RESEARCH PAPER

"Comparison Of Hemodynamic Changes In Cardiac Surgery During Induction With Etomidate And Thiopentone"

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Background: Hemodynamic stability during induction of anesthesia is a critical determinant of perioperative outcomes in cardiac surgery. Induction agents can significantly influence cardiovascular parameters such as heart rate, blood pressure, and systemic vascular resistance. Among commonly used intravenous anesthetic agents, Etomidate is known for its cardiovascular stability, whereas Thiopentone (thiopental sodium) has been associated with myocardial depression and hypotension. Given the high-risk profile of cardiac surgery patients, the choice of induction agent plays a crucial role in minimizing perioperative morbidity and mortality.
Aim: This study aims to compare the hemodynamic changes during induction of anesthesia using etomidate and thiopentone in patients undergoing cardiac surgery.
Materials and Methods: This prospective, randomized comparative study was conducted in a tertiary care hospital on 60 adult patients (ASA III–IV) scheduled for elective cardiac surgery. Patients were randomly divided into two groups: Group E (n=30) received etomidate (0.2–0.3 mg/kg), and Group T (n=30) received thiopentone (3–5 mg/kg) for induction. Standard monitoring was applied, including electrocardiography, non-invasive blood pressure, pulse oximetry, and invasive arterial pressure monitoring. Hemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at baseline, after induction, immediately after intubation, and at 1, 3, and 5 minutes post-intubation. Statistical analysis was performed using appropriate tests (Student's t-test and repeated measures ANOVA), with $p < 0.05$ considered statistically significant.
Results: Both groups were comparable in demographic characteristics and baseline hemodynamic parameters. Following induction, Group T (thiopentone) showed a significant reduction in SBP, DBP, and MAP compared to Group E (etomidate) ($p < 0.05$). The decrease in MAP was more pronounced in the thiopentone group, indicating greater cardiovascular depression. In contrast, Group E demonstrated minimal changes in blood pressure, maintaining better hemodynamic stability. Heart rate increased in both groups following intubation; however, the rise was more significant in the thiopentone group. Etomidate provided superior stability during the critical phases of induction and intubation. No significant adverse effects were observed in either group, although mild myoclonus was noted in a few patients receiving etomidate.
Conclusion: Etomidate is superior to thiopentone in maintaining hemodynamic stability during induction of anesthesia in cardiac surgery patients. It produces minimal changes in blood pressure and heart rate, making it a safer and more reliable induction agent in high-risk cardiac patients. Thiopentone, although effective, is associated with significant hypotension and cardiovascular depression, which may be detrimental in compromised patients. Therefore, etomidate should be preferred as an induction agent in cardiac surgical procedures where maintaining stable hemodynamics is essential.

Keywords: Etomidate, Thiopentone, Hemodynamic Changes, Cardiac Surgery, Induction of Anesthesia, Mean Arterial Pressure.
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INTRODUCTION

General anesthesia involves induction to facilitate tracheal intubation. Laryngoscopy and tracheal intubation are painful stimuli associated with sympathoadrenal response. This response has been noticed and reported 60 years ago. [1]

Patients presenting for valve replacement surgeries have an already compromised myocardium, and they poorly tolerate intubation response which may lead to hypertension, tachycardia and arrhythmias; an imbalance in myocardial supply and demand can result in myocardial ischemia. Hence anesthetic induction in patients undergoing valve replacement are based on

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techniques for minimizing intubation response, optimizing myocardial oxygen supply and maintaining hemodynamic stability.[2]

The precise mechanism of the intubation response is elusive but it has been established that it has both a sympathetic and parasympathetic element. The effect is transient occurring 30 seconds after intubation and lasting for less than 10 minutes thereafter.[3]

The sympathetic response is a polysynaptic pathway with the glossopharyngeal and vagus nerve forming the afferent arc to the sympathetic nervous system via the brain stem and spinal cord. This ensures a diffuse autonomic response at the efferent side including increased firing of the cardio-accelerator fibres and release of adrenergic mediators including norepinephrine, epinephrine and vasopressin. The net effect of this autonomics urge is an increase in blood pressure (BP) and heart rate (HR) [4,5] which can be harmful to any patient, more so in patients with increased cardiac risk.

The possibilities to offset or blunt the intubation response are numerous. Options include pharmacological , peripheral blocks and variations in techniques including various blades and conduits for intubations. Many pharmacological methods, like beta - blockers, deep inhalational anaesthesia, intravenous lignocaine,calcium channel blockers and direct acting vasodilators, have been tried to blunt these harmful pressor responses associated with laryngoscopy and endotracheal intubation.

Studies have been conducted to investigate the effects of variety of induction agents such as Propofol, Thiopental, Etomidate, Midazolam, Fentanyl and Ketamine, on these hemodynamic changes. [6,7]

Thiopentone has a direct negative effect on myocardial performance and both arterial and venous peripheral vasculature, with secondary effects on the circulatory system mediated via the sympathetic nerves and catecholamine release. Etomidate does not inhibit sympathetic tone or myocardial function [8,9] and at typical anaesthetic induction doses (0.3mg/kg) produces minimal blood pressure and heart rate changes in patients, including those with valvular disease or ischemic heart disease.

This study is conducted to compare the hemodynamic changes seen when Etomidate and Thiopentone are used as induction agents in patients subjected to anaesthesia for cardiac surgery.

PHARMACOLOGY

THIOPENTONE

Sodium thiopentone , also known as Sodium Pentothal is a rapid-onset ,short-acting and fairly prompt recovery barbiturate general anesthetic that is an analogue of Thiobarbital .

STRUCTURE OF THIOPENTONE:

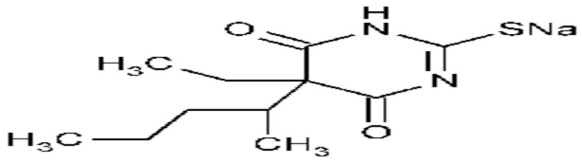

Figure 1 : Structure of thiopentone

Table 1 : Physicochemical properties of thiopentone

Chemical formula	C11H17N2NaO2S
Molecular weight	264.32gm/mol
Colour	Sodium salt
Concentration	Yellow amorphous powder. 500 mg ,1 gm
Lipid solubility	Highly soluble
Ph	10.5
Pka	7.6

STRUCTURE-ACTIVITY RELATIONSHIPS

Barbiturates are drugs derived from Barbituric acid. Barbituric acid, which lacks central nervous system (CNS) activity, is a cyclic compound obtained by the com- bination of urea and malonic acid. Barbiturates with sedative -hypnotic properties result from substitutions at the number 2 and 5 carbon atoms of Barbituric acid. Barbiturates that retain an oxygen atom on the number 2 carbon of the barbituric acid ring are designated as oxybarbiturates. Replacement of this oxygen atom with a sulfur atom results in thiobarbiturates, which are more lipid soluble than oxybar-
biturates.

MECHANISM OF ACTION

Barbiturates produce their sedative-hypnotic effects through an interaction with the inhibitory neurotransmitter gamma aminobutyric acid (GABA) in the CNS. [10] The ability of barbiturates to uniquely depress the reticular activating system, which is presumed to be important in the maintenance of

wakefulness, may reflect the ability of barbiturates to decrease the rate of dissociation of GABA from its receptors.

Table 2: Dosage of Thiopentone

INDUCTION	3-7 mg/kg
MAINTANENCE	50 – 100mg every 10-20 mins

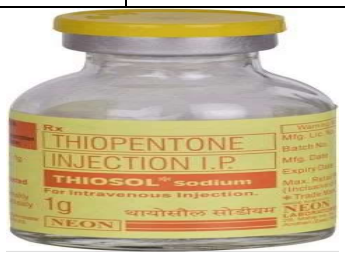

Figure 2: Thiopentone vial

PHARMACOKINETICS

Prompt awakening after a single intravenous dose of Thiopental reflects its , redistribution from the brain to inactive tissues. Ultimately, however, elimination from the body depends almost entirely on metabolism, because <1% of these drugs are recovered unchanged in urine [11] . The time required for equilibration of the brain with the Thiopental concentration in the blood (effect -site equilibration time) is rapid. Distribution of barbiturates in the body is determined by their lipid solubility (most important), protein binding, and degree of ionization.

