Comparative evaluation of induction characteristics of Propofol and Etomidate during general anaesthesia

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Abstract

Introduction: In general anaesthesia, induction of patients with intravenous anaesthetic agents is a common practice. Induction is a very crucial time as at this time the patient is liable to undergo sudden unexpected haemodynamic changes due to the exaggerated physiological effects of the induction agents. Anaesthetist all the time needs to choose an agent with least adverse effects for the safety of the patient.

Aim and Objective: In this study, our objective was to observe the effects of propofol and etomidate on the haemodynamics during induction of general anaesthesia.

Materials and Method: The study included 60 ASA Grade I and II patients aged between 18 and 60 years who were given general anaesthesia for elective surgery. The patients were allocated to two groups randomly with 30 patients in each group. Patients induced with propofol 2mg/kg were assigned to Group P and those induced with etomidate 0.3 mg/kg were assigned to Group E. The groups were compared for the changes in systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP)* The data collected was statistically analysed using the computer software SPSS. A "p" value of 0.05 or less was considered as statistically significant.

Observation and Results: It was observed that in Group P after induction with the study drug there was a significant decrease in the haemodynamic parameters – systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) as compared to the parameters before induction ($p \leq 0.05$). On the other hand in Group E the post induction values of haemodynamic parameters were not statistically different than the values before induction ($p \geq 0.05$).

Conclusion: Thus from our study, we came to the conclusion that etomidate when used for induction of general anaesthesia offers greater stability of haemodynamics than propofol and hence can be preferred as the agent of choice for induction of patients and especially more so for those with cardiac disease in whom stable haemodynamics are all the more important.

Keywords: Induction, General Anaesthesia, Propofol, Etomidate, Hemodynamic

Introduction

General anaesthetic induction agents decrease arterial blood pressure by decreasing myocardial contractility, arterial and venodilatation and attenuation of autonomic nervous system.[1-4] Induction is a critical step in conduction of general anaesthesia as the patients are susceptible to sudden and unexpected haemodynamic changes. One of the most common way of inducing anaesthesia is by intravenous anaesthetic agents. Thiopentone, Propofol, Ketamine are the common anaesthetic agents given intravenously for induction in present times. Because of high incidence of adrenocortical depression use of etomidate for induction was stopped in the past.[5] But rediscovery of the advantages with use of etomidate and absence of any new reported incidences of adrenocortical suppression has brought about a renewed interest among anaesthesiologists for the use of etomidate.[6]

Intravenous induction agents when given in an adequate dose, lead to unconsciousness within an arm circulation time.

Propofol gained popularity as induction agent with its favourable features of rapid and smooth induction and faster recovery, decreased incidence of nausea and vomiting etc.[7,8] On the other hand fall in blood pressure, depression of ventilation with higher dose and pain on injection are the major unfavourable effects.[9-11]

Etomidate is characterized by rapid onset and faster recovery with greater haemodynamic stability, minimal or no respiratory depression and neuro protective effects. Stable haemodynamic parameters after etomidate induction are explained by its lack of effect on sympathetic nervous system and baroreceptor reflex regulatory system. Some studies have observed that it results in increased coronary perfusion and so it is an induction agent of choice in patients with cardiac disease.[12-15] However, pain on injection, thrombophlebitis and myoclonus are some of the adverse effects.[16,17]

McCollum J S et al[18] compared the induction characteristics of the four induction agents - thiopentone, etomidate and methotrexate and propofol and they observed that propofol caused significantly more hypotension as compared to the other three induction agents.

Ebert T J et al[19] compared the effect of propofol and etomidate induction on sympathetic responses and came to a conclusion that etomidate maintains a greater stable heart rate by keeping both sympathetic outflow and autonomic reflexes intact.

Djordjevic B et al[20] compared thiopentone, propofol and etomidate for the incidence of adverse effects after induction and came to a conclusion that propofol is more efficacious as induction agent as it is tolerated better and the incidence of side effects is least with propofol among the three induction agents.

Yang C Y et al[21] did hemodynamic comparison of thiopental and propofol induction in different patients during endotracheal intubation and observed that fall in systolic and diastolic blood pressure was more marked with propofol than thiopentone and with thiopentone they observed a rise in heart rate.

Criado et al[22] studied the hemodynamic effects of induction with etomidate in 36 patients and their results showed that although etomidate has a negative inotropic effect, the variables remained within acceptable limits.

