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Original research article

Mean heart rate (bpm) changes in response to laryngoscopy and intubation – A comparative study between I.V. esmolol hydrochloride and I.V. clonidine

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Abstract

The tracheal intubation following laryngoscopy is not only accompanied by increased sympathetic activity but also increased sympathoadrenal activity. Increased hypothalamic activity and traffic in sympathetic efferent tracts are observed. Release of trophic hormones from hypothalamus stimulate release of ACTH, TSH, GH, FSH, luteinizing hormone and prolactin in addition to ADH from the pituitary. 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. Repeated measure ANOVA study showed significant variations in heart rate 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 our study, heart rate increased by 41.1% when compared with preinduction value in control group ($p< 0.001$). Similar increase was seen with the esmolol and clonidine groups - 15.4% and was 25.8%. The difference in heart rate between control and clonidine group remains statistically significant at all times of assessment ($p< 0.001$). Both esmolol and clonidine attenuated the heart rate which was highly significantly (P 0.001).

Keywords: Mean Heart Rate, Esmolol Hydrochloride, Clonidine

Introduction

Laryngoscopy and tracheal intubation are frequently associated with sympathetic response. Diagnostic laryngoscopy under anaesthesia and tracheal suctioning are also associated with adverse circulatory changes. Severe hypertension, tachycardia, increase in intracranial pressure can also be seen [1].

Supraglottic traction during laryngoscopy or superficial stimulation of airway and passage of tracheal tube into trachea may be associated with reflex sympathetic changes [2].

Other contributory factors to hypertension and tachycardia like anxiety, baroreceptor mediated reflex after induction are less important than laryngeal stimulation. The tracheal intubation following laryngoscopy is not only accompanied by increased sympathetic activity but also increased sympathoadrenal activity. Increased hypothalamic activity and traffic in sympathetic efferent tracts are observed. Release of trophic hormones from hypothalamus stimulate release of ACTH, TSH, GH, FSH, luteinizing hormone and prolactin in addition to ADH from the pituitary [3, 4].

Afferent impulses are carried through trigeminal, glossopharyngeal, vagus and sympathetic nerves from the airway. These impulses are relayed in cranial nerve nuclei, vasomotor and autonomic regulatory areas.

Key areas that integrate CVS responses and maintain CVS homeostasis are nucleus solitarius, dorsal vagal nucleus, nucleus ambiguus and parabranchial nucleus. The nucleus solitarius is the area of primary central synapse for baroreceptor mediated reflexes and relay station for peripheral information to hypothalamic sympathetic control centers. It projects directly to interomediolateral nucleus of the spinal cord, the common pathway for preganglionic sympathetic outflow. This along with nucleus ambiguous play an important role in control of secretion of vasopressin [5, 6].

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

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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 Body Weight Distribution

Body weight (kg)	Group-I (Control)		Group-II (Esmolol)		Group-III (Clonidine)	
	Number of Patients	Percent	Number of Patients	Percent	Number of Patients	Percent
40 – 44	2	6.7	2	6.7	3	10
45 – 49	9	30.0	4	13.3	5	16.7
50 – 54	11	36.7	10	33.3	8	26.7
55 -59	4	13.3	4	13.3	7	23.3
60 – 64	2	6.7	2	6.7	4	13.3
65 – 70	2	6.7	8	26.7	3	10.0
Total	30	100	30	100	30	100
Mean ± SD	52.60±5.75		52.93±9.92		51.63±7.91	

Table-2 shows the body weight distribution of the patients. The minimum body weight in all groups were 40 kg. The maximum body weight in groups I, II, and III were 70 kg. The mean body weight in Group I (control)was 52.6±5.75, in Group II (esmolol) it was 52.92±9.92 and group III (clonidine) it was 51.63±7.91 There was no significant difference in the body weight of patients between the Group I, II and Group III group (p>0.05).

Table 2: Sex Distribution between Group I, II and Group III

Sex	Group-I (Control)		Group-II (Esmolol)		Group-III(Clonidine)	
	Number of Patients	Percent	Number of Patients	Percent	Number of Patients	Percent
Male	20	66.7	17	56.7	15	50
Female	10	33.3	13	43.3	15	50
Total	30	100	30	100	30	100

No significant difference was observed in sex wise distribution of the cases between three groups (p>0.05)

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Table 3: Showing type of surgical procedures

Type of surgery	Number of Patients		
	Group-I(control)	Group-II (Esmolol)	Group-III(clonidine)
General surgeries	19	22	21
Orthopedic surgeries	02	03	04
ENT surgeries	08	05	05
Miscellaneous surgeries	01	00	00
Total	30	30	30

Table 4: Showing the intergroup comparison of mean heart rate (bpm) changes in response to laryngoscopy and intubation

