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Comparison of Haemodynamic Profile of Thiopentone and Etomidatein to Pressor to Laryngoscopy and Intubation

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Abstract: ***Aim and Objective: To quantify and compare cardiovascular response to direct laryngoscopy and endotracheal intubation using intravenous Thiopentonesodium and intravenous Etomidate. Materials and methods: This study was carried out in the Department of anesthesiology, Acharya VinobaBhave Rural Hospital, affiliated to Jawahar Lal Nehru Medical College, Sawangi (Meghe), Wardha.This study comprised of 100, ASA I and II patients who were randomly allocated into two groups of 50 each - Etomidate Group (E) and Thiopental Sodium Group (T). Result: At laryngoscopy and1 min after intubation, PR increased significantly in both the groups. Increase was significantly more in Group T than in Group E. At 4 minute after intubation, increase in PR was significantly greater in Group T than in Group E. At 5 minutes, PR decreased in both the groups, difference being statistically significant. SBP, DBP, MAP and RPP decreased significantly after induction and intubation at 1, 2, 3, 4 and5 min in Group E than in Group T. Conclusion: Inj. etomidate at 0.3mg/kg has a better haemodynamic profile as compared to inj. Thiopentone sodium in attenuation of pressor response to laryngoscopy and endotracheal intubation by significantly suppressing sympatho-adrenal reflex activity.***

Keywords: Etomidate, Thiopentone, Pressor response, Induction, Laryngoscopy, Intubation

1. Introduction

The word "Anaesthesia" is derived from Greek meaning (an "without" and aesthesia Perception") without feeling.

Laryngoscopy and tracheal intubation frequently induce a cardiovascular stress response, characterized by hypertension, tachycardia and increased serum concentrations of catecholamines (5). This sympatho-adrenal response to laryngoscopy results in an increase in cardiac workload which, in turn, may culminate in perioperative myocardial ischaemia and acute heart failure in susceptible individuals(5). This response is undesirable in any patient with heart disease undergoing surgery, irrespective of the nature of surgery.

The hemodynamic responses to laryngoscopy and tracheal intubation were first recognized as early as in 1940s by Reid and Brace et al(6).

General anaesthesia may be induced by either inhalational or intravenous routes to a major extent. It may be produced by several drugs which depress the central nervous system including sedatives, tranquilizers and hypnotics. The introduction of two thiobarbiturates by Lundy and Waters in 1934(7,8) marked the first successful use of intravenous route to produce anaesthesia of rapid onset and short duration. One of these, Thiopentone, has since become widely accepted. Thiopentone has proved as useful as an intravenous anaesthetic, that it remains the standard drug against which all the recently introduced drugs are compared. But thiopentone has certain limitation for its use in clinical practice like long-elimination half-life, inability to blunt the haemodynamic and sympathetic nervous system responses to laryngoscopy and endotracheal intubation(9). In addition it was also found to cause prolonged recovery and emergence delirium in addition to dose-dependent accumulation and reduction in cardiac output, stroke volume and systemic vascular resistance associated with a compensatory tachycardia(10, 11).

Etomidate, a new imidazole intravenous induction agent, was first introduced in the 1970s; has an action rapid in onset and of short duration. There was minimal alteration in cardiorespiratory function and recovery was found to be uneventful, discerned by Morgan M, et al. in 1975(12) and further reiterated by Fragen RJ et al. in 1976(13). Initially, etomidate possessed two undesirable side-effects: pain on injection and excessive involuntary movements during induction. There were also concerns about reductions in the serum cortisol levels(16, 17, 18). The introduction of a new preparation of etomidate, studied by Hendry JGB, et al. in 1977(14) and the use of a rapid induction sequence studied in 1974 by Downing et al. (15) has reduced the frequency of both problems. In recent times due to its very stable cardiovascular profile and has been reintroduced in India(19, 20, 21). It is now recommended for induction in patients with poor left ventricular (LV) function (22, 23).

