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Research Article

A comparative study of haemodynamic effects of propofol and etomidate used as induction agent in general anaesthesia

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Abstract:

Background: As an induction agent, a variety of anaesthetic medications have been utilised. Despite being the most widely used induction drug, propofol induces a considerable decrease in arterial pressure. Another drug, etomidate, has the advantage of lowering blood pressure. **Materials and Methods:** The research enrolled fifty patients who were scheduled for surgery under general anaesthesia and were randomly assigned to one of two groups. Over the course of 30-60 seconds, all patients received intravenous fentanyl citrate (2ug/kg) followed by a study medication. The propofol group (Gr P) got 2.5 mg/kg of propofol, whereas the etomidate group (Gr E) received 0.2 mg/kg of etomidate. Before induction, at the conclusion of induction (lack of eyelid reflex), at the end of intubation, and after 5 minutes of intubation, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and SpO2 were measured. Pain upon injection and myoclonus were also reported as side effects. **Results:** Mean heart rate, SBP, DBP, and MAP recorded at different time intervals were lowest in Gr P. Pain on injection was significantly increased in Gr P (56%). Myoclonus was seen in Gr E (12%). **Conclusion:** Induction with 0.2 mg/kg of etomidate is better for its hemodynamic stability over propofol (2.5 mg/kg) along with less incidence of pain on injection. Only drawback was incidence of myoclonus.

Keywords- propofol, etomidate, mean arterial pressure, myoclonus, pain on injection.

Introduction

Incidence of coronary artery disease is steadily on rise and coronary artery bypass grafting (CABG) surgery is the commonest performed cardiac surgery. Patients with low left ventricle ejection fraction (LVEF) undergoing CABG constitute a high risk group. Anaesthetic induction agents produces variable degree of hypotension while laryngoscopy and endotracheal intubation produces hypertension and tachycardia. These changes in hemodynamics may alter the balance between myocardial oxygen supply and demand which can be detrimental in this high risk group of patients undergoing CABG. Various anaesthetic agents like Thiopentone, propofol, midazolam and Etomidate are in current use as an induction agents but no single anaesthetic agent is suitable for all patients as all of these agents have their advantages and disadvantages. Propofol, an alkylphenol derivative, provides rapid onset and short duration of action. It causes considerable reduction in systemic vascular resistance and arterial pressure 15% to 40% after iv induction with 2mg/kg. Its effect on HR is variable. It causes direct myocardial depression at doses above 0.75mg/kg. Etomidate is a carboxylated imidazole derivative, has a rapid onset (10-60 sec), a brief duration of action (3-5 min), and hydrolyses primarily in liver. It provides hemodynamic stability in both noncardiac and cardiac disease patients after dosage of 0.15 to 0.30 mg/kg. It directly inhibits 11-beta hydroxylation, which results in temporary reduction in biosynthesis of cortisol and aldosterone.

Propofol, 2, 6 - diisopropylphenol, a non-barbiturate anaesthetic agent, has recently been accepted as a viable alternative to the time-tested thiopentone sodium for intravenous anaesthesia induction due to its smooth and rapid induction, better intubating condition by maintaining upper airway integrity, and, most importantly, rapid recovery from anaesthesia. [1,2] Hemodynamic instability and cardiovascular problems, such as hypotension, are the most serious adverse effects of this medicine. When anaesthesia was produced with 2 mg/kg body weight of propofol, systolic blood pressure was lowered by 26-28 percent, diastolic blood pressure by 19 percent, and mean arterial pressure by 11 percent from baseline, with no significant changes in stroke volume or cardiac output. [3,4] It can also cause bradycardia by increasing nitrous oxide production and release, which has been observed in 4.2 percent of patients. [5]

Etomidate was initially launched in the early 1970s with the benefit of lowering blood pressure. It is an induction agent of choice in cardiac illness patients due to its lack of effects on the sympathetic nervous system, baroreceptor reflex regulation system, and effects of enhanced coronary perfusion even in patients with significant cardiac dysfunction. [6] One of the drug's most serious adverse effects is the inhibition of adrenocortical function by

inhibiting the 11-hydroxylase enzyme, as well as myoclonic movements in 30-40% of patients. [7]

Given the widespread use of propofol and etomidate for anaesthesia induction, as well as the importance of maintaining patients' hemodynamic stability during induction, this study compared the effects of these two drugs on the cardiovascular responses of patients undergoing general anaesthesia surgery.

