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## A comparative study of hemodynamic changes and serum cortisol levels of induction agents: Thiopentone, propofol, Etomidate

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### Abstract

**Objective:** Haemodynamic changes are inevitable while induction of general anesthesia with anaesthetic drugs. This present study records the haemodynamic changes that is caused by three different drugs (thiopental, propofol, and etomidate) used for induction of general anaesthesia.

**Methods:** A Randomized and double-blinded study, 90 patients were assigned to one of the three groups (n=30 each). Propofol- 2 mg kg<sup>-1</sup> in Group 1, Thiopentone- 5 mg kg<sup>-1</sup> in Group 2 or Etomidate - 0.3 mg kg<sup>-1</sup> in Group 3. Heart rate (HR) Noninvasive measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), was performed on admittance, after giving fentanyl, immediately before the induction of anaesthesia, 1,2,3,4,5,6,7,10 mins thereafter intubation. Serum cortisol levels were measured at baseline, after intubation, 30 minutes after induction.

**Results:** Following the administration of propofol (Group 1), a greater decrease of systolic and diastolic blood pressure was observed when compared with that of etomidate (Group 3) or thiopentone (Group 2).

**Conclusion:** In this study, It can be concluded that etomidate is safer than propofol and thiopental groups in terms of haemodynamic stability.

**Keywords:** Propofol, thiopental, etomidate, induction, haemodynamic changes

### Introduction

For more than 70 years, development of intravenous anaesthetics has been an important component of anaesthetic management. Any Intravenous induction agent is selected based on their rapidity of action, effect on hemodynamic parameters and their action in suppressing intubation response. It increases cardiac workload and thus the oxygen consumption, leading to ischemia. Catecholamines are released during tracheal and laryngeal tissue stimulation, increasing the sympathetic activity and thus increasing heart rate and systemic blood pressure<sup>[1, 2]</sup>.

Thiopentone is an ultra-short acting barbiturate. It is one of the oldest and commonly used intravenous induction agent for general anesthesia. Propofol was discovered in 1977. It was one of the most commonly used intravenous induction agent for general anesthesia. Hemodynamic instability and cardiovascular complications like hypotension may present with propofol<sup>[3, 4, 5]</sup>.

In 1973, Etomidate was introduced and was used in induction of general anaesthesia. Etomidate induction gives us a stable hemodynamic condition to perform endotracheal intubation

In this study we compared the Hemodynamic responses and serum cortisol changes of three Induction agents - Thiopentone, Propofol, Etomidate while induction of general anesthesia and following endotracheal intubation

### Methods

After getting approval from the ethics committee of Meenakshi Medical College Hospital and Research Institute (Ref.No 03/IEC/MMCHRI/2017), the study involved 90 patients aged between 18-60 years who were undergoing elective surgery and who were classified in group I-II-III according to the risk classification of American Society of Anesthesiology (ASA)

Written informed consent was obtained from the patients during their preoperative examinations, and they were informed about the method. Patients who had hepatic and renal failure, Uncontrolled hypertension, those who were allergic to the medications and who might have difficulty in intubation were excluded from the study.

All patients who were operated were monitored using Electrocardiogram, pulse oximeter and non-invasive blood pressure). Vascular access was established on the hands of the patients with a 18 G cannula, and 0.9% NaCl infusion was initiated at a rate of 10 mL hour<sup>-1</sup>.HR, Non-invasive SBP, DBP, MAP was recorded after giving fentanyl. Patients were induced with study drug according to group stratification, Group 1 – Received Inj. Propofol 2mg/kg. Group 2 - Received Inj. Thiopentone sodium 5mg/kg, Group 3 - Received Inj. Etomidate 0.3 mg/kg. Were recorded after induction with test drug. Inj. Vecuronium 0.1mg/kg iv was given and intubated. Anaesthesia was maintained by using O<sub>2</sub>: N<sub>2</sub>O (50:50) and sevoflurane 2%. HR, SBP, DBP, MAP was recorded after intubation, 1 min, 2,3,4,5,6,7,10 mins after intubation. Measurement of Serum Cortisol levels was done at baseline, after Intubation, 30 mins after induction.

**Statistical analysis**

Statistical analysis was done using statistical package for social sciences windows version 15. Results expressed in this study were given as mean and standard deviation. All continuous variables like age, weight, HR, SBP, DBP, MAP were compared using ANOVA (Analysis of Variance). Chi square test used to compare between sex and ASA. Bonferroni-corrected Mann-Whitney U test was used as a post hoc test and chi-square test was used for comparing qualitative data. The results were evaluated with 95% confidence interval and a significance value of  $p < 0.05$ .