Etomidate has emerged as a superior intravenous anaesthetic agent that can be used to inhibit or attenuate the haemodynamic response to laryngoscopy and endotracheal intubation. Our study compared the pressor response to induction, laryngoscopy and endotracheal Intubation with intravenous Thiopentone and Etomidate in 100 ASA Grade I and II patients.

2. Materials and Methods

This study was carried out in the Department of anesthesiology, Acharya VinobaBhave Rural Hospital, affiliated to Jawahar Lal Nehru Medical College. For this study, the Institutional Ethics committee clearance was

obtained for 100 ASA grade I and II patients between the ages of 20 to 60 years of either sex who were posted for elective general surgery procedures. Written consent was taken from each patient and they were randomly allocated into two groups of 50 each. Group T received Inj. Thiopental Sodium 6mg/kg and Group E received Inj. Etomidate 0.3mg/kg. Pregnant patients, patient refusal and patients with a history of hypertension, heart disease, cerebrovascular disease, arrhythmias, shock, chronic obstructive pulmonary disease, tuberculosis, epilepsy, diabetes were excluded from the study.

Patients with anticipated difficult intubation or previous history of difficult intubation were also excluded. Any patient that required more than one attempt for intubation was also excluded from the study. Patients were thoroughly investigated with complete blood count, bleeding and clotting time, urine examination, kidney function tests, liver function tests, blood sugar, ECG, chest x-ray was done where needed.

All the patients included in the study were kept nil per oral for a period of atleast 8 hours.

Anaesthesia work station with abains circuit, appropriate size of endotracheal tube, laryngoscope, oral and nasal airways, oxygen supply, suction machine, anaesthetic and emergency drugs were kept ready. In all patients, an intravenous line was secured with 18 gauge cannula on dorsum of hand or wrist in operation theatre and all patients received ringer lactate-normal saline. Monitors like pulse oximeter, blood pressure,ECG, were applied to all patients. Patients in both the groups were premedicated with injection glycopyrrolate 0.2mg, Injection midazolam 0.03 mg/kg and injection fentanyl 2µg/kg. After 3minutes, pulse rate, systolic, diastolic blood pressure and mean arterial pressure was recorded as baseline data. All patients were preoxygenated with 100% O2 for 3minutes. Group T received injection Thiopentone 6mg/Kg and group E received inj. Etomidate0.3 mg/kg. Injection rocuronium0.9mg/kg was given as muscle relaxant for intubation. Patients were manually ventilated with 100% oxygen before intubation was performed. Direct laryngoscopy was performed after 60 seconds and tracheal intubation was accomplished within 15 seconds. After confirming the placement of endotracheal tube, anaesthesia was maintained on oxygen (40%), nitrous oxide (60%) and isoflurane. Muscle relaxation was maintained with injection vecuronium (0.08 mg/kg). The following parametersPulse Rate (PR), Systolic Arterial Blood Pressure (SBP) and Diastolic Arterial Blood Pressure(DBP) and Mean Arterial Pressure(MAP) were noted before induction (3minutes after premedication), at laryngoscopy, at endotracheal intubation and each minute after intubation, for 5 minutes. Rate pressure product was calculated from the obtained values

Hypertension was defined as a MAP more than 30% of a patient's baseline value, or 130 mm Hg, whichever was greater. Hypotension was defined as a MAP less than 70% of a patient's baseline value, or 65 mm Hg, whichever was less. Tachycardia and bradycardia were defined as a HR greater than 120 beats/minutes and less than 60 beats/minutes, respectively. The incidence of hypertension, hypotension, tachycardia, and bradycardia was recorded during the study period and compared among the two groups. The incidence of dysrhythmia after intubation was also compared among the two groups.