Materials & Methods

This randomised interventional study was done on patients with ASA grade I and II, ages 18 to 65, of either sex, who were scheduled for a treatment under general anaesthetic after receiving clearance from a research ethics board. The patients were told about the study's goal and method before being enrolled after providing written informed permission. All patients scheduled for elective surgery had a pre-anaesthetic examination. All patients had a detailed history, physical examination, and basic investigation the day before surgery to ensure anaesthetic fitness. To rule out any serious systemic ailment, a medical history was gathered. On the night before surgery, all patients were kept fasting overnight and given alprazolam 0.25-0.5 mg and ranitidine 300 mg orally.

Patients in all groups were given inj. glycopyrolate 0.2 mg intravenously (IV) and inj. ondansetron 4 mg IV soon before induction on the day of surgery. Standard monitoring (ECG, pulse oximetry, NIBP) was set up on the operating table, and baseline vital data such as heart rate (HR), blood pressure (BP), and arterial oxygen saturation (SpO2) were collected. Intravenous fluid was begun after an intravenous line was established using an 18G cannula in the non-dominant hand.

Patients were randomly assigned to one of two groups: propofol group (Gr P) or etomidate group (Gr E) (Gr E). An anaesthesiologist who was not aware of the study prepared the study medicines. All of the patients were administered 2g/kg of fentanyl citrate intravenously and were preoxygenated with 100% oxygen for 3 minutes. The induction agent (study medication) was administered 30-60 seconds after the fentanyl was provided. Inj. rocuronium bromide 0.9 mg/kg at 90 seconds was used to assist endotracheal intubation, and anaesthesia was maintained using oxygen, nitrous oxide, isoflurane, and an intermittent dosage of inj. rocuronium bromide. With neostigmine 0.05 mg/kg and glycopyrolate 0.008 mg/kg, residual neuromuscular blockade was reversed. After obtaining a protective airway reflex, endotracheal extubation was performed.

After thorough scrutiny and checking of the data, statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS), 24 version. Numerical/continuous variables

were reported as mean ± SD (standard deviation) and for qualitative/categorical variables, chi-square test or Fischer's exact probability test were used. The two group means were compared by independent sample test (t- test) and χ^2-test was applied for categorical variables. All comparisons were two- sided and the p-values of < 0.05 and < 0.01 were treated as the cut off values for significance and highly significance respectively.

Results

50 patients were recruited to the study. Both the groups were comparable with respect to demographic variables such as age, sex, weight and ASA physical status (Table 1).

Table 1: Comparison of demographic profiles between the groups

Variables	**Propofol Group**	**Etomidate Group**	**P value**
Age	37.32±11.14	36.08±9.78	0.678
Gender	F:M=11:14	F:M=13:12	0.571
Weight	59.36±10.91	63.56±9.79	0.159
ASA status	I:II=19:6	I:II=18:7	0.747

Heart rate between groups was studied here, using independent sample t-test. There was statistically significant difference in heart rate at the end of induction, after intubation and 5 minutes after intubation (Fig 1).

