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Comparison of the Hemodynamic Effects of Intravenous Induction with Thiopentone Sodium, Protocol and Etomidate in Patients Undergoing General Anesthesia

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Abstract:
AIM:*To compare thehaemodynamic effectsof thiopentone,propofol and etomidate and to study the side effects****.MATERIALS AND METHODS****:After taking institutional ethical committee approval and informed consent ,90 patients aged between 20-50 yrs of ASA Grade 1&11 undergoing elective surgeries under general anaesthesia were randomly divided into3groups Group T, Group P and Group E.Group T- patients were induced with thiopental 5mg/kg, Group P – patients received propofol 2mg/kg and Group E received etomidate 0.3mg/kg. Haemodynamic variables like H.R,B.P(systolic and diastolic) and Spo2 recorded before induction and at 1,3.5,10.15 and 30 mts post induction and S.E if any are noted.****RESULTS :****There was significant fall in HR in propofol group compared to thiopentone and etomidate groups. The re was also significant decrease in systolic blood pressure , diastolic blood pressure and mean blood pressure in patients of propofol and thiopentone groups than those of etomidate groups****.***
Conclusion*: Present study concludes that etomidate is an effective induction agent with good cardiovascular stability when compared with thiopentone and propofol.*

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I. Introduction

- Hemodynamic variations are inevitable during induction of anaesthesia ,laryngoscopy , intubation , surgical stimulus and extubation during general anaesthesia.
- Intravenous induction of anesthesia has many advantages over inhalational agents. It provides a smooth and pleasant induction, and avoids the fear of suffocation of face mask. Intravenous induction agents have rapid onset of action, predictable loss of consciousness with no "second stage" of anesthesia, smooth recovery and minimal postoperative sickness (Dundee JW 1985).
- An ideal intravenous induction agent should be water soluble, with lack of pain on injection, venoirritation, local tissue damage following extravasation; should have rapid and smooth onset in one arm brain circulation ; should have rapid clearance and metabolism with no active metabolites, low potential for histamine release or hypersensitivity reactions ,have high therapeutic ratio, and lack of acute cardiovascular and respiratory depression ; rapid and smooth return of consciousness and cognitive skills with residual analgesia with absence of postoperative nauses, vomiting,amnesia, psychomimeticreactions,dizziness, head ache or prolonged sedation.[1]
- All the currently available intravenous induction agents have been far from being ideal .Hence the search for newer induction agents continues.
- Commonest drugs currently in use for induction are thiopentone, propofol, ketamine, Benzodiazepines and opioids.
- This study is designed to compare the hemodynamic effects with 3 inducing drugs – commonly used Thiopentone sodium, propofol and newer drug Etomidate

II. Aim of the Study

Objectives Of The Study To Compare Thiopentone, Propofol And Etomidate As Anaesthetic Induction Agents In General Anaesthesia With Respect To Hemodynamic Changes

1. To Evaluate And Compare Hemodynamic Effects Of Thiopentone, Propofol And Etomidate Used For Induction Of General Anaesthesia.
2. Untoward Side Effects

III. Materials and Methods

- **Type of study :** prospective ,randomised , double blinded study
- **Source of data :**
- This study was conducted in 90 patients aged between 20-50 yrs who have undergone elective surgeries under general anaesthesia in Government General Hospital, Siddhartha medical college , vijayawada.
- **Study period** : Jan 2016 – June 2017

Method of collection of data :

● After institutional ethical committee approval , 90 patients aged between 20-50 yrs undergoing elective surgeries under general anaesthesia were selected. A detailed history , complete physical examination and investigations done for all patients. Informed written consent taken. The study population were randomly divided in to 3 groups with 30 patients in each group.

- Group **T** – patients were induced with thiopental 5 mg/kg
- Group **P** – patients were induced with propofol 2 mg/kg
- Group **E** – patients were iinduced with etomidate 0.3 mg/kg

Inclusion criteria :

- Age group between 20-50 yrs
- ASA grade I and II patients
- Elective surgeries
- Mallampati grade I and II

Exclusion criteria :

- Patient refusal
- ASA grade III / IV
- Mallampati grade III / IV
- Children < 20 yrs
- Pregnant women
- Emergency procedures
- Patient with history of hypersensitivity to thiopentone , propofol and etomidate
- Presence of known primary or secondary adrenal insufficiency or on steroid medication.
- Known case of porphyria

IV. Method

This study was conducted in 90 patients. They were randomly alloted into 3 groups , comprising of 30 patients in each group. All the patients started with an intravenous line .All the patients pre-medicated with Inj.ranitidine 50 mg , inj.ondansetron 4 mg , Inj.Midazolam 0.01 mg/kg before shifting the patient to the operation theatre , Inj.Glycopyrrolate 0.2mg IV before the induction of anesthesia, Inj .fentanyl 1microgms/kg i.v was given.