Metabolism

Metabolism of Thiopental occurs at a slow rate, wi th 10% to 24% being metabolized by the liver each hour. Ultimately, metabolism of Thiopental is almost complete (99%). In paediatric patients the elimination half time of Thiopentone is shorter than adults. [12]

Renal Excretion

All barbiturates are filtered by the renal glomeruli, but the high degree of protein binding limits the magnitude of filtration,whereas high lipid solubility favors reabsorption of any filtered drug back into the circulation.

CLINICAL USES

The principal clinical uses of barbiturates are for:
1. Induction of anaesthesia
2. Treatment of increased intracranial pressure (ICP).

Other clinical uses of barbiturates are declining in frequency because these drugs:

- Lack specificity of effect in the CNS,

Can interfere with cardiovascular stability,
Have a lower therapeutic index than do benzodiazepines,
Result in tolerance more often than do benzodiazepines,
Have a greater liability for abuse, and
Have a high risk for drug interactions.

EFFECTS ON ORGAN SYSTEMS:

Cardiovascular System:

The decrease in systemic blood pressure that acompanies the induction of anaesthesia with Thiopentone is principally due to peripheral vasodilation, reflect -ing depression of the medullary vasomotor center and decreased sympathetic nervous system outflow from the CNS. Hypovolemic patients, who are less able to compensate for the peripheral vasodilating effects of barbiturates, are highly vulnerable to marked decreases in systemic blood pressure when these drugs are administered rapidly for the intravenous induction of anaesthesia.

Respiratory system:

Thiopentone administered intravenously for the induction of anaesthesia produce dose-dependent depression of medullary and pontine ventilatory centers. The resumption of spontaneous ventilation after a single intravenous induction dose of Thiopentone is characterized by slow frequency of breathing and decreased tidal volume. Laryngeal reflexes and the cough reflex are not depressed until large doses of barbiturates have been administered. Stimulation of the upper airway as by laryngoscopy, intubation of the trachea, or secret ions in the presence of inadequate depression of laryngeal reflexes by Thiopentone may resul t in laryngospasm or bronchospasm.

Central nervous system:

A continuous infusion of Thiopental, 4 mg/kg, produces an isoelectric EEG that is consistent with near -maximal decrease in cerebral metabolic oxygen requirements. Barbiturate induced depression of

cerebral metabolic oxygen requirements when the EEG is isoelectric is about 55%, reflecting a decrease in neuronal needs for oxygen. Hypothermia is the only reliable method for decreasing the basal cellular metabolic requirements for oxygen.

Somatosensory Evoked Responses:
Doses of thiopental sufficient to produce an isoelectric EEG fail to render any component of these responses unobtainable (thiopental is an acceptable drug to administer when the ability to monitor somatosensory evoked potentials in patients is desirable). [13]

Liver:
Thiopental , in the absence of other drugs, produces only modest decreases in hepatic blood flow. Induction doses of thiopental do not alter postoperative liver function on tests.

Enzyme Induction:
Thiopentone stimulate an increase in liver microsomal protein content (enzyme induction) after 2 to 7 days of sustained drug administration. Altered drug responses and drug interactions may reflect barbiturate-induced enzyme induction, resulting in accelerated metabolism of (a) other drugs, such as oral anticoagulants, phenytoin, and tricyclic antidepressants; or (b) endogenous substances, including corticosteroids, bile salts, and vitamin K. Thiopentone also stimulate the activity of a mitochondrial enzyme (in contrast to a microsomal enzyme) known as D-aminolevulinic acid synthetase. As a result , the production of heme is accelerated, and acute intermittent porphyria may be exacerbated in susceptible patient s who receive barbiturates.

Kidneys:
The renal effects of Thiopental may include modest decreases in renal blood flow and glomerular filtration rate.

SIDE EFFECTS:
- Local infection
- Venous thrombosis occurring after the intravenous administration
- Skin necrosis
- Allergic reactions [14 ,15,16,17]
- Immunosuppression
- Hiccups & coughing
- Respiratory depression
- Laryngospasm & bronchospasm
- Postoperative disorientation
- Vertigo
- Euphoria (delirium)

ETOMIDATE
Etomidate is a carboxylated imidazole-containing compound that is chemically unrelated to any other drug used for the intravenous induction of anaesthesia.

STRUCTURE OF ETOMIDATE:

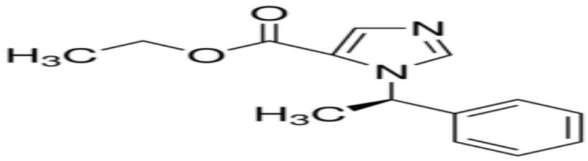

Figure 3: Structure of Etomidate

Table 3: Physicochemical properties of Etomidate

Chemical formula	C14H16N2O2
Molecular weight	244.289g/mol
Colour	Milky white
Concentration	2mg/ml in 35% propylene glycol
Lipid solubility	Acidic pH lipid soluble
Ph	6.9
PKa	4.2

Commercial Preparation
Etomidate is prepared as a fat emulsion, and pain on injection and venous irritation is unlikely. Administration through the oral mucosa results in direct systemic absorption while bypassing hepatic metabolism. The result is an achievement of higher blood concentrations more rapidly, compared with drug that is administered orally for delivery to the gastrointestinal tract .

Mechanism of Action
Etomidate is unique among injectable and inhaled anesthetics in being administered in a single isomer in clinical practice.The anesthetic effect of Etomidate

resides predominantly in the R (+) enantiomer, which is approximately five times as potent as the S (-) isomer. Etomidate is believed to exert its effects on GABAA receptors by binding directly to a specific site or sites on the protein and enhancing the affinity of the inhibitory neurotransmitter (GABA) for these receptors.

Table 4: Dosage of Etomidate

INDUCTION	0.2-0.6 mg/kg
MAINTANENCE	10 mcg/kg/min

Figure 4: Etomidate vial

Pharmacokinetics
The volume of distribution (Vd) of Etomidate is large, suggesting considerable tissue uptake. Etomidate penetrates the brain rapidly, reaching peak levels within 1 minute after intravenous injection [18] . Prompt awakening after a single dose of Etomidate principally reflects the redistribution of the drug from brain to inactive t issue sites. Rapid metabolism is also likely to contribute to prompt recovery.

Metabolism
Etomidate is rapidly metabolized through the hydrolysis of the ethyl ester side chain to its carboxylic acid ester, resulting in a water-soluble, pharmacologically inactive compound. The clearance of Etomidate is about five times that for thiopental ; this is reflected as a shorter elimination halftime of 2 to 5 hours. Likewise, the context -sensitive halftime of Etomidate is less likely to be increased by continuous infusion, as compared with thiopental .

Clinical Uses
Etomidate (0.2 to 0.4 mg/kg IV) may be viewed as an alternative to Propofol or barbiturates for the induct ion of anaesthesia, especially in the presence of an unstable cardiovascular system. Awakening after a single intravenous dose of Etomidate is more rapid than after barbiturates , and there is little or no evidence of a hangover or cumulative drug effect .

EFFECTS ON ORGAN SYSTEMS:
Cardiovascular System:
Etomidate does not inhibit sympathetic tone or myocardial function and at typical anaesthetic induction doses(0.3mg/kg) produces minimal blood pressure and heart rate changes in patients,including those with valvular or ischemic heartdisease.[19] For the same reason, Etomidate does not block sympathetic responses to laryngoscscopy and intubation, and these are often blunted by premedication with opioids [20, 21] . Because of its remarkably benign hemodynamic effects, Etomidate has proven useful for general anaesthetic induction in patients undergoing cardiac surgery and those with poor cardiac function. [22]

Central Nervous System:
Etomidate is a potent direct cerebral vasoconstrictor that decreases cerebral blood flow and CMRO2 (comparable to changes produced by thiopental). The frequency of excitatory spikes on the EEG is greater with Etomidate than with Thiopental and Methohexital , suggesting caution in the administration of Etomidate to patients with a history of seizures. Like Methohexital , Etomidate may activate seizure foci , manifesting as fast activity on the EEG. For this reason, Etomidate should be used with caution in patients with focal epilepsy. Conversely, this characteristic has been observed to facilitate the localization of seizure foci in patients undergoing the cortical resection of epileptogenic tissue.

