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"AN OBSERVATIONAL STUDY TO COMPARE LOW DOSE ESMOLOL AND LOW DOSE LABETALOL FOR ATTENUATION OF SYMPATHOMIMETIC RESPONSE TO LARYNGOSCOPY AND INTUBATION"

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ABSTRACT

INTRODUCTION: Laryngoscopy and endotracheal intubation are associated with cardiovascular & neurological changes. Studies comparing esmolol with labetalol to attenuate pressor response are lacking.

AIM: To compare the effects of low doses of esmolol and labetalol for attenuation of sympathomimetic response to laryngoscopy and intubation.

METHODS:

Study Design: Observational study

Study Site: Dhiraj Hospital,Piparia

Study Duration: 1year

Study Population: After ethical committee's approval, this study was carried out on 60 patients, randomly and equally allocated to any of the two groups using chit method.

HR,SBP,DBP,MAP,RPP&ECG changes were recorded prior to induction, at-intubation and 1,3,5&10min post-intubation.

RESULTS: Analysis showed no significant variation in HR, SBP &DBP at intubation for both the studied drugs but post-intubation analysis revealed lower HR,SBP,MAP&RPP in labetalol group($p<0.001$).

CONCLUSION(s) : The measurement of baseline and postintubation parameters revealed statistically significant variation in HR, SBP, MAP&RPP in Esmolol as compared to Labetalol thus proving our study.

KEYWORDS : Esmolol, Labetalol, Laryngoscopy, Sympathomimetic Response

INTRODUCTION

Despite the emergence of new airway devices in the recent years, rigid laryngoscopy and tracheal intubation still remain the gold standard in airway management. Laryngoscopy and endotracheal intubation are mandatory for most patients undergoing general anesthesia, which is invariably associated with certain cardiovascular changes such as tachycardia or bradycardia, rise in blood pressure and a wide variety of cardiac arrhythmias. Various attempts have been made to suppress this pressor response. Various pharmacological methods aimed at efferent, afferent, or both limbs of response are volatile inhalational agents.[1] lignocaine,[2] opioids,[3] sodium nitroprusside,[4] nitroglycerine[5] calcium channel blockers,[6] and adrenergic blockers[7] etc. Most workers have used esmolol[8] (cardioselective beta blocker) as a bolus and in infusion and found it to be effective. Other beta blockers like metoprolol[9] and labetalol[10] have been useful not only in attenuating the response of laryngoscopy and intubation but also in preventing perioperative cardiovascular events. However studies comparing esmolol with labetalol (non selective adrenergic blocker) as an attenuating agent for pressor response are lacking.

Esmolol hydrochloride is a beta 1- selective (cardio selective) adrenergic receptor blocking agent with rapid distribution half-life of about 2 minutes and an elimination half- life of about 9 minutes. Esmolol hydrochloride is rapidly metabolized by hydrolysis of the ester linkage, chiefly by the esterases in the cytosol of red blood cells.

Labetalol, a combined α1 and non-selective β– adrenergic blocking drug has shown a better safety profile and hemodynamic stability. Onset time after IV administration is 5 minutes; peak effect is seen at 5-15 minutes, with a half-life of 4-6 hrs. It reduces systemic vascular resistance & reflex tachycardia and not associated with rebound hypertension. It has low placental transfer due to high degree of ionization at physiological pH.

As there are very few studies comparing Esmolol and labetalol in attenuating pressor response, we undertook the study to compare them.

AIM & OBJECTIVES:

The present study is aimed to test the hypothesis to compare the effects of esmolol and labetalol, in low doses, for attenuation of sympathomimetic response to laryngoscopy and intubation viz. HR, SBP, DBP,MAP&RPP.

MATERIALS AND METHODS

Study Design: Observational study

Study Site: SBKS Medical Institute and Research Centre, Sumandeep Vidyapeeth University, Piparia, Vadodara, Gujarat

Study Duration: 1 year

Study Population: After ethical committee's approval, this observational study was carried out on 60 patients in the department of anaesthesiology of Dhiraj Hospital. All the patients were subjected to pre-anaesthetic checkup. A protocol was used for gathering the information regarding the efficacy and the tolerability of the drugs. These patients were kept nil by mouth overnight. Selected patients were equally allocated to any of the two groups using chit method.

Group E (esmolol)0.5 mg/kg diluted with 0.9% saline to 10ml i.v.
Group L (labetalol)0.25 mg/kg diluted with 0.9% saline to 10ml i.v.

- Patients willing to sign the informed written consent, American Society of Anaesthesiologist (ASA) grade I and II patients of either sex, Undergoing elective surgical procedure, Aged 18-45 years, Patients requiring general anaesthesia and orotracheal intubation were included in our study.
- Patient's refusal, Patients with cardiovascular, pulmonary, hepatic and renal diseases, bleeding disorder; Pregnant woman, Patients on beta-blockers, Patients with ASA III and above, Patients included in study but required more than two attempts for laryngoscopy were excluded from our study.

All the patients posted for planned surgery were assessed for height, weight, pulse rate, blood pressure, respiratory rate, temperature and complete systemic examination(cardiovascular, respiratory, abdominal and central nervous system).

