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ORIGINAL ARTICLE

A COMPARATIVE EVALUATION OF HEMODYNAMIC CHARACTERISTICS OF THE THREE INDUCTION AGENTS – ETOMIDATE, THIOPENTONE AND PROPOFOL

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ABSTRACT: BACKGROUND: Induction is an important step, while conducting general anaesthesia. Patients were susceptible to hemodynamic lability at the time of induction. Thus, an agent with least effect on hemodynamics would be the agent of choice. **AIMS AND OBJECTIVE:** To evaluate the hemodynamic effects of etomidate in comparison to those of thiopentone and propofol during induction of general anaesthesia. **SETTINGS AND DESIGN:** The study was conducted in the department of anaesthesia of SRMS IMS, over a period of one year from June 2013-2014, on patients undergoing elective surgery under general anaesthesia. **MATERIAL AND METHODS:** 105 adult patients aged 18 – 50 years, belonging to ASA grade 1 and 2, undergoing elective surgery under general anaesthesia, were divided randomly into three groups of 35 patients each. Group A patients were induced with injection thiopentone sodium 5 mg/kg, Group B with injection propofol 2mg/kg and Group C with injection etomidate 0.3 mg/kg intravenously. **STASTICAL ANALYSIS:** Data are presented as mean and standard deviation. The statistical analysis was performed using SPSS version 20. A "p" value of less than 0.05 was taken as significant. **RESULTS:** There was no significant change in mean heart rate at one, two and three minute after induction as compared with the mean heart rate at the time of induction in all the groups($p>0.05$). In Groups A and B there was a significant fall in systolic blood pressure, diastolic blood pressure and mean arterial pressure at one, two and three minute after induction, as compared to the induction value ($p<0.05$). In Group C however, there was no significant change in systolic, diastolic and mean arterial pressure ($p>0.05$). **CONCLUSION:** Etomidate offers superior hemodynamic stability during induction compared to thiopentone and propofol. Thus etomidate is a better induction agent for general anaesthesia.

KEYWORDS: Induction, general anaesthesia, thiopentone, propofol, etomidate.
MESHTERMS: Aged, Anaesthesia, Etomidate, Injection, Propofol.

INTRODUCTION: Induction is an important step in the conduction of general anaesthesia, because of hemodynamic susceptibility of the patient at the time of induction. It is a standard practice in the present time to induce general anaesthesia by using intravenous anaesthetic agents. Traditionally anaesthesia meant making patient unconscious by inhaling gases. The apparatus used to deliver these gases were complicated and these inhaled gases did not produce balanced anaesthesia.[1,2]

Discovery of barbituric acid derivatives leads to the advent of modern intravenous anaesthesia. An ideal intravenous anaesthetic drug should provide hypnosis, amnesia, analgesia and muscle relaxation without any side effects.[3]

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Thiopentone sodium was synthesized in 1932 and introduced in clinical practice in 1934 by Lundy. It was considered gold standard inducing agent because of its rapid onset of action and short duration of action without excitatory effects as seen during induction with inhalation gases.[4,5]

Later, studies showed that it causes peripheral vasodilatation, decrease in blood pressure, increase in heart rate and direct negative inotropic effect on heart.[6]

In 1970, 2, 6 di-isopropofol was discovered and introduced in clinical practice in 1977. It was considered superior to thiopentone because of faster onset, rapid recovery, potent attenuation of aiway reflexes, adequate depth of anaesthesia and antiemesis.[7-9] But the major disadvantage is the rapid fall in blood pressure.[8]

Etomidate was synthesized in 1964 and introduced in clinical practice in 1972 in Europe and in 1983 in United States.[10] It provided faster onset and rapid recovery with hemodynamic stability and minimal respiratory depression. Use of etomidate was associated with minor side effects like pain on injection, myoclonus and post-operative nausea and vomiting. But its use declined due to reports of adrenocortical suppression.[9]

Etomidate suppresses corticosteroid synthesis by reversibly inhibiting 11-beta-hydroxylase, an enzyme important in adrenal steroid production leading to primary adrenal suppression[11.] However, due to lack of studies showing demonstrable negative effect of temporary adrenocortical suppression associated with induction doses of etomidate, as well as the finding that the mean cortisol levels usually remain in the low normal range after etomidate induction, suggests that the adrenocortical suppression following etomidate induction may not be clinically significant.