Respiratory system
The depressant effects of Etomidate on ventilat ion seem to be less than those of barbiturates, although apnea may occasionally accompany a rapid intravenous injection of the drug.The depression of ventilation may be exaggerated when Etomidate is combined with inhaled anesthetics or opioids during continuous infusion techniques.

SIDE EFFECTS:
1. Pain on Injection
Pain on injection and venous irritation has been virtually eliminated with use of Etomidate preparations utilizing a lipid emulsion vehicle rather than propylene glycol .

2. Myoclonus

Myoclonus (spontaneous movements) occurs in 50% to 80% of patients receiving Etomidate in the absence of premedication. The prior administration of an opioid (fentanyl, 1 to 2 mcg/kg IV) or a benzodiazepine may decrease the incidence of myoclonus associated with the administration of Etomidate.

3. Adrenocortical Suppression
Etomidate causes adrenocort ical suppression by producing a dose-dependent inhibition of the conversion of cholesterol to cortisol . This enzyme inhibition lasts 4 to 8 hours after an intra venous induction dose of Etomidate.

4. Allergic reactions following the administration of Etomidate are very rare.

Aims
- To determine the hemodynamic changes between Etomidate and Thiopentone , when used for induction in patients posted for elective cardiac surgery. .

Objectives
- Determine hemodynamic change in Etomidate, when used for induction in patient for cardiac surgery (valve replacement).
- Determine hemodynamic change in Thiopentone, when used for induction in patient for cardiac surgery (valve replacement).

MATERIAL
Patients who will meet the inclusion criteria will be randomly allocated to group A and group B (30 patients in each group) generated by the computer generated random numbers. All patients will be premedicated with 0.15mg/kg of oral diazepam 1 hour prior to surgery. Electrocardiogram, invasive arterial blood pressure, central venous line and pulse oximeter monitoring will be initiated for all patients and baseline systolic and diastolic arterial blood pressure (SAP, DAP), mean arterial pressure (MAP) and heart rate(HR) will be recorded.
After preoxygenation for 3 minutes, patients in group A will be induced with Thiopental sodium 3 mg/kg and group B with Etomidate 0.2mg/kg. Both the groups will receive 5 mcg/kg of Fentanyl and 50 mcg/kg of Midazolam. The end point of anesthesia induction will denote as loss of eyelash reflex. All patients will receive 0.6 mg/kg Rocuronium for muscle relaxation to facilitate intubation. One to two minute after Rocuronium administration, tracheal intubation will be performed.
Hemodynamic variables including SAP, DAP, MAP and HR will be measured every minute for 5 minutes after induction and every 2 minutes till 10 minutes after intubation. The duration of laryngoscopy and intubation will be recorded for each patient. Hypotension (drop in SBP<90 mm Hg) will be treated with Trendelenberg position and ephedrine bolus (6 mg iv).Hypertension and tachycardia will be corrected by Inj . Fentanyl 2mcg/kg or Inj .Metaprolol 1-2 mg IV.

The primary study endpoint will be comparison of hemodynamic changes between the two groups.
Patients undergoing elective cardiac surgery (valve replacement surgery) at NIMS Hospital, Jaipur is to be enrolled in this study .This study will be conducted after obtaining approval from the Institutional Department of Research. The surgeons will be duly informed about the study. Consent from the Patients will be obtained prior to the study.

INCLUSION CRITERIA :
- Age: 18-80 years
- Weight : 35-100kgs
- Physical status: ASA II and III
- Elective valve replacement surgery

EXCLUSION CRITERIA :
- Physical status - ASA IV and V
- Ejection fraction less than 35%
- Emergency surgery
- Use of steroids in the preceding 6 months
- Use of Etomidate or thiopental within one week preoperatively
- Known sensitivity to Thiopentone or Etomidate

SAMPLE SIZE FORMULA

The formula for determining sample size is given as :

$$n = \left(\frac{Z_{\alpha/2} \cdot \sigma}{E}\right)^2$$

Where ,
n = Sample size
σ = Population standard deviation
e = Margin of error
Z = The value for the given confidence interval

- The confidence level is estimated at 95%
- Standard deviation 25.68
- With a z value of 1.96
- The confidence interval or margin of error is estimated at +/- 1.80
- Assuming that 80 percent as power of the study, minimum

sample size required for the study was calculated to be 52.

In our study 60 subjects were choosen 30 in each group

(n=30 in Thiopentone Group and n=30 in Etomidate Group)
Sample size was determined based on
Hemodynamic responses to Etomidate versus Ketamine -Thiopental sodium combination for ana esthetic induction in coronary artery bypass graft surgery patients with low ejection fraction: a double-blind, randomized, clinical trial .

Authored by Mohammad Reza Habibi et al

In this study it has been observed that systolic blood pressure three minutes after intubation for Ketamine + Thiopental showed as 119.96 ± 25.68

DATA ANALYSIS

Descriptive statistics was done for all data and were reported in terms of frequency analysis and percentage was used for categorical variables and the mean and SD were used for continuous variables. To find significant difference between continuous variables in independent groups the Unpaired sample t-test was used . To find the significance in categorical variable Chi-Square test and Fisher's Exact was used. Statistical significance was taken as $P < 0.05$.The data was analysed using IBM SPSS Statistics for Windows, Version 29.0.2.0.

RESULTS

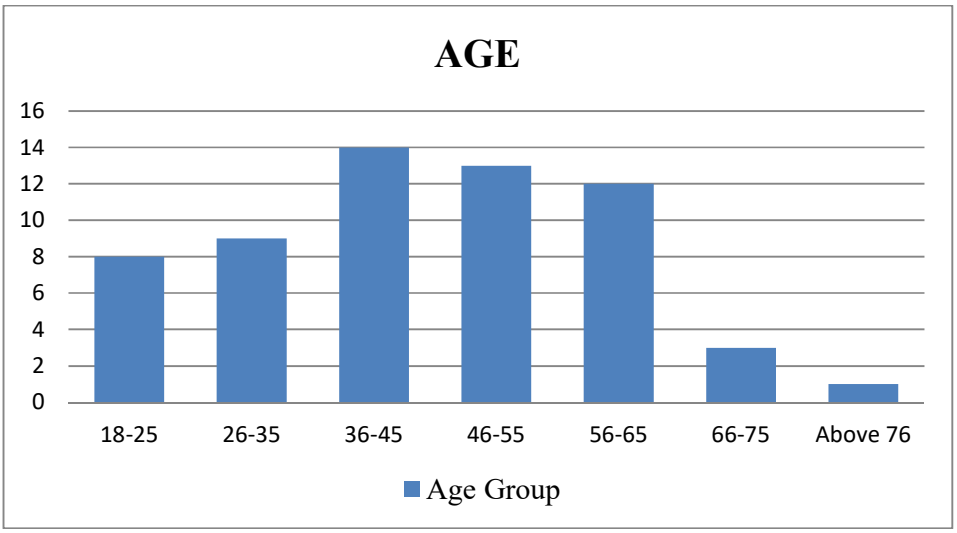

Figure 5: Age Groups Distribution

Table 5: Age groups distribution

Age Distribution		
Age Group	**Frequency**	**Percentage**
18-25	8	13.3
26-35	9	15
36-45	14	23.3
46-55	13	21.7
56-65	12	20
66-75	3	5
Above 76	1	1.7
Total	60	100

Comparison of Age Between groups:

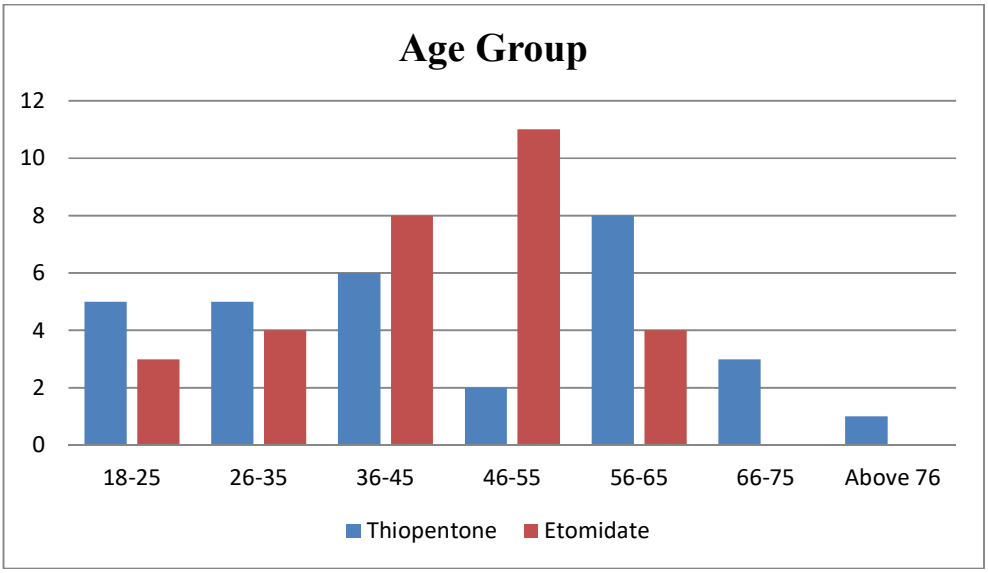

Figure 6 : Comparison of Age Between Groups

Table 6 : Comparison of Age Between Groups

Age Distribution			
Age	**Group**		**Total**
	Thiopentone	**Etomidate**	
18-25	5	3	8
26-35	5	4	9
36-45	6	8	14
46-55	2	11	13
56-65	8	4	12
66-75	3	0	3
Above 76	1	0	1
Total	30	30	60
P value		0.052	

p value : 0.052, p value > 0.05 is not statistically significant
Majority of the Thiopentone group patients belonged to 56 - 66 years age . In the Etomidate group patients, majority belonged to 46-55 years.

Conclusion:
The association between the intervention groups and age distribution is considered to be not statistically significant since p > 0.05 as per chi-square test .

GENDER STATUS

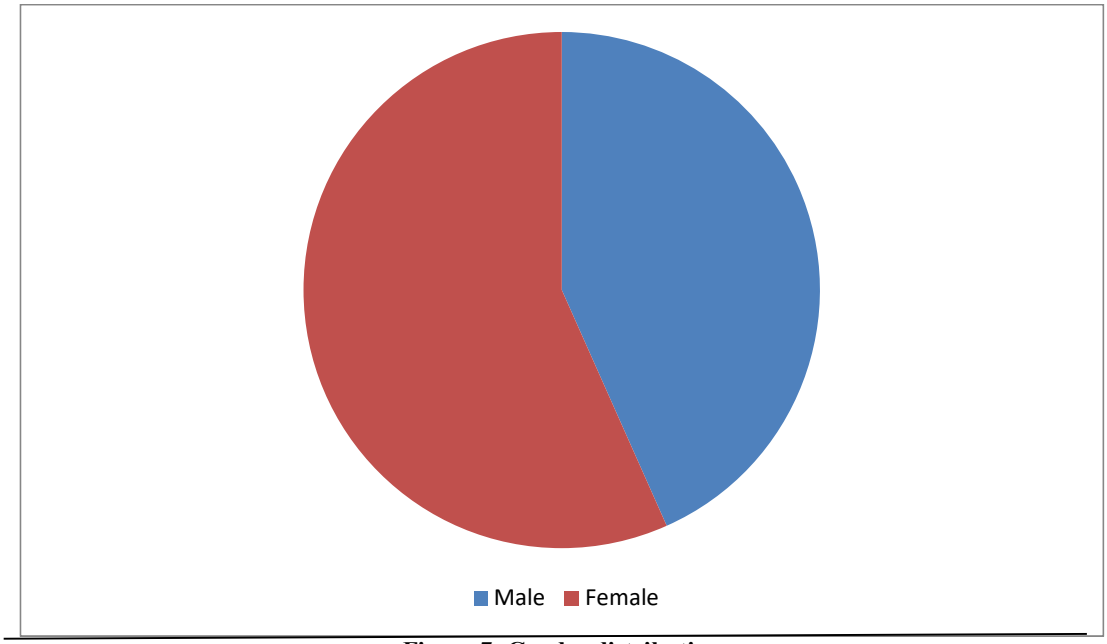

Figure 7: Gender distribution

Table 7: Gender Distribution

Gender	Frequency	Percentage
Male	26	43.33
Female	34	56.67
Total	60	100

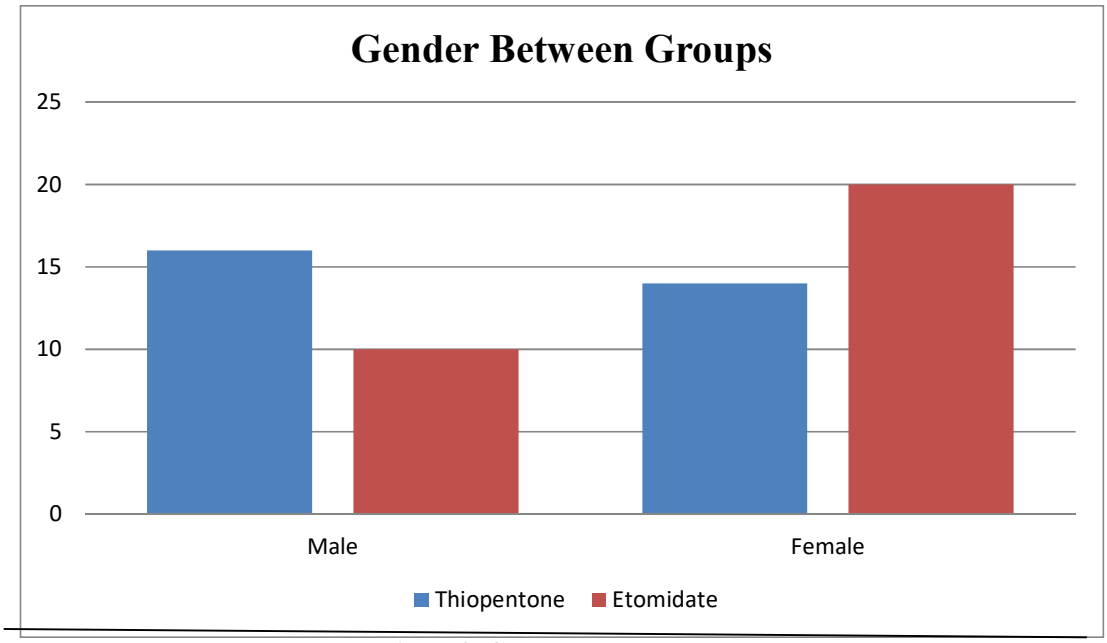

Figure 8 :Gender between groups

Table 8: Comparison of gender between groups

Gender	Groups		Total
	Thiopentone	Etomidate	
Male	16	10	26

Female	14	20	34
Total	30	30	60
p-value		0.193	

p value : 0.193, p value >0.05 is not statistically significant

Conclusion:
The association between the intervention groups and gender status is considered to be not statistically significant since p > 0.05 as per chi squared test .

WEIGHT

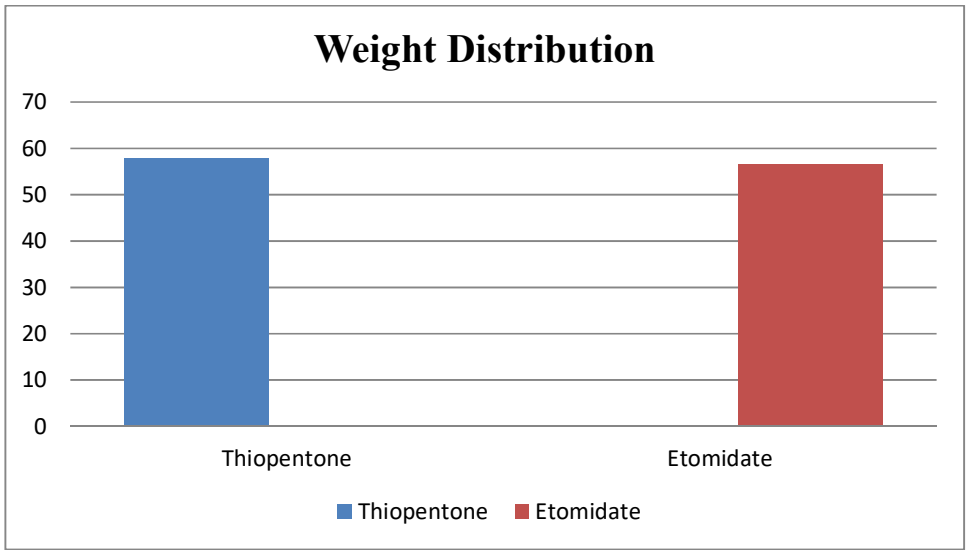

Figure 9: Weight distribution

Table 9: Comparison of weight between the groups

Weight	**Thiopentone**	**Etomidate**
N	30	30
Mean	57.933	56.500
SD	11.688	9.254
p-value		0.601

p value : 0.601, p value > 0.05 is not statistically significant
Majority of the Thiopentone group patients belonged to 41 - 60 kg weight class interval (n=16, 53.33%) with a mean weight of 57.93 kg. In the Etomidate group patients, majority belonged to 41-60 kgs weight class interval (n=20, 66.67%) with a mean weight of 56.50 kgs.

