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Haemodynamic Changes and Blood Sugar Levels Before and After Induction of General Anaesthesia with Thiopentone Sodium and Etomidate - A Comparative Study

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Abstract: The aim of this study is to compare the efficacy of two different anesthesia induction approach i.e Inj Thiopentone sodium and Inj. Etomidate in maintaining hemodynamic stability during induction and following endotracheal intubation in elective surgery. After obtaining Ethical committee clearance, 90 patients aged 15 to 60 years of either sex or ASA physical status I or II scheduled for elective surgery under general anaesthesia were taken for study. Written and informed consent was taken from the patients. This was conducted at Kamineni Academy of Medical sciences and research centre, Hyderabad. The patients were randomly placed into two groups. Group T induced with Inj.Thiopentone sodium (5 mg/kg) intravenous, Group II with Inj. Etomidate (0.3 mg/kg) intravenously. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and oxygen saturation (SPO2) were noted at different time interval. Heart rate in all study groups decreases after induction and it was more in group T compared to group E and after intubation HR increases in two groups but this increase is greater in group E than groupT. MAP among all three groups decreases after induction and it was more in group T than group E and Significant increase in MAP was seen at 1 min after intubation in all three groups but this increase was not sustained and returned to baseline in group II. The etomidate has better hemodynamic stability than thiopentone sodium at 1 min after intubation and was equally stable at other points of time.
Keywords: Thiopentone sodium, Etomidate, anesthesia.

INTRODUCTION

An ideal intravenous induction agent should produce minimal disturbance of cardiovascular and respiratory functions, should induce sleep in one arm brain circulation time, should chemically be stable, non-inflammable, nontoxic, easy to administer. The considerations for induction of anesthesia in patients undergoing cardiac surgery include hemodynamic stability, attenuation of the stress responses and maintenance of balance between myocardial oxygen demand and supply. Various intravenous (IV) inducing agents like thiopentone, etomidate, propofol and midazolam have been used for anesthetising these patients [1, 2].

The introduction of thiopental in to clinical practice in 1934 represents one of the most significant advances in the development of Anaesthesiology. Thiopentone sodium is a derivative of barbituric acid it is the sulphur anologue of pentobarbitone agent. Thiopentone has been the faster induction agent of anaesthesia because of its rapid action. The main draw-back is increased incidence of laryngospasm, bronchospasm allergic reaction, and decrease in arterial blood pressure. Due to its cardiorespiratory depressive effects thiopentone is not the drug of choice in shocked patients [3]. But thiopentone had certain limitation for its use in clinical practice like Long- elimination half-life, inability to blunt the haemodynamic and sympathetic nervous system responses to laryngoscopy and endotracheal intubation2, accumulation on repeated incremental doses or as a continuous infusion [4].

Etomidate is also a short-acting drug, which is usually used for induction and maintenance of anaesthesia [5]. Etomidate, carboxylated imidazole is characterized by hemodynamic stability, minimal respiratory depression and cerebral protective effects. Its lack of effect on sympathetic nervous system, baroreceptor reflex regulatory system and its effect of increased coronary perfusion even on patients with moderate cardiac dysfunction makes it an induction agent of choice in patients with cardiac disease [6]. However, the adverse effects such as pain on injection, thrombophlebitis and myoclonus are some undesirable adverse effects [7]. Studies have shown that plasma cortisol levels decrease with induction of anesthesia with etomidate [8].

Present study is a comparative study of haemodynamic changes and blood sugar levels before and after induction of general anaesthesia with thiopentone sodium and etomidate in elective patients induced under general anaesthetic management.

MATERIALS AND METHODS

After having approval from the institutional scientific and ethics committee, prospective randomized clinical study on 100patients, with 50 patients in each group.i.e.Group T (Thiopentone) and Group E (Etomidate). The study was undertaken at OT complex in Kamineni Academy of Medical sciences and Research Institute, Hyderabad during November 2015 to October 2017 i.e. two years. Patients those were included in the study were age 15 to 45 years of both sex, ASA grade I and II, not known allergic to mentioned anaesthetic drugs, non-diabetic patient, haemodynamically stable patients. Exclusion criteria was patient not fulfilling inclusion criteria, lack of patient consent, hypothyroid and hyperthyroid patients, heart block and active disease of CNS were excluded.

