

## Comparison of induction characteristics of etomidate versus thiopentone sodium

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### Abstract

**Introduction:** Induction with suitable drug by intravenous route for induction of anaesthesia is an important element of anaesthesia management. Patients are susceptible to hemodynamic liability at the time of induction. Thus, an agent with least effect on hemodynamics would be the agent of choice. **Aim:** To compare the induction characteristics of Etomidate and Thiopentone Sodium during induction of general anaesthesia. **Objective:** To observe the Hemodynamic changes during induction with Etomidate and Thiopentone sodium (Heart rate, Systolic Blood pressure, Diastolic Blood pressure, Mean arterial pressure). **Settings and design:** The study was conducted in the department of anaesthesia of BVP MCH, over a period of two year from June 2014-2016, on patients undergoing elective surgery under general anaesthesia. **Methods:** 60 adult patients aged 18 – 50 years, belonging to ASA grade 1 and 2, undergoing elective surgery under general anaesthesia, were divided randomly into two groups of 30 patients each. Group T patients were induced with injection thiopentone sodium 5 mg/kg, Group E with injection etomidate 0.3 mg/kg intravenously. **Statistical analysis:** Data are presented as mean and standard deviation. The statistical analysis was performed using SPSS version 20. A “p” value of less than 0.05 was taken as significant. **Results:** There was no significant change in mean heart rate at one, two and three minute after induction as compared with the mean heart rate at the time of induction in both groups (p>0.05). In Groups T and E there was a significant fall in systolic blood pressure, diastolic blood pressure and mean arterial pressure at one, two and three minute after induction, as compared to the induction value (p<0.05). **Conclusion:** Etomidate offers superior hemodynamic stability during induction compared to Thiopentone. Thus Etomidate is a better induction agent for general anaesthesia.

**Keywords:** Induction, General anaesthesia, Thiopentone, Etomidate.

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### Introduction

General anaesthesia is a pharmacologically induced state which is temporary and reversible and is characterized by the development of unconsciousness, analgesia, amnesia, myorelaxation and attenuation of autonomic response to painful stimulation. The purpose of anaesthesia is not only hypnosis but also a combination of safe analgesia, amnesia and immobilization of patients during surgery.

Thiopentone sodium is an established intravenous induction agent, rapid onset short acting barbiturate used since 1930s. It acts on Gamma-Amino Butyric Acid (GABA) receptors in brain and spinal cord[1]. It is used in a dose of 5-7mg/kg body weight with an onset of action of 10- 30 seconds.

Etomidate was synthesized in 1965 and introduced in clinical practice in 1972. Etomidate is a carboxylated imidazole derived non-barbiturate, non-narcotic hypnotic agent with least impact on cardiovascular stability and less ventilatory depressant effect[1,2,3]. It has GAB A like effect and acts by modulating and mimicking type A receptor mediated chloride current. It is given in a dose of 0.2 to 0.4mg/kg body weight[1]. Clinical evaluation of etomidate shows it to be useful for anaesthetic induction in adults and children more than 10 years old. The properties of etomidate include hemodynamic stability, minimal respiratory depression, cerebral protection, and favourable pharmacokinetics enabling rapid recovery after a single dose.

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Use of this drug waned significantly after number of studies. As a result of rediscovery of etomidate’s beneficial physiologic profile combined with a lack of any new reports describing clinically significant adrenocortical suppression after an induction dose or brief infusions; renewed interest in etomidate led to increasing use in present scenario.

Thiopentone sodium and Etomidate are now in use as Intravenous induction agents. We decided to compare induction characteristics of these two agents regarding hemodynamic and other effects.

### Methods

After approval by the college ethical committee, the study was undertaken in attached teaching hospital between years 2014-2016. This study was conducted as a prospective comparative study.

### Patient Randomization

Randomization was done through chit method and patients were enrolled in two different groups:

- **Group T:** In this group Thiopentone sodium was used as induction agent in a dose of 5 mg/kg.
- **Group E:** In this group Etomidate was used as induction agent in a dose of 0.3 mg/kg.

