

# Prevention of Haemodynamic Changes during Laryngoscopy and Endotracheal Intubation- A Clinical Study of Oral Ivabradine

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## ABSTRACT

**Introduction:** Laryngoscopy and Intubation causes lot of haemodynamic changes which can have deleterious effects on patients. This study evaluates the role oral Ivabradine on haemodynamics during laryngoscopy and intubation of trachea during general anaesthesia.

**Material and methods:** A prospective randomised study was conducted in fifty ASA grade-I patients undergoing various procedures under general anaesthesia. They were randomly divided into two groups. The group I (Test group, n=25) received oral Ivabradine 5mg one Tab. at 9.00 pm on the evening before the day of surgery and another one hour before intubation. Patients in group II (control group, n=25) received the placebo.

**Results:** The result of the study was that haemodynamic parameters were more stable in Test group as compared to Control group.

**Conclusion:** Ivabradine is extremely useful drug to prevent the abnormal increase in heart rate and blood pressure during laryngoscopy and tracheal intubation.

**Keywords:** Ivabradine, Attenuation, Haemodynamic, Laryngoscopy, Intubation.

## INTRODUCTION

Endotracheal intubation, commonly performed procedure can cause a rapid and dramatic haemodynamic changes which can adversely affect the patient in perioperative period.<sup>1</sup> Hypertension and tachycardia have been recognised since 1950. They have been commonly associated with intubation under light general anaesthesia due to manipulation during laryngoscopy and stimulation of epiglottis. Though they have little consequences in healthy but can be disastrous in patients with hypertensive, raised intracranial pressure, aneurismal vascular disorders and ischaemic heart disease.<sup>2</sup> Complications that might arise are acute left ventricular failure, arrhythmias, intracranial haemorrhage and pulmonary oedema. Convulsion may be precipitated in eclmptic patients. Almost all types of arrhythmias have been documented. Various types of techniques have been advocated in high risk patients<sup>3</sup> which includes topical and or Intravenous Lignocaine, Deep inhalational anaesthesia, Ganglion blockers, precurarization, Narcotic analgesics, Adrenoceptor blocking drugs, Nitroglycerine, Calcium channel blockers and techniques like minimising laryngoscopy time (less than 15 sec), the use of LMA's etc.

Ivabradine is a very unique drug being classified as cardiotoxic agent which is highly selective inhibitor of "I<sub>f</sub>" channels. This blockade results in decrease in slope of spontaneous depolarisation leading to increase in time interval between successive action potentials in SA node thereby decreasing the heart rate. As Ivabradine's binding site is located intracellular, it requires an open "I<sub>f</sub>" channel to reach to its binding site.

It is quite different from the beta blockers as Ivabradine reduces the rate without compromising haemodynamics in unhealthy, compromised patients.<sup>4</sup> The drug can be used in both hypertensive and normotensive patients. It has no negative inotropic effects and can be used in asthmatics too where beta blockers are contraindicated. It does not blunt the hypoglycaemic response, does not increase the sensitivity of diabetics to oral hypoglycaemic agents.<sup>5</sup> It reduces heart rate without producing precipitous fall in blood pressure hence it is useful in patients with angina, CAD, Cardiac failure and Obstructive cardiomyopathies where the risk of oxygen supply may be of prime importance.<sup>6,7</sup> Aim of our study was to evaluate the attenuation of haemodynamic response by Oral Ivabradine during Laryngoscopy and Intubation in general anaesthesia.

## MATERIAL AND METHODS

The study was conducted on fifty patients. They were selected randomly from General surgery and Gynaecology departments undergoing various procedures in general anaesthesia belonging to ASA Grade-I. The patients were in age group of 30-50 years comprising both sexes were included in our study. Their informed consent and ethical clearance was obtained from patients and college ethical board respectively.

Patients selected underwent open cholecystectomies, Abdominal and Vaginal Hysterectomies, Uterine fibroid and Tubo-ovarian surgeries. All the patients were assessed clinically preoperatively and presence of any medical disorder and history of any drug intake was ruled out. Patients with any systemic problems were excluded from the study. Patients with heart rate less than 60 per minutes and systolic blood pressure less than 100mm of Hg or ECG abnormality were also excluded from study. Difficult intubation cases were also not been taken. All patients underwent investigations namely complete urine analysis, Haemogram, Blood chemistry, X-Ray chest and ECG.