In order to randomize computer generated randomization table was used. Among the two groups, the first group (Group T) treated with inj Thiopentone sodium and second (Group E) patients were treated with Inj. Etomidate. All the patients underwent a thorough pre-anaesthetic checkup and investigated for all the routine and special investigations as per hospital protocol. Study was carried out after getting informed written consent from the patient.

All patients were premedicated with I.M glycopyrrolate 0.2 mg half an hour before induction. After receiving the patient in Operation Theater (OT), an intravenous line (IV) was secured with IV cannula and Normal Saline drip was started. Thereafter random blood sugar (RBS) recorded 5 min before induction (5 min BI).Before induction base line vital parameters were recorded; including blood pressure and pulse rate.

In the OT patient received IV midazolam 0.03 mg/kg and IV fentanyl 2mcg/kg five minutes before induction, and was preoxygenated with 100% oxygen. Then patient was induced with IV Etomidate at the dose of 0.3 mg/kg body weight as a induction agent in group E and thiopentone IV 5 mg/kg body weight for Group T respectively using peripheral cannula, until the patient's verbal response was lost. Then IV succinylcholine 1.5mg/kg was used as muscle relaxant in both the groups and intubation was done after IPPV, connected to work station and continued with nitrous oxide and oxygen mixture (70:30) and inhalational agent was used to maintain the anaesthesia. After 5 mins of induction, patients' blood sugar was recorded in both the groups. Later on as soon as intermediate muscle relaxant was administered with injection atracurium 0.5mg/kg and continued.

Simultaneously patient's haemodynamic - SBP, DBP, MAP and HR were recorded at 1 min, 2 min, 3min, 5min and 10 min after induction. The patients hemodynamic indicators such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP),heart rate (HR)were recorded before induction(T1),1 min (T2), 2min(T3), 3min(T4), 5min(T5) and 10min(T6) after Induction. Hypertension was defined as increase in SBP >20%, Hypotension <20% of baseline, tachycardia as HR > 20% and bradycardia is defined as < 60/min of baseline recordings.

STATISTICAL ANALYSIS

All statistical analyses was performed using the SPSS version 18.0 (SPSS Inc., chicago ,IL, USE). Quantitative data was presented as means and standard deviation (mean ±sd) and qualitative data as frequency and 95% confidence interval (CI).Age, weight and sex will be analyzed using frequencies test. Systolic, diastolic and mean arterial pressure, as well as heart rate was analysed using unpair student's t test and analysed with chi-2 or student's t test. Significance defined as $p<0.05$

RESULTS

In this study a total of 100 patients undergoing elective surgery under general anaesthesia were randomized in two groups comprising 50 patients each. In order to randomize computer generated randomization table was used. Among the two groups, the first group (Group T) all the patients were induced with Inj. Thiopentone and second (Group E) patients were induced with Inj. Etomidate.

Table 1: Demographic data in two groups

Group	Group T	Group E
Age (years)	34.775±9.75	34.7±9.14
Weight (Kgs)	64.65±10.66	64.9±10.45
Sex M/F	35/15	38/12
ASA I/II	29/21	30/20

The haemodynamic parameters like systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate were shown in table 2,3,4,5 respectively.

Table 2: Systolic blood pressure [SBP]

SBP at different time	T(mmofHg)	E(mmofHg)
T1	126. 9±8.6	124.3±7.5
T2	122. 4±11.6	114.1±7.8*
T3	131. 2±12.6	119.8±10.2
T4	130.5±10.6	118.1±11.2
T5	128.5±11.3	115.7±10.3
T6	127.7±11.1	112.5±11.3

The above table shows the mean of the systolic blood pressure of the two groups, there was statistically significant difference regarding blood pressure between two groups. There was fall in SBP after induction (T2) in two groups it is below the base line values in Etomidate group and increase in blood pressure from (T3) onwars above base line in thiopentone group.

