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Research Article

Effect of Esmolol on variation of rate-pressure product due to tracheal intubation – An evaluation using invasive arterial pressure monitoring

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Abstract

Introduction: Laryngoscopy and tracheal intubation produce sympathetic over drive by catecholamine release resulting in hypertension and tachycardia. This is usually tolerated by healthy individuals but susceptible patients are likely to succumb to the hemodynamic fluctuations. Various agents are being tried to combat the intubation response over years. This study is aimed at evaluating the efficacy of Esmolol in attenuating the rise in rate- pressure product secondary to laryngoscopy and tracheal intubation.

Methodology: 60 patients scheduled for general anesthesia were divided into two groups, E and C with 30 patients in each group. Hypertension, diabetes mellitus, thyroid disease, treatment with beta blockers and difficult airway constituted the exclusion criteria. Group-E patients received Esmolol 0.5mg/kg and group-C patients received normal saline [placebo] as intravenous premedication over 5min before a rapid sequence induction and tracheal intubation. Blood pressure and heart rate were measured using invasive arterial line and rate pressure product[RPP] was calculated at various time points including baseline, before induction, before intubation, at every 5sec after intubation up to 1min and at 5, 10 and 15min. Mean change in RPPs from the baseline were compared between the groups at the said time points.

Results: Mean fall in RPP in Esmolol group was significantly more than that in control group at almost all the time points of measurement.

Conclusion: Esmolol is effective in attenuating the hemodynamic response to laryngoscopy and tracheal intubation.

Keywords: Esmolol, Rate- pressure product, Intubation response, Laryngoscopic response

1. Introduction

The techniques of laryngoscopy and tracheal intubation are essential not only in anesthetic practice, but also in emergency and critical care medicine for airway protection and mechanical ventilation. Circulatory response to laryngeal and tracheal stimulation was known since1940[1]. Laryngoscopy and tracheal intubation elicit stress response manifested as increased blood pressure, heart rate and arrhythmias. The magnitude of hemodynamic changes may depend on depth of anesthesia and duration of stimulus. The principle mechanism behind hypertension and tachycardia is an exaggerated sympathetic action [2,3] due to increased catecholamine release.[4]

Laryngoscopic response in compromised and susceptible individuals can precipitate myocardial insufficiency, pulmonary edema, arrhythmias, left ventricular failure, and cerebrovascular hemorrahage[5,6]. Intravenous anaesthetic induction agents do not always adequately suppress the circulatory responses evoked by tracheal intubation[7]. Since tachycardia appears to be associated more frequently with myocardial ischemia than does hypertension,[8] interesting approach towards attenuating cardiac responses to laryngeal stimulation is the use of β-adrenergic antagonists. Among the β-adrenergic antagonists Esmolol (Methyl 3-4-{2-hydroxy-3- (isopropyl amino) propoxy–phenyl} propionate hydrochloride) is an effective option because it is an intravenously administered ultra short acting agent. We sought to evaluate the role of Esmolol in stabilizing the hemodynamics during laryngoscopy and tracheal intubation by beat to beat monitoring of blood pressure and heart rate using invasive arterial line in this prospective randomized double blind controlled study.

1.1. Objectives

To compare the hemodynamic variations in response to laryngoscopy and tracheal intubation measured as rate-pressure product [RPP], between the patients receiving Esmolol and normal saline (placebo) as intravenous premedication under continuous arterial line monitoring.

2. Materials and methods

Approval from institutional ethics committee was obtained before starting the study. Written informed consent was obtained from all the patients enrolled in the study. Patients in the age group of 20 to 50 years belonging to ASA status 1 and 2 scheduled for general anesthesia from July 2013 to December 2013 were included in the study. Patients with heart disease, hypertension, diabetes mellitus, thyroid abnormalities and those on treatment with beta blockers were excluded from the study. Patients with an anticipated difficult airway and those in whom tracheal intubation took more than 30 seconds were also excluded from the study. Patients were randomly segregated into two groups E and C using a computer generated randomization programme. Patients in group- E received Esmolol 0.5 mg/kg body weight in 20ml normal saline over 5minutes before induction. Patients in group- C received 20ml normal saline over 5min before induction. After shifting the patient into the operating room, non invasive blood pressure [NIBP] monitor, pulse oxymeter and ECG were connected and an intra venous [IV] line was secured with 18G canula. Inj Midazolam 1mg was given IV as premedication. Arterial line was secured in radial artery after giving local anesthesia and base line hemodynamics was recorded. All patients were pre oxygenated for 5minutes during when the study drugs were also administered as IV infusion. The study drugs were loaded by an anesthetist who was blinded to the study in 20ml syringe, coded and handed over to another anesthetist who was blinded to the drug present in the syringe for administration. After 5minutes of infusion and pre oxygenation, anesthesia was