Rediscovery of the beneficial effects of etomidate and lack of new reports of adrenocortical suppression lead to a renewed interest in etomidate.[12] The drug was reformulated using lipid emulsion and reintroduced in 2007 in India.

Due to lack of many studies comparing hemodynamic effects of the three intravenous inducing agents, especially in an Indian setting, we made an attempt to evaluate the hemodynamic effects of etomidate in comparison to those of thiopentone and propofol during induction of general anaesthesia.

MATERIAL AND METHODS: After approval from the institute's ethical committee, the study was carried out in 105 adult patients belonging to ASA grade 1 and 2, aged between 18–50 years, undergoing elective surgery under general anaesthesia. The patients were divided randomly into three groups of 35 patients each. A thorough pre-anaesthetic evaluation with detailed history, clinical examination and investigations was performed.

On the day of surgery, preoperative baseline values of heart rate and blood pressure were recorded. Patients were pre medicated with injection midazolam 0.05 mg/ kg intravenously and injection fentanyl 2µg/ kg intravenously. One minute after premedication, heart rate and blood pressure were recorded. Patients were pre oxygenated with 100% oxygen for 3 minutes. Group A patients were induced with injection thiopentone sodium 5 mg/kg intravenously, Group B patients were induced with injection propofol 2mg/kg intravenously and Group C patients were induced with injection etomidate 0.3 mg/kg intravenously.

All patients had continuous pulse oximeter, ECG and blood pressure monitoring. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressures were recorded at induction and at one, two and three minute after induction.

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Data are presented as mean and standard deviation. The statistical analysis was performed using SPSS version 20. Analysis of demographic data was done by Chi-square test and for quantitative data paired t-test was used to assess within group change and ANOVA (Analysis of Variance) was used to compare intergroup differences. A "p" value of less than 0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS: The objective of the study was to compare the hemodynamic effects of etomidate with that of thiopentone and propofol during induction of general anaesthesia.

The hemodynamic parameters were compared just before induction, at the time of induction and at one, two and three minute after induction.

The patients in all three groups were comparable for age and sex as shown in Table 1. Table 2 shows the changes in mean heart rate in the three groups. There was no significant change in mean heart rate at one, two and three minute after induction as compared with the mean heart rate at the time of induction in all the groups.

Table 3 shows the changes in mean systolic blood pressure in the three groups. In Groups A and B there was a significant fall in mean systolic blood pressure at one, two and three minute after induction as compared with induction value, with a maximum fall occurring in two minutes. In Group C however, there was no significant change in mean systolic blood pressure at one, two and three minute after induction when compared with that at induction.

Table 4 shows the changes in mean diastolic blood pressure in the three groups. In Groups A and B there was a significant fall in diastolic blood pressure and mean arterial pressure at one, two and three minute after induction, whereas in Group C there was no significant fall in diastolic and mean arterial pressure at one, two and three minute after induction as compared to that at the time of induction ($p< 0.05$).

Table 5 shows the changes in mean arterial pressure in the three groups. In Groups A and B there was a significant fall in mean arterial pressure at one, two and three minute after induction, whereas in Group C there was no significant fall in mean arterial pressure at one, two and three minute after induction as compared to that at the time of induction ($p>0.05$).

DISCUSSION: Induction is an important step, while conducting general anaesthesia. Patients were susceptible to hemodynamic lability at the time of induction. Thus, an agent with least effect on hemodynamics would be the agent of choice. For induction of anaesthesia, anaesthetic agents may be administered by various routes including inhalation, intravenous, oral and rectal.

Most general anaesthetics today are induced either by intravenous injection or by inhalation of gases. Intravenous induction has a faster onset than inhalation induction and is the preferred mode of induction of general anaesthesia in most cases. Most commonly used intravenous agents are thiopentone, propofol, etomidate and ketamine.

