.484	30
	Esmolol	143.88	12.036	30
	Clonidine	134.46	10.554	30
	Total	143.42	12.963	90
S.B.P. 5 min	Control	142.52	13.451	30
	Esmolol	136.48	10.809	30
	Clonidine	129.21	11.383	30
	Total	136.16	12.981	90
S.B.P. 7 min	Control	134.96	10.620	30
	Esmolol	130.20	11.533	30
	Clonidine	126.21	10.245	30
	Total	130.51	11.259	90
S.B.P. 10 min	Control	130.92	9.849	30
	Esmolol	127.56	11.976	30
	Clonidine	125.83	10.520	30
	Total	128.14	10.882	90

Table 1A: Tests of Within-Subjects Effects

Source		Type III Sum of Squares	DF	Mean Square	F	Sig.
SBP	Greenhouse-Geisser	25111.061	3.262	7696.912	202.291	<0.001
SBP * Group	Greenhouse-Geisser	4513.850	6.525	691.781	18.181	<0.001

Interpretation
The yellow marking shows significant difference in the change of Systolic Blood Pressure from time period 1 to 7 Green marking shows that there is significant difference in the Systolic Blood Pressure change between the groups.

Posthoctest: Tukey HSD

Table 1B: Multiple Comparisons

(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Esmolol Clonidine	3.67	2.929	.427	-3.34	10.68
Clonidine	Esmolol	8.58	2.960	.014	1.50	15.66
		4.91	2.960	.228	-2.17	12.00
Based on observed means.						

The error term is Mean Square (Error) = 107.251.

Interpretation of posthoc
The main difference is between control and clonidine.

Analysis of Systolic Blood Pressure
The changes and statistical analysis in systolic blood pressure assessed before and after induction of anaesthesia and at various time intervals from the onset of laryngoscopy and intubation in control and study groups are presented.

Control group
The mean systolic blood pressure was 129.28±9.693. It decreased to 125.96±9.541 (4.12%) after induction. A rise of 20.0% (154.32±10.082) was noticed after 1 minute from the onset of laryngoscopy and intubation ($p< 0.001$). It remained almost at the same level 151.56±10.484 (19.0%) by the end of 3 minutes. It further decreased to (142.52±13.451) 10.4% and 3.5% (134.96±10.620) at the end of 5 and 7 minutes. At the end of 10 minutes the mean systolic blood pressure was equal to preinduction level (130.92±9.849).

Clonidine group
A decrease in systolic blood pressure of 1.2% (128.83±12.157) from the basal level of 128.84±12.040 occurred with induction of anaesthesia. With the onset of laryngoscopy and intubation rise in systolic blood pressure was only 6% (137±11.085) at 1 minute. Subsequent observation showed fall to 4.2% (134.46±10.554) at 3 minutes and reached to the pre induction level at the end of 5 minutes

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(129.21±11.383). A 3.1% lower value than the basal value (125.83±10.520) was recorded at 10 minutes.

Esmolol Group

A small insignificant fall in systolic blood pressure of 1.2% from preinduction level of 130.52±12.316 was observed following induction. The rise in systolic blood pressure was 11.7% at 1 minute with the onset of laryngoscopy and intubation (146.36±11.254). Then it decreased to 10.1% and 3.2% at 3 (143.88±12.036) and 5 (136.48 ±10.809) minutes. A 3.1% lower value than the basal value (127.56±11.976) was recorded at the end of 10 minutes.

Repeated measures ANOVA test was done to compare the trend of systolic Blood Pressure seen in control, Clonidine and Esmolol administration. Looking at the Greenhouse – Geisser values it is seen that from the preinduction to the 7 min post induction the values differ significantly and there is significant difference in the levels between the three groups.

Repeated measure ANOVA study showed significant variations in systolic blood pressure before and after induction and at time intervals of 1, 3, 5, 7 and 10 minutes from the onset of laryngoscopy and intubation ($p< 0.001$). In control group systolic blood pressure increased maximally after 1 minute from onset of laryngoscopy and intubation. It gradually decreased to preinduction level over 10 minutes. With administration of esmolol, the maximum increase compared to the preinduction value was 11.7% and with clonidine, it was only 6.0%. Both when compared with control showed significant suppression. The difference in systemic blood pressure between control and clonidine groups remains significant at all times of assessment ($p< 0.014$) and the difference in systolic blood pressure between control and esmolol group remains statistically significant at all times of assessment ($p< 0.427$). The systolic blood pressure response difference between esmolol and clonidine group is clinically and statistically highly significant at all times of assessment ($p< 0.228$). Among the two drugs clonidine showed better result ($p< 0.001$).