**Results**

The demographic data of the groups are presented in Table 1. In the comparison of the groups for SAP values, The decreases seen in Group 1 after induction was statistically significantly different than the SAP values of Group 2 and Group 3 that were recorded at the same time ( $p < 0.05$ ) (Figure 1).

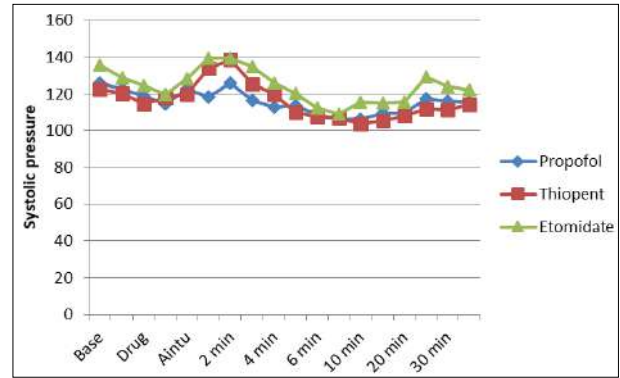
In the comparison of the groups for DAP values, the decrease by 13mmHg in Group 1 before intubation was found to be statistically significantly different from the simultaneously recorded DAP values of Group 2 and Group 3 ( $p < 0.01$ ) (Figure 2).

In the comparison of the groups for MAP values, the decreases seen in Group 1 (10 mmHg) after induction and in the 1st minute after intubation were statistically significantly different than the MAP values of Group 2 and Group 3 that were recorded at the same time ( $p < 0.01$ ) (Figure 3).

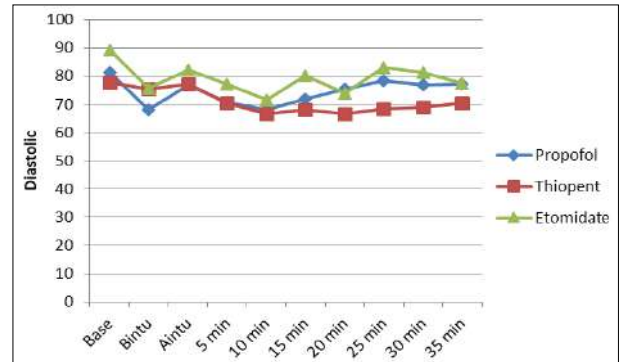
In terms of HR values, the groups were compared, and no statistically significant difference was found (Figure 4).

**Table 1:** The demographic data of the groups are presented

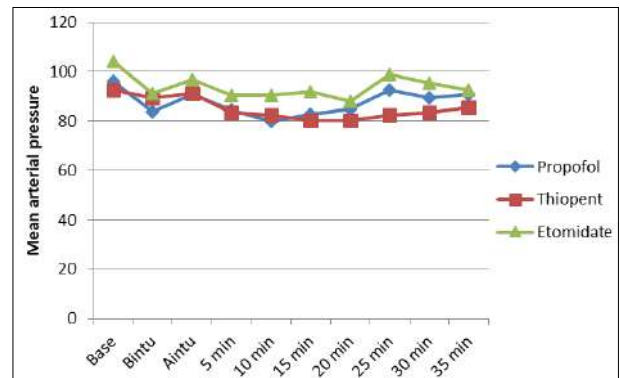
Parameter	Group 1 Mean ±S.D	Group 2 Mean ±S.D	Group 3 Mean ±S.D	P value
Age in years	38.97 ±11.48	41.84 ±15.5	42.1 ±13.0	0.6
Gender	30 ±32.6	31 ±33.7	31 ±33.7	0.9
Weight in kgs	65.0 ±9.02	67.71 ±11.5	67.35 ±11.05	0.5
ASA Status	30 ±32.6	31 ±33.7	31 ±33.7	0.13



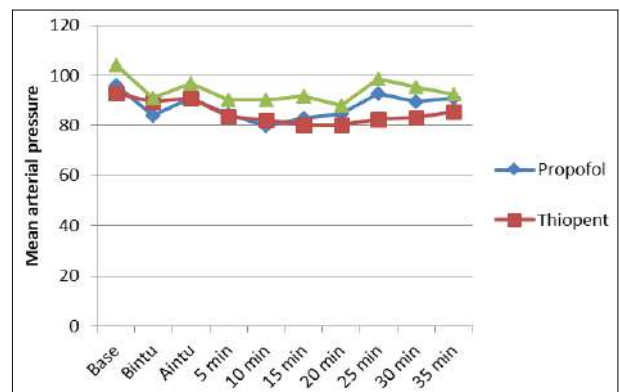
**Fig 1:** Systolic arterial pressure measurements of the groups



