



## Anaesthesiology

## A RANDOMISED CLINICAL STUDY OF HEMODYNAMIC EFFECTS OF ETOMIDATE AND THIOPENTONE SODIUM AS AN INDUCTION AGENTS IN GENERAL ANAESTHESIA

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**ABSTRACT**

**Introduction :** As there are very few studies available regarding the comparison of effects of etomidate and thiopentone over hemodynamic changes during anaesthesia in elective procedures, this study is done **Methods and methodology :** 60 patients belonging to ASA physical status I or II, who were between 15 years to 60 years of age were selected randomly. The drugs used for induction were either inj Etomidate 0.3 milligrams/kg Or inj Thiopentone 5milligrams/kg intravenously administered for 30-60 seconds. Hemodynamic changes during induction and endotracheal tube intubation were recorded and analysed. **Results :** In the thiopentone group, Pre induction rate was  $13.4 \pm 1.9$  and decreased to  $12.1 \pm 1.7$  at 1 min,  $10.3 \pm 2.3$  at 2 min,  $10.2 \pm 2.1$ . In the Etomidate group, there were no significant changes pre-induction rate was  $12.2 \pm 1.7$  after induction increased to  $13.1 \pm 1.9$  at 1 min,  $12.1 \pm 2.2$  at 2 min touches the pre-induction rate at 3 min. Thiopentone group shows fall in both systolic and diastolic blood pressures but were not significant  $p > 0.005$  but Etomidate group shows very minimal changes in both systolic and diastolic blood pressures. After intubation diastolic blood pressures were recorded in both thiopentone and etomidate groups at 1,2,3-minute intervals. The diastolic blood pressure in the Thiopentone group  $87 \pm 17$  mmHg ( $p < 0.005$ ) at 1 min,  $87 \pm 19$  mmHg at 2 min,  $85 \pm 18$  mmHg at 3 min and  $77 \pm 17$  at 1 min,  $76 \pm 16$  at 2 min,  $74 \pm 19$  at 3 minutes in the etomidate group respectively. There was a significant increase in diastolic blood pressures of etomidate with a p-value of  $< 0.05$ . **Conclusion :** This study concludes that the Etomidate has a lesser induction time compared to thiopentone, but the incidence of apnea attack was more with thiopentone. From all the above studies we can finally conclude that etomidate is safe, hemodynamically stable induction agent compared to thiopentone and can be used as an effective alternative for general anaesthesia induction.

**KEYWORDS :****Introduction :**

Stress response of the body during endotracheal intubation or procedures will lead to hemodynamic changes in the body . These changes might vary from mild changes in heart rate to accelerated hypertension. Hence pre procedural induction with anaesthetic agents will facilitate the ease of the procedure minimising the haemodynamic changes. However administration of these drugs itself might lead to severe adverse events like hypotension and bradycardia . These events are important in elderly patients particularly with underlying ischaemic heart disease because these events might further compromise in cardiac perfusion leading them to ischaemia<sup>1</sup>.

Various drugs such as Etomidate, Ketamine, and Propofol have been explored with varying degrees of success in the hunt for a better inducing agent that has adequate control of hemodynamic changes during intubation. Because of its quick and predictable effect, thiopentone has been used as a standard anaesthetic induction drug since the 1930s. Cardiovascular and respiratory depression, higher incidence of laryngospasm and bronchospasm, and allergic responses are the primary downsides. As an intravenous anaesthetic medication, thiopentone has stood the test of time.

FUCHS T.et al. carried out a study on 60 patients by selecting them randomly into one of the two study groups. Induction of anaesthesia was done with Alfentanil 10 microgram/kg followed by thiopentone sodium 5 mg/kg (group 1) or Etomidate 0.3 mg/kg (group 2), and both groups received Rocuronium 0.6 mg/kg. The intubation response was less in group 2 compared to group 1. The study concluded that Etomidate as an induction agent containing Alfentanil and Rocuronium decrease intubation response compared to thiopentone<sup>2</sup>

DE SANTOS P et al. did a study on 40 ASA physical status I-II women who were randomly selected into two groups containing 20 in each group who were posted for uterine curettage. Induction of anaesthesia was done with 2.5% Thiopentone (5mg/kg) or Etomidate (0.3mg/kg) was maintained with inhalational agent isoflurane, maintained with supplemental doses as and when required. Their study concluded that in healthy patients who were subjected to short-duration surgeries etomidate show no advantage over thiopentone as an inducing agent.