Conclusion:
The association between the intervention groups and weight distribution is considered to be not statistically significant since p > 0.05 as per unpaired t test .

HEIGHT

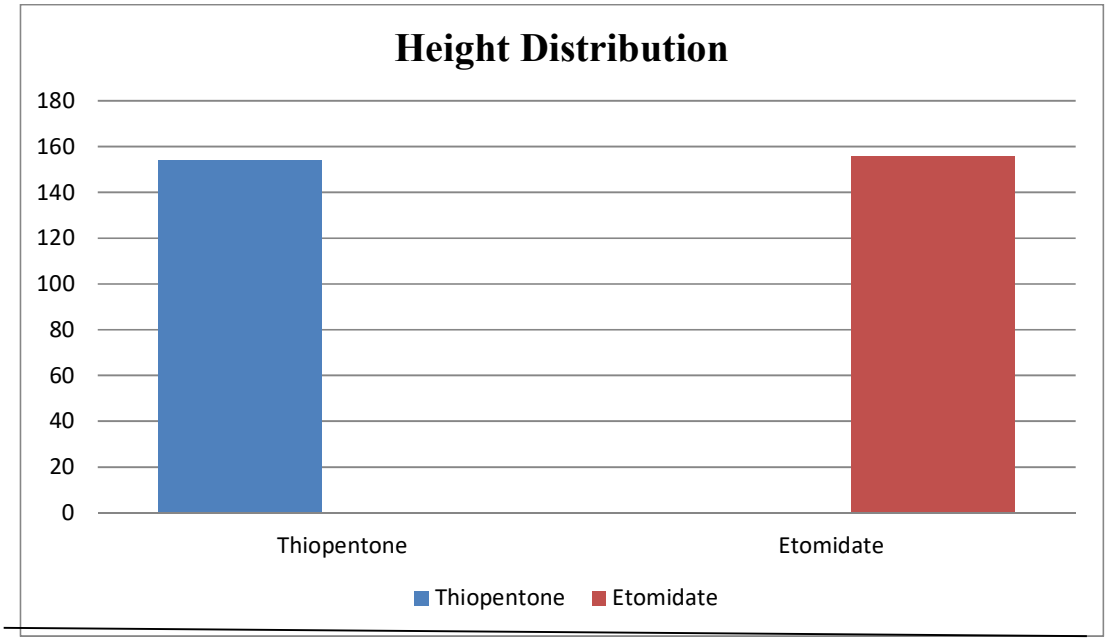

Figure 10 : Height distribution

Table 10 : Comparison of Height between the groups

Height	**Thiopentone**	**Etomidate**
N	30	30
Mean	153.86	155.73
SD	9.51	8.26
p-value		0.421

p value 0.421, p value > 0.05 is not statistically significant

Majority of the Thiopentone g roup patients belonged t o ≤ 150 cms height class interval (n=13, 43.33%) with a mean height of 153.86 cms. In the Etomidate group patients, majority belonged to 151-160 cms height class interval (n=14, 46.67%) with a mean height of 155.73 cms.

Conclusion:
The association between the intervention groups and height distribution is considered to be not statistically significant since p > 0.05 as per unpaired t test .

PROCEDURE

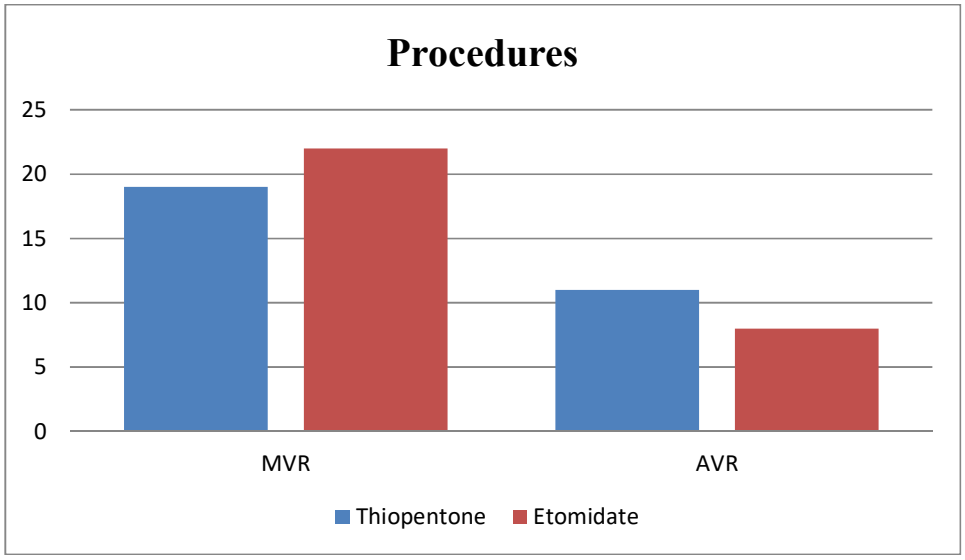

Figure 11 : Procedure between groups

Table 11 : Comparison of Procedure Between the Groups

Group	MVR	AVR	Total
Thiopentone	19	11	30
Etomidate	22	8	30
Total	44	16	60
p-value			0.405

p value 0.405 , p value > 0.05 is not statistically significant

Conclusion:
The association between the intervention groups and procedure status is considered to be not statistically significant since p > 0.05 as per chi squared test .

SYSTOLIC ARTERIAL PRESSURE

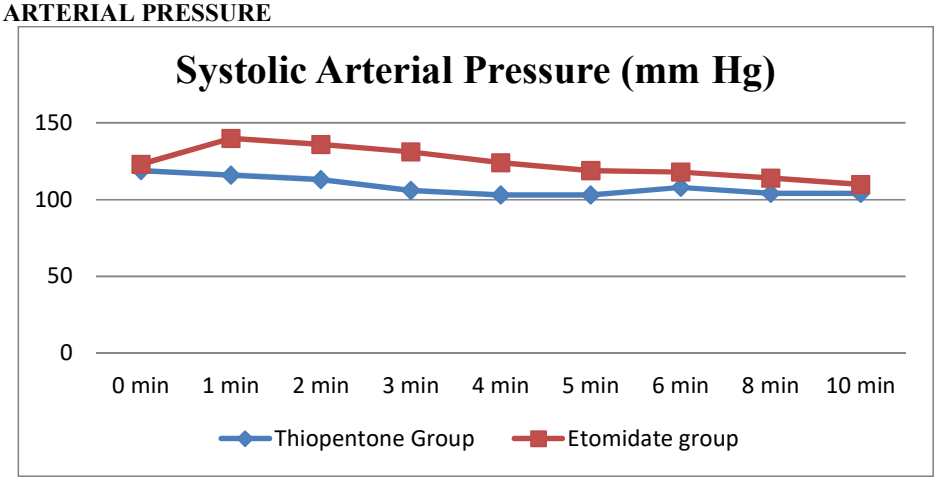

Figure 12: Comparison of systolic blood pressure between the groups

Table 12: Comparison of systolic blood pressure between the groups

Systolic Arterial Pressure(mm Hg)	Thiopentone Group		Etomidate Group		P value
	Mean	SD	Mean	SD	

0 min	119	8.85	122.60	11.86	0.1879
1 min	116.20	22.09	139.63	26.44	0.0004
2 min	113.07	23.32	136.33	25.75	0.0007
3 min	106.20	20.70	130.83	24.03	0.0001
4 min	102.93	20.99	123.90	22.21	0.0004
5 min	103.43	18.71	119	20.63	0.0033
6 min	108.07	19.48	118.23	20.70	0.0449
8 min	104.10	16.30	113.90	19.19	0.0373
10 min	104	15.15	109.93	16.36	0.1504

p value is < than 0.05 at 1 – 8 minutes which is significant

In patients belonging to Thiopentone group, the mean systolic blood pressure between 1-8 minutes during the procedure is 108 mm Hg. In Etomidate group the mean systolic blood pressure between 1-8 minutes during the procedure is 126 mm Hg.