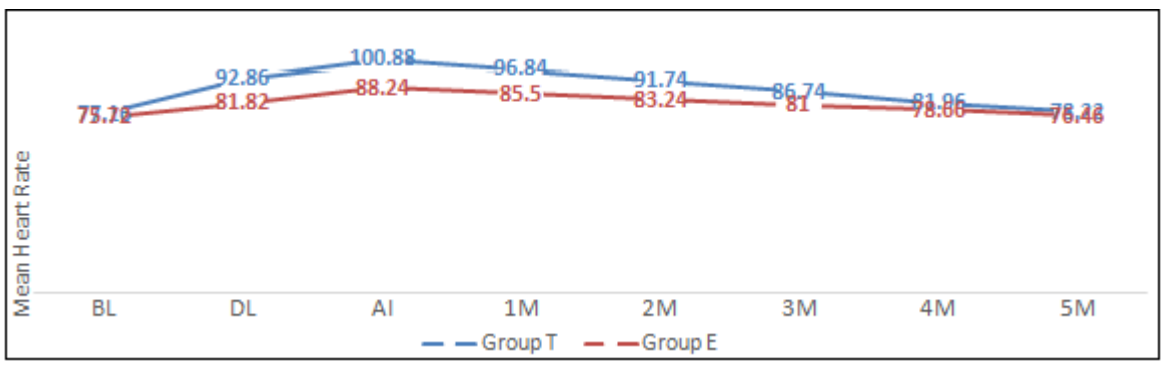
Statistical Methods

Student's t test was used to compare the groups. Chi square test will be used for analysis of nonparametric data.P value of < 0 .05 will be considered statistically significant.

3. Observations and Results

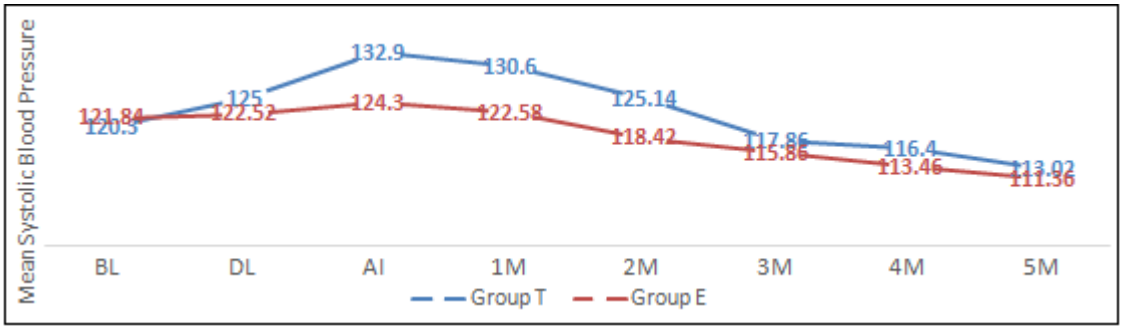
The demographic profile (age, gender, weight and ASA grading) was similar in both the groups.

	Group T	Group E
Age Group(yrs)		
Mean±SD	37.92±12.55	38.62±11.41
Range	20.60 yrs	21-60 yrs
Gender		
Male	31(62%)	27(54%)
Female	19(38%)	23(46%)
Weight(kg)		
Mean±SD	56.06±9.28	55.82±7.53
Range	45-89 kg	39-72 kg
ASA Grading		
Grade I	34(68%)	39(78%)
Grade II	16(32%)	11(22%)