Table 2: Showing Comparison of mean arterial blood pressure

	Group	Mean	Std. Deviation	N
Map pi	Control	94.28	6.786	30
	Esmolol	95.08	6.626	30
	Clonidine	93.84	5.864	30
	Total	94.40	6.371	90
Map poi	Control	90.64	6.626	30
				30
	Esmolol	93.48	6.456	30
	Clonidine	92.5	5.510	30
	Total	92.45	6.267	90
Map 1 min	Control	111.96	6.107	30
				30
	Esmolol	106.08	5.604	30
	Clonidine	98.88	4.978	30
	Total	105.64	7.702	90
Map 3 min	Control	110.36	6.383	30
				30
	Esmolol	104.72	4.946	30
	Clonidine	97.52	5.084	30
	Total	104.20	7.584	90
Map 5 min	Control	104.56	7.405	30
				30
	Esmolol	99.52	4.001	30
	Clonidine	94.20	5.331	30
	Total	99.43	7.094	90
Map 7 min	Control	98.72	6.215	30
				30
	Esmolol	94.52	4.788	30
	Clonidine	92.68	5.360	30
	Total	95.31	5.980	90
Map 10 min	Control	95.28	6.086	30
				30
	Esmolol	92.80	5.831	30
	Clonidine	92.20	5.323	30
	Total	93.43	5.834	90

Table 2A: Tests of Within-Subjects Effects

Source		Type III Sum of Squares	DF	Mean Square	F	Sig.
MAP	Greenhouse-Geisser	12791.406	3.188	4012.855	313.779	.000

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MAP * GROUP	Greenhouse-Geisser	2966.606	6.375	465.334	36.386	.000

Interpretation
There is significant differences in the MAP from time period 1 to 7 as well as between the groups.

Posthoctest: Tukey HSD

Table 2B: Multiple Comparisons

(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Esmolol	2.80	1.501	.156	-.79	6.39
	Clonidine	6.18	1.501	<0.001	2.59	9.77
Clonidine	Esmolol	3.38	1.501	.070	-.21	6.97
Based on observed means.						
The error term is Mean Square (Error) = 28.163.						

Interpretation of posthoc
The difference is between the clonidine group and control.

Analysis of Mean Arterial Blood Pressure
The changes in mean arterial pressure assessed at pre and post induction and at various time intervals from the onset of laryngoscopy and intubation in control and study groups and their comparative statistics are shown in the table.

Control group
The pre induction mean arterial pressure is 94.28±6.786. It showed 2.7% decrease after induction (90.64±6.626). It increased by 18.1% (111.96±6.626) at 1 minute from the onset of laryngoscopy and intubation. It is highly significant (P<.001). After 3 minutes it is 17.4% above pre induction value (110.36±6.383). It decreased in subsequent intervals i.e. at 5 mins (104.56±6.215), at 7 mins (98.72±6.215) and is almost equal to basal level at 10 minutes (95.28±6.086).

Clonidine group
The pre induction mean value is 93.8± 5.864 which is lowered by 1.3% with the induction (92.5±5.510). A maximum rise of 4.9% (98.88±4.978) was found after 1 minute. After 3 minutes the value 97.52±5.084. Subsequently it reached near basal value at 5 minutes (94.20±5.331). A small decrease was seen at 7 (92.68±5.360) and 10 minutes (92.20±5.323).

Esmolol group
The pre induction mean value is 95.08±6.626. A decrease of 2.1% was seen with induction (93.48±6.456). The maximum rise in mean arterial pressure was by 10.7% (106.08±5.604) at 1 minute interval. It further reduced at 3 (104.72±4.946) and 5(99.52±4.001) minutes interval. A small fall was found at 7 (94.52±4.788) and 10 (92.80±5.831) minutes.
Repeated measures ANOVA test was done to compare the trend of Mean Arterial Blood Pressure seen in control, clonidine and Esmolol administration. Looking at the Greenhouse – Geisser values it is seen that from the preinduction to the 7 min post induction the values differ significantly and there is significant difference in the levels between the three groups.
Repeated measure ANOVA study showed significant variations in mean arterial blood pressure before and after induction and at time intervals of 1, 3, 5, 7 and 10 minutes from the onset of laryngoscopy and intubation (p< 0.00). The mean arterial pressure increased by 18.1% from the preinduction value in control group at 1 minute (P0.001) and gradually reached basal level over 10 minutes, esmolol the maximum rise to 10.7% (p< 0.01) while clonidine to only 4.9% (p< 0.001). It reached preinduction level over 7 minutes esmolol group and 5 minutes in clonidine group. The difference in the diastolic blood pressure between control and esmolol group remains statistically significant at all times of assessment (p< 0.156). The diastolic blood pressure difference between esmolol and clonidine group is clinically and statistically highly significant at all times of assessment (p< 0.070). The efficacy of clonidine over esmolol has been verified in many other studies. Both esmolol and clonidine together is also recommended to suppress the pressor response.