Conclusion:

The decreased mean systolic blood pressure between 1 -8 minutes during the procedure in Thiopentone group compared to the Etomidate group is statistically significant with lowest p values of 0.0001 as per unpaired t - test indicating a true difference among study groups.

DIASTOLIC ARTERIAL PRESSURE

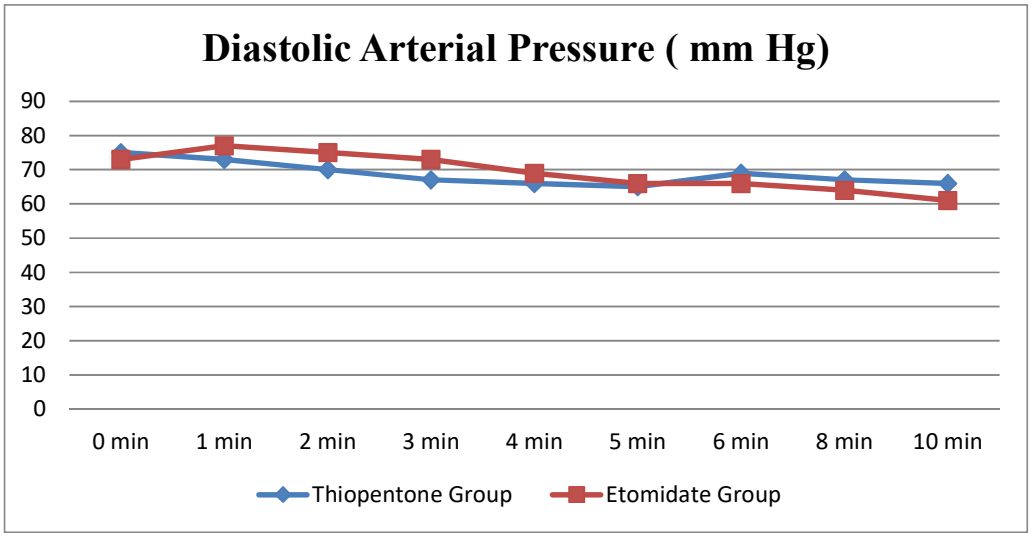

Figure 13: Comparison of diastolic blood pressure between the groups

Table 13: Comparison of diastolic blood pressure between the groups

Diastolic Arterial Pressure (mm Hg)	Thiopentone Group		Etomidate Group		P value
	Mean	SD	Mean	SD	

0 min	75	9.38	73	9.52	0.4158
1 min	72.82	14.39	76.97	13.28	0.2523
2 min	70.33	15.38	74.70	19.02	0.3322
3 min	66.57	14.75	72.87	12.40	0.0785
4 min	65.87	12.90	68.77	12.94	0.3883
5 min	64.60	12.21	65.77	13.78	0.7297
6 min	68.50	12.33	66.20	13.80	0.4986
8 min	67.10	9.22	63.93	11.58	0.2463
10 min	66.40	9.52	61.07	8.75	0.0277

p value is < 0.05 at 10 minutes which is significant
In patients belonging to Thiopentone group, the mean diastolic blood pressure at 10 minutes during the procedure is 66 mm Hg. In Etomidate group the mean diastolic blood pressure at 10 minutes during the procedure is 61 mm Hg.

Conclusion:
The increased mean diastolic blood pressure at 10 minutes during the procedure in Thiopentone group compared to the Etomidate group is statistically significant with lowest p values of 0.0277 as per unpaired t - test indicating a true difference among study groups.

MEAN ARTERIAL PRESSURE

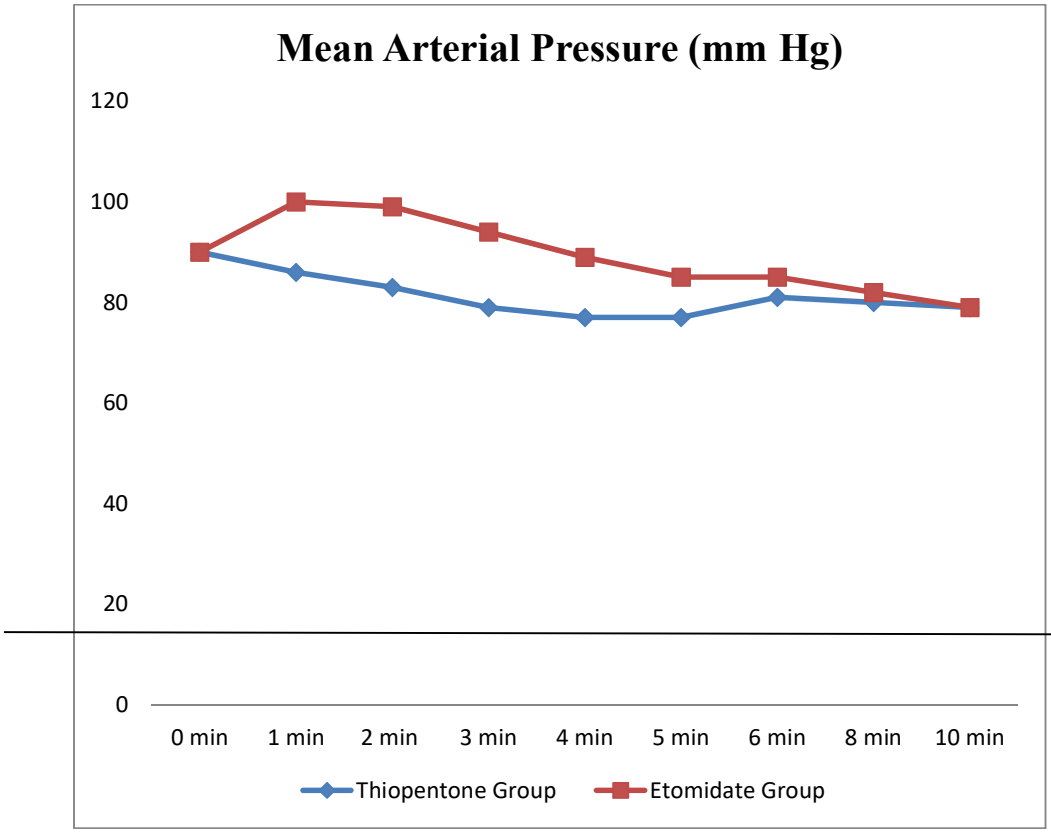

Figure 14: Comparison of mean arterial pressure between the groups

Table 14: Comparison of mean arterial pressure between the groups

Mean Arterial Pressure (mm Hg)	Thiopentone Group		Etomidate Group		P value
	Mean	SD	Mean	SD	
0 min	89.60	8.05	89.70	9.40	0.9649

1 min	85.87	13.87	99.80	18.32	0.0016
2 min	82.73	15.54	98.93	18.54	0.0005
3 min	78.70	15.66	94.07	17.20	0.0006
4 min	77.17	14.42	89	16.27	0.0042
5 min	76.70	13.61	84.60	17.30	0.0442
6 min	80.83	14.94	84.97	16.93	0.3202
8 min	79.50	11.42	82	15.04	0.4712
10 min	79	11.32	78.63	11.24	0.9002

p value is <0.05 at 1 – 5minutes which is significant
In patients belonging to Thiopentone group, the mean MAP between 1-5 minutes during the procedure is 80 mm Hg. In Etomidate group the mean MAP between 1-5 minutes during the procedure is 93 mm Hg.

Conclusion:
The decreased mean MAP between 1-5 minutes during the procedure in Thiopentone group compared to the Etomidate group is statistically significant with lowest p values of 0.0005 as per unpaired t - test indicating a true difference among study groups.