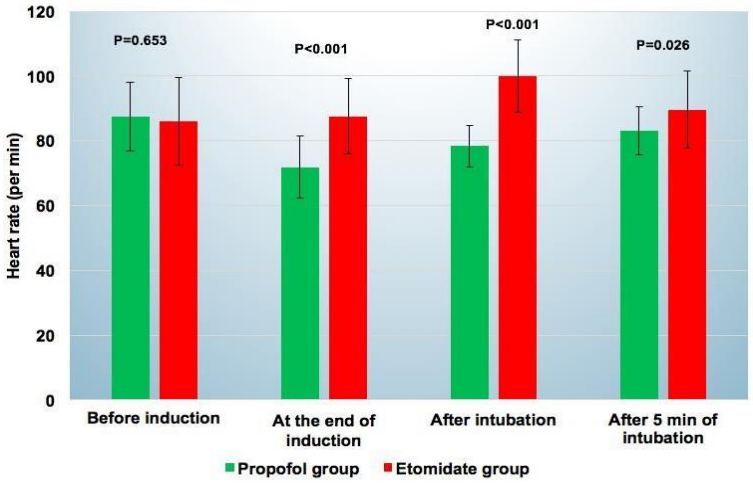

Fig. 1 showing comparison of heart rate between the groups

The pre-induction systolic blood pressure of both groups were comparable with no significant differences. But the systolic blood pressure of both the groups after induction were statistically and clinically different with p value of <0.05. There were significant differences between both the groups at the end of induction and after intubation. However, SBP after 5 minutes in both groups were comparable (Table 2).

Table 2: Comparison of systolic blood pressure (mmHg) between the groups

SBP (mm Hg)	Propofol group	Etomidate group	P value
Before induction	135.12±10.84	130.88±13.02	0.217
At the end of induction	113.88±11.63	123.52±11.97	0.006**
After intubation	120.12±11.08	141.88±10.24	<0.001**
After 5 min of intubation	133.48±8.78	134.44±13.51	0.767

It is seen from table 3, that pre-induction DBP were comparable in both groups with no statistical significant differences (p>0.05). But DBP of both groups at the end of induction, and after intubation were different both clinically and statistically, with p value <0.05.

Table 3: Comparison of diastolic blood pressure (mmHg) between the groups

DBP (mm Hg)	Propofol group	Etomidate group	P value
Before induction	83.28±9.33	78.72±9.02	0.085+
At the end of induction	70.92±9.93	78.08±7.60	0.006**
After intubation	74.68±9.11	85.32±8.91	<0.001**
After 5 min of intubation	81.40±8.26	81.96±12.1	0.849

The pre-induction MAP were comparable in both groups with no statistical significant differences (p>0.05). But MAP of both groups at the end of induction, after intubation were different both clinically and statistically, with p value <0.05. MAP values after 5 minutes of intubation was insignificant and hence comparable (Table 4).

Table 4: Comparison of mean arterial pressure (mmHg) between the groups

MAP (mm Hg)	Propofol group	Etomidate group	P value

Before induction	100.68±8.92	96.12±9.36	0.084+
At the end of induction	85.28±9.68	93.24±8.53	0.003**
After intubation	89.72±8.65	104.24±8.53	<0.001**
After 5 min of intubation	98.72±7.44	99.40±11.63	0.807

The incidence of pain on injection in both the groups is shown in fig 2 and incidence of pain is higher in group P (56%) as compared to group E (0%). In group P, 9 cases (36%) had grade 1 on pain scale followed by 4 cases (16%) had grade 2 and only one case had grade 3 pain (Fig. 2).

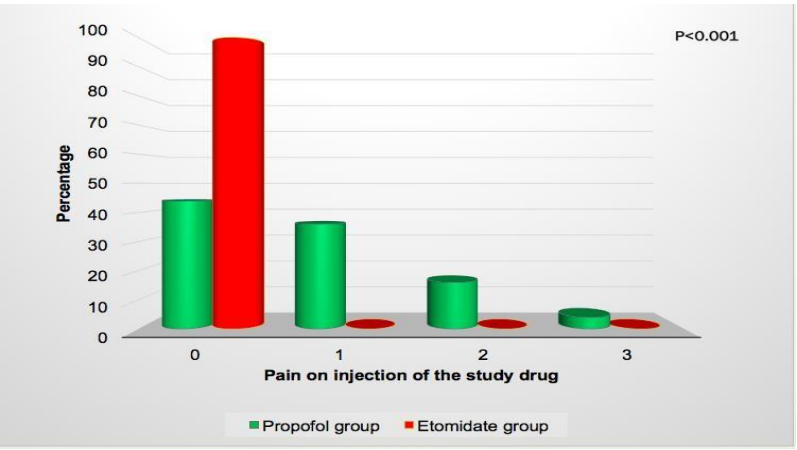

Fig. 2 Pain on injection of the study drugs

In the present study myoclonus was observed in 3 patients (12%) in group E, in which 2 cases (8%) had grade 1 and 1 case (4%) had grade 2 myoclonus during the study (Fig. 3).