**Group-1 (Test Group):** Comprising 25 patients, who received Oral Ivabradine (5mg) one tablet. At 9.00 PM in the night before the day surgery planned. Another 5mg tab. was given one hour before Laryngoscopy and intubation.

**Group-2 (Control Group):** Comprising 25 patients who received placebo.

The premedication, induction agent and muscle relaxant to

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facilitate intubation were standardised for both the groups. Intravenous line was put and Ringer Lactate solution was started. Premedication with Inj. Midazolam 1 mg and Ondansetran 4mg were given slowly intravenously about 20 minutes before induction. Patient were also connected with Nihon Kohden Multipara Monitor to monitor ECG Lead II, NIBP, SpO<sub>2</sub> Respiration and EtCO<sub>2</sub>. All patients were preoxygenated by 100% O<sub>2</sub> for 3 minutes. Patients were induced with Inj. Propofol 2.5mg /kg intravenously. Intubation was facilitated with succinyl Choline 1.5 mg/kg. Lungs ventilated with 100% O<sub>2</sub> for one minutes. In whole process intubation was timed at 60 minutes, after Ivabradine treatment in Group-1 as well as after Group-2 the Placebo group. Intubation achieved with appropriate size of cuffed Portex tube orally by Macintosh laryngoscope blade. Intubation was achieved within 15-20 seconds. Anaesthesia was maintained by Vecuronium Bromide 0.08mg/kg top-up doses; and intermittent positive pressure ventilation with O<sub>2</sub> and N<sub>2</sub>O (50%:50%) using circle absorber connected to Dragers Fabius Plus workstation.

Surgery was not allowed to commence till the recording were completed which was around 10 minutes. After that inj. Fentanyl 2mcg/kg and Isoflurane were started for maintaining the anaesthesia needed for surgical procedure. Patients were reversed with Inj. Neostigmine 0.05mg/kg and Glycopyrrulate 0.04mg/kg. All patients were followed in the post-operative period for any side effectsof in both the groups.

**The Parameters recorded were:** Heart Rate, Systolic Blood Pressure, Diastolic Blood pressure and Mean Arterial Pressure.

**The recordings we noted at various intervals as -** Preoperatively (after Premedication), At Induction or Intubation, 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation, 8 minutes after intubation, 10 minutes after intubation.

**STATISTICAL ANALYSIS**

SPSS version 21 was used for statistical analysis. Test of significance between groups were carried out by student t-test or modified t-test.

**RESULTS**

Fifty patients, undergoing elective surgery were selected for the study. The patients were randomly divided into two groups of 25 patients each.

**Group-1 (test group):** Patients who received oral Ivabradine pre-treatment.

**Group-2 (Control group):** Who received placebo. The test group comprises of 12 males and 13 females, and the Control Group comprises 10 male and 15 females. The range for age was 30-50 years while the range for weight was 45-63 kg in both groups.

Mean heart rate which was 102.86 at preoperative time was gone up to 120.88 during intubation and it was still at 110.64/ min. after 10 minutes, while in test group it was 82.6/min. which rose only upto 85.43 during intubation and came down to 73.46 at 10 minutes (Table-1 and Graph-1).

In control group Mean systolic blood pressure which was 128.65 preoperatively gone up to 140.90 mm of Hg.at 1min. and it was still 136.09 mm of Hg at 10 min. while in test group it

remained 119.76 at preoperatively went to 127.60 at 1 min. and was 120.20 at 10 min (Table-2 and Graph-2).