After pre-oxygenation, the induction agent,either Thiopentone or propofol or etomidate was injected over a period of 20-30 seconds . Thiopentone was used in a dose of 5mg/kg, propofol in a dose of 2 mg/kg, Etomidate in a dose of 0.3 mg/kg. Hemodynamic variables like heart rate (HR) , blood pressure (systolic, diastolic and mean) and Spo_2 recorded before induction and at 1 ,3, 5 , 10 15 and 30mts post induction . After the patient was induced, Inj.vecuronium 0.08 - 1 mg/kg is given IV and the patient intubated with appropriate sized endotracheal tube made of PVC. Anesthesia maintained with 66% nitrous oxide and 33% oxygen ;sevoflurane 1 vol % and Inj.Vecuronium bromide 0.02 mg/kg increments thereafter. At the end of the surgery, the neuromuscular blockade was reversed with Inj.Neostigmine 0.07mg/kg and Inj.Glycopyrrolate 0.01mg/kg body weight**.**

STATISTICAL ANALYSIS-

Date are presented as mean and standard deviation. Statistical analysis of demographic data was done by using chi-square test. The paired Student t-test was used for quantitative data and $p < 0.05$ is considered significant.

RESULTS : COMPARISION OF DEMOGRAPHIC DATA IN THREE GROUPS – AGE Table 1

	Group						F-value	P-value
	Etomidate		Propofol		Thiopentone			
	Mean	SD	Mean	SD	Mean	SD		
Age	32.77	8.57	32.47	7.40	32.03	8.03	.063	.94

GENDERTable 2

Sex	Group					
	Etomidate		Propofol		Thiopentone	
	Count	%	Count	%	Count	%
Female	18	60.0%	16	53.3%	15	50.0%
Male	12	40.0%	14	46.7%	15	50.0%
Total	30	100.0%	30	100.0%	30	100.0%
Chi-square value = 0.63; P = 0.73						

The demographic data for gender is comparable in all the three groups as shown in table 2

CHANGES IN MEAN SYSTOLIC BLOOD PRESSURE IN THREE GROUPS : Table 3a

SBP	Group					
	Etomidate		Propofol		Thiopentone	
	Mean	SD	Mean	SD	Mean	SD
at 0	126.03	16.17	131.93	11.13	131.27	15.00
at 1	126.13	16.69	127.73	13.21	128.07	17.39
at 3	126.23	16.30	123.53	14.77	121.40	15.43
at 5	126.27	15.66	113.40	16.32	113.67	15.94
at 10	126.17	15.79	107.77	11.92	115.20	16.59
at 15	125.90	16.16	108.37	11.17	112.93	15.36
at 30	126.07	16.4	111.10	13.32	112.90	14.70

Table 3b

Paired comparison	P-value		
	E	P	T
SBP at 0 - SBP at 1	.816	.012	.097
SBP at 0 - SBP at 3	.695	.002	.002
SBP at 0 - SBP at 5	.69	<0.001	<0.001
SBP at 0 - SBP at 10	.8	<0.001	<0.001
SBP at 0 - SBP at 15	.77	<0.001	<0.001
SBP at 0 - SBP at 30	.95	<0.001	<0.001

CHANGES IN MEAN DIASTOLIC BLOOD PRESSURE IN THREE GROUPS :

Table 4a

DBP	Group					
	Etomidate		Propofol		Thiopentone	
	Mean	SD	Mean	SD	Mean	SD
at 0	80.10	10.88	84.30	9.20	81.60	11.10
at 1	80.27	10.81	81.03	13.47	82.13	13.67
at 3	80.23	11.03	77.47	12.88	79.37	13.59
at 5	80.27	11.50	70.97	13.44	74.00	11.79
at 10	80.27	11.12	67.17	10.85	75.40	15.46
at 15	80.60	10.28	70.53	11.36	74.23	11.74
at 30	80.07	11.23	71.70	9.23	72.67	12.00

