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Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation using oral ivabradine – Randomised controlled trial

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ABSTRACT

Introduction: Endotracheal intubation is one of the most common procedures, and anesthesiologists play an important role in patient care. During laryngoscopy and intubation, the patient can experience rapid and drastic hemodynamic changes that are potentially fatal.
Aim: The purpose of this study is to know the efficacy of ivabradine in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation.
Materials and Methods: In this prospective randomised double-blinded study, fifty patients belonging to ASA 1 and 2 were randomised to group A - ivabradine 5mg (first dose on the evening before the day of surgery and the second dose one hour before intubation). Patients in group B received tablet MVT (placebo) (first dose on the evening before the day of surgery and the second dose one hour before intubation).
Results: Patients in group A showed attenuation of heart rate during laryngoscopy and intubation till 10minutes after intubation. Patients in group B showed a rise in blood pressure during laryngoscopy and intubation till 10 minutes after intubation. Patients in group A and group B showed no significant difference in hemodynamics when monitored intraoperatively. All patients recovered fully from anaesthesia and had no complications such as severe bradycardia.
Conclusion: Ivabradine effectively attenuates the hemodynamic stress response without a fall in blood pressure and without severe bradycardia.

1. Introduction

Direct laryngoscopy and endotracheal intubation are the most common methods for securing the airway and giving positive pressure ventilation. Endotracheal intubation has become necessary for most patients undergoing surgery under general anesthesia. Unfortunately, laryngoscopy and endotracheal intubation can result in a cascade of physiological and pathophysiological reflex responses.[1,2]

Intubation under light anesthesia has been linked to increased blood pressure and heart rate, which is particularly noticeable during laryngoscopy and endotracheal intubation. These changes start at about 15seconds, and it peaks at 35-45 seconds and returns to normal within 5-10 minutes. These changes are of little value in healthy patients. However, failure to attenuate the intubation response has deleterious effects in patients with systemic hypertension, raised intracranial pressure, aneurysmal vascular disease and also in ischaemic heart disease patients.[3]

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Even in normotensive patients, reactive sympathoadrenal reactions cause myocardial ischaemia, resulting in a 40mmHg rise in systolic blood pressure after laryngoscopy and endotracheal intubation.[4] However, hypertensive patients' increased heart rate and blood pressure are significantly exaggerated.[5] Complications include left ventricular failure, arrhythmias, intracranial bleeding, and pulmonary edema. Additionally, pre-eclampsia patients may experience convulsions.

Various methods and techniques are used to blunt the hemodynamic stress response for laryngoscopy and endotracheal intubation. The methods are the use of narcotics, beta-blockers, intravenous lignocaine, clonidine, nitroglycerine, ivabradine.[6]

Ivabradine is a newer drug. It is a selective funny channel (If) blocker which acts on the S.A. node causing a decrease in heart rate.[7]

2. Aim

The purpose of this study is to know the efficacy of ivabradine in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation.

3. Materials and Methods

This was a prospective, randomized, double-blinded, placebo-controlled study. After Institutional ethical committee approval obtained, the patients were consented to participate in the study. This study was done from March 2017 to August 2017 in the Institute of anaesthesiology and Critical care (IACC), madras medical college, Chennai. Fifty patients of

This study group included randomly selected patients with an ASA physical status of 1 or 2 who were undergoing an elective surgical procedure under general anaesthesia with endotracheal intubation.

3.1. Inclusion criteria

1. Age: 15 years to 50 years
2. ASA: I and II
3. Both sexes
4. Surgery: elective surgery in urology
5. Who have given valid informed consent

3.2. Exclusion criteria

1. Patient with difficult airway
2. Patient posted for emergency surgery
3. Baseline heart rate less than 60
4. Baseline blood pressure less than 90/60
5. Abnormal ECG
6. Hypertensives on beta-blockers
7. History of chest pain, palpitation, and syncope
8. Allergy to the drug used
9. Pregnancy
10. Patient refusal
11. Patients with severe cardiovascular, respiratory, renal, hepatic diseases.
12. Lack of written informed consent

A pre-operative visit is done to allay anxiety and to develop a good rapport with the patients. Baseline values noted, which include heart rate, blood pressure. The randomized drug first dose was given the day before surgery at 6 pm. After that, the patient was monitored in the ward continuously. On the day of surgery, one hour before intubation second dose of the randomized drug was given with sips of water.

Premedication, induction agent, inhalational agent, the neuromuscular blocking agent was standardized in all patients.