Table 3: Showing Comparison of diastolic blood pressure

	GROUP	Mean	Std. Deviation	N
D.B.P pi	Control	76.84	6.289	30
	Esmolol	77.52	5.810	30

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	Clonidine	76.36	5.453	30
	Total	76.91	5.801	90
D.B.P poi	Control	73.24	6.566	30
	Esmolol	75.76	5.725	30
	Clonidine	75.56	4.925	30
	Total	74.85	5.814	90
D.B.P 1 min	Control	90.72	5.216	30
	Esmolol	86.20	4.619	30
	Clonidine	80.32	5.170	30
	Total	85.75	6.541	90
D.B.P 3 min	Control	89.64	5.392	30
	Esmolol	85.04	3.623	30
	Clonidine	79.40	4.690	30
	Total	84.69	6.212	90
D.B.P 5 min	Control	85.56	6.634	30
	Esmolol	80.92	3.523	30
	Clonidine	76.72	4.198	30
	Total	81.07	6.101	90
D.B.P 7 min	Control	80.52	5.432	30
	Esmolol	77.00	4.778	30
	Clonidine	76.00	4.770	30
	Total	77.84	5.307	90
D.B.P 10 min	Control	78.16	5.886	30
	Esmolol	75.44	4.691	30
	Clonidine	75.28	5.087	30
	Total	76.29	5.342	90

Table 3A: Tests of Within-Subjects Effects

Source		Type III Sum of Squares	DF	Mean Square	F	Sig.
DBP	Greenhouse-Geisser	8226.411	3.455	2380.703	187.931	<0.001
DBP * Group	Greenhouse-Geisser	1986.743	6.911	287.479	22.693	<0.001

Interpretation
There is significant difference in the DBP as well as the three groups.

Posthoctest: Tukey HSD

Table 3B: Multiple Comparisons

(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Esmolol clonidine	2.40	1.299	.162	-.71	5.51
Clonidine	Esmolol	5.01	1.299	.001	1.90	8.11
		2.61	1.299	.118	-.50	5.71
Based on observed means.						
The error term is Mean Square (Error) = 21.095.						

Interpretation of posthoc
The main differences are between the control and clonidine groups

Analysis of Diastolic Blood Pressure
The changes in diastolic blood pressure assessed at pre and post induction and at various time intervals from the onset of laryngoscopy and intubation in control and study groups and their comparative statistics are shown in the table.

Control group
The mean diastolic blood pressure before induction was 76.84±6.289. With the induction of anaesthesia this blood pressure decreased by 3.5% i.e., mean of 73.24±6.566. From the onset of laryngoscopy and tracheal intubation a rise of 17.2% (90.72±5.216) was noticed at the end of 1 minute. It remained at 89.64±5.392 (16.6%) at 3 minutes. At 5 (85.56±6.634) and 7 (90.72±5.216) minutes it decreased further to 10.4% and 3.1%. It was almost nearer to preinduction level at 10 minutes

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Clonidine group

Pre induction value is 76.36±6.634. Maximum increase in diastolic blood pressure was 14.8% (90.72±5.216) from the basal level following a small decrease by 1.7% (75.56± 4.925) after induction of anaesthesia. Maximum increase was at 1 minute interval. It decreased to 79.40±4.690 i.e., 3.5% at 3 minutes and 76.9±5.6 at 5 minutes. The mean values at 7 (76±4.770) and 10 (75.28±5.087) minutes were slightly less than basal level.

Esmolol group

This group showed mean preinduction value of 77.52±5.810. There was a small fall to 75.76±5.725 (1.8%) after induction. The maximum rise found at 1 minute was 10.0% more than preinduction value (86.20±4.619). It decreased to 85.04±3.623 i.e.8% at 3 minutes and 80.92±3.523 i.e., 3.4% at 5 minutes. The mean values at 7 (77.00 ±4.778) and 10 (75.44±4.691) minutes showed a small decrease.

Repeated measures ANOVA test was done to compare the trend of Diastolic Blood Pressure seen in control, Clonidine and Esmolol administration. Looking at the Greenhouse – Geisser values it is seen that from the preinduction to the 7 min post induction the values differ significantly and there is significant difference in the levels between the three groups.

Repeated measure ANOVA study showed significant variations in diastolic blood pressure before and after induction and at time intervals of 1, 3, 5, 7 and 10 minutes from the onset of laryngoscopy and intubation ($p< 0.001$). Maximum increase in diastolic blood pressure was 14.8% when compared with preinduction value in control group ($p< 0.001$). It was 10.0% and 4.8% in esmolol and clonidine groups respectively. The difference in diastolic blood pressure between control and clonidine groups remains significant at all times of assessment ($p< 0.001$) but it returned to near basal level at 5 minutes. The difference in the diastolic blood pressure between control and esmolol group remains significant ($p< 0.162$). The diastolic blood pressure difference between esmolol and clonidine group is clinically and statistically highly significant at all times of assessment ($p< 0.118$). Thus, among the two drugs clonidine showed better result in attenuating the diastolic blood pressure.