Table 4b

Paired comparison	P-value		
	E	P	T
DBP at 0 - DBP at 1	.69	.080	.804
DBP at 0 - DBP at 3	.707	.004	.245
DBP at 0 - DBP at 5	.69	<0.001	.000
DBP at 0 - DBP at 10	.61	<0.001	.031
DBP at 0 - DBP at 15	.307	<0.001	<0.001
DBP at 0 - DBP at 30	.94	<0.001	<0.001

CHANGES IN MEAN HEART RATE: Table-5a

HR	Group					
	Etomidate		Propofol		Thiopentone	
	Mean	SD	Mean	SD	Mean	SD
at 0	81.57	10.50	89.60	15.91	87.97	11.08
at 1	81.57	11.70	87.63	16.54	85.73	13.51
at 3	81.57	11.70	86.97	17.48	86.77	15.03
at 5	80.43	12.04	85.20	14.39	88.00	14.59
at 10	80.23	12.39	84	15.07	88.07	13.36
at 15	80.30	11.98	82.87	14.17	86.47	14.92
at 30	81.23	11.64	82.43	14.06	87.47	15.47

Table 5b

Paired comparison	P-value		
	E	P	T
HR at 0 - HR at 1	.516	.03	0.204
HR at 0 - HR at 3	.127	.17	.576
HR at 0 - HR at 5	.127	0.013	.986
HR at 0 - HR at 10	.153	0.009	.966
HR at 0 - HR at 15	.143	0.006	.533
HR at 0 - HR at 30	.019	0.002	.825

CHANGES IN MEAN BLOOD PRESSURES IN THREE GROUPS: Table6a

MAP	Group					
	Etomidate		Propofol		Thiopentone	
	Mean	SD	Mean	SD	Mean	SD
at 0	95.43	12.09	100.23	8.86	97.90	11.91
at 1	95.43	11.84	96.50	12.48	97.57	15.13
at 3	95.43	11.98	92.73	12.92	93	12.84
at 5	95.53	11.99	85.07	13.50	87.20	12.58
at 10	95.43	11.83	80.53	10.24	88.60	15.43
at 15	95.53	11.54	83.07	10.16	87.37	13.37
at 30	95.23	11.94	84.60	9.87	86.00	12.51

Paired comparison	P-value		
	E	P	T
MAP at 0 - MAP at 1	1	0.25	0.864
MAP at 0 - MAP at 3	.83	0.02	0.02
MAP at 0 - MAP at 5	.609	<0.001	<0.001
MAP at 0 - MAP at 10	1	<0.001	0.002
MAP at 0 - MAP at 15	.67	<0.001	<0.001

MAP at 0 - MAP at 30	.311	<0.001	<0.001

Table 6b

INCIDENCE OF NAUSEA IN THREE GROUPS:

Nausea	Group					
	Etomidate		Propofol		Thiopentone	
	Count	%	Count	%	Count	%
No	18	60.0%	27	90.0%	19	63.3%
Yes	12	40.0%	3	10.0%	11	36.7%

INCIDENCE OF MYOCLONUS IN THREE GROUPS Table 8

Myoclonus	Group					
	Etomidate		Propofol		Thiopentone	
	Count	%	Count	%	Count	%
No	21	70%	30	100.0%	30	100.0%
Yes	9	30%	0	0.0%	0	0.0%

INCIDENCE OF PAIN ON INECTION IN THREE GROUPS Table 9

Pain on injection	Group					
	Etomidate		Propofol		Thiopentone	
	Count	%	Count	%	Count	%
No	26	86.7%	18	60.0%	30	100%
Yes	4	13.3%	12	40.0%	. 0	0

V. Discussion

Hemodynamic variations are inevitable during induction of anaesthesia ,laryngoscopy , intubation , surgical stimulus and extubation during general anaesthesia.

Intravenous induction of anesthesia has become widely popularasIt provides a smooth and pleasant induction, and avoids the fear of suffocation of face mask.

An ideal intravenous induction agent should be water soluble, with lack of pain on injection, venoirritation, local tissue damage following extravasation; should have rapid and smooth onset in one arm brain circulation ; should have rapid clearance and metabolism with no active metabolites, low potential for histamine release or hypersensitivity reactions ,have high therapeutic ratio, and lack of acute cardiovascular and respiratory depression ; rapid and smooth return of consciousness and cognitive skills with residual analgesia with absence of postoperativenausea, vomiting, amnesia psychomimetic reactions ,dizziness, head ache or prolonged sedation.All the currently available intravenous induction agents have been far from being ideal.

