Comparative Study of Thiopentone & Etomidate For Pressor Response in Hypertensive Patients Posted For Elective Surgeries

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ABSTRACT
Background & objective: The present study aims at comparing the hemodynamic effects of thiopentone and etomidate during induction in hypertensive patients and also to assess any untoward side effects of either drug. Methods: This study was conducted among 60 patients in the age group of 18 – 75 yrs undergoing various elective laminectomy and orthopaedic procedures. They were divided into 2 groups of 30 each. General anaesthesia was induced in Group E with Inj. etomidate 0.3mg/kg and in Group T with Inj. Thiopentone 5mg/kg. Inducing agent has been given over a period of 60 seconds in all the patients. Inj. Vecuronium bromide (0.1mg /kg. body wt.), was injected after loss of eye lash reflex in both groups. Nitrous oxide and oxygen was used for mask ventilation in both study groups. Subsequently, heart rate, SBP, DBP and MAP and ECG changes were recorded at one, two and three minutes after induction. Results: It has been observed that there is no clinically significant difference between in hemodynamic parameters (HR, SBP, DBP and MAP) following induction with etomidate and thiopentone. Conclusion: From our study, it has been concluded that there is no significant difference regarding hemodynamic parameters following induction with thiopentone and etomidate in adult hypertensive patients posted for elective surgery.

KEYWORDS
Thiopentone, Etomidate, Pressor response.

INTRODUCTION
Hypertension is one of the leading causes of death worldwide. Approximately 7.6 million deaths i.e. 13 to 15 percent of the total and 92 percent disability adjusted life years are attributable to high blood pressure. Hypertension doubles the risk of cardiovascular diseases like congestive heart failure, coronary heart disease, ischemic and haemorrhagic stroke, renal failure and peripheral artery disease.

Patients with arterial hypertension generally exhibit exaggerated hypotension after induction and excessive pressor response to stresses such as laryngoscopy and intubation, surgical incision and extubation. A statistically significant association has been obtained between hypertensive patients and perioperative cardiac outcomes. Intraoperative maintainance of blood pressure is more crucial than preoperative blood pressure control in terms of decreasing perioperative cardiac complications in mild to moderately hypertensive patients. Induction is a critical phase especially in patients with limited cardiac reserve. Hence an induction agent that cause minimal hemodynamic changes should be selected.

Introduction of thiopentone by Water and Lundy revolutionized the usage of intravenous anesthetics because of its rapid onset and ultrashort action. But it was thought that it was the major culprit in causing a grossly increased mortality in pearl harbor bombing incident in 1941. Later it was learnt that the improper use of thiopentone rather than the drug itself was responsible for the increased deaths. Since then, till date it enjoyed the clinical success that no other barbiturate had.

Etomidate, an intravenous anaesthetic was introduced in 1972. It is well known for its cardiovascular stability and minimal respiratory depression. Also the margin of safety of etomidate is much wider than that of thiopentone. These properties led to the wide spread use of etomidate for induction, maintenance and sedation in intensive care units especially in geriatric patients and those with significant cardiovascular disease where hemodynamic stability is desired. Major disadvantage which led to the withdrawl of etomidate is temporary inhibition of steroid synthesis. But recently etomidate usage is being expanded because of rediscovery of its physiological profile and also due to the lack of studies supporting clinically significant adrenocortical suppression after a single induction dose or brief infusions.

The present study aims at comparing the hemodynamic effects of thiopentone and etomidate during induction in hypertensive patients and also to assess any untoward side effects of either drug.

MATERIALS AND METHODS
Type of study: Interventional – Randomized double blind controlled trial.
Size of study: 60
Duration of the study: May 2013 to April 2014
Place of study: Government general hospital, Kurnool.