Etomidate is a short acting intravenous anaesthetic agent used for the induction of general anaesthesia.[13] It has a very stable cardiovascular profile[14-17] and has been recently reintroduced in India as an induction agent. Due to absence of any study using etomidate in Indian setting, we conducted a study to evaluate the hemodynamic effects of etomidate in comparison to those of thiopentone and propofol during induction of general anaesthesia.

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In our study the demographic data were comparable in all the three groups. Patients in Group a showed an increase in heart rate at one, two and three minute after induction (Graph 1). The maximum increase in mean heart rate was 3.66 beats per minute, which is comparable to that observed in a study conducted by Edward M et al[6] in 1969. This increase in heart rate however was not statistically significant (P> 0.05). The increase in heart rate is due to decrease in sensitivity of baroreceptors by thiopentone. In Group B, there was a decrease in heart rate as compared to heart rate at induction, but the decrease was not statistically significant (P>0.05). Similar findings were seen in previous studies conducted by Grounds R. M et al[18] and Versichelen L et al.[19]

They attributed the decrease in heart rate to the resetting of the baroreflex mechanism. In Group C, there was no change in mean heart rate after induction from the pre induction value. Similar results were found in the studies conducted in the past.

McCollum J S et al[20] compared the induction characteristics of thiopentone, etomidate and methotrexate to those of propofol. They observed that propofol caused significantly more hypotension than thiopentone. Ebert T J et al [15] studied the sympathetic responses to induction of anaesthesia with propofol or etomidate.

They concluded that etomidate induction preserved muscle sympathetic nerve activity (MSNA), forearm vascular resistance and blood pressure, whereas propofol reduced MSNA by 76±5% leading to a reduction in forearm vascular resistance and a significant hypotension. Both cardiac and sympathetic baroslopes were maintained with etomidate but were significantly reduced with propofol. Etomidate maintains stability in heart rate through preservation of both sympathetic outflow and autonomic reflexes.

In our study, the mean systolic blood pressure at one, two and three minute after induction in Groups A and B was significantly lower than the mean systolic blood pressure at the time of induction (P<0.05). The maximum fall in mean systolic blood pressure was 7.46 mm Hg in Group A and 12.41 mm Hg in Group B. But in Group C, the fall was 0.74 mm Hg which is not statistically significant (P>0.05).

Similar results were observed by Mackenzie et al[9] in their study where mean systolic blood pressure was reduced by 15% after induction with thiopentone and 20% after induction with propofol. They concluded that the fall in blood pressure during induction with thiopentone and propofol is due to decrease in systemic vascular resistance and decrease in cardiac output and alteration in baroreceptor sensitivity.

In our study, the mean diastolic blood pressure in Groups A and B at one, two and three minute after induction was significantly lower when compared to mean diastolic blood pressure at induction (P<0.05). The maximum fall in mean diastolic blood pressure was 4.08 mm Hg in Group A and 11.63 mm Hg in Group B. But in Group C, the fall in mean diastolic blood pressure was 1.03 mm Hg which is not statistically significant (P>0.05).

In our study, the mean arterial pressure was significantly lower in Groups A and B at one, two and three minute after induction when compared to mean arterial pressure at induction. The maximum fall in mean arterial pressure was 7.69 mmHg in Group A and 11.06 mm Hg in Group B. However, in Group C the maximum fall in mean arterial pressure was 1.03 mm Hg which is not statistically significant. McCollum J S et al[20] also observed similar results.

The mean arterial pressure in their study decreased by 10% after induction with thiopentone, by 15% after induction with propofol and only 5% after induction with etomidate.

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Pandey AK[21] et al compared the effects of propofol and etomidate induction on hemodynamic parameters and serum cortisol levels in patients undergoing coronary artery bypass graft (CABG) and found that hemodynamically etomidate group was more stable than propofol group following induction of anaesthesia (P <0.05).