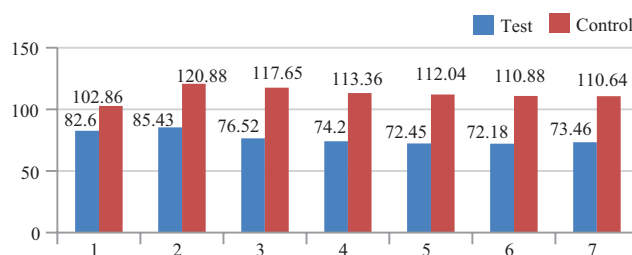
In control group Mean diastolic pressure which was 83.09 at preoperative level rose to 91.43 at intubation and reached to 87.56 mm of Hg at 10 min. while in Test group the values were 76.62 at preoperative to 82.04 at intubation which came down to 74.21mm of Hg at 10 min (Table-3 and Graph-3).

In control group Mean blood pressure which was 98.35 at preoperative level rose to 108.65 at 1min. and was still at 101.56 mm of Hg at 10 min. while in Test group the values were 92.00 at preoperative to 95.12 at 1min. which came down to 89.90 mm of Hg at 10 min (Table-4 and Graph-4).

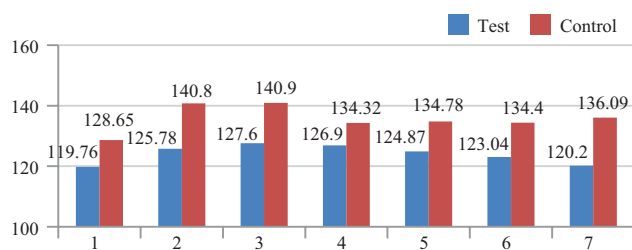
The above tables and graphs show that haemodynamic parameters recorded in preoperative period, during intubation and after 1,3,5,8 and 10 min. were found to be very significant( p value <0.05).

**DISCUSSION**

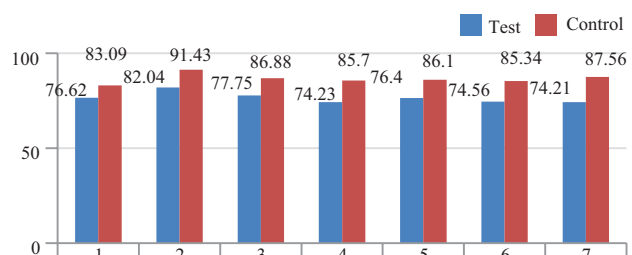
Cardiac and hemodynamic disturbances following



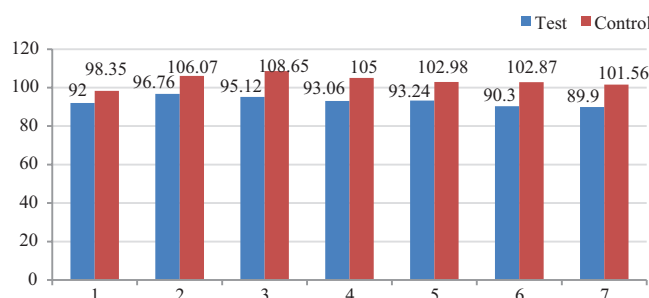
**Graph-1:** Heart rate variations



**Graph-2:** Systolic blood pressure variations



**Graph-3:** Diastolic blood pressure variations



**Graph-4:** Mean blood pressure variations

Groups	Pre Op.	Intubation	At 1 min.	At 3 min.	At 5 min.	At 8 min.	At 10 min.
Test	82.60	85.43	76.52	74.20	72.45	72.18	73.46
Control	102.86	120.88	117.65	113.36	112.04	110.88	110.64
P value	0.000	0.000	0.000	0.000	0.000	0.000	0.000

**Table-1:** Heart rate variations (Test n=25, Control n=25)

Groups	Pre Op.	Intubation	At 1 min.	At 3 min.	At 5 min.	At 8 min.	At 10 min.
Test	119.76	125.78	127.60	126.90	124.87	123.04	120.20
Contro	128.65	140.80	140.90	134.32	134.78	134.20	136.09
P value	0.012	0.000	0.000	0.000	0.000	0.000	0.000

**Table-2:** Systolic blood pressure variations (Test n=25, Control n=25)

Groups	Pre Op.	Intubation	At 1 min.	At 3 min.	At 5 min.	At 8 min.	At 10 min.
Test	76.62	82.04	77.75	74.23	76.40	74.56	74.21
Control	83.09	91.43	86.88	85.70	86.10	85.34	87.56
P value	0.014	0.000	0,000	0,000	0.000	0,000	0.000