Kaur S et al[23] in their study compared induction with propofol and etomidate in cardiac patients posted for non cardiac surgery. They found a less decrease in heart rate and blood pressure in the etomidate group than in propofol group.

Materials and Method

This prospective, randomised, observational study was carried out after receiving clearance from the ethical committee of our institute. The study included 60 adult patients belonging to American Society of Anaesthesiologist (ASA) physical status 1 and 2 posted for elective surgery under general anaesthesia. The patients were divided using simple random sampling technique into two groups of 30 patients each.

Selection Criteria: The patients were enrolled in the study on the basis of following inclusion and exclusion criteria.

Inclusion Criteria:

1. Age between 18 to 60 years
2. Weight between 45 kg to 70 kg
3. ASA Grade 1 and 2
4. Elective surgery under general anaesthesia
5. Informed consent given

Exclusion Criteria:

1. Consent not given
2. ASA Grade 3 and above
3. Hypersensitivity to study drugs
4. Pregnant females
5. Emergency surgery
6. Altered sensorium before induction
7. Presence of seizure disorder
8. History of steroid medication
9. Hypotension

Sample Size Estimation: Number of patients to be enrolled in the study was calculated by normal distribution theory while fixing type 1 error (α) at 0.05 and the power (1β) at 0.8. A minimum of 25 patients were required for a significant result and so we decided on a sample size of 30.

Materials and Method

All the patients who fulfilled the inclusion criteria were randomly divided into 2 groups of 30 patients each. Group P received Propofol 2mg/kg and Group E received Etomidate 0.3 mg/kg intravenously.

All the patients were thoroughly evaluated and examined before the day of surgery and required investigations were ordered. On the day of surgery, preoperative baseline values of heart rate and blood pressure were recorded. As premedication patients were given injection midazolam 0.05 mg/kg iv and injection fentanyl 2µg/kg iv. Patients were pre-oxygenated with 100% oxygen for 3 minutes. Heart rate and blood pressures were noted at induction. Group P patients were induced with 2 mg/kg propofol and Group E patients were induced with etomidate 0.3 mg/kg iv. Heart rate and blood pressure were monitored at 1 min, 3 min, and 5 min after induction and recorded.

Data Compilation and Analysis: The statistical analysis was performed by using computer software SPSS version 20. Analysis was done by Chi-square test, paired t test and Student's t-test. The difference was considered as statistically significant for a p- value of less than 0.05.

Observations and Results

The aim of the present study was to compare the effects of etomidate with that of propofol on heart rate and blood pressure during induction of general anaesthesia.

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

The patients in both groups were comparable for age and sex as shown in Table 1. The mean age in Group P was 32.69 years and in Group E the mean age was 37.66 years (p=0.079). In Group P there were a total of 30 patients of which 13 were male patients and 17 were female patients whereas in Group E there were a total of 30 patients of which 18 were male patients and 12 female patients (p=0.212). The total number of patients was equal in both groups and the gender ratio was comparable. The haemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure) were monitored throughout the surgery but to compare the induction characteristics the statistical analysis was done for five minutes only as the duration of action of the induction dose is 5 minutes and also after this time inhalational agents and intermediate acting muscle relaxants are also given which can have their own effects on the haemodynamics. Table 2 shows the mean heart rate in the two groups before and after induction. There was no significant change in mean heart rate at one, three and five minute after induction as compared with the mean heart rate at the time of induction in both groups.

Table 3 shows the change in mean systolic blood pressure in the two groups before and after induction. In

Group P the mean systolic blood pressure at one, three and five minute after induction was significantly lower as compared with induction value(p=0.000), with maximum fall occurring at three minutes. In Group E, however there was no significant change in mean systolic blood pressure at one, three and five minute after induction when compared with that at the time of induction(p> 0.05).

Table 4 shows the mean diastolic blood pressure in the two groups at different times. In Group P the diastolic blood pressure at one, three and five minute after induction (p=0.001) decreased significantly whereas in Group E there was no significant decrease in diastolic blood pressure at one, three and five minute after induction as compared to that at the time of induction (p> 0.05).

Table 5 shows the changes in mean arterial pressure (MAP) in the two groups. In Group P the mean arterial pressure at one, three and five minute after induction (p = 0.001) was significantly lower than the pre induction value whereas in Group E there was no significant fall in mean arterial pressure at one, three and five minute after induction as compared to that at the time of induction (p>0.05).

