

# Efficacy of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation by Using Oral Ivabradine and Oral Gabapentin

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Conflict of interest: Nil

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## Abstract

**Background:** Laryngoscopy and endotracheal intubation are fundamental skills that an anaesthesiologist is supposed to achieve in order to administer anesthesia safely. Some studies have been reported in literature suggesting the role of Ivabradine and Gabapentin in inhibiting the hemodynamic responses to laryngoscopy and endotracheal intubation separately, but none of them have compared their efficacy.

**Aim and Objective:** To evaluate the efficacy of oral Ivabradine and oral Gabapentin in attenuating the hemodynamic response occurring due to Laryngoscopy and Endotracheal intubation.

**Material and Method:** This was the Hospital based prospective, randomized double blind clinical trial, conducted on Patients undergoing elective surgical procedure under general anesthesia, in which 120 patients were included in Group I (Patient has received Ivabradine 5 mg.) Group G (Patients has received Gabapentin 800mg) for the duration of one year, in one of the tertiary care center Government medical college, Siddipet, after getting informed consent and followed inclusion and exclusion criteria.

**Results:** There was no statistically significant difference in gender between the groups, and also we found age between the groups was comparable. Mean heart rate, SBP, DBP and MAP at pre op was higher in Group I compared to Group G, only at induction it was increased and higher compared to group G and at intubation and later on it was lower compared to Group G and mean difference in of these parameters were statistically highly significant between the groups.

**Conclusion:** we can conclude that both the drugs provides good degree of hemodynamic stability during the surgeries, but ivabradine is maintaining the vital at all points and providing good hypotensive effects also by using ivabradine was more effective in addition to the avoidance of some side effects.

**Keywords:** Laryngoscopy, Endotracheal Intubation, Ivabradine, Gabapentin etc.

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## Introduction

Laryngoscopy and endotracheal intubation are fundamental skills that an anaesthesiologist is supposed to achieve in order to administer anesthesia safely. Both these procedures have been an

indispensable aspect of general anesthesia since the twentieth century. Endotracheal intubation is one of the most frequently accomplished procedures, wherein drastic hemodynamic changes occurs rapidly

during the peri-operative time period that can adversely affect the patient's health. [1]

Conventionally, Laryngoscopy has been utilized as a traditional means to ease the procedure of endotracheal intubation. Tracheal intubation refers to the procedure of placing a flexible plastic tube within the trachea to preserve a clear airway and to provide a way for administering oxygen and other inhalational agents. [2,3] Both laryngoscopy and endotracheal intubation are of critical importance since they have the tendency to increase the sympathoadrenal response resulting in tachycardia, arrhythmias and hypertension. [4,5]

These hemodynamic responses to laryngoscopy and endotracheal intubation were first identified by Reid et al during early 1940s. [6] This transient rise in the hemodynamic (blood pressure and heart rate) responses are uncertain and irregular. The sympathoadrenal response usually appears within 30 seconds following laryngoscopy and intubation, which often persists for less than 10 minutes. [7,8] These hemodynamic alterations secondary to laryngoscopy and tracheal intubation occurs in all the patients, but it is stated that normal healthy individuals have a better tendency to tolerate them. However, in some patients, these hemodynamic alterations have been proven to be harmful to the patient's health as well as the end result of the procedure. [9]

In non-cardiac surgery of long duration, hypertension and tachycardia are both independent risk factors for unfavorable outcomes. [10] There is an increased risk of morbidity and mortality as a result of tachycardia and hypertension in patients with history of cerebral or cardiovascular diseases. [11] In such patients, these hemodynamic responses may also result in severe complications including left ventricular failure, myocardial ischemia, ventricular dysrhythmias, pulmonary oedema and cerebral hemorrhage. [12] Because of these reasons, it becomes

mandatory for the clinician to search for other approaches to decrease the pressor response due to laryngoscopy and endotracheal intubation. However, inability to reduce the pressor response might result in unfortunate outcomes in patients with raised intracranial pressure, hypertension, aneurysmal vascular disease, ischemic heart disease or diseases affecting cerebral vasculature. [13]

Some studies have been reported in literature suggesting the role of Ivabradine and Gabapentin in inhibiting the hemodynamic responses to laryngoscopy and endotracheal intubation separately, [9] but none of them have compared their efficacy. Thus the present comparative study was undertaken in order to evaluate the efficacy of oral Ivabradine and oral Gabapentin in attenuating the hemodynamic response occurring due to Laryngoscopy and Endotracheal intubation.