**Table-3:** Diastolic blood pressure variations (Test n=25, Control n=25)

Groups	Pre Op.	Intubation	At 1 min.	At 3 min.	At 5 min.	At 8 min.	At 10 min.
Test	92.00	96.76	95.12	93.06	93.24	90.30	89.90
Control	98.35	106.07	108.65	105.00	102.98	102.87	101.56
P value	0.002	0.000	0.000	0.000	0.000	0.000	0.000

**Table-4:** Mean blood pressure variations (Test n=25, control n=25)

laryngoscopy and endotracheal intubation with traditionally used anaesthetic techniques were first reported by REID and BRACE in 1940<sup>7-9</sup> They reflect as rise in heart rates and blood pressure (systolic, diastolic and mean arterial pressures) specially peaks are seen after 30-45 seconds after laryngoscopy. These changes may be transient but may have serious and life threatening consequences if patients has cardiovascular and cerebral disorder. Sympathetic response to laryngoscopy has been studied and tackled in past by topical anaesthesia of pharynx, superior laryngeal nerve block, tracheal spray of lignocaine, increasing the depth by inhalational agents, alpha and beta blockers, both alpha and beta blockers e.g. Labetelol, Nitroprusside, Calcium channel blockers, Nitroglycerine and strong narcotics etc.<sup>10-13</sup>

King et al in 1951 described pressure response to laryngoscopy and intubation during anaesthesia.<sup>14</sup> Study of Prys Roberts et al in 1970 concluded that reflex response occurred in both treated and untreated hypertensive patients and the risk was more in later. They suggested Beta –Blockers to attenuate the response.<sup>15</sup> J. Gilbert Stone et al in 1988 have shown exaggerated haemodynamic responses undoubtedly cause a large increase in oxygen demand. Beta Blocking prophylaxis was given by Pierce Fox, John Sear Lynne in 1988 for patients with hypertension and Ischaemic heart disease and concluded that reflex response to Laryngoscopy and intubation was blocked by Labetalol more effectively than Atenolol or Oxprenolol. In 1994 Wang et al studied the effectiveness of bolus dose of Esmolol in attenuating haemodynamic response.<sup>16</sup> In the present study, oral Ivabradine, was used to attenuate the haemodynamic responses to laryngoscopy and endotracheal intubation and the same were compared with a placebo group. Blood pressure and heart rate response to laryngoscopy and intubation was studied in both the groups. The pre-induction parameters of haemodynamic (i.e. after premedication) showed a slight increase in the systolic, diastolic

and mean arterial pressures, when compared to the values noted at the pre anaesthetic evaluation. The difference was not statistically significant, and these values were taken as basal values. After induction and intubation the surgeon was not allowed to operate till ten minutes (duration of observation) because ivabradine has no analgesic properties and skin incision could have raised the heart rate and blood pressure giving false result.

The advantage of Ivabradine in our study were – Good attenuation of heart rate response,<sup>14-20</sup> mild attenuation in blood pressure response, intraoperative protection against abnormal cardiovascular response in perioperative period, good response to pressure effects during extubation, drug with minimal side effects. No side effects with these dosages were observed during study. The drug in our study as we observed can be used even in normotensive patients to prevent unwanted tachyarrhythmias commonly seen during induction of general anaesthesia. Ivabradine is simple, safe, economical and easy to use drug for achieving satisfactory haemodynamic goal during induction, laryngoscopy, intubation, perioperative and also in immediate postoperative period.<sup>21</sup>

## CONCLUSION

Ivabradine is extremely useful drug to prevent abnormal rise in heart rate during laryngoscopy and intubation. It also minimises, though not fully effectively, the rise of blood pressure but helps to bring down baseline blood pressure within short period of time (approx. 3 minutes.). It has proved safe in patients with diabetes mellitus, asthma, Ischaemic heart disease, angina pectoris and cardiomyopathies. Its stabilizing effect of haemodynamics also extends up to extubation and immediate post-operative period. With the dosages we used in our study there were no side effects seen in patients.

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