HEART RATE

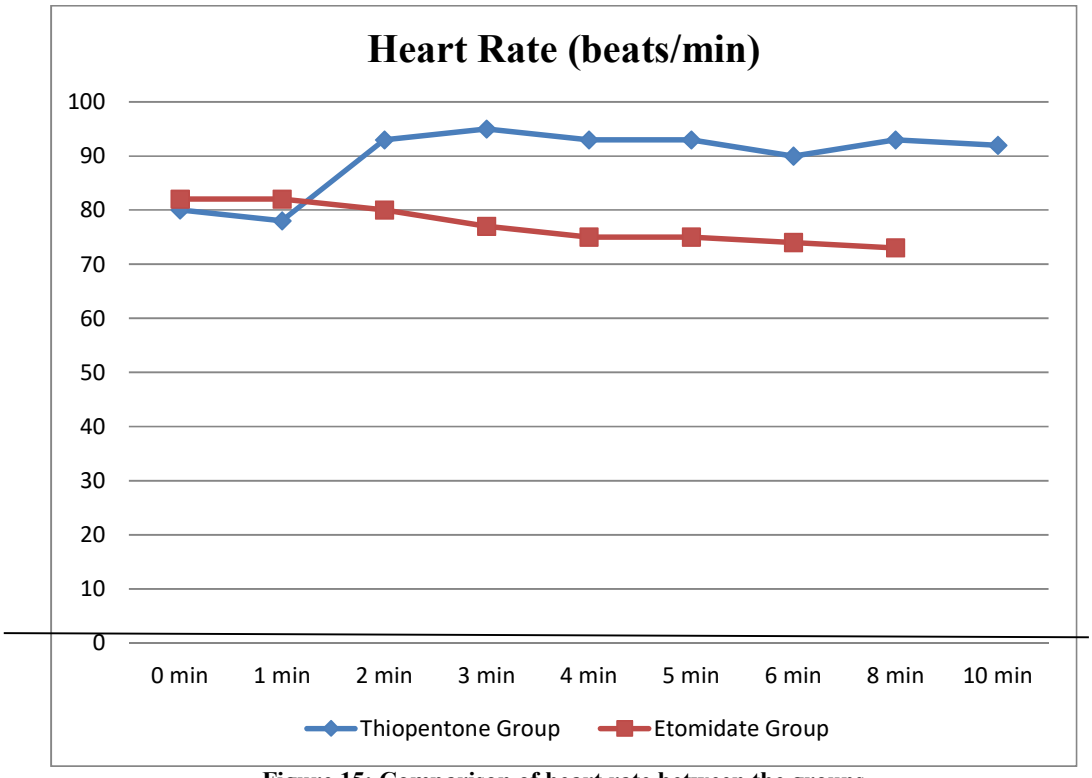

Figure 15: Comparison of heart rate between the groups

Table 15: Comparison of heart rate between the groups

Heart Rate (beats/min)	**Thiopentone Group**		**Etomidate Group**		**P value**
	Mean	**SD**	**Mean**	**SD**	

0 min	79.77	10.58	82.47	10.18	0.3180
1 min	77.67	10.68	81.67	13.91	0.2167
2 min	92.93	16.29	79.53	13.51	0.0010
3min	94.97	19.61	76.80	12.28	0.0001
4 min	93.37	18.02	74.70	13.44	<0.0001
5 min	93.03	15.99	74.57	13.44	<0.0001
6 min	90.03	12.83	73.93	13.60	<0.0001
8 min	92.87	12.02	73.47	12.71	<0.0001
10 min	91.90	13.44	70.37	11.86	<0.0001

p value is < 0.05 at 2 – 10 minutes which is significant
In patients belonging to Thiopentone group, the mean heart rate between 2-10 minutes during the procedure is 93 beats per minute. In Etomidate group the mean heart rate between 2 -10 minutes during the procedure is 75 beats per min.

Conclusion :
The increased mean heart rate between 2-10 minutes during the procedure in Thiopentone group compared to the Etomidate group is statistically significant with lowest p values of <0.0001 as per unpaired t- test indicating a true difference among study groups.

PERIPHERAL CAPILLARY OXYGEN SATURATION

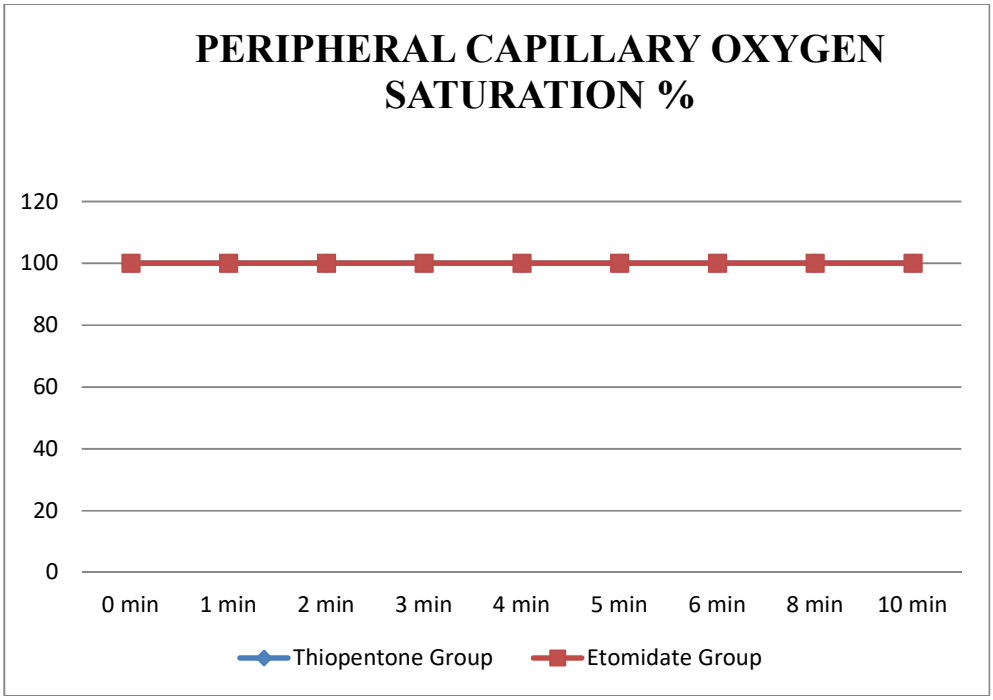

Figure 16: Comparison of peripheral capillary oxygen saturation between the groups

Table 16: Comparison of peripheral capillary oxygen saturation between the groups

Peripheral Capillary Oxygen Saturation (%)	Thiopentone Group	Etomidate Group	P value

	Mean	SD	Mean	SD	
0 min	100	00	100	00	0.999
1 min	100	00	100	00	0.999
2 min	100	00	100	00	0.999
3 min	100	00	100	00	0.999
4 min	100	00	100	00	0.999
5 min	100	00	100	00	0.999
6 min	100	00	100	00	0.999
8 min	100	00	100	00	0.999
10 min	100	00	100	00	0.999

p value is > 0.05 from 0 – 10 minutes which is not significant

In patients belonging to Thiopentone group, the mean SPO2 during the procedure is 100%. In Etomidate group the mean SPO2 during the procedure is 100%.

Conclusion:

SPO2 measurements during the procedure in Thiopentone group compared to the Etomidate group is statistically not significant since p value is > 0.05 as per unpaired t - test .

DISCUSSION

Induction of general anesthesia may be a critical period during valve replacement surgery. Both HR and BP are determinants of delivery and demand of oxygen. An increase in heart rate deleteriously affects both supply and demand of oxygen[33] . All the vital organs like the brain, heart and kidneys depend on systemic pressure to maintain perfusion pressure.

The harmful effects of anesthetic agents in patients suffering from cardiac diseases are well-known. Various authors have concern regarding induction of anesthesia with agents such as Thiopentone, Propofol, Ketamine and Midazolam.

Thiopentone directly depresses the contractile force of the heart , reducing cardiac output and blood pressure. There may be a compensatory increase in heart rate. It also decreases venous tone, causing pulling of blood in the peripheral veins; increasing the degree of hypotension.