The patients were investigated for standard pre-operative profile. All the patients were kept nil by mouth for more than 12 hours, a night before surgery.

Method:

On arrival of the patient in the operating room, an 18-gauge intravenous line was secured in the unaffected limb and Ringer's lactate was started. The patients were connected to multichannel monitor which records Heart rate (HR), non-invasive measurements of systolic, diastolic and mean arterial pressure(SBP, DBP, MAP), continuous ECG monitoring and oxygen saturation. All patients were pre medicated intravenously 10 min prior to induction with inj.

Glcopyrolate 0.004mg/kg, inj. Ondansetron 0.1 mg/kg, inj. Ranitidine 1 mg/kg and inj. midazolam 0.05 mg/kg IV.

In the esmolol group, 0.5 mg/kg of esmolol (diluted with 0.9% saline to 10 ml) was given 2 min prior to intubation. In the labetalol group 0.25 mg/kg of labetalol (diluted with 0.9% saline to 10 ml) 2 min prior to intubation.

The patients were pre-oxygenated with 100% 02 by a face mask for 3 min. Induction was done with inj. propofol 2 mg/kg IV and after 30 seconds, relaxation achieved with inj succinylcholine 2 mg/kg. & the patient was intubated using a Macintosh laryngoscope. Tracheal tubes of ID 7.0 mm and 8.0 mm were used for female and male patients, respectively. Anesthesia was maintained by N2O (60%) and O_2 (40%), and Inj.Atracurium bolus followed by intermittent doses of atracurium intravenously. At the end of surgery, neuromuscular blockade was reversed with inj. Neostigmine (0.05 mg/kg IV) and inj. Glycopyrrolate (0.008mg/kg) IV.

Measures:
HR,SBP,DBP,MAP,RPP&ECG changes were recorded prior to induction, at time of laryngoscopy and intubation and 1,3,5,&10 min after intubation.

RESULTS
Analysis of patients' results revealed no differences in the demographic characteristics of the two groups (Table 1).

TABLE 1: DEMOGRAPHIC DATA

	GROUP E	GROUP L
AGE	39±11.2	38.76± 13.2
SEX(M:F)	2:1	1:1
WEIGHT (Kg)	56.4	57.8

The pre-induction values of pulse rate were comparable between two groups (Table 2). Post-intubation 5&10 min, heart rate was significantly lower in labetalol group compared to the esmolol group ($p<0.001$).

TABLE 2: PULSE RATE

	GROUP E	GROUP L	P value E & L
Pre intubation	85.83±7.65	84.9 ±6.95	0.6240
At intubation	89.03 ±7.26	87.53 ± 6.74	0.4103
Post intubation			
1 min	88.16±6.90	83.8±6.01	0.0115
3 min	85.06 ±6.61	79.56±6.45	0.0019
5 min	82.2±6.32	75.83±5.69	<0.0001
10 min	77.7±5.92	69±7.31	<0.0001

The pre-induction values of SBP were comparable between two groups (Table 3). SBP increased in both esmolol and labetalol groups at the time of intubation. SBP was significantly lower at 3&10 min post-intubation in the labetalol group ($p<0.0001$) which was extremely statistically significant.

The pre-induction and post-induction values of DBP were comparable between two groups(Table 3).

The pre-induction values of MAP were comparable between two groups (Table 3). MAP was statistically significantly less in the labetalol group at 5&10 min post-intubation ($p<0.01$ and $p<0.0001$ respectively).

The pre-induction values of RPP were comparable between two groups(Table 3). RPP was statistically significantly less in the labetalol group at 5&10 min post-intubation ($p<0.0001$).

TABLE 3: TABLE SHOWING STATISTICAL ANALYSIS OF SBP, DBP, MAP & RPP DURING THE STUDY

SYSTOLIC BLOOD PRESSURE				DIASTOLIC BLOOD PRESSURE			
	GROUP E	GROUP L	P VALUE		GROUP E	GROUP L	P VALUE
Pre-intubation	132.93±6.85	123.23±8.18	<0.0001	**Pre-intubation**	77.53±5.58	77.66±6.01	0.9311
At intubation	135.26±5.99	133.26±7.79	0.0281	**At intubation**	79.63±5.3	79.66±7.01	0.9851
Post-intubation				**Post-intubation**			
1 min	130.03±5.87	135.93±6.97	0.2695	**1 min**	79.93±5.69	81.06±5.05	0.4192
3 min	125.33±5.77	125.53±7.17	0.9057	**3 min**	79.83±5.23	78.86±4.91	0.4619
5 min	120.96±5.50	112.53±7.98	<0.0001	**5 min**	77.43±5.68	77.33±5.51	0.9451
10 min	113.13±5.90	102.40±5.46	<0.0001	**10 min**	73.60±5.88	72.23±5.12	<0.3398
MEAN ARTERIAL PRESSURE				**RATE PRESSURE PRODUCT (RPP)**			
	GROUP E	GROUP L	P VALUE		GROUP E	GROUP L	P VALUE
Pre-intubation	96.26±4.41	92.85±4.86	0.0061	**Pre-intubation**	11407.1±1145.72	10474.67±1220.21	0.0034
At intubation	98.17±4.05	97.53±4.58	0.5686	**At intubation**	12407.77±1164.90	11670.87±1193.48	0.0201
Post-intubation				**Post-intubation**			
1 min	96.63±4.18	99.35±4.18	0.0145	**1 min**	11475.4±1156.41	11407.87±1193.83	0.8247
3 min	95±3.73	94.42±4.05	0.5662	**3 min**	10670.57±1059.58	9993.53±1045.32	0.0156
5 min	91.94±3.83	89.06±4.39	0.0089	**5 min**	9948.63±947.86	8530.53±852.12	<0.0001
10 min	86.77±4.05	82.28±3.66	<0.0001	**10 min**	8795.96±877.33	7069.46±872.87	<0.0001