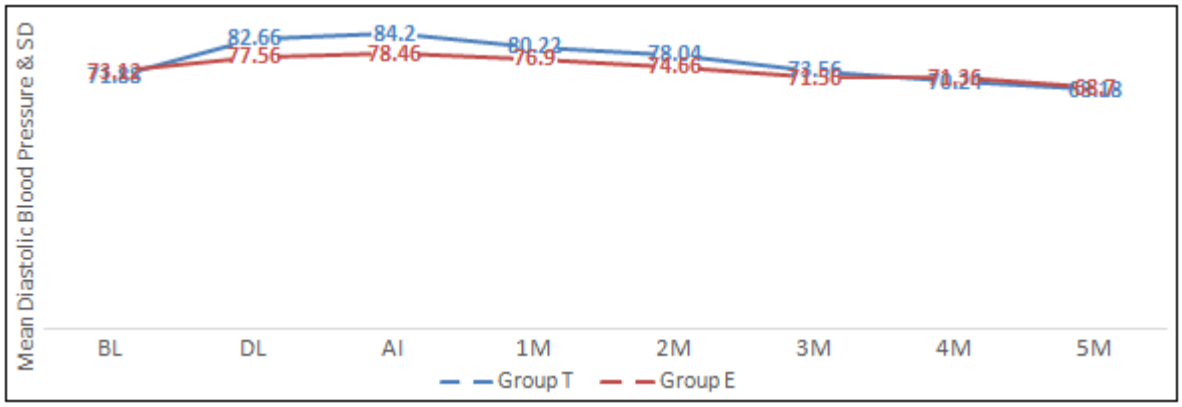


Graph 1: Comparison of mean heart rate at different time intervals with its baseline in patients in both the Thiopentone group and Etomidate group.

Graph 1 indicates changes in pulse rate in both the groups. There was a more significant (p<0.001) increase in PR after induction in Group T than Group E. At 1minute after laryngoscopy and intubation, PR increased significantly (p < 0.001) in both the groups. Increase was significantly more in Group T than in Group E (p < 0.001). By the2nd minute after intubation, PR progressively decreased in both groups. Increase in PR was significantly greater (p<0.001) in Group T than in Group E. At 5 minutes after intubation, PR decreased in both the groups with a greater fall in Group T than in Group E. While comparing Group T with Group E, difference was statistically significant (p > 0.043).



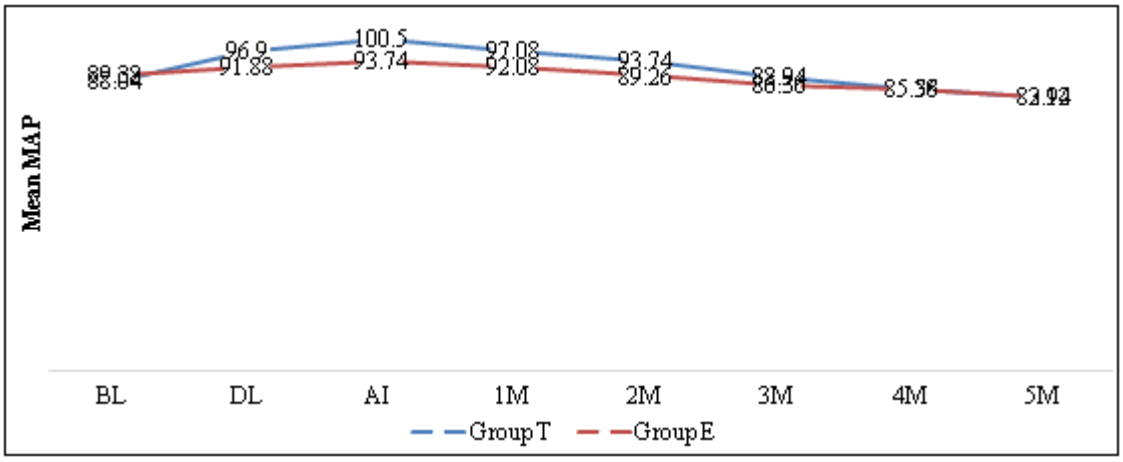
Graph 2: Comparison of systolic blood pressure at different time intervals with its baseline in patients in both Thiopentone group and Etomidate group