**Fig 2:** Diastolic arterial pressure measurements of the groups



**Fig 3:** Mean arterial pressure measurements of the groups



**Fig 4:** Heart rate measurements of the groups

**Table 2:** Serum Cortisol Changes

Time interval	Group 1 Mean $\pm$ S.D	Group 2 Mean $\pm$ S.D	Group 3 Mean $\pm$ S.D	f value	P value
Baseline	7.09 $\pm$ 2.57	6.67 $\pm$ 3.45	7.93 $\pm$ 6.3	0.61	0.54
After intubation	9.83 $\pm$ 2.78	9.32 $\pm$ 3.6	10.0 $\pm$ 6.67	0.18	0.83
30 min	14.07 $\pm$ 4.43	16.0 $\pm$ 5.09	12.87 $\pm$ 7.61	2.22	0.11

### Discussion

Soon after introducing the general anaesthesia, it was made possible to induce a controlled unconsciousness state in the patient so that they are unaware of the events happening throughout the surgical procedure and totally insensitive to pain. These anaesthetised patients are generally not able to maintain adequate airway, and here comes the need to employ an artificial airway device such as endotracheal tube.

The mainstay in safeguarding the airway in such patients is through Laryngoscopy and endotracheal intubation. Though intubation has its own advantages such as a safe, secured airway which aids in prevention of aspiration and as a route for delivery of anaesthetic gases, it has got its own complications. Both Laryngoscopy and endotracheal intubation can be a noxious stimuli to the body which is meant to produce a spectrum of stress responses

Haris *et al.* [6] evaluated thiopental (4 mg kg<sup>-1</sup>), etomidate (0.3 mg kg<sup>-1</sup>) and propofol (2.5 mg kg<sup>-1</sup>) in tracheal intubation by adding 2  $\mu$ g kg<sup>-1</sup> fentanyl or not. They detected that there was a significant decrease in SAP values in the group receiving only propofol, and there were significant increases in SAP values in the group receiving only thiopental and etomidate after intubation. In our study, remarkable decreases in SAP values were observed, especially in the propofol group after induction. No significant differences were seen in HR values. Our results are consistent with those of a study conducted by Harrison *et al.*

Schmidt *et al.* [7] found that propofol causes hypotension by reducing preload and afterload that is not synchronized with compensatory responses such as increased HR and cardiac output which was consistent with our study report

Mehrdad *et al.* [8] conducted study on patients posted for elective orthopedic surgeries. 2 drugs (propofol and etomidate) were compared by their cardiovascular responses: SBP, DBP, MAP, HR, and O<sub>2</sub>sat before laryngoscopy, during induction with Etomidate (0.3 mg/kg) in group A and propofol (2-2.5 mg/kg) in group B and at 1, 3, 5, 10 min after the induction. They found that patients who received Etomidate had more stable hemodynamic condition and it can be preferred over propofol for patients undergoing elective surgery under general anaesthesia

One more study correlating with our result by Prasad R *et al.*, observed that a significant decreased in blood pressure after induction of general anaesthesia was seen in propofol group of patients [9]. Etomidate is better than Propofol in induction because it preserves autonomic reflexes and sympathetic outflow, so there is only minimum changes in vitals after giving the drug. [10, 11]

Administering Etomidate prior to laryngoscopy and endotracheal intubation can increase Serum Cortisol level after 30 minutes of induction by 5 mcg/dl while Thiopentone and propofol increases serum cortisol level by 10 mcg/dl. so, this smaller increase by Etomidate (though it is not statistically significant) could be because of the adrenal suppression that is caused by Etomidate (Table 2.)

Huiku *et al.* told that the blood cortisol changes that takes

place during intraoperative period in whom total intravenous anaesthesia was given to thirty five ASA 1 and 2 patients. Serum cortisol levels was found to be raised 30 minutes after extubation

### Conclusion

In our study, it was detected that among three different groups, etomidate (Group 3) affected haemodynamic responses the least, and propofol (Group 1) affected haemodynamic responses the most.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Meenakshi Medical College Hospital and Research Institute.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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