### Materials and Method

This was the Hospital based prospective, randomized double blind clinical trial, conducted on Patients undergoing elective surgical procedure under general anesthesia, for the duration of one year, in one of the tertiary care center Government medical college, Siddipet, after getting consent from patients, following inclusion and exclusion criteria and approved by institutional ethical committee of our institute.

### Inclusion Criteria:

1. Males and Female patients of American Society of Anesthesiologists (ASA) physical status I/II.
2. Aged between 18 and 65 years.
3. Normal ECG and Mallampati Grading I & II

### Exclusion Criteria:

1. Patients refusal or not consented to participate in the study.
2. H/O Chest Pain/ Palpitations/Syncope
3. H/o Respiratory Problems
4. Hepatic or renal Problems

5. Baseline HR<60, SBP<100 mmHg
6. Patients with ECG abnormality
7. Patients with difficult airway

### Study Group:

Patients undergoing elective surgical procedure under general anesthesia under following groups.

- **Group I** – Patients will receive Ivabradine 5 mg.
- **Group G** – Patients will receive Gabapentin 800mg

### Sample Size :

According to the study conducted by Rajendra Gosawi et al, on the basis of proportion of adverse effects of drugs, considering alpha error 5% and power of the test 80% sample size calculated as 43 in each groups, and taking 15% extra final sample size calculated was 50 in each group, sample size was calculated by using software G\*power for sample size calculation.

### Methodology

All patients undergoing elective surgeries at Government Medical College, Siddipet were enrolled for study after obtaining, written and informed consent from patient regarding the study in his/her vernacular language and English. PAC and necessary investigations were done, one day prior to surgery, patients were instructed as per standard oral guidelines. Both the drugs are given with sips of water one hour before induction. Patients of both the groups were not permitted with any sedative drugs before surgery. The observer anesthesiologist who did the peri-operative observation was unaware of the study drug. After shifting the patients to operation theater, all the baseline parameters like

heart Rate(HR), blood pressure, Reparatory Rate and Oxygen saturation were recorded. Standard anesthetic regimen was administered for patients of both groups. With Inj. Glycopyrrolate 10 mcg/Kg intravenous (IV). Inj. Ondansetron 0.1mg/Kg IV, Inj. Tramadol 1 mg/Kg IV as premedication prior to induction. After preoxygenation for 3 min with 100% SPO<sub>2</sub>, all patients were induced with Inj. Thiopentone sodium 5mg/Kg IV and intubated with succinylcholine 1.5mg/kg IV. Using appropriate size cuffed, endotracheal tube by the aid of Macintosh laryngoscope blade. Maintenance of anesthesia was done with Inj. Vecuronium 0.1mg/Kg IV, with 60% N<sub>2</sub>O and 40% O<sub>2</sub> and intermittent positive pressure ventilation using circle absorber system connected to the Boyles Machine. Surgery was not allowed to commence till the recordings were completed up to 10 Min. Parameters to be recorded are heart Rate, systolic blood pressure, diastolic blood pressure, Mean arterial pressure. Ten minutes after intubation, after taking the recordings of hemodynamic parameters, inhalational agent was introduced into the anesthetic technique. Reversal was done with Inj Neostigmine 0.05 mg/kg and Inj Glycopyrrolate 0.01 mg/kg. All patients were monitored for any adverse effects of Ivabradine and gabapentine in post Op period. The recordings were noted at preoperative (after Premedication) at induction, at intubation, 1,3,5,8,10,30 minutes , 1,2,4,6,12 Hours after intubation.