Discussion

The most important laryngoscopic factor influencing the cardiovascular response is found to be the duration of laryngoscopy. A linear increase in heart rate and mean arterial pressure during first 45 seconds has been observed. Further prolongation has little effect. As duration of laryngoscopy is normally less than 30 seconds the result of studies in which it takes longer than this have less clinical relevance. The force applied during laryngoscopy has only minor effect. In our study the duration of laryngoscopy and intubation was limited to 30seconds [7].

In a study conducted showed that greater time needed to perform blind oral intubation was not associated with a more pronounced haemodynamic or hormonal stress response. Infact patients intubated with direct laryngoscopy showed significant response [8].

Excluding hypoxia and hypercarbia other contributory causes of hypertension and tachycardia could be continued manifestation of anxiety concerning anaesthesia and operation, atropine premedication, reflex baroreceptor effect after thiopentone and possible effect of suxamethonium. They seem to be less important than laryngotracheal stimulation during laryngoscopy and intubation.

We observed in our study, in the control group systolic blood pressure increased maximally after 1 minute from onset of laryngoscopy and intubation and then it gradually decreased to preinduction level over 10 minutes. When we compare esmolol, we found statistical significant difference of a higher fall of the systolic blood pressure in clonidine groups.

It was seen in our study that the maximum increase in diastolic blood pressure was in the control group when compared with pre induction value of the other groups. When we compare clonidine, we found statistical significant attenuation of the diastolic blood pressure response to laryngoscopy and intubation than seen in the esmolol group [9].

We observed in our study, in the control group, similarly the mean arterial pressure increased in the pre induction at 1 minute and gradually reached basal level over 10 minutes. Similar increase with esmolol was seen. It was seen that both esmolol and clonidine attenuated the mean arterial blood pressure with a statistical significance. In the esmolol group it was noted the mean arterial blood pressure reached the preinduction level over 7 minutes while in 5 minutes in clonidine group. When we compare esmolol, we found statistical significant difference of a higher fall of mean arterial blood pressure in clonidine groups. The efficacy of clonidine over esmolol has been verified in many other studies.Both esmolol and clonidine together is also recommended to suppress the pressor response [10].

Conclusion: Clonidine in a dose of 3 microgms/kg was more effective than esmolol 1.5 mg/kg and control group for attenuating haemodynamic response to laryngoscopy and intubation.

References

1. Smith JE, Mackenzie AA, Scott- Knight VCE. Comparison of two methods of fibroscope guided

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tracheal intubation. Br J Anaesthesiology. 1991;66:546-50.
2. Pernerstorfer T, Krafft F, Fitzgerald RP, Krenn CG, Chiari A, wagner O, *et al*. Stress response to tracheal intubation; direct laryngoscopy compared with blind oral intubation. Anaesthesia. 1995;50:17-22.
3. Devault M, Greifenstein FE, Harris JRLC. Circulatory responses to endotracheal intubation in light general anaesthesia; The effect of atropine and phentolamine Anaesthesiology. 1960;21:360-362.
4. William M, Splinter MD FRCP, Frank Cervenko MD FRCP. Haemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients: effects of fentanyl, lidocaine and thiopentone. Canadian journal of Anaesthesia. 1989;36(4):370-376.
5. Crawford DC, Fell D, Achola KJ. Effect of Alfentanyl on the pressure and catecholamine response to tracheal intubation. British journal of Anaesthesia. 1987;59:707-712.
6. Scheinin B, Schenin M, Vuorinen J. Alfentanyl obtunds the cardiovascular and Sympathoadrenal responses to suxamethonium facilitated laryngoscopy and intubation British journal of Anaesthesia. 1989;62(4):385-393.
7. Kay B, Nolan D, Mayall R, Healy TEJ. The effects of sufentanil on the Cardiovascular response to tracheal intubation. Anaesthesia. 1987;42:382-386.
8. Robert Stoelting RK. Attenuation of blood pressure to laryngoscopy and tracheal intubation with sodium nitroprusside. Anaesthesia Analg. 1979;58(2):116-119.
9. Nielson DJ. The effect of intranasally administered nitroglycerine on the blood pressure response to laryngoscopy and intubation in patients undergoing coronary artery bypass graft surgery. Acta Anaesthesiologica Scandinavia. 1986;30:23-27.
10. Yoshitaka Fujii MD, Yuhji Saitosh MD, Shinji Takahashi MD, Hidenori Toyooka MD. Diltiazem-lidocaine combination for the attenuation of cardiovascular responses to tracheal intubation in hypertensive patients. Canadian Journal of Anaesthesia. 1998;45:935-937.