Table 1: Profile of patients according to age and sex

	Group P Mean ±SD	**Group E Mean ±SD**	**P Value**
Age (Years)	32.69 ± 9.25	37.66 ± 10.32	0.071
Sex (M:F)	13:17	18:12	0.212

Table 2: Mean heart rate (beats per minute)

	Group P Mean±SD	**P Value**	**Group E Mean±SD**	**P Value**
Baseline	82.12±12.80		84.37±11.04	
Induction	80.49±10.07		79.17±10.14	
1 min	78.47±09.75	0.122	79.20 ±8.98	0.941
3 min	78.32±10.10	0.083	79.34 ±9.61	0.641
5 min	80.52±10.74	0.898	79.22± 9.95	0.907

Table 3: Mean systolic blood pressure (mmHg)

	Group P Mean±SD	**P Value**	**Group E Mean±SD**	**P Value**
Baseline	135.54±6.10		130.89±10.78	
Induction	120.59±5.88		118.85±12.23	
1 min	110.33±10.32	0.000	117.82±12.35	0.417
3 min	106.48±10.33	0.000	118.73±13.12	0.408
5 min	110.33±10.65	0.000	118.62±13.25	0.311

Table 4: Mean diastolic blood pressure (mmHg)

	Group P Mean±SD	**P Value**	**Group E Mean±SD**	**P Value**
Baseline	86.54±7.83		84.14±8.85	
Induction	76.68±8.24		75.20±11.54	
1 min	68.80±11.37	<0.001	74.35±11.28	0.230
3 min	64.36±9.75	<0.001	73.99±11.88	0.469
5 min	71.92±10.89	<0.001	73.35±12.54	0.349

Table 5: Mean arterial pressure (mmHg)

	Group P Mean±SD	**P Value**	**Group E Mean±SD**	**P Value**
Baseline	102.48±6.29		100.21±8.58	
Induction	92.35±8.37		90.54±13.05	
1 min	81.89±11.05	<0.001	89.35±11.85	0.226
3 min	80.73±9.63	<0.001	89.39±11.98	0.529
5 min	85.86±12.32	<0.001	89.28±12.67	0.275

Discussion

While conducting general anaesthesia, induction of the patient with an intravenous anaesthetic agent is an important part as the patients are susceptible to hemodynamic lability at the time of induction. Thus, an anaesthetist has to choose an agent with minimum or no effect on hemodynamics. Anaesthesia may be induced by administering induction agents by inhalation, intravenous, oral and rectal routes. In the present time, general anaesthesia is most commonly induced either by intravenous injection or by inhalation of gases. As compared to inhalation induction, intravenous induction has a faster onset and hence is the preferred mode of induction for general anaesthesia in most cases. Four most commonly used intravenous agents are thiopentone, propofol, etomidate and ketamine.

The mechanism by which propofol induces a state of general anaesthesia involves facilitation of inhibitory neurotransmission mediated by GABA. The high lipid solubility of propofol results in a rapid onset of action. After a single induction dose, recovery is also rapid due to a very short distribution half life.

Etomidate depresses the reticular activating system and mimics the inhibitory effects of GABA. Etomidate is characterised by a very rapid onset of action due to its high lipid solubility and large non ionized fraction a physiological pH. Long term infusions in ICU lead to adrenocortical suppression that was associated with high mortality in critically ill patients. Because of this etomidate was removed from the market and was not used for a long time. But induction doses of etomidate only transiently inhibit enzymes involved in cortisol and aldosterone synthesis. Because of this etomidate was again launched in the market. Due to re-introduction of etomidate in Indian market and an increased interest in it, we conducted a study to evaluate the effects of etomidate in comparison to that of propofol during induction of general anaesthesia.

In our study the demographic data were comparable in all the three groups. There was no statistical difference in the mean age of patients in the two groups (p=0.071). Also the gender of patients in the two groups was comparable (p=0.212). While analysing the change in heart rate, it was observed that in Group P, there was a decrease in heart rate after induction as compared to heart rate before induction, but the fall in BP was not significant statistically (P>0.05) as is evident from Graph 1. Bradycardia or a decrease in heart rate by propofol is vagally mediated reflex due to a drop in preload. Similar findings were seen in previous studies conducted by Grounds R.M et al[24] and Versichelen L et al.[25] They attributed the decrease in heart rate to the resetting of the baroreflex mechanism. On the other hand, it was observed that in Group E, there was no change in mean heart rate after induction from the pre induction value which is similar to the results found in the studies conducted in past. McCollum J S et al[13] compared thiopentone, etomidate, methotrexate and propofol for their induction characteristics. Ebert T J et al[14] in 1992, studied the cardiovascular responses by induction of anaesthesia with propofol or etomidate. They observed that the patients induced with etomidate were haemodynamically more stable than those induced with propofol. Stable heart rate with etomidate can be explained by its preservation of sympathetic outflow and autonomic reflexes.