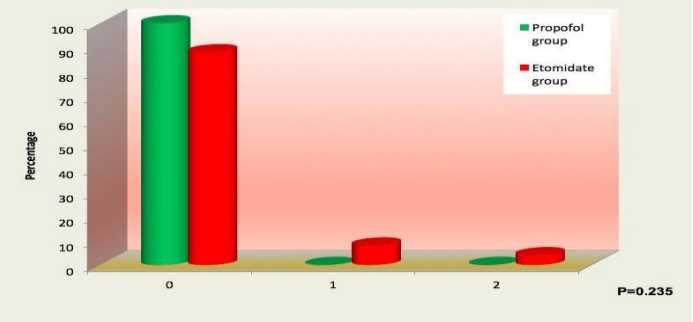

Fig. 3 Incidence of myoclonus observed with study drugs

Discussion

All the surgical procedures are performed under anaesthesia, which is categorized in to general anaesthesia (GA), regional anaesthesia (RA) and local infiltration, depends on patient general condition, and type of surgery. Induction of GA can be done by intravenous (IV) and inhalational anaesthetic agents but in most of the cases IV agents are preferred over inhalational because of rapid and smooth induction with minimal systemic effects. Recently various type of IV agents are used e.g. thiopentone, midazolam, Propofol and etomidate, opiod etc. During induction of anaesthesia many complications are noted like sudden fall in blood pressure, arrhythmias, cardiac arrest, hypoxia so it is desirable to use a safe agent with minimum systemic side effects. In present study we compared the Propofol and etomidate as induction agents of GA for their effect on hemodynamic parameters and various adverse effects on patient.

This was a 50-patient research comparing ASA I and II patients undergoing surgery under general anaesthesia with propofol or etomidate as the inducing drug. Group P (n=25) got 2.5 mg/kg of inj. propofol intravenously, whereas group E (n=25) received 0.2 mg/kg of inj. etomidate intravenously.

Induction of anaesthesia is accompanied with modest to severe hemodynamic variations, depending on a variety of circumstances. In comparison to etomidate, propofol induced a drop in heart rate during induction in our research. In response to a drop in systolic blood pressure, the mean heart rate for the propofol group at the time of induction was reduced compared to the pre-induction (Fig. 1). The findings of Das M et al [8] (before induction heart rate vs. post induction heart rate) are supported by our findings. Propofol may trigger a resetting of the baroreflex processes, which allows for a lower heart rate to be maintained despite lower arterial pressure. [9] However, induction with etomidate causes no change in heart rate which is comparable to the findings of Aggarwal S et al[10], Colvin MP et al[11] and Das M et al[8].

Propofol causes hypotension by inhibiting the sympathetic nervous system and impairing baroreflex regulation systems. Etomidate, on the other hand, preserves hemodynamic stability by preserving sympathetic outflow and autonomic responses. A research on the haemodynamic impact of propofol during coronary artery bypass surgery was conducted by Pensado A et al[3]. They discovered that after 1 minute of propofol injection, the systolic arterial pressure dropped to its lowest point. This conclusion is consistent with our findings, which showed a considerable drop in systolic blood pressure following induction compared to the baseline. Skinner et al[13] found a substantial reduction in SBP after induction in the propofol group

and a significant rise in SBP after intubation in the etomidate group, which is comparable to the current findings. Rise in SBP post-intubation was less in our study which may be due to the use of fentanyl as it blunts the hemodynamic responses to intubation.