Fifty patients of both sexes of ASA physical status 1 or 2 undergoing surgery under general anesthesia were randomly assigned to two groups. GROUP A (Tab. Ivabradine 5mg)- comprising 25 patients, the first dose was given in the evening before the day of surgery at 6pm. And the second dose is given one hour before intubation. GROUP B (Tab. MVT(Placebo)- comprising 25 patients, the first dose was given in the evening before the day of surgery at 6 pm.

And the second dose is given one hour before intubation.

Intravenous cannulation was done with an 18G cannula and connected to ringer lactate solution. They were premedicated glycopyrrolate 0.2mg i.m (20 minutes before the start of surgery) and injection fentanyl 2mcg/kg given intravenously. It is done with 100% oxygen for 3minutes.

The patient was induced with a thiopentone sodium injection (5mg/kg). Supinylcholine 2mg/kg was used to facilitate intubation. For 60 seconds, the lungs were ventilated with 100 percent oxygen. Intubation was timed 60 minutes after pretreatment with ivabradine in group A and 60 minutes after pretreatment with placebo in group B. (correlating with the peak action of the drug). With the aid of the macintosh laryngoscope blade, an appropriate size oral cuffed, portex endotracheal tube was intubated. The time required for intubation was less than 20 seconds (intubation that needed more than 20 seconds was excluded from the study). Atracurium besylate 0.5mg/kg injection, 0.1mg/kg top-up dose, and intermittent positive pressure ventilation with nitrous oxide and oxygen in a 50:50 ratio using a circle absorber system connected to a Boyles machine were used to maintain anaesthesia.

Surgery could not begin until the recordings were complete, which took approximately ten minutes. Hemodynamics were continuously monitored intraoperatively. At the conclusion of surgery, neostigmine (0.05mg/kg) and glycopyrrolate (10mcg/kg) were used to reverse the neuromuscular blockade. All patients were followed postoperatively. In comparing two groups, we looked for any incidence of ivabradine-related adverse

effects.

4. Results

In ivabradine group, 41-50 years age group was higher (n=17, 68%) and same in MVT group (n=18, 72%). The majority of the ivabradine group study subjects were males (n=16, 64%) and the same in the MVT group (n=14, 56%). In ivabradine group, 61-70 kgs weight group were higher (n=13, 52%) and same in MVT group (n=13, 52%). In the ivabradine group, percutaneous nephrolithotomy patients were higher (n=19, 76%) and the same in the MVT group (n=14, 56%). The majority of the study subjects in the ivabradine group were classified as ASA 1 (n=15, 60%) and ASA II in the MVT group (n=15, 60%)

Heart rate comparison between Ivabradine and MVT group shown statistical significance in Laryngoscopy and Intubation till laryngoscopy till 10 mins post-intubation. (Figure 1)

Systolic blood pressure comparison between Ivabradine and MVT group shown statistical significance in Laryngoscopy and Intubation till laryngoscopy till 10 mins post-intubation. (Figure 2)

Diastolic blood pressure comparison between Ivabradine and MVT group shown statistical significance in Laryngoscopy and Intubation till laryngoscopy till 10 mins post-intubation. (Figure 3)

Mean arterial pressure comparison between Ivabradine and MVT group shown statistical significance in Laryngoscopy and Intubation till laryngoscopy till 10 mins post-intubation. (Figure 4)

Peripheral capillary comparison between Ivabradine and MVT group shown statistical insignificance in Laryngoscopy and Intubation till laryngoscopy till extubation. (Figure 5)

All patients recovered fully from anaesthesia and exhibited no adverse effects such as severe bradycardia. (heart rate less than 50 beats per minute).