induced with Thiopentone 5mg/kg body weight and Succinyl choline 2mg/kg body weight in a rapid sequence followed by tracheal intubation by a reasonably experienced anesthetist. Subsequently Fentanyl 2mcg/kg and Vecuronium 0.1mg/kg body weight were administered intra venous and the anesthesia was maintained on Sevoflurane in oxygen and nitrous oxide gas mixture. Invasive systolic blood pressure [SBP] and heart rate[HR] were recorded before giving the study drug, before induction of anesthesia, before tracheal intubation, immediately after tracheal intubation, at every 5seconds in the first minute and at 5min, 10min and 15min after tracheal intubation. The rate-pressure product [RPP] was calculated with the above parameters at all the said time points. Percentage change in RPP value from baseline was also calculated at all the time points of measurement. The data was tabulated and analysed.

2.1 Statistical analysis

Descriptive and inferential statistical methods were used to analyse the data. In descriptive statistics, calculation of means, standard deviation [SD] and differences in average RPPs were done with the help of Microsoft Excel. In inferential statistics, student's t-test of difference between two means, Z test of difference between two proportions were used to analyse the differences. Difference in demographic profile was analysed with the help of t-test of two independent means and Z test of proportions was used to analyse the difference in proportion of males and females in both the groups. In-silico project support for life sciences online statistical calculator was used for performing t-test and Z-test. Power of the study was calculated using online power calculator for two independent sample study.

3. Results

A total of 60 patients were enrolled in the study with 30 in each group. Power of the study with 30 as size in each sample was 96%. So the sample size was adequate. The demographic profile was comparable in two groups[table 1]. Decrease in the RPP was observed to be more at almost all the time points in Esmolol group [Fig 1]. The difference in the RPP variation from the baseline was statistically significant at 16 time points out of 19 [Table 2]. However at 45th second after intubation, the decrease in RPP was significantly less in control group than in the Esmolol group.

Table 1: Demographic Profile

Patients characteristics	Group E	Group C	Z-Value	t-value	P-value	Result
Age (years) (Mean±SD)	33.6±6.14	33.3±6.91		-0.118	0.9	NS
WEIGHT(Kg) (Mean±SD)	54±9.7	57±7.7		1.27	0.2	NS
Males	19	19	0		NA	NS
Females	11	11	0		NA	NS

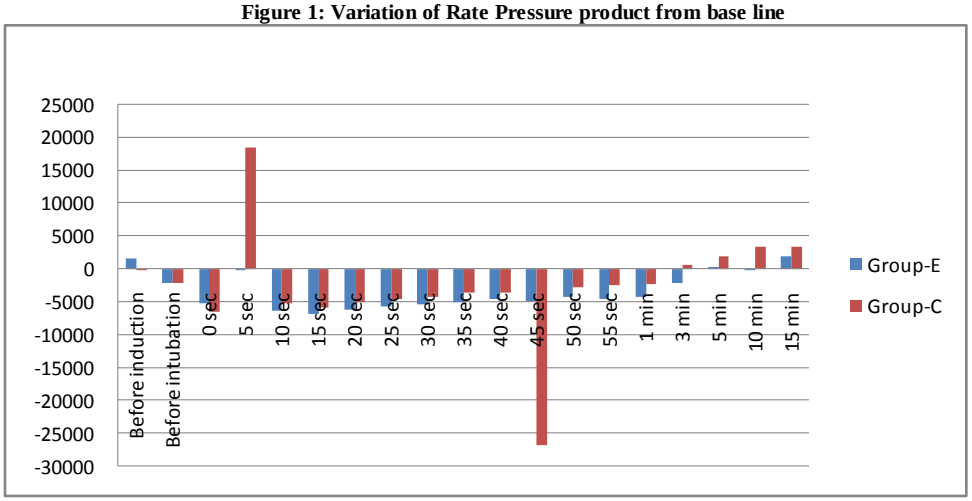
SD- Standard Deviation NS-Not Significant NA-Not Applicable