Table-3: Diastolic Blood Pressure [DBP] Monitoring

DBP at different time interval	T(mmofHg)	E(mmofHg)
T1	82.7±6.9	81.1±6.3
T2	78.7±6.7	74.9±5.6
T3	84.4±10.9	78.9±7.5
T4	83.5±11.2	79.3±6.8
T5	81.7±10.3	80.8±7.0
T6	79.5±9.1	80.3±7.1

The mean of the diastolic blood pressure of the two groups, there exist statistically significant difference. There was fall in DBP after induction (T2) in two groups it is below the base line values in Etomidate group at T3-T5 and increase in blood pressure from (T3) onwards above base line in thiopentone group.

The below table shows the mean arterial blood pressure in two groups, the difference among the groups was statistically significant (Table-3).

Table-3: Mean Arterial Pressure [MAP] Monitoring

DBP at different time interval	T(mm of Hg)	E(mm of Hg)
T1	95.6±7.0	96.5±6.4
T2	94.8±7.8	92.0±5.8
T3	100.7±10.5	99.0±8.2
T4	98.3±8.9	98.5±7.3
T5	96.7±13.1	96.5±6.6
T6	94.3±8.6	95.6±7.1

Table-4: Heart Rate [HR] Monitoring

HR beats per min	T Mean ±sd	E Mean ±sd
T1	82.9±10.4	82.0±12.3
T2	83.0±11.1	77.8±13.1
T3	88.6±11.1	85.5±15.1
T4	87.5±13.25	81.3±12.57
T5	83.6±12.23	80.3±11.4
T6	81.2±11.36	80.7±11.3

The above table shows the HR changes among two groups, there was a statistically significant difference in HR after induction (Table-4).

Random Blood Sugars was measured in both groups at base line and 5 minutes after induction in both the groups it was significantly increased in Etomidate group (Table 5).

Table 5: RBS Monitoring in two groups

Group	Rbs 5 Mins. Before Induction	Rbs 5 Mins. After Induction
T	96.88±10.48	95.32±11.05
E	97.98±9.92	103.04±7.72*

DISCUSSION

An Ideal inducing Agent for general Anaesthesia should have hemodynamic stability, Minimal respiratory side effects and rapid clearance. The present study compared the efficacy of inj. Thiopentone and inj. Propofol for controlling cardiovascular responses. The observations showed that there was a significant difference among two groups regarding SBP, DBP and MAP after induction period. The results of our study showed that Etomidate significantly maintained HR, SBP, DBP and MAP after induction and 1,3,5,10 min after endotracheal intubation as compared to Thiopentone.

The properties of etomidate (Amidate, Hypnomidate) include hemodynamic stability, minimal respiratory depression, cerebral protection, and pharmacokinetics enabling rapid recovery after either a single dose or a continuous infusion. In animals, etomidate also provides a wider margin of safety (ED50/LD50) than thiopental [9]. These beneficial properties led to widespread use of etomidate for induction, for maintenance of anesthesia, and for prolonged sedation in critically ill patients. Anesthesiologists' enthusiasm for etomidate was tempered, however, by reports that the drug can cause temporary inhibition of steroid synthesis after single doses and infusions [10].

Etomidate has been used for induction and maintenance of anesthesia.The induction dose of etomidate is 0.2 to 0.6 mg/kg and it is reduced by premedication with an opiate, a benzodiazepine, or a barbiturate. Onset of anesthesia after a routine induction dose of 0.3 mg/kg of etomidate is rapid (one arm–brain circulation) and is equivalent to anesthesia obtained with an induction dose of thiopental or methohexital[11]. The duration of anesthesia after a single induction dose is linearly related to the dose each 0.1 mg/kg administered provides about 100 seconds of loss of consciousness [12]. Repeat doses of etomidate by bolus or infusion prolong the duration of hypnosis. Recovery after multiple doses or an infusion of etomidate is still usually rapid [13]. The addition of small doses of fentanyl with etomidate for short surgical procedures reduces the required dose of etomidate and allows earlier awakening. IN children, induction by rectal administration of etomidate has been obtained with 6.5 mg/kg. Hypnosis occurs in 4 minutes. At this dose, hemodynamics are unaltered, and recovery is still rapid [14].