Descriptive Statistics				
	Group	Mean	Std. Deviation	N
HR PI	Control	81.04	6.804	30
	Esmolol	81.52	6.917	30
	Clonidine	79.08	5.908	30
	Total	80.55	6.556	90
HR POI	Control	90.52	10.005	30
				30
	Esmolol	83.60	6.788	30
	Clonidine	79.88	5.525	30
	Total	84.67	8.775	90
HR 1 MIN	Control	116.64	10.468	30
				30
	Esmolol	102.36	7.610	30
	Clonidine	93.32	5.129	30
	Total	104.11	12.500	90
HR 3 MIN	Control	115.08	13.868	30
				30
	Esmolol	97.84	9.612	30
	Clonidine	89.32	4.862	30
	Total	100.75	14.710	90
HR 5 MIN	Control	106.52	14.518	30
				30
	Esmolol	92.40	7.205	30
	Clonidine	84.40	5.723	30
	Total	94.44	13.438	90
HR 7 MIN	Control	91.48	9.161	30
				30
	Esmolol	84.88	7.412	30
	Clonidine	81.64	6.357	30
	Total	86.00	8.668	90
HR 10 MIN	Control	83.84	5.550	30
				30
	Esmolol	81.62	6.413	30
	Clonidine	79.68	6.123	30
	Total	81.72	7.005	30
				90

Table 4A: Tests of Within-Subjects Effects

Source		Type III Sum of Squares	DF	Mean Square	F	Sig.
HR	Greenhouse-Geisser	40189.691	3.658	10985.581	217.943	<0.001
HR * GROUP	Greenhouse-Geisser	7305.440	7.317	998.446	19.808	<0.001

Interpretation

The yellow marking shows significant difference in the change of heart rate from time period 1 to 7. Green marking shows that there is significant difference in the heart rate changes between the groups.

Table 4B: Post hoc test: Tukey HSD

(I) Group	Multiple Comparisons		Std. Error	Sig.
	(J) Group	Mean Difference (I-J)		
Control	Esmolol	8.61*	1.819	<0.001

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	Clonidine	14.06*	1.819	<0.001
Clonidine	Esmolol	5.45*	1.819	.010
Based on observed means. The error term is Mean Square (Error) = 41.355.				
*. The mean difference is significant at the .05 level.				
Interpretation of posthoc.				

The differences are between all the three groups in any combination.

Analysis of Heart Rate

Statistical analysis of changes in the heart rate assessed at pre and post induction and at different time intervals from the onset of laryngoscopy and intubation in control and study groups and their comparative statistics are presented.

Control group

The mean heart rate in this group before induction of anaesthesia was 81.04±6.84. Following induction it increased by 8.7% with mean value of 90.52±10.005. At one minute from the onset of laryngoscopy and intubation heart rate increased by 41.1% with mean of 116.64±10.468 and remained at the same significantly higher level with mean heart rate of 115.08±13.868 at the end of 3 minutes. A decreasing trend was noticed from 5 minutes; mean heart rate of 106.52±14.518 which is 27% higher than preinduction value. Subsequently decrease to 11.4% at the end of 7 minutes, mean heart rate of 91.48±9.161 and only 2.5% at the end of 10 minutes with mean of 83.84±5.550 was noticed. The heart rate at the end of 10 minutes from the onset of laryngoscopy and intubation is clinically not significantly different or higher from preinduction heart rate.

Clonidine group

This study group shows the mean heart rate of 79.08±5.908 before induction of anaesthesia. After induction of anaesthesia it increased by 1.1% with the mean of 79.88±5.525. An increase of 15.4% in heart rate was observed at 1 minute from the onset of laryngoscopy and intubation, having a mean value ± standard deviation 93.32±5.129. It decreased to 12.5% (89.32±4.862) after 3 minutes. Further decrease to 6.2% (84.40±5.723) and 2.0% (81.64±6.357) above preinduction level was observed at the end of 5 and 7 minutes respectively. At the end of 10 minutes heart rate was 0.6% below preinduction level (79.68±6.123).

Esmolol group

The mean pre induction heart rate in this group of patients was 81.52±6.917. There was 2.8% increase in heart rate (83.60±6.788) after induction. A 25.8% increase of heart rate (102.36±7.610) was noticed at the end of 1 minute from the onset of laryngoscopy and intubation. A decrease in heart rate to 22.4% (97.84±9.612) was observed at the end of 3 minutes. Further decrease to 13.8 (92.4±7.205) and 3.8% (84.887.412) was seen. At the end of 10 minutes the heart rate 0.1% below the pre induction level (81.62±6.413).

Repeated measures ANOVA test was done to compare the trend of heart rate 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 heart rate 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 our study, heart rate increased by 41.1% when compared with preinduction value in control group ($p<$ 0.001). Similar increase was seen with the esmolol and clonidine groups - 15.4% and was 25.8%. The difference in heart rate between control and clonidine group remains statistically significant at all times of assessment ($p<$ 0.001). Both esmolol and clonidine attenuated the heart rate which was highly significantly (P 0.001). It reaches to a level which is clinically less significant by the end of 7 minutes in control group, and 5 minutes in esmolol and clonidine groups. Suppression of maximum rise in heart rate by clonidine is statistically highly significant when compared with esmolol (P 0.001). It remains significant till 7minutes.