Etomidate may differ from most other intravenous anesthetics in that the depressiv e effects on myocardial contractility are minimal at the concentrations needed for the induction of anesthesia. Cardiovascular stability (minimal changes in heart rate, stroke volume, cardiac output) is characteristic of induct ion of anesthesia using0.2 mg/kg IV of Etomidate. Etomidate has been proposed for the induction of anesthesia in patients with little or no cardiac reserve. [34, 35, 36, 37, 38]

Hence a study is undertaken at NIMS University and Hospital to compare the hemodynamic changes in cardiac surgeries with Etomidate and Thiopentone.

Sixty patients between the age group of 18 – 80 years of either sex belonging to ASA physical status II, III and IV posted for elective cardiac surgery (valve replacment) were randomly assigned to two groups of 30 each , group A (Thiopentone) and group B (Etomidate).

1. Group A received 3mg/kg i.v of Thiopentone for induction.
2. Group B received 0.2 mg/kg i.v of Etomidate for induction.

DEMOGRAPHY:

In our study there is no statistically significant difference in age, sex, height and weight distribution between Group A and Group B.

PROCEDURE:

In our study there was no statistically significant difference in type of surgery between Group A and Group B.

HEMODYNAMIC PARAMETERS:

The baseline values of the hemodynamic parameters (SBP, DBP, MAP and HR) were comparable between the Etomidate and Thiopentone group.

SYSTOLIC BLOOD PRESSURE:

In patients belonging to Thiopentone group, the mean systolic blood pressure betw een 1-8 minutes during the

procedure is 108 mm Hg. In Etomidate group, the mean systolic blood pressure between 1-8 minutes during the procedure is 126 mm Hg. The mean systolic blood pressure between 1-8 minutes during the procedure was less in Thiopentone group compared to the Etomidate group by mean difference 18 mm Hg (14% decrease).

Supriya Aggarwal et al [32] conducted a study to compare Propofol and Etomidate for their effect on hemodynamics and various adverse effects on patients in general anaesthesia. In this study there was a decrease in the SBP in Propofol group than compared to Etomidate group. But there was no significant change in systolic blood pressure between both the groups.

Fuchs T et al [25] conducted a study comparing Etomidate and Thiopentone. They used Alfentanil and Rocuronium in both the groups. The hemodynamic parameters were monitored. In this study there was a decrease in systolic blood pressure in the Thiopentone group than that of the Etomidate group after induction. But no statistiical significance was present . This study concluded that Etomidate reduces the stress response during intubation when compared to Thiopentone.

DIASTOLIC BLOOD PRESSURE:

In patients belonging to Thiopentone group, the mean diastolic blood pressure at 10 minutes during the procedure is 66mm Hg. In Etomidate group the mean diastol -ic blood pressure at 10 minutes during the procedure is 61 mm Hg. The mean dias -tolic blood pressure at 10 minutes during the procedure was meaningfully more in Thiopentone group compared to the Etomidate group by mean difference 5 mm Hg (8% increase).

As an institutional practice in the event of hypotension, the patient will be given Trendelenburg position and infused with a bolus of crystalloids (which was require -d more in the Thiopentone group). Thiopentone has a higher effect on the vascular tone (vasodi latat ion) than that of Etomidate. This probably explains why the Thiopentone group had a higher diastolic blood pressure at 10 mins after induction.

Habibi MR [29] et al conducted a study to compare the hemodynamic responses to Etomidate (0.2mg/kg) versus Ketamine -Thiopental sodium (Ketamine 1mg/kg, Thiopentone 5mg/kg) combination for anaesthet ic induction in CABG surgery patients with low ejection fraction (EF<45%). He states that in his study there was significant fall in diastolic blood pressure between Etomidate and Ketamine - Thiopetone groups. The addition of Ketamine to Thiopentone explains the higher DBP in that group compared to that of Etomidate.

Supriya Aggarwal et al [32] in her study states that there was no significant change in diastolic blood pressure in the Etomidate group.

MEAN ARTERIAL PRESSURE:

In our study in patients belonging to Thiopentone group, the mean arterial pressure between 1-5 minutes during the procedure is 80 mm Hg. In Etomidate group the mean arterial pressure between 1-5 minutes during the procedure is 93 mm Hg. The mean arterial pressure between 1-5 minutes during the procedure was meaning fully less in Thiopentone group compared to the Etomidate group by mean difference 13 mm Hg (14 % decrease).

Habibi et al [29] states that there was no significant difference in mean arterial blo -od pressure in Etomidate and Ketamine-Thiopentone group.

Singh R et al [27] conducted a study to compare the hemodynamic effects of anest -hesia induction with Etomidate, Thiopentone, Propofol, and Midazolam in patient with coronary artery disease and left ventricular dysfunction. This study states that there was a significant fall in mean arterial pressure between the groups(Etomidate, Thiopentone, Ketamine and Midazolam) with Thiopentone showing more decrease than Etomidate.

Baradari AG et al [31] conducted a study to compare the effects of Etomidate, combination of Propofol-Ketamine and Thiopental -Ketamine as induction agents on hemodynamic response to laryngoscopy and intubation. In their study there was minimal decrease in the MAP in the Etomidate Group than compared with Thiopentone - Ketamine group. There was no significant fall in the MAP in the Propofol – Ketamine group.

HEART RATE:

In our study in patients belonging to Thiopentone group, the mean heart rate betwe -en 2-10 minutes during the procedure is 93 beats per minute. In Etomidate group the mean heart rate between 2-10 minutes during the procedure is 75 beats per min. The mean heart rate between 2-10 minutes during the procedure was meaningfully more in Thiopentone group compared to the Etomidate group by mean difference 18 beats per minute (19 % increase).

Singh R et al [27] in their study state that there was a least significant decrease of mean heart rate in Thiopentone (7%) than compared to the other agents.

Naresh Dawan et al [26] conducted study on 30 children with congenital cardiac sh unt lesions 15 children having congenital Right to left group A and 15 children with left to right shunt group B. He states that there was no significant change in the heart rate between the two groups and concludes that Etomidate is a safer induction agent in cardiac surgeries in children.

Supriya Aggarwal et al [32] states that there was significant increase in heart rate in the Propofol group than compared with that of Etomidate group.

Kaushal et al [30] conducted a study to find out the effect of Etomidate and Propofol induction on hemodynamic and endocrine response in patients undergoing coronary artery bypass grafting/mitral valve and aortic valve replacement surgery on cardiopulmonary bypass. In this study there was increase in heart rate in the Propofol group after induction and intubation than compared with that of the Etomidate group.

PERIPHERAL CAPILLARY OXYGEN SATURATION:

In our study in patients belonging to Thiopentone group, the mean SPO2 during the procedure is 100%. In Etomidate group the mean SPO2 during the procedure is 100%. SPO2 measurements during the procedure in Thiopentone group compared to the Etomidate group is statistically not significant .

SUMMARY

A comparative randomized control study titled "Comparison of hemodynamic changes in cardiac surgeries during induction with Etomidate and Thiopentone" was done in the Department of Anesthesiology at NIMS University and Hospital.

Sixty patients between the age group of 18 – 80 years of either sex belonging to ASA physical status II and III posted for elective cardiac surgeries (Valve replacement) were randomly assigned to two groups of 30 each, Group A (Thiopentone) received 3mg/kg i.v. Group B (Etomidate) received 0.2 mg/kg i.v. of Etomidate for induction.The objective of this study was to compare the hemodynamic changes during induction with Etomidate and Thiopentone in cardiac surgeries .Demographic variables were comparable between the two groups.

There was statistically significant difference in SBP between Thiopentone and Etomidate groups at 1, 2, 3 ,4, 5, 6, and 8 mins.

There was statistically significant difference in DBP between Thiopentone and Etomidate groups at 10 mins.

There was statistically significant difference in MAP between Thiopentone and Etomidate groups at 1,2,3,4 and 5 mins.

There was statistically significant difference in heart rates between Thiopentone and Etomidate groups at 1,2,3,4 and 5 mins.

There was no significant difference in peripheral capillary oxygen saturation between both the groups.

CONCLUSION

Etomidate is associated with minimal changes in blood pressure (systolic, diastolic, mean) and heart rate when compared with Thiopentone. Etomidate is a better induction agent in patients particularly prone to hemodynamic fluctuations at induction like valve replacement. Hence we conclude that Etomidate can be safely used as an anaesthetic induction agent in cardiac patients.

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