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ORIGINAL RESEARCH

A COMPARATIVE STUDY ON THE HEMODYNAMIC EFFECTS OF PROPOFOL AND ETOMIDATE USED AS INDUCING AGENTS IN GENERAL ANAESTHESIA

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Abstract:

Introduction: One of the most common way of inducing anaesthesia is by intravenous anaesthetic agents.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.

Methods: The present Retrospective analytical comparative study is carried out on the records of100 subjects. The study included records of 100 adult patients belonging to American Society of Anaesthesiologist (ASA) physical status 1 and 2 who were posted for elective surgery under general anaesthesia. The patients were divided into two groups of 50 patients each using propofol in Group A & Etomidate in Group B. In both the groups the records had Heart rate and blood pressure were been monitored at 1 min, 3 min, and 5 min after induction and recorded.

Results: The mean age in Group A was 34.85 ± 4.73 years and in Group B the mean age was 36.41 ± 3.63 years (p=0.094).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.

Conclusions: 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 also a better induction agent. Thus, etomidate can 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.

Keywords: Propofol, Etomidate , Comparative study , Haemodynamic changes

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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.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.

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Methodology:

The present Retrospective analytical comparative study is carried out on 100 subjects was carried. The study included records of 100 adult patients belonging to American Society of Anaesthesiologist (ASA) physical status 1 and 2 who were posted for elective surgery under general anaesthesia. The patients were divided using simple random sampling technique into two groups of 50 patients each.

This Retrospective Analytical study involved Prior Consent from Hospital Authorities / Medical Superintendents of the Local Randomly selected Secondary & Tertiary care Radio-diagnostic Centres / hospitals including ours to see the records of the patients from their Medical Records Departments (MRD). The study was conducted within ethical standards and only those were selectedwho were posted for elective surgery under general anesthesia in hospitals in past 2 year. Randomization was done using computer tables in selecting data. Only those Patients records were selected who underwent standard clinical examinations, routine biochemical and hematological investigations& Radiological Investigations. Medical record numbers were used to generate the data for analysis.

For the purpose of the present study, data of 100 of the randomly selected patients (candidates / study subjects) who seek care for care were retrospectively identified with age ranging from 18 to 65 years.

Selection Criteria

Onlyrecords of the patients were enrolled in the study which followed the following inclusion and exclusion criteria.

Inclusion Criteria

1. Age between 18 to 65 years
2. Weight between 45 kg to 80 kg
3. ASA Grade 1 and 2
4. Elective surgery under general anesthesia
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

All the patients who fulfilled the inclusion criteria were randomly divided into 2 groups of 50 patients each. Group “A” received Propofol 2mg/kg and Group “B” received Etomidate 0.3 mg/kg intravenously. It was observed that all the patients were thoroughly evaluated and examined before the day of surgery and required investigations were ordered. It was observed

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in records that 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 A patients were induced with 2 mg/kg propofol and Group B patients were induced with etomidate 0.3 mg/kg iv. In both the groups the records had Heart rate and blood pressure were been monitored at 1 min, 3 min, and 5 min after induction and recorded.

Statistical Analysis

The data obtained were analyzed in detail using the statistical software SPSS 21 for Windows. Data are reported as mean ± SD or proportions and 95% confidence intervals. Statistical analysis was performed by tests of significance.

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.

Result:

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 .The mean age in Group A was 34.85 ± 4.73 years and in Group B the mean age was 36.41 ± 3.63 years (p=0.094). In Group A there were a total of 50 patients of which 23 were male patients and 27 were female patients whereas in Group B there were a total of 50 patients of which 28 were male patients and 22 female patients (p=0.351). The total number of patients was equal in both groups and the gender ratio was comparable. It was made sure that in the records 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 1 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 2 shows the change in mean systolic blood pressure in the two groups before and after induction. InGroup A 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 B, 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 3 shows the mean diastolic blood pressure in the two groups at different times. In Group A the diastolic blood pressure at one, three and five minute after induction (p=0.001) decreased significantly whereas in Group B 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 4 shows the changes

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in mean arterial pressure (MAP) in the two groups. In Group A 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 B 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: Mean heart rate (beats per minute)

	Group A Mean±SD	P Value	Group B Mean±SD	P Value
Baseline	81.42±11.80		83.97±10.04	
Induction	80.19±10.07		79.27±10.64	
1 min	77.17±08.91	0.122	78.20 ±7.98	0.841
3 min	78.12±11.10	0.083	79.74 ±10.41	0.941
5 min	81.52±11.74	0.898	80.22± 10.95	0.707

Table 2: Mean systolic blood pressure (mmHg)

	Group A Mean±SD	P Value	Group B Mean±SD	P Value
Baseline	134.24±6.10		132.49±9.38	
Induction	119.41±5.88		118.25±10.23	
1 min	111.33±9.32	0.000	119.82±11.35	0.617
3 min	106.48±10.33	0.000	118.73±13.12	0.808
5 min	110.33±10.65	0.000	118.62±13.25	0.511

Table 3: Mean diastolic blood pressure (mmHg)

	Group A Mean±SD	P Value	Group B Mean±SD	P Value
Baseline	85.14±6.83		84.34±7.85	
Induction	77.48±8.24		76.28±10.54	
1 min	67.10±10.47	<0.001	73.35±10.28	0.271
3 min	65.36±10.75	<0.001	72.99±11.18	0.549
5 min	70.92±11.89	<0.001	71.35±10.94	0.712

Table 4: Mean arterial pressure (mmHg)

	Group A Mean±SD	P Value	Group B Mean±SD		P Value
Baseline	101.48±7.29		101.21±9.58		
Induction	91.35±9.37		90.54±11.05		
1 min	82.91±10.05	<0.001	90.35±09.85		0.226
3 min	81.73±9.63	<0.001	88.39±11.98		0.529
5 min	84.86±11.32	<0.001	91.28±12.67		0.275

Discussion:

While conducting general anesthesia, induction of the patient with an intravenous anesthetic agent is an important part as the patients are susceptible to hemodynamic lability at the time of induction. Thus, an anesthetist has to choose an agent with minimum or no effect on

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hemodynamics. Anesthesia may be induced by administering induction agents by inhalation, intravenous, oral and rectal routes. In the present time, general anesthesia 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 anesthesia 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 anesthesia 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 characterized 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 . Also the gender of patients in the two groups was comparable . While analysing the change in heart rate, it was observed that in Group A, 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 ($P>0.05$) . 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 B, 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 anesthesia with propofol or etomidate. They observed that the patients induced with etomidate were hemodynamically 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 A was significantly lower than the mean systolic blood pressure at the time of induction ($P =0.001$).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

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pressure in Group A at one, three and five minute after induction was significantly lower as compared to mean diastolic blood pressure before induction(P<0.001).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.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 pressureafter induction with propofol whereas after induction with etomidate the decrease in MAP was only 5%.

Mausumi Das et al[27] did comparative study on hemodynamic 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 also a better induction agent. Thus, etomidate can be preferred over propofol as the induction agent of choice in patients with co-

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existing cardiac illness in whom maintaining stable hemodynamic parameters is very important during induction for a favourable outcome.

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Conflict of interest

None declared

Consent

Yes

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