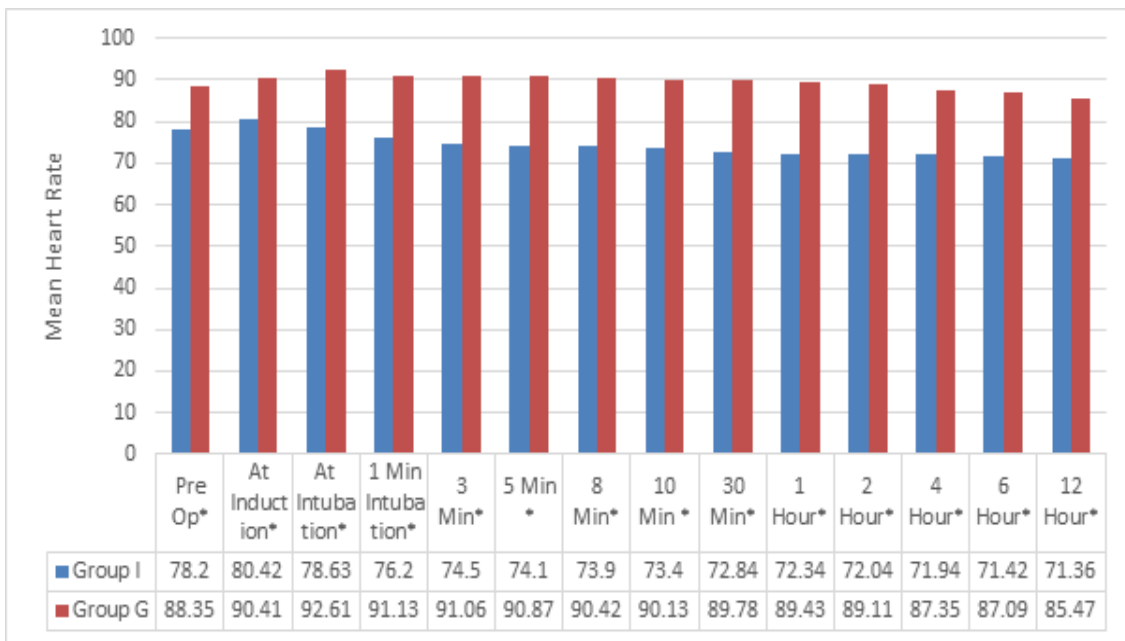
### Observation and Results

In the study we have included total 120 patients for various elective surgeries, divided into two different groups, and observation given bellow in the tables and figure.

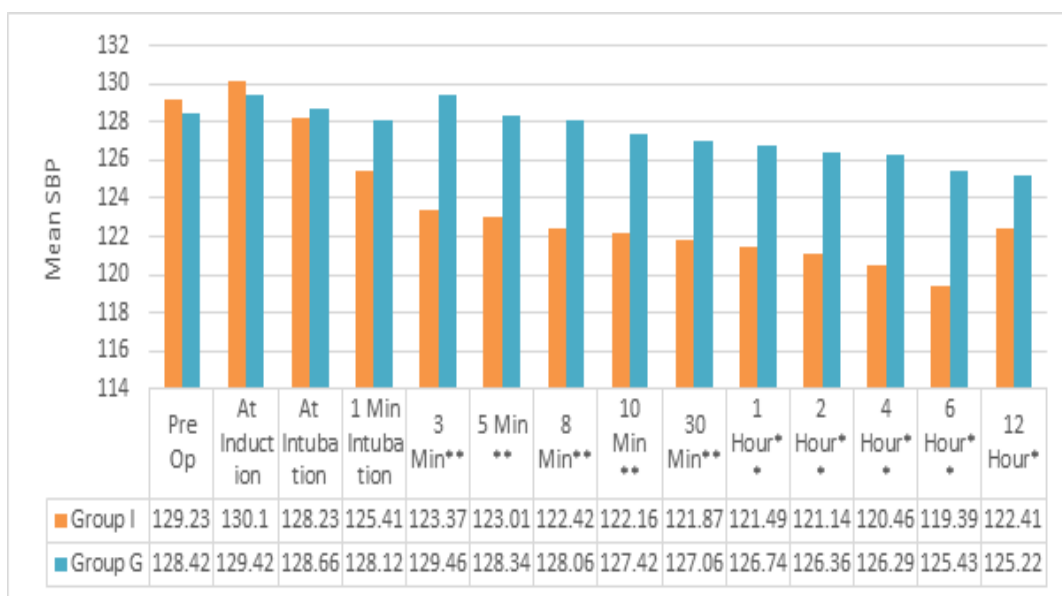
**Table 1: Demographic profiles of study population between the groups.**

Parameter	Group I	Group G	Chi-square/t-test	P-value
<b>Gender</b>				
Male	22	19	0.334	0.5636
Female	38	41		
<b>Age</b>				
Mean ±SD	38.24±7.84	40.27±8.59	1.35	0.1789
<b>ASA Status</b>				
Grade I	32	34	0.1347	0.7136
Grade II	28	26		

It was observed that there was no statistically significant difference in gender between the groups, and also we found age between the groups was comparable.