In our study, the mean systolic blood pressure at one, three and five minute after induction in Group P was significantly lower than the mean systolic blood pressure at the time of induction (P =0.001). The greatest decrease in mean systolic blood pressure was 14.02 mm Hg from the pre-induction value in Group P. But in Group E, the fall was only 0.82 mm Hg from the pre-induction value which is not statistically significant (P>0.05). Similar results were observed by Mackenzie et al[26] in their study where there was a 20% reduction in mean systolic blood pressure after induction with propofol. They concluded that induction with propofol causes vasodilatation leading toa decrease in systemic vascular resistance and therefore hypotension. Propofol also causes a decrease in cardiac output and alters the sensitivity of baroreceptors, thus explaining the fall in blood pressure observed after induction with it.

In our study, the mean diastolic blood pressure in Group P at one, three and five minute after induction was significantly lower as compared to mean diastolic blood pressure before induction(P<0.001). The greatest decrease in mean diastolic blood pressure was 12.32 mm Hg from the pre-induction value in Group P. But in Group E, the greatest decrease in mean diastolic blood pressure was 1.23 mm Hg from the pre-induction value which was not statistically significant (P>0.05).

In our study, there was a significant fall in mean arterial pressure in Group P at one, three and five minute after induction as compared to mean arterial pressure before induction. The greatest decrease in mean arterial pressure was 11.62 mm Hg from the pre-induction value in Group P. On the other hand, in Group E the greatest decrease in mean arterial pressure was 1.15 mm Hg from the pre-induction value which was found to be statistically not significant (p≥0.05). Etomidate has minimal effects on the cardiovascular system. A mild reduction in peripheral vascular resistance is responsible for a slight decrease in arterial pressure. Myocardial contractility and cardiac output are usually unchanged. The decrease in blood pressure by propofol is due to inhibition of sympathetic vasoconstrictor activity leading to a drop in systemic vascular resistance, decreased cardiac contractility and preload. Propofol markedly impairs the normal arterial baroreflex response to hypotension.

McCollum J S et al[13] in their study also observed results that are similar to that of our study. In their study there was a 15% fall in mean arterial pressure

after induction with propofol whereas after induction with etomidate the decrease in MAP was only 5%.

Mausumi Das et al[27] did comparative study on haemodynamic responses during intubation using etomidate, propofol and thiopentone in laparoscopic surgeries. They observed no change in heart rate, systolic, diastolic and mean arterial pressure after induction and after intubation in etomidate group. In propofol group, they observed that though heart rate decreased significantly from pre induction to post induction but systolic, diastolic and mean arterial pressure decreased more significantly.

In our study, we observed that the heart rate, systolic and diastolic blood pressure and mean arterial pressure of patients were not altered significantly after induction with etomidate in comparison to propofol. However, in our study the patients were of ASA physical status I and II only and did not include hemodynamically compromised patients or those with limited cardiac reserve. Changes in heart rate and cardiac output caused by propofol are usually transient and insignificant in healthy patients. But patients with impaired ventricular function may experience a significant drop in cardiac output as a result of decreases in ventricular filling pressures and contractility. But etomidate, is expected to show similar hemodynamic stability in such patients also. Thus, to further evaluate the effects of etomidate induction on hemodynamic parameters, a study on patients with low cardiac reserve and hemodynamic instability will be needed. Also, the study had a small number of patients. Maybe a study with more number of patients is required to further prove the haemodynamic stability of etomidate.

Conclusion

It is common to induce general anaesthesia by administering intravenous induction agents. Thiopentone and Propofol are the most commonly used induction agents. Patients undergoing surgery under general anaesthesia when induced with thiopentone and propofol exhibit significant changes in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure, which can sometimes be detrimental to the patient outcome.. But as observed in the present study the group of patients which was induced with etomidate did not show any statistically significant change in the haemodynamic parameters after induction. The patients induced with etomidate exhibited a more stable heart rate and blood pressure. It can be concluded from the study that etomidate is a better induction agent compared to Propofol and Etomidate. Thus, etomidate should be preferred over propofol as the induction agent of choice in patients with co-existing cardiac illness in whom maintaining stable hemodynamic parameters is very important during induction for a favourable outcome.

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