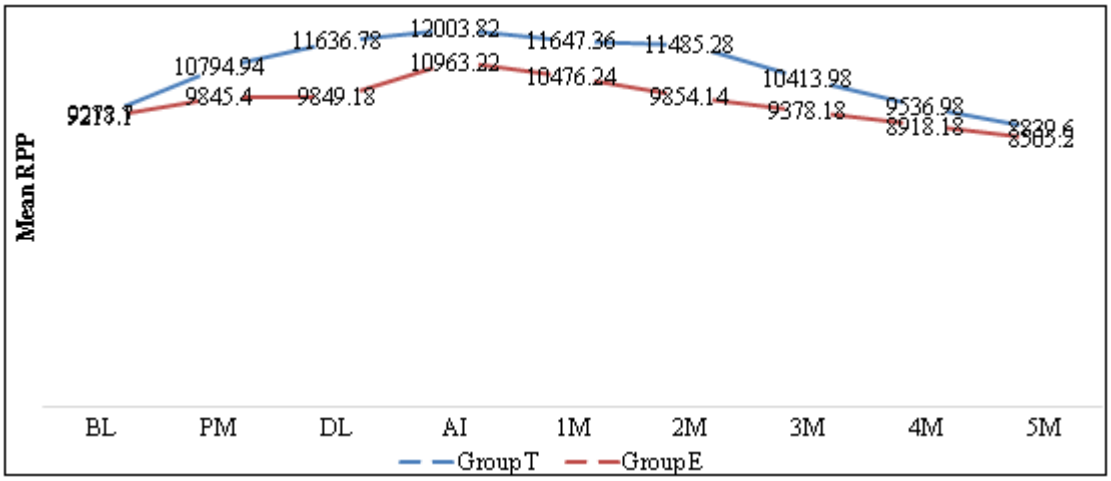
Graph 3: Comparison of diastolic blood pressure at different time intervals with its baseline in patients in both Thiopentone group and Etomidate group

Changes in SBP, DBP, MAP and RPP (**Graph 2, 3, 4, 5**) showed significant, rapidincrease after intubation in group T. It increased above the baseline values significantly (p < 0.001) in group E from post-induction values, but the rise was smaller and gradual (p<0.001). Both groups saw a peak increase at intubation, though the peak value was greater in group T than in group E. From the 1st minute after intubation up to the 5thminute after intubation, mean SBP, DBP, MAP and RPP decreased in group T. It remained above than baseline mean values till the 5th minute. In group E, the mean SBP, DBP, MAP and RPP also decreased. It remained below the baseline values on the 4th and 5th minute after intubation.

On comparing Group T and E, SBP, DBP, MAP and RPP decreased significantly (p < 0.001) in group E than in group T. At 1, 3 and 5 minutes after intubation, SBP,DBP,MAP and RPP was above the baseline values in group T, while it was below the baseline values in group E. Difference between two groups was significant (p < 0.001). There was no case of bradycardia or hypotension among three groups. No ST segment depression or other electrocardiogram changes was noted in either group. On asking about pain on injection post-operatively to all thepatients in both the groups, 6 patients in etomidate group complained of pain. No other side effects were observed.



Graph 4: Comparison of mean arterial pressure at different time intervals with its baseline in patients in both Thiopentone group and Etomidate group



Graph 5: Comparison of rate pressure product at different time intervals with its baseline in patients in both Thiopentone group and Etomidate group

4. Discussion

Most general anaesthetic procedures in the modern anaesthesia practice are carried out with endotracheal intubation. Laryngoscopy and tracheal intubation are considered as the most critical events during administration of general anaesthesia as they provoke a transient, but marked sympatho-adrenal response manifesting as hypertension and tachycardia[1].