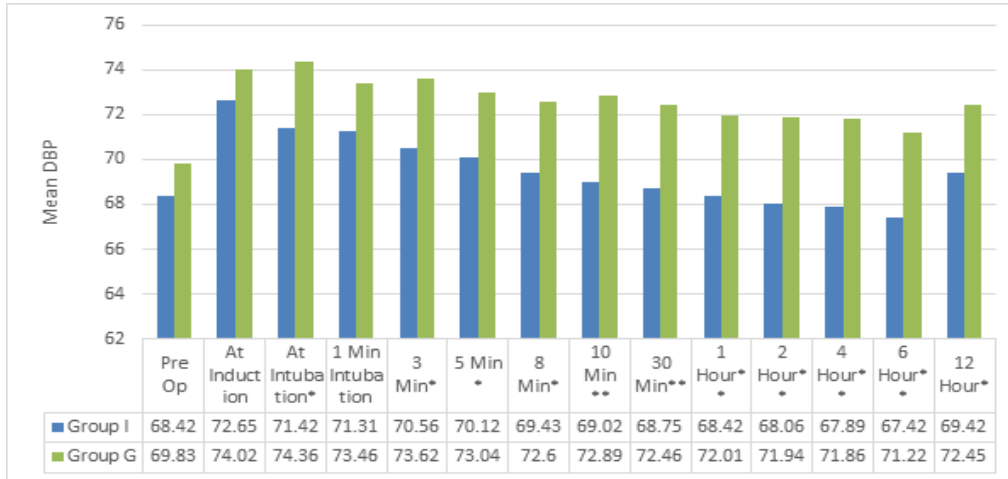
**Figure 1: Mean heart rate distribution between the groups.**



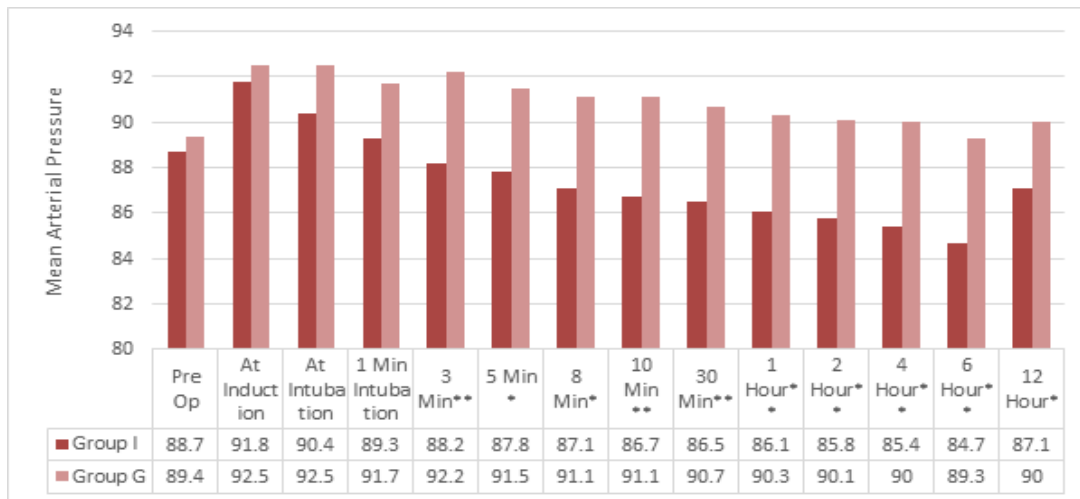
**Figure 2: Mean Systolic Blood Pressure distribution between the groups.**

**Table 2: Distribution of Adverse effect between the groups.**

Adverse Effect	Group I	Group G
Vomiting	1	4
Nausea	1	2
Bradycardia	0	0
Hypotension	0	0



**Figure 3: Mean Diastolic Blood Pressure distribution between the groups.**



**Figure 4: Mean arterial pressure distribution between the groups.**

Above table showed, mean SBP, DBP and MAP at pre op was higher in Group I compared to Group G, only at induction it was increased and higher compared to group G and at intubation and later on it was lower compared to Group G and mean difference in heart rate was statically highly significant between the groups. Also mean heart rate at pre op was lower in Group I compared to Group G, only at induction it was increased and at intubation and later on it was lower compared to Group G and

mean difference in heart rate was statically highly significant between the groups.

**Discussion**

Rapid and dramatic hemodynamic changes are adversely affecting the patient. It may occur during perioperative period. Hypertension and tachycardia have been recognized since 1950’s as commonly associated with intubation under light anesthesia and is most evident during laryngoscopy and manipulation of

epiglottis. The effect is temporary arising in 30 seconds after endotracheal intubation and lasts for less than 10 minutes thereafter. Sympathetic response to laryngoscopy has been studied and managed in past by topical anesthesia 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. Labetalol, Nitroprusside, Calcium channel blockers, Nitroglycerine and strong narcotics etc. Stress response is a neuroendocrine complex occurring due to anaesthesia and surgery. Even with stable anaesthesia, laryngoscopy alone without intubation can cause a supraglottic stimulus. This stimulus leads to an increase in BP which is due to norepinephrine, and increase in HR which is due to epinephrine discharge. Placing the endotracheal tube can cause an infraglottic stimulus.

