



ATTENUATION OF HEMODYNAMIC RESPONSE TO ENDOTRACHEAL INTUBATION USING ORAL IVABRADINE - A PROSPECTIVE RANDOMISED CONTROLLED DOUBLE BLIND STUDY

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ABSTRACT

BACKGROUND: Rapid and dramatic hemodynamic changes which adversely affect the patient may occur during laryngoscopy and intubation. The present study evaluates the effect of oral ivabradine on the hemodynamics during laryngoscopy and endotracheal intubation in patients undergoing surgical procedures under general anaesthesia with ETT.

STUDY DESIGN: A prospective, randomized, controlled, double-blind study.

MATERIAL AND METHODS: 90 ASA I and II patients who underwent elective surgeries under general anaesthesia at Dr Jeyasekharan Hospital and Nursing Home, were randomly divided into two groups of 45 each. Group A received Tab Ivabradine 5 mg and group B received Tab B complex. The hemodynamic parameters namely HR, SBP, DBP and MAP were monitored prior to the study drug as baseline and at the following time intervals; after induction, after intubation, after 1, 3, 5, 8 and 10 minutes after intubation.

RESULTS: HR was significantly lower in the ivabradine group compared to control group at all time interval after study drug. SBP, DBP & MAP were significantly lower in the Ivabradine group compared to control group after induction, after intubation, and 1, 3, 5, 8 and 10 minutes after intubation.

CONCLUSIONS: Ivabradine given before intubation prevents significant rise in HR and SBP, DBP, MAP compared to placebo in patients during laryngoscopy and endotracheal intubation.

KEYWORDS :

INTRODUCTION

Laryngoscopy and intubation is needed for most patients undergoing surgical procedures under general anaesthesia. Hypertension and tachycardia have been commonly associated with intubation under general anaesthesia due to manipulation during laryngoscopy and stimulation of epiglottis.

Ivabradine is a cardiotonic agent which is highly selective inhibitor of "I_f" channels, results in decrease in slope of spontaneous depolarization leading to increase in time interval between successive action potentials in SA node thereby decreasing the heart rate. Ivabradine reduces the heart rate without compromising hemodynamics, can be used in both hypertensive patients and normotensive patients.

MATERIAL AND METHODS

After obtaining the clearance from the institutional scientific and ethical committee study was undertaken AT Dr. Jeyasekharan Hospital and Nursing Home Nagercoil, Kanyakumari district, Tamilnadu. The study period was 18 months from September 2017 to February 2018.

Pre-anesthetic checkup was done including proper history, general and systemic examination for ASA grading and also for inclusion in the study. 90 patients aged above 15 years (ASA I and II) of either sex were selected and they were randomly allocated into two groups as per randomization method.

Group A – Comprising 45 patients who received oral ivabradine.

Group B – Comprising 45 patients, who received a placebo

Written and informed consent were obtained from the patient and standard protocols followed for anaesthesia in both group patients. All patients were kept nil per oral for 6 hours prior to surgery time at Operation theatre. Premedication with Inj. Ondansetron 4mg IV + Inj. Rabeprazole 20 mg IV were given for all patients 1 hour prior to surgery in the pre-operative room. A nurse not clinically involved in the study followed the randomization sequence using a computer generated random number chart with a block size of four and a 1:1 allocation ratio.

The same nurse prepared sequentially numbered, opaque and sealed envelopes to implement the sequence, with either Tab Ivabradine 5mg or placebo and administered it to the patient with sips of water about 1 hour before intubation, after obtaining permission from the researcher without disclosing the name of the tablet. All patients and care providers, including anaesthesiologists and study personnel were blinded during group allocation. All patients had intravenous infusion of IV fluid Ringer's lactate on flow prior to induction.

Patient was shifted into the Operating room and connected to monitors after placing supine on the OT table. Pulse Rate (PR), Respiratory Rate (RR), Non-invasive blood pressure (NIBP), Oxygen Saturation (SpO₂) and Electrocardiogram (ECG) monitoring was done using a standard calibrated monitor. The premedication, induction agent and muscle relaxant to facilitate intubation were standardized for both the groups.

Baseline HR, SBP, DBP and MAP were recorded and preoxygenation done for 3 min with a facemask. The patient induced by Inj Propofol 2mg/kg and Inj Fentanyl 1 mcg/kg. Intubation facilitated by using Inj. Vecuronium 0.1mg/kg i.v.

The lungs ventilated with 100% oxygen for 60 seconds. Intubation done at around 60 minutes after Ivabradine pre-treatment in group-1 and 60 min after placebo in group -2 (correlating with peak action of the drug).