Thiopentone sodium was discovered by Volwiler and introduced in to clinical practice by Sir Ralph Water in 1934. Thiopentone sodium is considered as "gold standard" inducing agent because of its rapidity of action , smooth induction and considerable safety. It's major disadvantages are delayedrecovery , decrease in systemic blood pressure and absence of suppression of upper airway reflexes. Howeveritdoes not possess all the properties of an ideal inducing agent. This lead to development of other inducing agents such as propofol and Etomidate.

Propofol was introduced into clinical practice in the year 1977.propofol provides faster onset of action, anti Emesis, rapid recovery, potent attenuation of upper airway reflexes and adequate depth of anaesthesia during intubation. Major disadvantage is decrease in s systemic blood pressure and pain during injection.

Another inducing agent Etomidate was introduced into clinical practice in 1972. It provides more cardiac stability with faster onset of action and rapid recovery with side effects like pain on Injection and myoclonus.

We conducted a study to evaluate the hemodynamics stability of Etomidate in comparison with Thiopentone and propofol following induction in general anaesthesia.

DEMOGRAPHIC VARIABLES-

In our study the demographic data were comparable for age and sex in all the three groups

VI. Hemodynamic Parameters

HEART RATE-

The mean heart rate was decreased significantly in **group P** at 1,3,15,10,15, and 30 minutes following induction. The maximum decrease in mean heart rate was 7 at 30 minutes following induction.

In **group T**,there was increase in mean heart rate at 5,10 minutes after induction but was not statistically significant.

In **group E,** there was no significant change in mean heart rate at 1,3,5,10 and 15 minutes following induction compared to induction value.

In the present study the heart rate was more stable in group E and group T as compared to propofol.Similar results were obtained in the studies conducted by McCollum.J.Sand J.W.Dundee[2] in 1986,by Ebert .T.J, Muzi.M, Berens.R, Goff.D in 1992.[3] and by Mousumi das etal[4].

Baroreceptor reflex control of heart rate may be depressed by propofol[5]. Bradycardia and asystole have been observed after induction of anesthesia with propofol, resulting in the occasional recommendation that anticholinergic drugs be administered when vagal stimulation is likely to occur in association with administration of propofol .Propofol may decrease sympathetic nervous system activity to a greater extent than parasympathetic nervous

system activity, resulting in a predominance of parasympathetic activity[6] how ever it does not alter sinoatrial or atrioventricular node function.[7]

In normovolemic subjects, thiopental, 5 mg/kg IV, produces a transient 10- to 20-mm Hg decrease in blood pressure that is offset by a compensatory 15 to 20 beats per minute increase in heart rate.[8]

Etomidate maintains hemodynamics stability through preservation of both sympatheticout flow and autonomic reflexes.

SYSTOLIC BLOOD PRESSURE-

The mean systolic blood pressure was significantly lower in **group P** at 1,3,5,10,15 and 30 minutes after induction when compared to mean systolic blood pressure at induction. The maximum decrease in mean systolic blood pressure in group P was 24 mm of Hg(19%) at 10 minutes following induction.

The mean systolic blood pressure was significantly lower in **group T**at 3,5,10,15 and 30 minutes after induction when compared to mean systolic blood pressure at induction

The maximum decrease in mean systolic blood pressure in group T was 19 mm hg and in group P was 24 mm of Hg (17% fall in thiopentone and 19% fall in propofol group)

In the present study , mean systolic blood pressure was stable at all points after induction in **group E**.Similar results were observed in the study by Ram Pravda kaushalandin[9] study by Geethakarkietal[10] , Mackenzie and Grant in 1985[11],

Propofol produces decreases in systemic blood pressure, which are greater than those evoked by comparable doses of thiopental .These decreases in blood pressure are often accompanied by corresponding changes in cardiac output and systemic vascular resistance. The relaxation of vascular smooth muscle produced by propofol is primarily due to inhibition of sympathetic vasoconstrictor nerve activity.[12]

Etomidate , maintains hemodynamic stability through preservation of both sympathetic out flow and autonomic reflexes whereas propofol induces hypotension by an inhibition of sympathetic nervous system and impairment of baroreflex regulatory mechanisms. Both Cardiac and Sympathetic barosreflexes were maintained with Etomidate but were significantly reduced with propofol , especially in response to hypotension.