As there are differences among various studies done earlier in comparison of these drugs we have done a study to compare the effect of these two drugs on the hemodynamics of the patient during

induction and during endotracheal intubation in elective procedures in our setting.

**Methodology :**

This clinical trial was conducted on 60 patients who were between 15 years to 60 years of age undergoing elective surgeries under general anaesthesia in NRI Institute of Medical Sciences,

**Visakhapatnam**

After attaining institutional ethical committee approval, 60 patients belonging to ASA physical status I or II, who were between 15 years to 60 years of age, undergoing elective surgeries under general anaesthesia were selected randomly. The patients were randomly allocated to one of the

following two groups :

Group-T: Includes 30 patients in which general anaesthesia is induced with inj thiopentone 5milligram / kg intravenously.

Group - E: Includes 30 patients in which general anaesthesia is induced with inj etomidate 0.3milligram/kg intravenously.

Parameters like Heart rate, blood pressure, respiratory rate, ECG and SPO2 were measured using Saturation Probe, ECG leads, Sphygmomanometer.

Before the start of anaesthesia, all patients were pre-treated with Injection fentanyl 2 micrograms for

each kg and Inj. Glycopyrrolate 0.2 mg IV 10 minutes before inducing with induction agents.

The drugs used for induction were either inj Etomidate 0.3 milligrams/kg (Group-E patients) Or inj

Thiopentone 5milligrams/kg (Group T patients) intravenously administered for 30-60 seconds.

**OBSERVED PARAMETERS:**

1) During Pre-Induction Period

Parameters like Heart rate Respiratory rate and Blood pressures were recorded at an interval of 1, 3,

5 minutes from immediately after premedication to before injection of inducing agents. These were considered baseline parameters for further comparison.

2) During Induction Period

- a) From the start of induction to loss of eyelash reflex induction time was recorded in seconds
- b) At intervals of 1,2,3 minutes hemodynamic parameters like heart rate respiratory rate and blood pressure were recorded
- c) Grading of pain on injection was done by visual analogue scale as No pain- zero, slight pain- one, moderate pain- two, severe pain- three
- d) Apnea: The cessation of respiration for more than 10 seconds was considered apnea.

1) Immediately after endotracheal intubation -At an interval of 1,2,3 minutes hemodynamic parameters like Blood pressure, Heart rate, Respiratory rate were recorded.

The data is analyzed using SPSS software. The descriptive statistics like mean and standard deviation were evaluated with 95% CI and a significant p value of <0.05.

RESULTS :

Table1: Demographic characteristics of patients

Parameter	Thiopentone (N=30)	Etomidate (N=30)
Age in years*	32.63±16.4	25.26±9.26
Weight in Kg*	49.8±10.8	48.86±7.6
Sex		
Male	17	14
Female	13	16

\* Mean±SD

The Distribution of patients according to weight was shown in group T and group E. The average mean weight was 49.8 ±10.8 kgs in group T and 48.86 ±7.6 kgs in group E, respectively. There was no significant difference between mean weights between the two groups.

Graph-1 -Demographic characteristics of patients

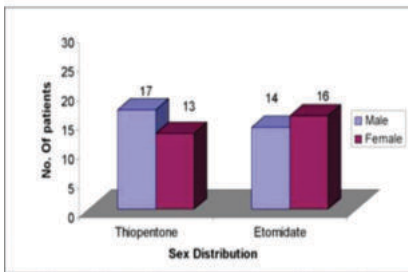


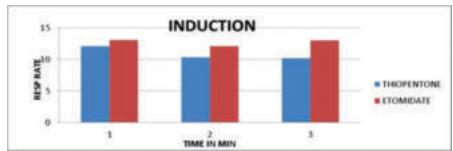
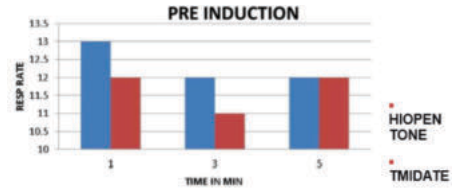
Table-2 -Comparison of respiratory rate between two groups