PATIENT SELECTION CRITERIA:
a) Patients diagnosed as hypertensives with or without medication.
b) Stage I & II hypertensive patients.
c) Only patients undergoing elective surgeries
d) MPG – I & II
e) ASA – II
f) Age - 18 - 75 yrs

Exclusion criteria:
a) Patients with other co-morbidities.
b) MPG - III & IV or any unexpected difficult intubation.

c) Severe hypertension patients (> 180/110 mm of hg).

d) Patients undergoing emergency surgeries.

e) Not a known hypertensive but with pre-op BP recordings > 140/90.

f) Patient refusal.

**OPERATIONS INCLUDED:**

Laminectomy and Orthopedic procedures (upper limb procedures).

**PROCEDURE:**

Following approval from institutional ethical committee and written informed consent from patients, this prospective double blinded randomised controlled trial was conducted in sixty adult hypertensive patients (33 males and 27 females) of ASA physical status II aged between 18-75 years who were to undergo elective laminectomy and orthopedic procedures. They were divided into two groups of thirty each.

**Group E** - Inj. Etomidate

**Group T** - Inj. Thiopental sodium

Randomization was done using computer generated random numbers.

A thorough pre anesthetic evaluation was done with particular attention to the duration of hypertension, treatment details, as well as pulse rate, blood pressures (systolic, diastolic and mean) recordings. Apart from general physical and systemic examination, routine investigations, blood urea, serum creatinine, serum electrolytes, ECG and x-ray chest were performed in all patients. All patients received Tab. Alprazolam 0.5 mg and Tab. ranitidine 150 mg on the night before surgery and all anti hypertensive medications except ACE inhibitors were continued up to and on the day of surgery. None of them were on ARBs. Those on ACE inhibitors were converted to CCBs 48 hrs prior to surgery. Upon arrival in the operating room, IV access was established and lactated Ringer’s infusion started. Monitors included an automated blood pressure cuff, electrocardiogram with lead II and V5 monitoring, peripheral pulse oximeter, and capnometer were connected.

Pre operative heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were recorded. After 2 minutes, patients in both the groups received inj. glycopyrrolate 0.2mg, inj. midazolam 0.02mg/kg, inj. ondansetron (0.08mg/kg) and inj. fentanyl 2mcg/kg iv. Pre oxygenation was done with 100% oxygen for 3 minutes. The above parameters were recorded again and noted as at level 0 and considered for comparison with subsequent recordings. Since it was a double blind study the observer entered the operating room after administration of the induction agent. General anaesthesia was induced in Group E with Inj. etomidate 0.3mg/kg and in Group T with Inj. Thiopental 5mg/kg. Inducing agent has been given over a period of 60 seconds in all the patients. Inj. Vecuronium bromide (0.1mg / kg. body wt.), was injected after loss of eye lash reflex in both groups. Nitrous oxide and oxygen was used for mask ventilation in both study groups. Respiration was controlled with rate between 12 to 14 cycles per minute and tidal volume adjusted to maintain EtCO2 between 30 to 35.

Subsequently, heart rate, SBP, DBP, MAP and ECG changes were recorded at one, two and three minutes after induction (level 1-3). During this period patient was left undisturbed except for the mask ventilation in order to avoid alterations due to stimulation. ECG was monitored through out to note down any rhythm or ischaemic changes. Any untoward complications such as pain on injection, myoclonus, hiccups during induction were noted down. Trachea was intubated at the end of 3 minutes. Patients were followed up for 24 hours for any untoward complications such as nausea, vomiting and haemodynamic changes.