Direct laryngoscopy and endotracheal intubation lead to increasing blood pressure and heart rate5. Mechanism of cardiovascular response to intubation is considered to be a reflex sympathetic response to the mechanical stimulation of larynx and trachea. Significant increase in serum levels of norepinephrine and epinephrine subsequent to laryngoscopy with and without tracheal intubation have been described[6,7]. These responses are transitory, variable and may not be significant in otherwise normal individuals. But in patients with cardiovascular compromise like hypertension, ischemic heart disease, and cerebrovascular disease and in patients with intracranial aneurysms, even these transient changes in haemodynamics can result in potentially deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral haemorrhage. Myocardial oxygenation in patients with coronary insufficiency may be severely compromised under these circumstances and ischaemic changes and actual infarction have been reported[2,3,4]. Hypertension and tachycardia predispose to dysrhythmias,[1,5] while the ejection fraction decreases during laryngoscopy and intubation[5,6]. Cases of frank left ventricular failure have been described[7]. Cerebral haemorrhage may also occur[7] and convulsions may be precipitated in mothers with pre-eclampsia[9].These are, by far, some of the most important indications to attenuate the haemodynamic response to laryngoscopy and tracheal intubation.

Many methods like the use of inhalational anaesthetic agents, lidocaine, opioids, direct acting vasodilators, calcium channel blockers and β – blockers have been tried by various authors for blunting haemodynamic responses to laryngoscopy and intubation. But all such manoeuvres have their limitations. For example, with opioids, respiratory depression and chest wall rigidity were potential problems, use of halothane was associated with dysrhythmias, calcium channel blockers produced reflex tachycardia, direct acting vasodilators needed invasive haemodynamic monitoring and lidocaine did not give consistent results in blunting the haemodynamic response to laryngoscopy and intubation. The search for the ideal technique or agents for attenuation of haemodynamic changes is still continuing.

Rate Pressure Product is an index of myocardial oxygen Consumption[4]. It is the product of systolic arterial pressure and the heart rate. Increases in heart rate have a marked deleterious effect on myocardial oxygen supply and demand. Rate pressure product exceeding 12,000 is commonly associated with myocardial ischemia and angina. An increase in blood pressure without a change in heart rare appears to be better for myocardial oxygenation than an increase in heart rate along with the increase in blood pressure. The present study was set out to compare pressor response during laryngoscopy and intubation following the use of two commonly used induction agents, intravenous Thiopentone and intravenous Etomidate.The results of our study showed that intravenous Etomidate significantly reduced PR, SBP, DBP, MAP, and RPP after induction and 1,3,5 min after endotracheal intubation as compared to Thiopentone. There were no cases of bradycardia, tachycardia, arrhythmias, ST segment or other ECG changes noted throughout the study.

5. Conclusion

We conducted a study to understand and observe the effectiveness of two induction agents, inj. Thiopentone sodium 6mg/kg and inj. Etomidate 0.3mg/kg on blunting the haemodynamic response to laryngoscopy and endotracheal intubation.

From this study we concluded that inj etomidate at 0.3mg/kg has a better haemodynamic profile as compared to inj. Thiopentone sodium at 6mg/kg in attenuation of pressor response to laryngoscopy and endotracheal intubation by significantly suppressing sympatho-adrenal reflex activity.

6. Limitations

1) The rate of administration of the induction agents were restricted to 15 seconds as the quantities of each drug varied by 2-4ml to each other. Considering the pharmacology of the two induction agents, speed of injection to loss of eyelash reflex was not compared or studied.
2) Although the laryngoscopy duration was kept to less than 30 seconds, no comparison was made between the duration of laryngoscopy and the stress response.
3) Bi-spectral Index System measurement was not applied to evaluate loss of consciousness and to determine depth of anaesthesia to events like laryngoscopy and endotracheal intubation.

7. Recommendations

In our study we found that patients falling under ASA grade I and grade II, intravenous thiopentone sodium 6mg/kg and etomidate 0.3mg/kg are effective and safe induction agents to enable laryngoscopy and endotracheal intubation.

Etomidate was found to be a relatively more haemodynamically stable induction agent as compared to thiopentone sodium where the pressor response to laryngoscopy and endotracheal intubation caused lower rise of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and calculated rate pressure product.

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