On arrival in operating room intravenous access was established and patients received normal saline (0.9%) solution 7 mL kg<sup>-1</sup>. Standard monitoring was established and heart rates, SP02, MAP were measured before induction of anaesthesia. All patients were given Fentanyl 2.5 µg kg<sup>-1</sup> 3 minutes before induction of anaesthesia. Anaesthesia was induced: Airway was secured using appropriate size PVC endotracheal tube. Anaesthesia was maintained with 1 MAC Isoflurane in combination with nitrous oxide 50% in oxygen. Further

boluses of Fentanyl 1µg/kg and Vecuronium 0.1mg/kg depending on decision of anesthesiologist were given. Ventilation was mechanically controlled. At the end of surgery neuromuscular blockade was antagonized with Neostigmine 70µg/kg and Glycopyrrolate 10µg/kg. After tracheal extubation patients were transferred to Post Anesthesia Care Unit (PACU).

The hemodynamic parameters like Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure were compared at baseline, pre-induction, immediate post-induction, at the 3, 6, 9, 12 and 15 minutes after induction. Other effects like apnoea, myoclonus and pain on injection were observed. The statistical analysis of the data represented as mean± standard deviation, was done by using one way ANOVA and t-test for the difference of means

for parametric data and chi-square test for the nominal data. These tests were referred for p values for their significance. Any p value less than 0.05 was taken to be statistically significant. The analysis of the data was performed by using statistical package for social sciences (SPSS version 20.00).

**Results**

In Our study, 60 patients were divided into two groups of 30 each. Group T in which thiopentone sodium was used as induction agent in a dose of 5 mg./kg. In Group E Etomidate was used as induction agent in a dose of 0.3 mg./kg. All the patients were comparable with regard to demographic profile (table 1).

**Table 1: Patient demographic characteristics**

Parameters	Group T	Group E	P Value
Number(N)	30	30	0.279
Age(years)	29.07 ± 9.88	29.60±10.18	0.838
Weight(kg)	61.50±8.87	62.50±10.99	0.567
Height(cm)	160.3±6.49	169.2±6.07	0.453
Gender(M/F)	21/9	22/8	0.768
ASA status I/II	25/5	26/4	0.445
Duration of surgery	161.00±7.59	158.50±6.58	0.347

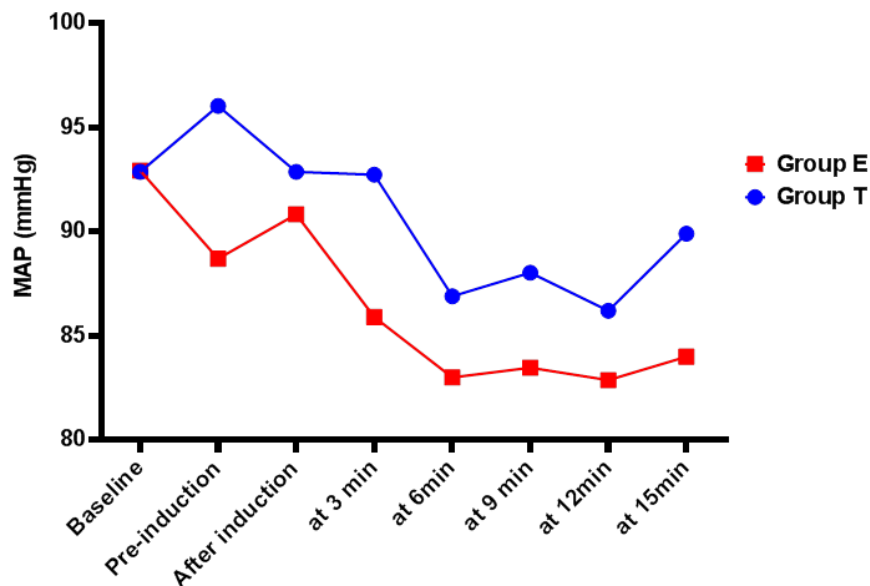
Values in the table are mean ± SD or absolute numbers (percentage). SD = Standard deviation, ASA = American Society of Anesthesiologists.