Time of assessment	Thiopentone	Etomidate	t value	P-value
	Mean±SD	Mean±SD		
Pre induction	13.4 ±1.9	12.2±1.7	1.97	0.59*
1 Min	12.8±2.1	11.7±1.3	1.23	1.71*
3 Min	12.4±1.9	12.4±1	1.02	1.11*
Induction	12.1±1.7	13.1±1.9	1.83	0.93*
1 Min	10.3±2.3	12.1±2.2	0.9	1.10*
2 Min	10.2±2.1	13±2	0.78	1.2*
3 Min	12	12	--	--
Post intubation (RR fixed) 1 Min	12	12	--	--
2 Min	12	12	--	--
3 Min	12	12	--	--

NOT SIGNIFICANT

There was a slight decrease in the respiratory rate in both groups after premedication after 2 min and returns to the normal value after 5 minutes which was not statistically significant. In the thiopentone group, Pre induction rate was 13.4±1.9 and decreased to 12.1±1.7 at 1 min, 10.3±2.3 at 2 min, 10.2±2.1. In the Etomidate group, there were no significant changes pre-induction rate was 12.2±1.7 after induction increased to 13.1±1.9 at 1 min, 12.1±2.2 at 2 min touches the pre-induction i.e., 12±1.7 value at 3 min.

Graph-2 - Comparison of Respiratory rate in the two study groups



POST INTUBATION

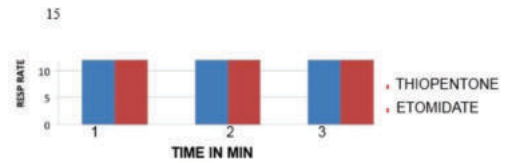


Table 3: Comparison of heart rate in the two study groups

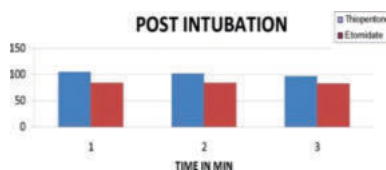
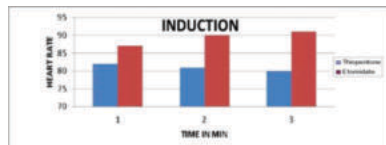
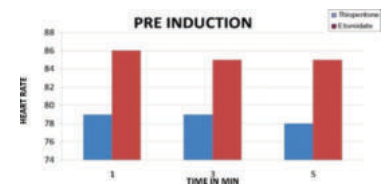
Time of assessment	Thiopentone	Etomidate	t value	P-value
	Mean±SD	Mean±SD		
Pre induction				
1 Min	79.4±18	86.2±17.7	1.57	0.22*
3 Min	79.8±21	85.7±19.3	1.4	0.31*
5 Min	78.8±19	85.2±21	1.8	0.11*
Induction				
1 Min	82±19	87.9±17	1.33	0.43*
2 Min	81.5±22	90.3±23	1.9	0.10*
3 Min	80±20	91±21	1.7	0.2*
Post intubation				
1 Min	105±24	84.7±19	3.04	0.004**
2 Min	102±23	84.5±15	3.9	0.005**
3 Min	97±19	83±17	4.32	

\*NOT/ SIGNIFICANT

There was only a slight decrease in heart rate in both the groups after premedication which was not statistically significant.

After induction, there was an increase in heart rate in the etomidate group from the pre-induction values, from 86±17 BPM before induction to 87.9±17 at 1 min, 90.3±23 BPM at 2 min 91±21 bpm at 3 min. Heart rate was decreased in the Thiopentone from the pre-induction values from 79.4±18 to 82±19 bpm at 1min. 81.5±2.2 bpm at 2 min. 80 ±20 bpm at 3 min. After intubation, there was a significant increase in heart rate in the Thiopentone group 105±24 bpm at 1 min. 102±23 bpm at 2 min. 97 bpm at 3 min compared to the Etomidate group which was statistically significant i.e. p<0.005.