Table 2: Variation of Rate Pressure product from base line

Mean change in RPP from baseline	Group-E	Group-C	t-value	P-value	Result
Before induction	1532.63	-88.466	-3.068	0.003	HS
Before intubation	-2187.3	-2111.8	-0.354	0.72	NS
0 sec	-5329.7	-6603.1	-0.64	0.52	NS
5 sec	-273.86	18404.3	6.42	<0.001	HS
10 sec	-6332.5	-5293	4.54	<0.0001	HS
15 sec	-6862.4	-5877	-6.64	<0.001	HS
20 sec	-6201.8	-5087.3	-6.051	<0.0001	HS
25 sec	-5790.1	-4669.9	-6.01	<0.0001	HS
30 sec	-5412.7	-4250.7	-5.6	<0.0001	HS
35 sec	-5017.6	-3672.3	-1.39	0.16	NS
40 sec	-4650.4	-3679.3	3.71	0.0005	HS
45 sec	-4860.2	-26828	-5.46	<0.0001	HS
50 sec	-4348.3	-2851.6	-4.78	<0.0001	HS
55 sec	-4653.2	-2515.3	-5.19	<0.0001	HS
1 min	-4331.3	-2365.1	-5.16	<0.0001	HS
3 min	-2251.2	646.3	-2.04	0.04	S
5 min	323.3	1853.8	2.14	0.03	S
10 min	-74.26	3291.16	2.88	0.005	HS
15 min	1809.23	3245.03	2.02	0.04	S

NS- Not Significant HS-Highly significant S- Significant

Figure 1: Variation of Rate Pressure product from base line



4. Discussion

Laryngoscopy and intubation are associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias. Less commonly bradycardia may occur as a result of vagal stimulation Ghaus *et al* (2002)[9]. These potentially dangerous changes disappear within 5 minutes of onset of laryngoscopy.[10] Although these responses of blood pressure and heart rate are transient and short lived they may prove to be detrimental in high risk patients especially in those with cardiovascular disease, increased intracranial pressure or anomalies of the cerebral blood vessels.

Variations of heart rate changes decrease with increasing age. Young patients show more extreme changes.[11] The most significant factor during laryngoscopy influencing cardiovascular responses is found to be the duration of laryngoscopy.[11] A linear increase in heart rate and mean arterial pressure during the first 45 seconds was observed. Further prolongation had little effect. As the duration of laryngoscopy is normally less than 30 seconds, the results of studies in which it takes longer than this have less clinical relevance. The force applied during laryngoscopy has only minor effect.[11] In our study, the duration of laryngoscopy and intubation was limited to 20 seconds. Marked fluctuations in haemodynamic responses are often seen in geriatric patients.[12,13] In our study we selected the optimal age range of 20 to 40 years.

We employed rate-pressure product as the comparing variable between the two groups. This is the product of systolic arterial pressure and heart rate and is an index of myocardial oxygen consumption[14]. It is said that the rate-pressure product of more than 22000 often signifies the risk of myocardial ischemia and angina[15]. A substantial amount of clinical research was done in this area previously evaluating the efficacy of Esmolol in countering the pressor response individually[16] as well as in comparison with other agents like Fentanyl[17] Lidocaine[18]. In most of the previous clinical trials, NIBP was employed to analyse the hemodynamic variations. The difference in the methodology of our study is employing invasive arterial blood pressure monitoring. It usually takes an average of 40 seconds to measure blood pressure in oscillometry through non invasive blood pressure monitoring. But hemodynamic fluctuations occur continuously during and after laryngoscopy and tracheal intubation. Thus with NIBP, recording the hemodynamic variations before 40 seconds is not possible. Our study is distinguished from several other similar studies in selecting the variable of comparison between the groups. In most of the previous studies, either blood pressure or RPP was compared between the groups at different time points. But technically the most appropriate factor of clinical relevance in a laryngoscopic response is the fluctuation of hemodynamic parameters from base line than the absolute value. Thus in our study we principally compared the percentage change of RPP from the baseline at similar points of time before and after laryngoscopy and tracheal intubation. The mean fall in RPP was not only observed to be more in Esmolol group at all time points, but also the difference was statistically significant at 12 time points out of 15 time points of measurement up to 3 minutes. Subsequently at 5, 10 and 15 minutes, the mean rise in RPP from the base line was significantly less in Esmolol group emphasizing the efficacy of Esmolol in blunting the pressor response to laryngoscopy and tracheal intubation. Our study certainly contributes to the improvement in the clinical practice of airway management in both elective and emergency scnerios. However, close hemodynamic monitoring is always an essential requirement whenever vaso-active agents are included in the pharmacological armamentarium. There is certainly a scope for further reaserch in the arena of hemodynamic stabilisation during airway management evaluating the relative merits and demerits of not only various pharmacological agents but also of different interventions and their related tools and equipment.

4. Conclusion

Elevation in the rate-pressure product due to laryngoscopy and tracheal intubation can be affectively countered using pre-treatment with esmolol. However, further research is needed to find out the least possible dose to acheive the same effect and also to explore the prospects of using other pharmacological agents in combination with esmolol to attain better results.

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