**Table 2: Onset of induction was faster with Etomidate as compared to Thiopentone sodium and this was statistically significant p value < 0.0001**

Onset	Group T	Group E
Minimum	23.00	15.46
Maximum	32.00	28.00
Mean	27.14	21.83
SD	3.023	3.105

Values in the table are mean ± SD or absolute numbers (percentage). SD = Standard deviation.

Mean Arterial Pressure decreased after the 1st minute in both the groups but the fall was slower in the Group T compared to group E. In the Group E, the fall in diastolic blood pressure was much more rapid. Coincidentally, as in case of mean systolic BP, pre induction value difference between two groups is statistically significant, Group E having low MAP (fig 1).



**Fig 1:MAP Comparison**

Myoclonus was noticed in none of the cases in Group T while 7 cases were reported having myoclonus in Group E. The findings were statistically significant with p value =0.011 (fig 2).

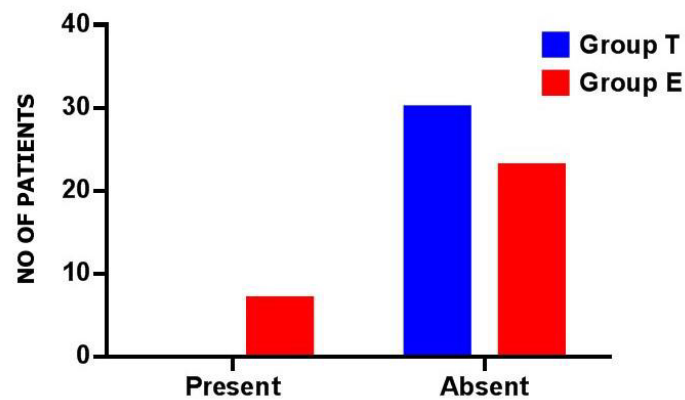


Fig 2:No. of patients' comparison

### Discussion

The ideal anaesthetic agent should have characteristics that include rapid induction, shorter duration of action, minimal side effects, and rapid recovery. Hemodynamic changes due to anaesthesia in various surgeries have become a great concern for anesthesiologists and evidence show that changes in blood pressure, either decrease or increase, independently are associated with side effects and complications in patients undergoing surgery[4].

Thiopentone sodium is a barbiturate that is most commonly used induction agent and it causes a dose-dependent reduction in cardiac output, stroke volume and systemic vascular resistance which associated with a compensatory tachycardia[5].

Etomidate, which is an imidazole derivative and an ester, is an anaesthetic induction agent and characterized by rapid onset, with minimal side effects on cardiovascular and respiratory functions, as well as minimum histamine release[6]. These properties make it especially useful for cardiac-compromised patients. Laboratory studies indicate that etomidate is 25X more potent and has a therapeutic index six times greater than thiopentone sodium[6]. Currently use of etomidate as induction agent is increasing.

In our study, we found that onset of induction with Etomidate was faster than Thiopentone sodium. Mean induction time with Etomidate was  $21.83 \pm 3.105$  and with Thiopentone group  $27.14 \pm 3.023$ , and reported significantly shorter onset time for Etomidate, with a p value statistically highly significant. Etomidate is frequently used as an anesthesia induction agent because of its fast onset of induction and recovery[7]. The patients receiving etomidate had a significantly shorter onset time of anaesthesia compared with those receiving the other intravenous induction agents. It also provides cardiovascular stability, leads to minor respiratory suppression, protects the brain, and induces smaller amounts of histamine secretion[7]. **Gill and Scott (1992)[8]** reported that the patients receiving etomidate had a significantly shorter onset time of neuromuscular block compared with those receiving thiopentone. There was a significant negative correlation between onset time of neuromuscular block and the maximum percent change in mean arterial pressure.