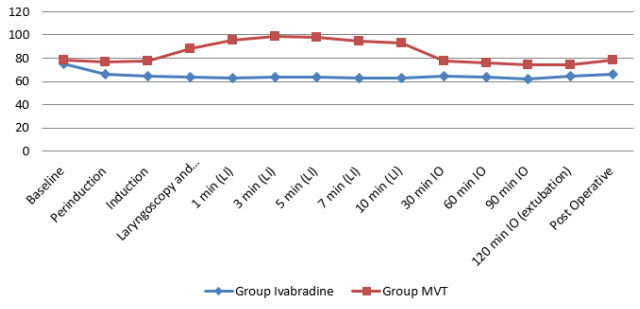

Figure 1: Heart rate (beats per min) distribution

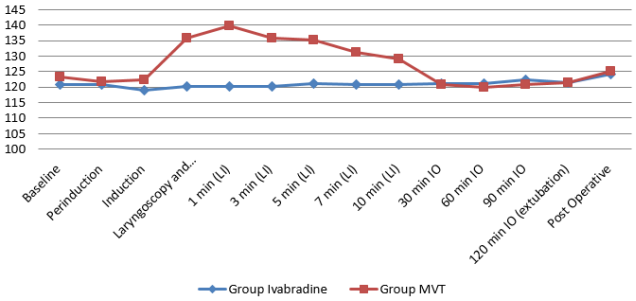

Figure 2: Systolic blood pressure (mm Hg) distribution

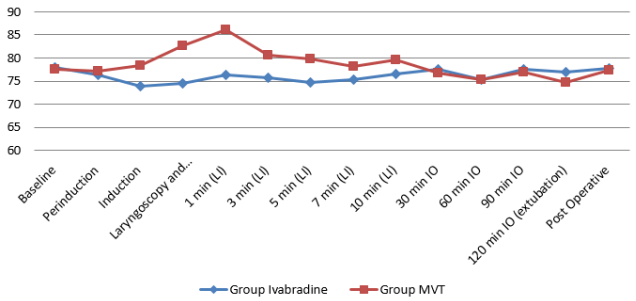

Figure 3: Diastolic blood pressure (mm Hg) distribution

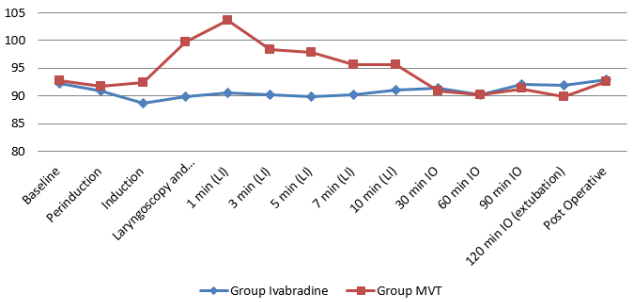

Figure 4: Mean arterial pressure (mm Hg) distribution

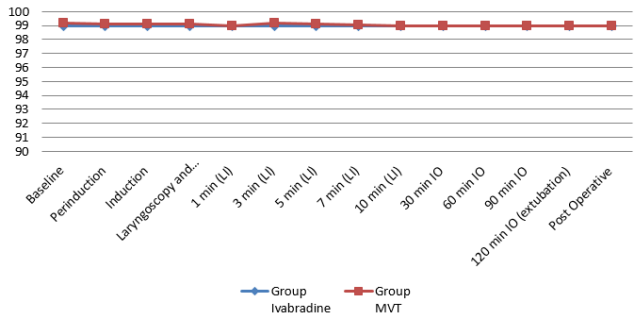

Figure 5: Peripheral capillary oxygen saturation (%) distribution

5. Discussion

Induction, laryngoscopy, and endotracheal intubation are linked to significant hemodynamics and autonomic reflex activity alterations, which is a concern in many high-risk patients. In general, all patients exhibit a hemodynamic stress response to laryngoscopy and endotracheal intubation, but healthy subjects tolerate it well. However, in high-risk patients, this stress response is detrimental to the health and good outcome of the patient. Patients with cardiovascular or cerebral disease are at an increased risk of morbidity and mortality as a result of the stress reflex induced by respiratory tract irritation.

At the time of intubation, hypertension and tachycardia increase the myocardium's oxygen demand. This increased requirement is met in normal healthy subjects by coronary vasodilation and increased coronary blood flow. However, the patient who has previously been diagnosed with ischaemic heart disease is at an increased risk of developing a new episode of myocardial ischaemia and myocardial infarction as a result of fixed coronary blood flow and a decline in cardiac index and ejection fraction.

Numerous techniques and medications have been developed to inhibit the hemodynamic stress response. They include deepening the plane of anesthesia, reducing the time for intubation, using beta-blockers, narcotics, vasodilators, topical airway anesthesia with lignocaine, and intravenous lignocaine. Unfortunately, only a few of these drugs and techniques are useful, and many have their own complications.

When statistically analysing heart rate distribution between the intervention groups, a trend of significantly lower heart rates in the ivabradine group is much more pronounced between laryngoscopy and intubation till 10 mins post-intubation was observed. The difference in the mean heart rate of patients in the ivabradine group and MVT group (31.43, 33% lower in the ivabradine group) between laryngoscopy till 10 mins post-intubation was found to bestatistically significant ($p < 0.05$). The difference in the mean heart rate of patients in ivabradinegroup and MVT group during baseline, pre-induction, induction, 10-30 mins post-intubation, extubation and post-operative periods was found to be statistically insignificant ($p > 0.05$). Reid LC et al.[8] concluded that direct laryngoscopy and endotracheal intubation are associated with increased blood pressure and heart rate and can cause dysrhythmias.