**OBSERVATION & RESULTS:**

1. Heart rate:

<table>
<thead>
<tr>
<th></th>
<th>E</th>
<th>T</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 0</td>
<td>85.5 +/- 13.81</td>
<td>81.20 +/- 13.94</td>
<td>0.115</td>
</tr>
<tr>
<td>Level 1</td>
<td>83.73 +/- 12.00</td>
<td>82.60 +/- 12.75</td>
<td>0.362</td>
</tr>
<tr>
<td>Level 2</td>
<td>82.00 +/- 11.08</td>
<td>83.80 +/- 11.78</td>
<td>0.272</td>
</tr>
<tr>
<td>Level 3</td>
<td>81.10 +/- 10.20</td>
<td>81.60 +/- 10.86</td>
<td>0.427</td>
</tr>
</tbody>
</table>

P values for comparison of HR between the two groups at levels 0, 1, 2 and 3 are 0.115, 0.362, 0.272 and 0.427. There is no statistically significant difference between heart rates at all levels between the two groups as P values are more than 0.05 at all levels.

Graph - 1

2. SBP:

<table>
<thead>
<tr>
<th></th>
<th>E</th>
<th>T</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 0</td>
<td>131.46 +/- 13.436</td>
<td>135.70 +/- 10.745</td>
<td>0.091</td>
</tr>
<tr>
<td>Level 1</td>
<td>123.06 +/- 12.716</td>
<td>126.26 +/- 26.734</td>
<td>0.278</td>
</tr>
<tr>
<td>Level 2</td>
<td>118.63 +/- 13.228</td>
<td>122.56 +/- 13.15</td>
<td>0.126</td>
</tr>
<tr>
<td>Level 3</td>
<td>118.90 +/- 13.502</td>
<td>120.9 +/- 12.554</td>
<td>0.277</td>
</tr>
</tbody>
</table>

P values for comparison of SBP between the two groups at levels 0, 1, 2 and 3 are 0.091, 0.278, 0.126 and 0.277. There is no statistically significant difference between SBP at all levels between the two groups as P values are more than 0.05 at all levels.

Graph - 2.
3. DBP:

<table>
<thead>
<tr>
<th>DBP</th>
<th>E</th>
<th>T</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 0</td>
<td>88.1 +/- 8.99</td>
<td>85.26 +/- 8.97</td>
<td>0.113</td>
</tr>
<tr>
<td>Level 1</td>
<td>83.8 +/- 10.85</td>
<td>81.13 +/- 5.89</td>
<td>0.121</td>
</tr>
<tr>
<td>Level 2</td>
<td>81.2 +/- 9.66</td>
<td>78.83 +/- 8.19</td>
<td>0.155</td>
</tr>
<tr>
<td>Level 3</td>
<td>80.5 +/- 9.34</td>
<td>77.06 +/- 8.29</td>
<td>0.069</td>
</tr>
</tbody>
</table>

P values for comparison of DBP between the two groups at levels 0, 1, 2 and 3 are 0.113, 0.121, 0.155 and 0.069. There is no statistically significant difference between DBP at all levels between the two groups as P values are more than 0.05 at all levels.

Graph 3:

4. MAP:

<table>
<thead>
<tr>
<th>MAP</th>
<th>E</th>
<th>T</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 0</td>
<td>102.5 +/- 10.26</td>
<td>101.93 +/- 8.6</td>
<td>0.408</td>
</tr>
<tr>
<td>Level 1</td>
<td>96.23 +/- 10.48</td>
<td>97.3 +/- 8.34</td>
<td>0.332</td>
</tr>
<tr>
<td>Level 2</td>
<td>93.5 +/- 9.902</td>
<td>92.96 +/- 10.6</td>
<td>0.42</td>
</tr>
<tr>
<td>Level 3</td>
<td>93.83 +/- 10.815</td>
<td>90.86 +/- 10.12</td>
<td>0.138</td>
</tr>
</tbody>
</table>

P values for comparison of MAP between the two groups at levels 0, 1, 2 and 3 are 0.408, 0.332, 0.42 and 0.138. There is no statistically significant difference between MAP at all levels between the two groups as P values are more than 0.05 at all levels.

Graph - 4

DISCUSSION:

In the present study, Among a total of 60 patients, 23 patients (38.66%) have been posted for upper limb surgeries and 37 patients, (61.33 %) have been posted for laminectomy. In our setting the most common indication for elective surgery under general anesthesia in adult population is laminectomy followed by upper limb surgeries and laparoscopic surgeries.