Etomidate is a potent direct cerebral vasoconstrictor that decreases cerebral blood flow and CMRO2 35% to 45%. As a result previously increased ICP is lowered by etomidate. These effects of etomidate are similar to those of changes compared to that of thiopental but without decreasing arterial pressure or cerebral perfusion pressure. Etomidate is an induction agent with less cardiovascular depression than thiopental or propofol[15]. Haemodynamic stability with etomidate results from reduced effects on sympathetic nervous system and baroreceptor reflex responses. The stability of cardiovascular function suggests a lack of significant effects on either the peripheral or pulmonary vascular beds or on the myocardium itself. In a study done in 11 human volunteers, etomidate has minimal effects on heart rate, stroke volume, cardiac output and ventricular filling pressures. A slight increase in heart rate (10%) was the only haemodynamic change noted to be of significance.

John M. *et al*.[16] conducted study in patients with coronary heart disease, coronary blood flow is substantially increased, resulting in a minimal increase in myocardial oxygen consumption. Etomidate was found to have haemodynamic stability following a dose of 0.3 mg/kg in patients at risk of cardiac disease.

Fuchs T. *et al.* [17] conducted a study on 60 adult patients induced with alfentanil 10 micro gram/kg followed by thiopentone 5 mg/kg (Goup I) or etomidate 0.3 mg/kg (Group II). Response to the intubation stimulus was significantly less pronounced in Group II compared to group me. It was concluded that etomidate as part of an induction regime containing alfentanil and rocuronium, attenuated the reaction to intubation to a greater extent than thiopentone.

Scott Jelish W. *et al*,[18] conducted a study on 66 patients divided into two groups. First control subgroup received low dose etomidate 0.4 to 0.6 mg/kg, the second control subgroup received thiopentone 3-6 mg/kg. The study group was given high dose etomidate 0.5 to 1.7 mg/kg to an early burst suppression pattern. They concluded that etomidate based anaesthesia induction, titrated to EEG burst suppression, and produced stable haemodynamics during laryngoscopy and intubation as compared with lower dose, more classic induction with etomidate and thiopentone.

Naresh Dhawan *et al*.[19] conducted study on 30 children with congenital cardiac shunt lesion. He concluded that the etomidate at 0.3 mg/kg produces very minimal changes in hemodynamic parameters and shunt fraction In children with congenital shunt lesion. Eames *et al*. [20] conducted a study on 75 patients. Anaesthesia was induced with 2.5 mg/kg Propofol, 0.4 mg/kg etomidate, or 5mg/kg thiopental. Respiratory resistance was measured at 2 minutes after induction. They concluded that the respiratory resistance after tracheal intubation is lower after induction with propofol than after with thiopental or after induction with high dose etomidate.

A study conducted by Famewo CE, *et al*. [21] on plasma potassium, sodium and blood sugar following induction of anesthesia with etomidate and suxamethonium. Blood sugar increased after the administration of etomidate but rises significantly after suxamethonium is given. This hyperglycaemic response was greater in etomidate than thiopentone is due to greater sympathetic nervous system activity. In our study similar results were found in etomidate group having slightly higher blood sugar level. Another study in contrast to our study was by Ram Prasad Kaushal *et al*. [22] studied 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. There was significant increase in blood glucose values during bypass and when weaning off cardio pulmonary bypass in both groups compared to baseline, but the rise was less in etomidate group due to decrease stress response because of inhibition of cortisol synthesis. This study results are contrast to our study results.

CONCLUSION

Etomidate provides more stable hemodynamic parameters when used for induction of anesthesia as compared to thiopentone. Blood sugar levels were found to be slightly increased after 5mins of induction than the baseline level in Etomidate group.

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