When statistically analysing systolic blood pressure distribution between the intervention groups, trend of significantly lower systolic blood pressure in the ivabradine group is much more pronounced between laryngoscopy till 10 mins post-intubation was observed. The difference in the mean systolic blood pressure of patients in the ivabradine group and MVT group (13.94, 10% lower in ivabradine group) between laryngoscopy till 10 mins post-intubation was found to be statistically significant ($p < 0.05$). The difference in the mean systolic blood pressure of patients in the ivabradine group and MVT during baseline, pre-induction, induction, 10-30 mins post-intubation, extubation and post-operative periods was found to be statistically insignificant ($p > 0.05$). Prof Ward and colleagues[9] demonstrated myocardial ischaemia as a result of sympathoadrenal reflex responses following direct laryngoscopy and endotracheal intubation, with a mean increase in systemic blood pressure of 40mmHg in normotensive individuals.

When statistically analysing diastolic blood pressure distribution between the intervention groups, A trend of significantly more pronounced lower diastolic blood pressure in ivabradine group between laryngoscopy till 10 mins post-intubation and higher measurements during other periods which is much was observed. The difference in the mean diastolic blood pressure of patients in the ivabradine group and MVT group (5.59, 7% lower in ivabradine group) between laryngoscopy till 10 mins post-intubation was found to be statistically significant ($p < 0.05$). The difference in the mean diastolic blood pressure of patients in the ivabradine group and MVT during baseline, pre-induction, induction, 10-30 mins post-intubation, extubation and post-operative periods was found to be statistically insignificant ($p > 0.05$).

Forbes A.M et al.[10] reported that an average rise immediately followed laryngoscopy and endotracheal intubation in mean arterial blood pressure of 25mmHg. When statistically analysing mean arterial pressure distribution between the intervention groups, A trend of significantly more pronounced lower mean arterial pressure in ivabradine group between laryngoscopy till 10 mins post-intubation and higher measurements during other periods, which is much was observed. The difference in the mean MAP of patients in the ivabradine group and MVT group (8.21, 8% lower in ivabradine group) between laryngoscopy till 10 mins post-intubation was found to be statistically significant ($p < 0.05$). The difference in the mean MAP of patients in the ivabradine group and MVT during baseline, pre-induction, induction, 10-30 mins post-intubation, extubation and post-operative periods was found to be statistically insignificant ($p > 0.05$).

Prys-Roberts et al.[5] discovered that hypertensive patients' increases in heart rate and blood pressure are greatly exaggerated and identified as a complication following laryngoscopy and intubation. When statistically peripheral capillary oxygen saturation distribution between the intervention groups, the difference in the mean SPO2 of patients in the ivabradine group and MVT group was statistically insignificant ($p > 0.05$).

There was good intraoperative hemodynamic stability in the intraoperative period and the immediate post-operative period. There were no adverse events observed during this study. The medication was readily available, simple

to administer, and reasonably priced. Ivabradine has been shown to be extremely effective at lowering heart rate in all patients, but especially in those for whom beta-blockers are contraindicated, such as those with bronchial asthma or diabetes. Even in difficult intubation cases requiring more than 20 seconds of intubation, ivabradine was effective in rapidly returning the heart rate to baseline levels.[11] This is a definite advantage of this drug. Beta-blockers have been used routinely to control intubation response. Though they are very potent drugs in attenuating the intubation response, they have many side effects like bradycardia, masking of hypoglycemic response, blunting the normal response to hypotension—i.e. tachycardia.

Throughout the study, none of our patients experienced abnormal hemodynamic responses as a result of severe bradycardia or hypotension. During intubation, blood pressure increased slightly but quickly returned to normal. Additionally, it is used to treat life-threatening conditions such as ischaemic heart disease, angina pectoris, diabetes, congestive heart failure, myocardial infarction, and obstructive cardiomyopathy.[12] Even in normotensive patients, this medication can be used to prevent inappropriate tachycardia during general anaesthesia. It is simple, safe, economical, and simple to use to maintain hemodynamic stability during intubation, intraoperative, and postoperative periods.

6. Conclusion

The study concluded that by obtunding the hemodynamic changes associated with laryngoscopy and endotracheal intubation with oral ivabradine 5mg (2 doses), the hemodynamic changes associated with these procedures could be safely and effectively obtunded. Ivabradine effectively attenuates the hemodynamic stress response without a fall in blood pressure and without severe bradycardia.

7. Source of Funding

None.

8. Conflict of Interest

None.

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