There is no statistically significant difference between both the groups regarding preoperative systolic and diastolic blood pressures. P value for pre-op SBP is 0.3703 and that for pre-op DBP is 0.569.

Equipotent doses of induction agents should be used in order to compare drugs with respect to hemodynamic effects. Induction doses of intravenous anaesthetics based on hypnotic potency alone usually differ from those found necessary by clinical experience. Hence taking into account the relevant literature and clinical experience we have used etomidate 0.3 mg/kg and thiopentone 5mg/kg to do a comparative study of the hemodynamic effects of both drugs and any side effects during the 3 minutes following induction.

In our study there was an increase in heart rate following induction of anaesthesia with thiopentone (81.2 +/- 13.81 to 83.8 +/- 11.789) but decrease in the heart rate following induction with etomidate (85.5 +/- 13.81 to 81.1 +/- 10.2).

The increase in heart rate noted by us following thiopentone was similar to that of, Prys Roberts, Joerg T. Arnow et.al and Gauss et.al., but differed from the study of Raven singh. This increase in heart rate following thiopentone induction is probably reflex tachycardia in response to peripheral vasodilation.

The decrease in the heart rate in our study following induction with etomidate was similar to that of price et.al and Raven singh et.al, but differed from the observations of Criado et.al, Gooding et.al and Colvin et.al.

In our study, the comparison of the extent of change in heart rate from level zero to post induction levels (1-5) between the two groups was insignificant at all levels. (p>0.05)(Table-7, graph-7,8). This observation was similar to that of Jeffery et.al, Robert J Fragen et.al and Joerg T. Arnow et.al. However Joerg T. Arnow et.al’s study showed a small increase in heart rate with thiopentone which is similar to that of our observation.

In the present study, there is no statistically significant difference between T and E regarding duration of hypertension. (P value = 0.883). The shortest duration being 3 months and the longest being 12 years. Hence both the groups are matched with regard to duration of hypertension.

C Prys Roberts et.al’s study showed severe reduction of arterial pressure following induction with thiopentone in both hypertensives and normotensives.

A.F.Van Eeden compared etomidate with methohexitone which showed that etomidate group had no cardiovascular instability.

In our study there was decrease in mean arterial blood pressure in both the groups. The decrease was from 101.933 +/- 9.6 to 90.86 +/- 10.12 in group T and from 102.5 +/- 10.26 to 93.5 +/- 9.9 in group E. Maximum post induction fall in mean arterial blood pressure from level zero occurred at 3 minutes in group T and at 2 minutes in group E.

The observation of fall in MAP in thiopentone group and in our study was similar to that of Raven singh et.al. The fall in MAP in etomidate group was similar to that of Cradio et.al, Colvin et.al and Raven singh et.al but differed from that of A F Van Eeden et.al, Gooding et.al and Peter J Zed et.al.

In our study, it has been observed that there is no clinically significant difference between in hemodynamic parameters (HR, SBP, DBP and MAP) following induction with etomidate and thiopentone.

Our results are similar to that of Jeffrey et.al, Robert J Fragen et.al, Joerg T Arnow et.al and Peter J Zed et.al.
et.al and Joerg T Arnow et.al which showed no difference regarding hemodynamic parameters between etomidate and thiopentone. But our study differed from Gauss et.al and Jellish et.al which concluded that etomidate had better hemodynamic stability.

There are widely varying observations among different studies regarding better hemodynamic stability of etomidate over conventional inducing agents like barbiturates. Hence a meta-analysis of all the available studies need to be carried out to actually know if this difference is statistically and clinically significant.

CONCLUSION:
From our study, it has been conclude that there is no significant difference regarding hemodynamic parameters following induction with thiopentone and etomidate in adult hypertensive patients posted for elective surgery.

REFERENCES