One patient had atrial ectopics on electrocardiogram (ECG) in the esmolol group while there were no ECG abnormalities detected, anytime, in the labetalol group.

DISCUSSION:
Very few clinical studies have been undertaken in the past to determine the effects of Esmolol and Labetalol on haemodynamic responses caused by laryngoscopy and endotracheal intubation.

Since the introduction of esmolol in 1982, it has found clinical application to control perioperative tachycardia and hypertension, to suppress intubation and extubation response, supraventricular tachycardia etc., and has been used as bolus and infusion to attenuate intubation response in doses varying from 0.4mg/kg to 2 mg/kg.

Gilakala Varaha Ganesh ***et al***, in the year 2015, conducted a study on 75 patients dividing the subjects into two groups receiving Esmolol 0.5mg/kg, labetalol 0.25 mg/kg, labetalol in 0.25 mg/kg dose showed better attenuation of sympathomimetic response to laryngoscopy and intubation compared to esmolol of 0.25mg/kg.

B. Sowbhagya lakshmi ***et al***(2014) conducted a study on 75 patients of ASA 1 And ASA 2 patients aged 18-45 yrs, undergoing elective surgical procedures requiring GA or orotracheal intubation. Patients were divided into three groups receiving labetalol at 0.5mg/kg, esmolol 1mg/kg and the control group received 10mlR of 0.9% NS. Study revealed that in low doses, labetalol is a better agent than esmolol in suppressing the hemodynamic response to laryngoscopy and intubation.

Amanathan ***et al*** conducted study in the Dept of Anaesthesia, General hospital of Athens[Greece] in June 2013,in which 60 patients were randomly allocated into three different groups who received Esmolol 0.5mg/kg, labetalol 0.25mg/kg and third group received NS as a control,given two minutes prior to endotracheal intubation, SBP, DBP, HR and MAP were recorded at 1,2,4 & 10. They Concluded that, Labetalol significantly attenuated the rise in SBP and HR during laryngoscopy and ET intubation when compared to esmolol [$p<0.05$].

Forbes AM et al stated that HR and BP returned to pre-laryngoscopy level in normotensives within 5 to 10 minutes due to adaptation and

gradual fatigue of receptors, cessation of stimulus and deepening of anesthesia. However, Chandola HC observed that in hypertensive patients, in whom pressor response was exaggerated, it took as long as 20 minutes to reach the baseline value. In the view of this, we excluded hypertensive patients from our study.

Sarvesh P Singh et al in 2010, conducted a study on 75 ASA 1 nd 2 patients aged 18 to 45 years. Patients were divided into three groups. Group c receiving 0.9% saline to 10 ml, group L receiving labetalol 0.25mg/kg and group Esmolol 0.5mg/kg 2 min prior to intubation. HR, SBP, DBP were recorded at 1,3,5,10 min after intubation. MAP and RPP were calculated. Abnormal ECG changes were also recorded. Compared to placebo and esmolol(0.5mg/kg), labetalol (0.25mg/kg) significantly attenuated the rise in heart rate, systolic blood pressure and RPP during laryngoscopy and endotracheal intubation.

In our study, when the effect of stimulus weans off, as occurs at 10 min postintubation, the drug's effect takes over and pulse rates go below baseline values. Labetalol prevented the increase in SBP significantly throughout the study period as compared to esmolol group ($p<0.05$). The rise in DBP was not attenuated in any of the study groups and inter-group study also, none of them is superior. When labetalol was compared with esmolol group, the MAP was significantly less at all points except at 10th min post intubation. Labetalol had a significantly ($p<0.05$) better effect than esmolol in controlling pulse rate at all points during the study. It seems that when instrumentation stimulus is present, labetalol maintains the pulse rate within normal ranges.

CONCLUSION(s)

We conclude that the measurement of the baseline vital parameters and parameters immediately after laryngoscopy and endotracheal intubation revealed a statistically significant percentage variation in heart rate, SBP, MAP and RPP in Esmolol as compared to Labetalol. Thus, low dose Labetalol(0.25mg/kg) is more effective and safe in attenuating sympathetic response to laryngoscopy and endotracheal intubation in comparison to low dose esmolol(0.5mg/kg).

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