Etomidate is advocated in patients with compromised cardiopulmonary function, because of its minimal cardio respiratory depressant effects and lack of histamine release[9]. **Rahman et al[9]** compared the effect of thiopental sodium/fentanyl with etomidate/fentanyl during anaesthetic induction in patients with coronary artery disease with poor left ventricular function. The changes of heart rate were insignificant between the groups (reduction of heart rate 8% versus 7%). **Shilpashri et al[10]** reported that mean heart rate increased in Thiopentone group compared to the Etomidate group. **Jellish et al[11]** showed that compared with baseline values, the thiopental sodium group had the highest increase in HR ( $22.9 \pm 4.4$  bpm.) after laryngoscopy and intubation compared to etomidate. **Karki et al[12]** and **Edward et al[13]** reported a non-

significant increase in heart rate at 1, 2 and 3 minutes after induction and the maximum increase in mean heart rate were 3.66 beats per minute in thiopentone group.

In our study, mean systolic blood pressure in two groups was found to be statistically significant with a p value of 0.007, the maximum rise in Systolic blood pressure was seen immediately after induction and rise was comparatively insignificant. Later systolic blood pressure decreased in both the groups but the fall was slower in group T than Group E. Sustained effect of etomidate was noted up to 12 minutes with a p value of 0.032. Regarding Diastolic blood pressure, rise in group T was seen at 3rd minute after induction with a p value of 0.047. Diastolic blood pressure decreased in both the groups but the fall was slower in group T compared to group E. The fall was much more rapid in group E. At 15 minutes post induction difference between mean diastolic BP in two groups was statistically significant with a p value of 0.016, group E had more fall. Etomidate is an anaesthetic induction agent in patients with significant cardiovascular disease[14].

In our study, we found a fall in Mean arterial pressure after 1st minute in both groups, but the fall was slower in group T compared to group E. In group E fall of diastolic blood pressure was much more rapid. Various studies have shown, stable cardiovascular profile of etomidate while others have shown stable haemodynamics with thiopentone in patients with good ventricular function[15,16]. **Rahman et al[9]** reported that reduction of MAP was greater in patients who received thiopental sodium/fentanyl induction (maximal decrease 32%) compared to etomidate/fentanyl induction (maximal decrease 12%) ( $p < 0.05$ ) in patients with coronary artery disease with poor left ventricular function. This indicates stable hemodynamics.

Apnea was observed in 6 cases in group T, No case had apnea in group E. Findings were statistically significant with p value of 0.024. Similar findings were reported by **Giese et al[17]** where patients in whom anaesthesia was induced with etomidate had a lesser incidence than patients in whom anaesthesia was induced with thiopental sodium. Fentanyl pretreatment significantly increased the incidence of apnea when anaesthesia was induced with etomidate. **Shilpashri et al[10]** reported that the incidence of apnea was more with thiopentone than Etomidate group.

Myoclonus was observed in 7 cases in group E, while it was not noticed in group T. The findings were statistically significant with a p value of 0.011. The new emulsion preparation of etomidate has decreased the incidence of some adverse effects eg. Thrombophlebitis and myoclonus [9]. **Habibi et al[10]** did not find any significant differences between the two groups (etomidate versus ketamine-thiopental sodium combination) regarding Muscle twitching. **Giese et al[17]** reported that patients in whom anaesthesia was induced with etomidate had a greater incidence of myoclonus than patients in whom anaesthesia was induced with thiopental sodium. Fentanyl pretreatment significantly decreased the incidence of myoclonus, but

it increased the incidence of apnea when anesthesia was induced with etomidate.

#### Limitations of the study

This study did not include poor cardiac reserve patients because of obvious ethical reasons. These findings in ASA1 and 2 patients may guide Etomidate's use in such patients.

The study only confirmed that Etomidate relatively has more sustained cardio stability as compared to thiopentone sodium though statistical significance is not seen consistently

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