Intubation achieved with an appropriate size oral, cuffed, portex endotracheal tube by the aid of Macintosh laryngoscope blade. HR,SBP, DBP and DBP were recorded post induction, post intubation and at predetermined intervals. Balanced anesthesia was maintained with Vecuronium bromide (0.02mg/kg) top-up doses; and intermittent positive pressure ventilation with nitrous oxide and oxygen in the ratio of 66%: 33% using circle absorber system connected to Anesthesia work station.

The surgeon was requested to defer putting the incision until 1,3,5,8 and 10 minutes recordings were completed .Any post induction hypotension (MAP < 20%) was managed with fluid bolus of NS 250 to 300 ml and ephedrine 6mg IV and with Inj atropine 0.6 mg if heart rate was less than 20% of baseline heart rate.

Parameters recorded were heart rate, systolic BP, diastolic BP,

Mean arterial pressure. Ten minutes after intubation, after taking the recordings of hemodynamic parameters, inhalational agent was introduced into the anesthetic technique. The study was discontinued once the sample size of 90 patients have been studied.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 2020 statistical Analysis Software. Significance level is decided before starting study-95% The parametric variables were collected and were analyzed by independent t- test.Statistical analysis was performed using Chi-Square for non-parametric samples. P<0.05 was considered as statistically significant.Master chart was prepared using the available individual data from the patient proformas , following which the data was analyzed.

RESULTS AND DISCUSSION

Present study was undertaken to study the hemodynamic changes following intubation between patients who received oral ivabradine and those who did not. Blood pressure and heart rate response to direct laryngoscopy and endotracheal intubation was studied in both the groups.

TABLE-1: HR CHANGES IN BOTH GROUPS

	PLACEBO(n=45)		IVABRADINE(n=45)		t	df	P VALUE
	Mean	sd	Mean	sd			
HEART RATE - BASELINE	84.22	11.419	77.13	8.05	3.404	79.069	0.001
HR-AT INDUCTION	87.29	10.593	79.02	7.823	4.211	88	<0.001
HR-AT INTUBATION	91.36	10.671	76.71	7.765	7.444	88	<0.001
HR-1 MIN AFTER INTUBATION	89.51	10.211	74.76	7.595	7.778	88	<0.001
HR-3 MIN AFTER INTUBATION	88.24	10.107	73.42	7.359	7.953	88	<0.001
HR-5 MIN AFTER INTUBATION	86.67	9.902	71.96	7.483	7.951	88	<0.001
HR-8MIN AFTER INTUBATION	86.4	9.804	71.13	7.307	8.376	88	<0.001
HR-10 MIN AFTER INTUBATION	85.64	9.815	70.71	6.992	8.313	79.516	<0.001

TABLE-2 : SBP CHANGES IN BOTH GROUPS

	PLACEBO(n=45)		IVABRADINE(n=45)		t	df	P VALUE
	Mean	sd	Mean	sd			
SBP-BASELINE	114.42	7.275	116	6.671	-1.072	88	0.287
SBP-AT INDUCTION	119.42	7.216	121.91	6.643	-1.702	88	0.092
SBP-AT INTUBATION	117.69	7.332	119.56	6.416	-1.285	88	0.202
SBP-1 MIN AFTER INTUBATION	115.56	7.573	117.04	6.684	-0.989	88	0.325
SBP -3MIN AFTER INTUBATION	113.42	7.347	114.73	6.545	-0.894	88	0.374
SBP-5 MIN AFTER INTUBATION	111.51	6.871	112.6	6.429	-0.776	88	0.44
SBP 8 MIN AFTER INTUBATION	109.84	6.829	111.18	6.114	-0.976	88	0.332
SBP-10 MIN AFTER INTUBATION	108.8	6.666	110.62	6.154	-1.347	88	0.181

TABLE-3 :DBP CHANGES IN BOTH GROUP

	PLACEBO(n=45)		IVABRADINE(n=45)		t	df	P VALUE
	Mean	sd	Mean	sd			
DBP-BASELINE	68.29	7.54	69.71	5.558	-1.019	88	0.311
DBP-PRE INDUCTION	72.18	7.114	73.67	5.669	-1.098	88	0.275
DBP-AT INTUBATION	70.93	6.607	71.53	5.599	-0.465	88	0.643
DBP-1 MIN AFTER INTUBATION	69.18	6.576	69.71	5.763	-0.409	88	0.683
DBP-3 MIN AFTER INTUBATION	67.62	6.461	68.31	5.744	-0.535	88	0.594
DBP-5 MIN AFTER INTUBATION	66.33	6.36	67.04	5.657	-0.56	88	0.577
DBP- 8MIN AFTER INTUBATION	65.51	6.24	66.18	5.293	-0.547	88	0.586
DBP-10 MIN AFTER INTUBATION	64.4	6.103	65.62	5.577	-0.992	88	0.324