Our study showed that the hemodynamic parameters of patients were maintained after induction with etomidate when compared to induction with thiopentone and propofol. However, the patients in our study were of ASA grade 1 and 2 only and did not include hemodynamically compromised patients or those with low cardiac reserve. But from the drug profile of etomidate, it is expected to show similar hemodynamic stability in such patients also. Thus, it would be interesting to evaluate the effects of etomidate induction on hemodynamic parameters of patients with low cardiac reserve and hemodynamic instability.

CONCLUSION: It is a standard practice in the present time to induce general anaesthesia by using intravenous anaesthetic agents. Most commonly used intravenous anaesthetic agents are thiopentone and propofol. But, both these agents have a significant effect on the hemodynamic stability of the patients. As shown in our study, on induction with etomidate, there are no significant change in heart rate, systolic, diastolic and mean arterial pressures.

Etomidate offers superior hemodynamic stability during induction compared to thiopentone and propofol. Thus etomidate is a better induction agent for general anaesthesia. It can be the induction agent of choice in patients with co-morbid cardiovascular illness in whom maintaining hemodynamic stability during induction is very crucial for a favorable outcome.

	GROUP A Mean ± SD	GROUP B Mean ±SD	GROUP C Mean ±SD	P Value
AGE	37.49 ± 9.15	32.69 ± 10.25	37.66 ± 11.52	0.079
SEX (M:F)	15:20	13:22	20:15	0.222

Table 1: Demographic profile of patients

	GROUP A Mean±SD	P Value	GROUP B Mean±SD	P Value	GROUP C Mean±SD	P Value
Baseline	90.77±13.96		88.14±14.82		84.37±11.04	
Induction	86.11±4.57		82.51±12.09		79.17±10.14	
1 min	88.75± 13.5	0.590	80.49±11.77	0.121	79.20 ±8.98	0.943
2 min	88.97±11.86	0.511	80.34±12.12	0.094	79.34 ±9.61	0.629
3 min	90.34±10.30	0.279	82.54±12.76	0.986	79.22± 9.95	0.877

Table 2: Changes in mean heart rate

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	GROUP A Mean±SD	P Value	GROUP B Mean±SD	P Value	GROUP C Mean±SD	P Value
Baseline	139.60±16.30		130.74±9.10		129.09±11.48	
Induction	122.17±14.81		117.69±6.68		116.25±13.03	
1 min	114.83±15.86	0.008	107.63±11.12	0.000	115.94±13.44	0.427
2 min	114.71±13.05	0.003	105.28±11.63	0.000	116.68±14.02	0.412
3 min	115.03±14.33	0.006	107.83±13.65	0.000	115.51±14.18	0.321

Table 3: Changes in mean systolic blood pressure

	GROUP A Mean±SD	P Value	GROUP B Mean±SD	P Value	GROUP C Mean±SD	P Value
Baseline	84.86±11.10		84.77±9.35		82.34±9.57	
Induction	79.51±12.15		74.86±9.19		73.00±12.37	
1 min	75.74±12.45	<0.001	66.63±10.59	<0.001	72.23±13.19	0.240
2 min	75.48±11.30	<0.001	65.23 ±9.81	<0.001	72.20±12.96	0.478
3 min	75.43±11.87	<0.001	68.80±11.09	<0.001	71.97±13.23	0.355

Table 4: Changes in mean diastolic blood pressure

	GROUP A Mean±SD	P Value	GROUP B Mean±SD	P Value	GROUP C Mean±SD	P Value
Baseline	103.11±11.49		100.09±8.47		98.11±9.85	
Induction	94.20±12.93		90.03±9.27		87.45±12.16	
1 min	88.86±13.20	<0.001	80.77±10.99	<0.001	86.85±12.81	0.230
2 min	88.51±11.49	<0.001	78.97±10.55	<0.001	86.91±12.89	0.536
3 min	88.51±12.26	<0.001	82.34±11.88	<0.001	86.42±13.07	0.270