Graph -3 Comparison of heart rate in the two study groups

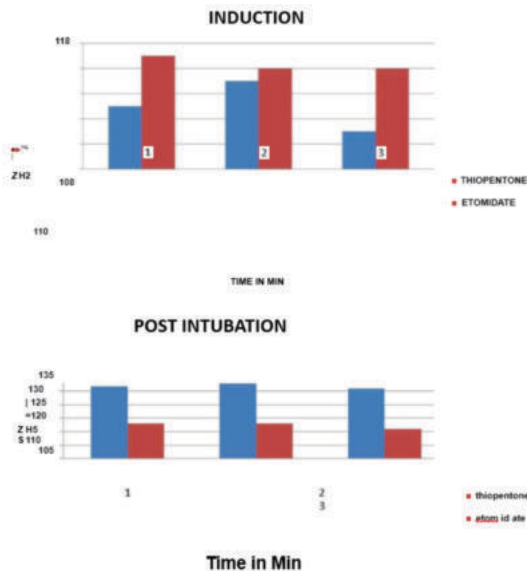


**Table 4: Comparison of Systolic blood pressure in the two study groups**

Time of assessment	Thiopentone	Etomidate	t value	P value
	Mean±SD	Mean±SD		
Pre induction				
1 Min	115±25.6	114±25.7	0.17	>0.05*
3 Min	115±23	115±24.3	0.23	>0.05*
5 Min	114±19	115±22.6	0.82	>0.05*
Induction				
1 Min	113±23	117±25	1.2	>0.05*
2 Min	114±22	116±24	0.9	>0.05*
3 Min	111±21	116±21	1.7	>0.05*
Post intubation				
1 Min	132±21	118±24	3.65	<0.05**
2 Min	133±24	118±23	3.9	<0.05**
3 Min	131±25	116±25	4.8	<0.05**

\*NOT SIGNIFICANT/^SIGNIFICANT

Thiopentone group shows fall in both systolic and diastolic blood pressures but were not significant  $p>0.005$  but Etomidate group shows very minimal changes in both systolic and diastolic blood pressures. In the thiopentone group, there was a significant rise in both systolic and diastolic blood pressures after intubation which was as follows at intervals of 1, 2, 3 minutes Systolic blood pressure in the Thiopentone group 132±21 mmHg at 1 min ( $p<0.005$ ), 133±24 mmHg ( $<0.005$ ) at 2 min 131±25 mmHg at 3min ( $<0.005$ ) and 118±24, 118±23, 116±25 at the interval of 1 2 3 minutes in etomidate group. Here p-value was found to be statistically significant i.e,  $p<0.05$ .



**Graph - 4: Changes in systolic blood pressure**

**Table-5- Comparison of Diastolic blood Pressures in both study groups**

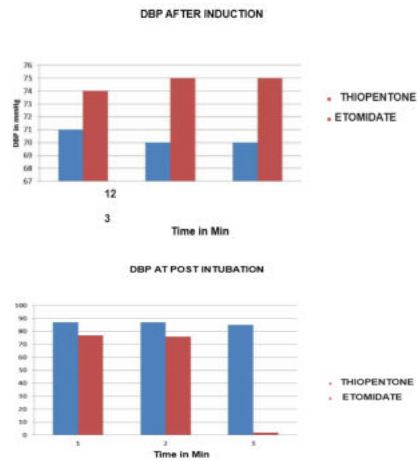
Time of assessment	Thiopentone	Etomidate	t value	P value
	Mean±SD	Mean±SD		
Pre induction				
1 Min	75.5±15.4	74±17.7	0.07	>0.05*
3 Min	73.6±15	73±16	0.65	>0.05*
5 Min	73±15	74±16	0.8	>0.05*
Induction				
1 Min	71±15	74±17	0.98	>0.05*
2 Min	70±14	75±16	1.49	>0.05*
3 Min	70±15	75±16	1.43	>0.05*
Post intubation				
1 Min	87±17	77±17	3.94	<0.05**
2 Min	87±19	76±16	3.76	<0.05**
3 Min	85±18	74±19	3.32	<0.05**

\*NOT SIGNIFICANT ^SIGNIFICANT

The diastolic blood pressure in the Thiopentone group

87±17mmHg( $p<0.005$ ) at 1 min.87±19mmHg at 2 min,85±18mmHg at 3 min and 77±17 at 1 min, 76±16 at 2 min, 74±19 at 3 minutes in the etomidate group respectively. There was a significant increase in diastolic blood pressures of etomidate with a p-value of  $<0.05$ .