TABLE-4 :MAP CHANGES IN BOTH GROUPS

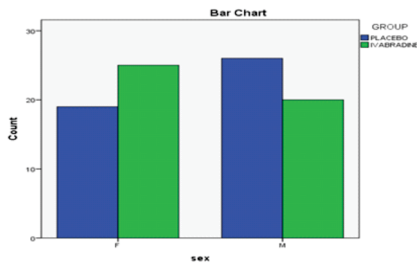
	PLACEBO(n=45)		IVABRADINE(n=45)		t	df	P VALUE
	Mean	sd	Mean	sd			
MAP-BASELINE	83.6756	6.52569	85.07	4.65037	-1.167	88	0.246
MAP- PRE INDUCTION	88.2422	6.23183	89.9133	4.8288	-1.422	88	0.159
MAP-AT INTUBATION	86.678	6.1195	87.538	4.8065	-0.741	88	0.46
MAP-1 MIN AFTER INTUBATION	84.7467	6.04414	85.446	4.91947	-0.602	88	0.549
MAP-3 MIN AFTER INTUBATION	82.9311	5.96356	83.766	5.4364	-0.694	88	0.489
MAP-5 MIN AFTER INTUBATION	81.58	5.77351	82.3111	4.92091	-0.647	88	0.52
MAP- 8 MIN AFTER INTUBATION	80.45111	5.584256	81.17756	4.654674	-0.67	88	0.504
MAP-10 MIN AFTER INTUBATION	79.5222	5.53776	80.5538	4.72255	-0.951	88	0.344

TABLE-5 : DISTRIBUTION OF AGE, WEIGHT, HEIGHT AND BMI

	PLACEBO(n=45)		IVABRADINE(n=45)		t	Df	P VALUE
	Mean	sd	Mean	Sd			
AGE	35.62	8.909	33.56	8.683	1.114	88	0.268
WEIGHT	61.5333	6.9922	57.6722	6.17956	2.776	88	0.007
HEIGHT	157.56	4.099	152.91	8.19	3.402	64.736	0.001
BMI	24.75111	2.552683	24.71778	2.585386	0.062	88	0.951

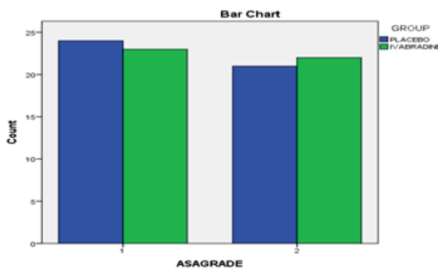
There is no significant difference in distribution of age, weight, height and BMI between two groups.

FIGURE-1: SEX DISTRIBUTION IN TWO GROUPS



No significant difference in distribution of sex and ASA between two groups.

FIGURE-2: ASA DISTRIBUTION IN TWO GROUPS



In this study HR was significantly lower with a p value <0.001 in the Ivabradine group compared to control group at all time interval after study drug. SBP, DBP&MAP were significantly lower in the Ivabradine group compared to control group after induction, after intubation, and 1,3,5,8 and 10 minutes after intubation.

DISCUSSION

Rapid and dramatic hemodynamic changes adversely affect the patient. These changes may occur during the perioperative period. Hypertension and tachycardia have been recognized as commonly associated with intubation under light anesthesia and is most evident during laryngoscopy and intubation. The effect is usually arising within 30 seconds after endotracheal intubation and lasting less than 10 minutes thereafter. Hence controlling hemodynamic changes is an important aspect of anesthetic management to prevent complications.

Various strategies have been implemented for the attenuation of hemodynamic response to laryngoscopy and intubation with tracheal spray of lignocaine, increasing the depth with inhalational agents, various drugs like Labetalol, Nitroprusside, Calcium channel blockers, etc but only few recent studies in southern part of India has been done with oral Ivabradine.

CONCLUSIONS

This study concluded that oral Ivabradine has better heart rate control than placebo for attenuation of hemodynamics during laryngoscopy and endotracheal intubation in ASA 1 and 2 patients without side effects.

Conflicting Interests Author declares no conflict of interest.

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Ethical approval - Obtained

Informed consent - Obtained

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