Table 5: Changes in mean arterial pressure

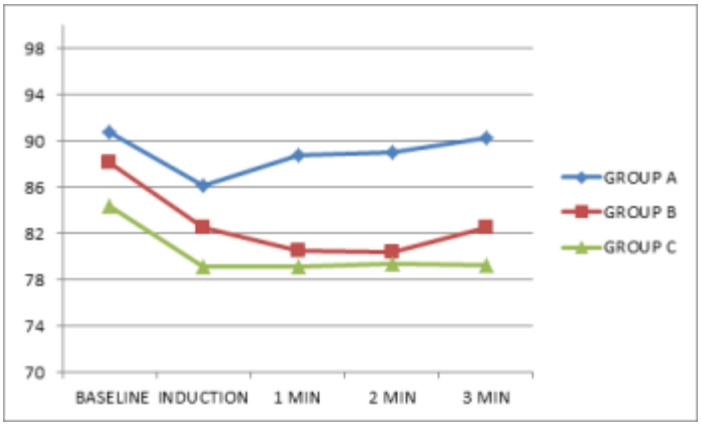

Fig. 1: Changes in mean heart rate

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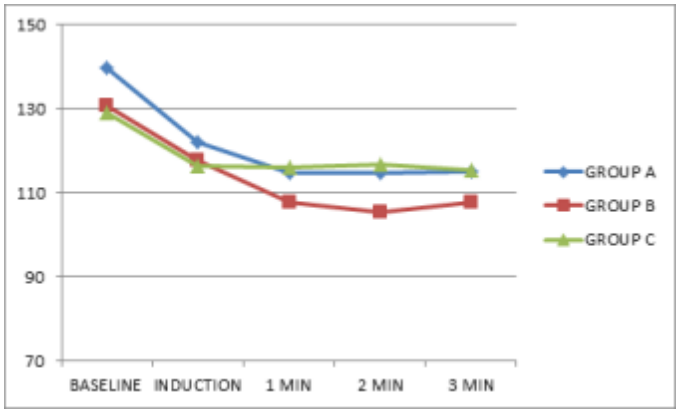

Fig. 2: Changes in mean systolic blood pressure

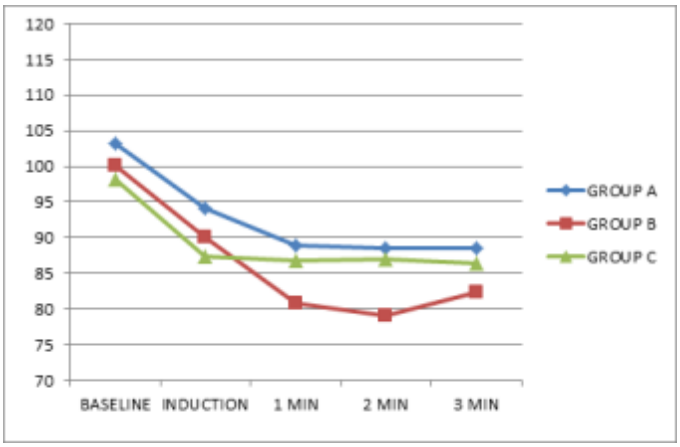

Fig. 3: Changes in mean diastolic blood pressure

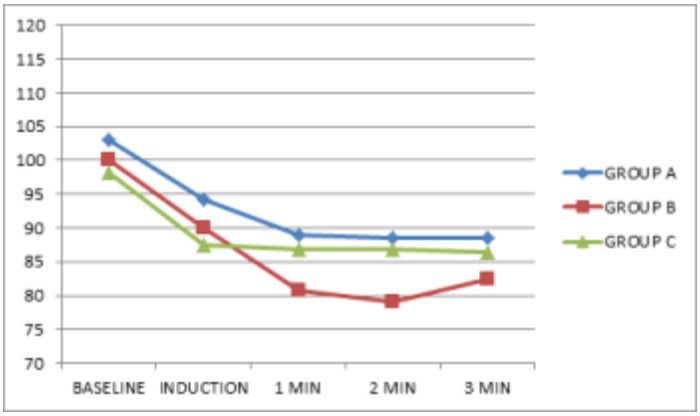

Fig. 4: Changes in mean arterial pressure

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