Ivabradine reduces the HR without producing a precipitous fall in blood pressure; hence, it is useful in patients with angina pectoris, coronary artery disease (CAD), cardiac failure, obstructive cardiomyopathies and in all conditions where the myocardial oxygen supply is endangered, and myocardial oxygen demand is increased. Gabapentin, as a single dose, when used as premedication, decreases hyperalgesia and allodynia associated with surgical manipulation by inhibiting membrane voltage-gated calcium channels and prevents peripheral and central sensitization.

Present study we have undertaken to find the Efficacy of Hemodynamic response to Laryngoscopy and Endotracheal intubation by using Oral Ivabradine and oral Gabapentin, in which we have included 120 patients, which was divided into two groups, group I and Group G, each groups had 60 patients. Study found predominance of female patients for elective surgeries in both the groups. The ratio of male is to female in group I and group G was 0.57 : 1 and 0.46 : 1 respectively and this gender difference between the groups was not

statistically significant (P-value = 0.8728). We have observed that mean age of group G was more than Group I, but mean age difference between the group was statistically not significant (P-value = 0.2241). Raghuram et al [13] in 2004, on patients with age group between 20 to 50 years and Ibrahim et al in 2016, on patients with age group 30 to 55 years age range showed similar results as compared to our study.

Present study observed that, from the beginning mean heart rate was more among patients from group G and it was found statistically significant (P-value < 0.01). At induction heart rate was increase in both group but also at induction we have observed it was statistically significant (P-value < 0.01) at intubation heart rate was reduced in group I but in group G it was again increased and it was statistically significant (P-value < 0.01), but after 1 minute of intubation in both the groups we have observed there was decreased in mean heart level. But we have observed that mean heart level in group G was lowering but not significantly, in group I we observed it was decreasing with stability and all the time it was lower to mean heart rate observed in group G, and all time after 1 Minute to the 12 hours it was statistically highly significant (P-value < 0.001). Study conducted by Vijay Mathur et al. [14] observed that there was significant and stable decrease of heart rate was observed between Ivabradine and Placebo (P-value < 0.01) till 12 hours. One study by Kunwar, et al. [15] observed that mean heart rate of the patients from group test (Ivabradine) was lower than control group, and it was lower and stable than control group and also statistically highly significant at all the time (P-value < 0.01).

Mean systolic blood pressure in both the groups was comparable during Preop no statistical significant difference was observed between the group at induction, and also at intubation (P-value = 0.6027, 0.6509, and 0.7783) but after 1 minute of

intubation systolic blood pressure was lower and decreasing steadily in group I compared to Group G and difference in the mean SBP was highly significant till 12 hours (P-value<0.05). also Diastolic blood pressure and mean arterial pressure from pre op to till intubation it was comparable between the groups (DBP : Pre op (P-value =0.257), at induction (P-value=0.273), at induction (P-value=0.023)) (MAP : Pre op (P-value =0.6036), at induction (P-value=0.6108), at induction (P-value=0.1413)) but at 1 minute of intubation diastolic blood pressure and mean arterial pressure was statistically highly significant between the group (P-value< 0.01) according to A.N. Ibrahim, R.Y. Atallah et al [16] there were mild increases in blood pressure and heart rate values in both groups after each stage, both ivabradine and propranolol provided a good general hemodynamic stability. However, ivabradine was more effective than propranolol with less changes in blood pressure and heart rate values. Arora et al [17] observed lower and stable mean SBP at all the time compared to control group and mean difference was found significant. Fassoulaki A et al. [18] reported that gabapentin attenuated the pressor response (SBP and DBP) but not tachycardia associated with laryngoscopy and tracheal intubation.

Our study observed some adverse side effects between the group, we have encountered with each one patients observed with Nausea and vomiting respectively as side effect in Ivabradine group, that was because of non-cooperation of the patients in that group, but in the group of gabapentin we have encountered with 4 patients had vomiting, and 2 patients had nausea as side effects. We have not found any of the patients with bradycardia or hypotension in our study. Study by Rajendra Gosavi et al [19] observed that there was more adverse effects was observed in gabapentine group compared to

clonide group which is supported to our study.

### Conclusion

From overall observation & results and after discussing with other studies, we can conclude that Ivabradine had better patient compliance in terms to attenuate the sympathetic response to laryngoscopy, endotracheal intubation. Ivabradine can be recommended in cases where beta blockers are contra indicated like in bronchial asthma, in actual in our study both the drugs provides good degree of hemodynamic stability during the surgeries, but ivabradine in maintaining the vital at all points and providing good hypotensive effects also by using ivabradine was more effective in addition to the avoidance of some side effects.

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