DIASTOLIC BLOOD PRESSURE-

The mean diastolic blood pressure was significantly lower in **group P** at 1,3,5,10,15,30 minutes after induction when compared to mean diastolic blood pressure at induction.

In **group T** there was significant fall in mean diastolic blood pressure at 5,10,15,30 minutes after induction compared to mean diastolic blood pressure at induction.

The maximum fall in mean diastolic blood pressure in group P was 17 mm of Hg and in group T was 9 mm of Hg.

In **group E** there was no significant increase or decrease in mean diastolic blood pressure at 1-30 minutes following induction compared to induction value.The results in the present study correlates with following studies-In the study by Ram Pravda kaushaletal[13] similar results were observed in study by Geethakarkietal,

MEAN ARTERIAL PRESSURE-

The mean blood pressure was significantly lower in **group P** at 1,3,5,10,15,30 minutes after induction when compared to mean blood pressure at induction.

The mean blood pressure was significantly lower in **group T** at 3,5,10,15,30 minutes after induction when compared to mean blood pressure at induction.

The maximum fall in mean blood pressure in **group T** was 11 mm of Hg and in group P was 17 mm of Hg.

The mean blood pressure was stable at all the points of comparison after induction in group E compared to mean blood pressure at induction time, maximum fall in group E was 0.3 mm of Hg which is not significant.

The results in the present study were comparable to studies conducted byWuJ etal[15], MC Collumetal[16] and by Geethakarkietal[17].

The decrease in systemic blood pressure by propofol is attributed to relaxation of vascular smooth muscles due to inhibition of sympathetic vasoconstrictor nerve activity and negative ionotropic effect of propofol resulting from decrease in intracellular calcium availability secondary to inhibition of trans sarcolemmal calcium influx.

Etomidate may differ from most other IV anesthetics in that depressive effects on myocardial contractility are minimal at concentrations needed for the production of anesthesia.Thus the present study showed that induction of anesthesia with etomidate there was insignificant fall in blood pressure

NAUSEA –

In the present study ,theincidence of nausea is observed in 12 patients out of 30 in group E , 11 out of 30 had nausea in group T and 3 out of 30 in group P.

The incidence in less in group P compared to group T and E

SV Korgaonkar[18], Jefery L Giese[19] et al found the incidence of nausea and vomiting was similar with both Etomidate and Thiopentone .

Propofol has a profile of CNS depression that differs from other anesthetic drugs. In contrast to thiopental, for example, propofol uniformly depresses CNS structures, including subcortical centers., and it is possible that propofol modulates subcortical pathways to inhibit nausea and vomiting or produces a direct depressant effct on the vomiting center

MYOCLONUS -

Most IV anesthetics can cause excitatory effects that manifest as spontaneous movements, such as myoclonus, dystonia, and tremor.Myoclonus occurred in 9 patients out of 30 in group E and there was no myoclonus in Thiopentone group T and group P. This is attributed to dis inhibition of subcortical structures that normally suppress extrapyramidal motor activity by EtomidateThis is similar to reports by Batra et al[20].,where the incidence of myoclonus was 28%of patients of Etomidate group and none in Thiopentone group.

PAIN ON INJECTION -

Pain during injection of anesthetic agent is a bad experience for patient while it is quite embarrassing situation for an anesthesiologist.Pain on injection was observed in 12 out of 30 Patients in group in P which is significantly high compared to 4 out of 30 in group E and none in group T.This is similar to study b SupriyaAggarwal et al.[20], where 50% of patients who received propofol had pain on injection compared to 4% in Etomidate group.Similarly in study by Wu J et al[21], pain on injection was significantly high in propofol group compared to etomidate group.

With Etomidate induction there was no significant change in Heart rate, SBP, DBP,and MAP .Etomidate offers the superior hemodynamic stability during induction. Etomidate is found to be a better induction agent for general anaesthesia with respect to hemodynamic stability compared to thiopentone and propofol .

VII. Conclusion

Present study concludes that Etomidate is an effective induction agent with good cardiovascular stability when compared to Thiopentone and Propofol. Hence in spite of its higher cost Etomidate can be a better alternative in hemodynamically unstable patients.However, association between Etomidate and adrenal insufficiency was not looked into in the present study.

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