**Graph - 5 Changes in Diastolic blood pressure**



**DISCUSSION**

Our study showed that thiopentone has a longer induction time in comparison with etomidate. The mean induction time in the Thiopentone group was 31±4.49 secs and with the Etomidate group was 25±3.19 secs ( $P<0.05$ ) which is significant. The comparative review is done by S.c Shah, et al., showed Etomidate in the portion utilized accomplished a quick and smooth acceptance of sedation<sup>4</sup>. These outcomes were reliable with our review as here too, the mean acceptance time with Etomidate was more limited than the mean enlistment time with Thiopentone.

In our study, following induction at 1, 2, and 3 minutes, both systolic and diastolic blood pressure decreased in the Thiopentone group, however, there was a modest increase in systolic and diastolic blood pressure in the Etomidate group ( $P$ -value  $> 0.05$ , not statistically significant). According to Batra et al., arterial pressure remained constant during the anaesthesia in the Etomidate group but fell in BP 80 per cent of Thiopentone patients. After Thiopentone, the incidence of hypotension was higher. In Etomidate, there was a negligible decrease in BP.

When comparing the Thiopentone and Etomidate groups, there is an increase in heart rate in the Thiopentone group. In the Thiopentone group, tachycardia was seen throughout the first minute. There was a trend for the heart rate to drop towards the preanesthetic value after 3 minutes. In the Etomidate group, the heart rate increased slightly compared to the pre- induction value, which was not statistically significant. Thiopentone raises heart rate and restores it to preinduction levels shortly before intubation, according to studies by C E Harris, et al<sup>5</sup>. Only 10% of patients' heart rates increased after receiving IV 0.3 mg/kg Etomidate, according to John M Gooding, et al<sup>6</sup>.

Respiratory rate: At 1, 2, and 3 minutes, the Thiopentone group's respiratory rate decreased. At 1, 2, and 3 minutes after induction, the Etomidate group demonstrated an increase in respiratory rate. Our findings are consistent with those of S V Korgaonkar et al.<sup>7</sup>, who found that the Respiratory rate increased by 80% and remained unchanged at 19.1% at 5 and 7 minutes following induction in the Etomidate group. The patients in the Thiopentone group had a lower respiratory rate, according to Batra et al. Ford SR, et al. reported that the respiratory rate increased by 72 per cent with Etomidate and decreased by 22 per cent with Thiopentone.

**Changes in Haemodynamic parameters after Endotracheal Intubation.**

Following intubation, the Thiopentone group had a significant rise in heart rate and blood pressure, both systolic and diastolic ( $P$  values were 0.005 and 0.05, respectively) both statistically and clinically these changes were considerable. There was no significant increase in both systolic and diastolic blood pressure in the Etomidate group. This is consistent with research by T Fuchs-Buder, et al., who found that

Etomidate combined with Alfentanil reduced the intubation response more than Thiopental. W Scott Jellish, et al., found that Etomidate-based induction resulted in stable hemodynamics during laryngoscopy and intubation and that the Thiopental group had a larger rise in both heart rate and blood pressure following laryngoscopy and intubation ( $p < 0.05$ )<sup>8</sup>.

After intubation, all groups' heart rates increased significantly, according to Jeffrey L Giese et al. A little amount of fentanyl reduces the elevated heart rate but does not completely eradicate the negative effects. The effects of intravenous etomidate on hemodynamic in children with congenital cardiac shunts were explored by Naresh Dhawan et al., who found that it causes minor hemodynamic alterations<sup>9</sup>.

## CONCLUSION

This study concludes that the Etomidate has a lesser induction time compared to thiopentone, but the incidence of apnea attack was more with thiopentone. Etomidate is a fast-acting induction drug that maintains stable hemodynamic parameters and the adverse effects of the drug can be decreased with premedication and proper intravenous anaesthetic methods.

From all the above studies we can finally conclude that etomidate is safe, hemodynamically stable induction agent compared to thiopentone and can be used as an effective alternative for general anaesthesia induction.

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