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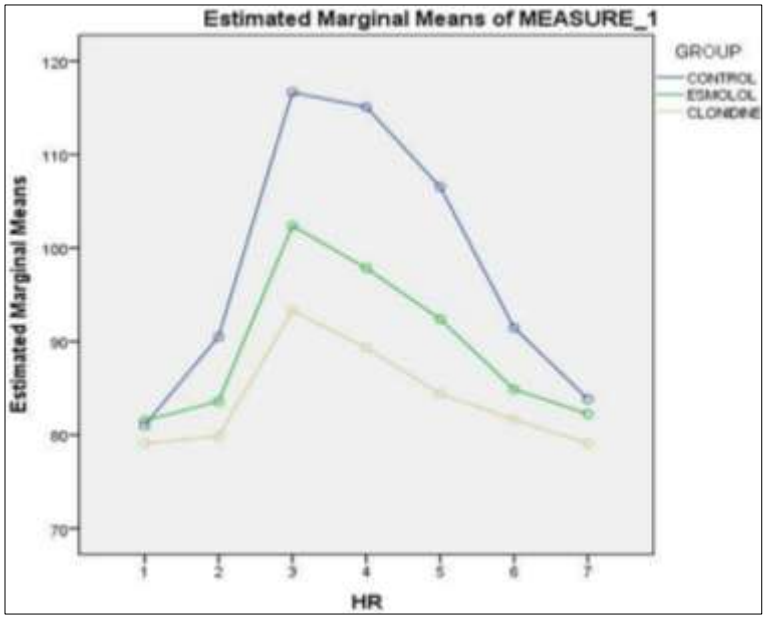

Fig 1: showing Comparison of heart rates

Discussion

Many factors affect the cardiovascular changes associated with laryngoscopy and intubation. Drugs, age, type of procedures, depth of anaesthesia, hypoxia, hypercarbia etc., influence the haemodynamic response.

We selected the optimal range of 18 to 50 years. This because, variability of heart rate changes decrease with increasing age and younger patients show more extreme changes.

We excluded the patients taking anti-hypertensive drugs as these may decrease the pressor response [2].

Thiopentone was selected for induction. In normovolemic patients thiopentone of 5mg/kg IV can transiently decrease 10-20 mmHg blood pressure and increase the heart rate by 15-20 beats/min. There is increase in catecholamine levels; both nor adrenaline and adrenaline. Blood pressure is usually offset by increase in heart rate [7].

Nitrous oxide may increase tone of the sympathetic nervous system. The direct action of N_2O is negative inotropism which is offset by increased sympathetic tone.

Nasotracheal intubation comprises three distinct stages: (a) nasopharyngeal intubation (b) direct laryngoscopy to identify the vocal cords and (c) passage of tracheal tube into the trachea. The nasopharyngeal intubation causes significant pressor response. This response is increased with the passage of tracheal tube into the larynx and trachea. Direct laryngoscopy did not increase the response significantly in a study. We included only laryngoscopy and orotracheal intubation in our study [2, 3].

Laryngoscopy alone may produce most of the cardiovascular responses reported after laryngoscopy and tracheal intubation during anaesthesia.

A diversity 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. Many techniques have been recommended. The drugs used were either partially effective or had other undesirable effects on the patients. Topical application of local anaesthetics, infiltration or nerve blocks, B-blockers, calcium channel blockers, droperidol, clonidine, sodium nitroprusside, lignocaine, fentanyl, esmolol etc. are being used. No single drug or technique is satisfactory [8].

In a study conducted criteria for selection of appropriate drug to prevent sympathetic response. The drug must be applicable regardless of patient collaboration, prevent impairment of cerebral blood flow, and avoid arousal of the patient. It should neither be time consuming nor affect the duration or modality of the ensuinganaestheisa. Intravenous esmolol and clonidine appear to best fulfill the above criteria.

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. A simple alternative is using bolus doses of esmolol and many study have investigated this and concluded it to be efficacious in attenuating the cardiovascular response to laryngoscopy and tracheal intubation.

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. Esmolol also prevented the bispectral index during induction of anaesthesia and orotracheal intubation [9].

In our study, the heart rate increased in control group when compared with pre induction value. Similar

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increase with esmolol was seen. It was seen that both esmolol and clonidine attenuated the heart rate with a statistical significance. When we compare esmolol, we found statistical significant difference of a higher fall of the heart rate in clonidine groups which remains significant till 7 minutes [10].

Conclusion

Repeated measure ANOVA study showed significant variations in heart rate 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).

The difference in heart rate between control and clonidine group remains statistically significant at all times of assessment ($p<$ 0.001). Both esmolol and clonidine attenuated the heart rate which was highly significantly (P 0.001).

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