The propofol group had lower mean diastolic blood pressure (DBP) than the etomidate group in the current investigation, which was tested at various time intervals up to 5 minutes. Clayes MA et al[4] discovered statistically significant reductions in diastolic arterial pressures 2 minutes after propofol induction (19%). This conclusion is in line with the findings of the current investigation, which showed a statistically significant reduction in DBP of 15% following propofol induction. DBP fell in both the propofol and etomidate groups at 2 and 3 minutes after induction, according to Shah SB et al[14]. The drop in DBP was large in propofol (27 and 30 percent, respectively) compared to etomidate (17 and 16 percent, respectively), which supports the findings of this study (Table 3). Criado A et al. [15] used etomidate (0.45 mg/kg) in non- premedicated patients and there was a significant decrease in DBP at 3 and 10 min interval after induction.

However, we noticed a 5-minute rise in DBP after induction in our trial. Increased SBP and DBP with etomidate after induction may be attributed to its CNS stimulant activity, which maintains BP directly, or increased muscular tone, which raises venous return and therefore blood pressure, according to Colvin MP and colleagues[11]. Recently, a mechanism has been postulated that explains etomidate's cardiovascular stability. Its steady haemodynamic profile is due to its ability to bind and excite peripheral alpha-2B adrenergic receptors, resulting in vasoconstriction. Abnormal responses during etomidate induction might be due to changes in the function or quantity of these receptors. [16]

The delivery of 2.5 mg/kg propofol resulted in the greatest reduction in MAP (15%) after induction (p0.003), which remained statistically significant throughout the investigation. When compared to etomidate, Aggarwal S and colleagues [10] found that propofol induction resulted in a considerable drop in mean arterial pressure (MAP) from baseline, but etomidate only resulted in a little change in MAP. This conclusion is consistent with our findings, in which the MAP in the propofol group is lower than the baseline during induction than in the etomidate group (Table 4). Our findings are similar to those of Shivanna S et al[7], who found that after induction, all indicators decreased significantly compared to baseline, including mean arterial pressure (27 to 32 percent, P = 0.001).Whereas, in the etomidate group, there was a significant increase from baseline in mean arterial pressure (P = 0.001) at 1 minute after intubation which corresponds to the present study (MAP at baseline and 1 minute after intubation of 96.12±9.36 and 104.24±8.53 respectively).

In the present study, oxygen saturation between the groups were comparable and statistically insignificant (>0.05) which is consistent with the findings of Masoudifar M and Beheshtian E (P = 0.21). [17]

Propofol is currently the preferred intravenous general anaesthetic drug with a smooth induction, pleasant sleep, rapid recovery, and low incidence of nausea and vomiting. Despite these positive properties, it also has adverse effects such as injection pain, which may cause discomfort in the induction of anesthesia. Earlier it was hypothesized that propofol might indirectly or directly interact with sensory nerve fibers located in the venous adventitia. A recent study claims that nonselective ligand-gated cation channels such as transient receptor potential (TRP) ankyrin 1 (TRPA1) and TRP vanilloid 1 (TRPV1) are the predominant molecular entities mediating activation of peripheral nerve endings by general anesthetics.[18]

In our study, pain on injection of propofol was observed in 56% population in comparison to etomidate (0%). This finding is similar to study by Saricaoglu F et al[19] in which the incidence was (83.8%) with propofol and in (63.2%) etomidate group. Low incidence of pain (in etomidate group) in our study may be due to slow injection of the drug consistent with findings of Colvin MP et al.[11]

The results of this study show that the incidence of myoclonus was 12% with etomidate and 0% with propofol. The incidence of myoclonus due to etomidate depends on the dosage and speed of injection.[20] Study by Kaushal RP et al[21] observed that myoclonus was not seen as the drug was injected slowly. Our study is also consistent with findings of Kaur S et al [22] where involuntary movements during induction were observed in none of the patients in the propofol group and were observed in 5 (16.7%) patients in the etomidate group. The low incidence of myoclonus in our study may be due to pre-treatment with fentanyl at a dose 2 □g/kg.

Conclusion

The current study concludes that induction with 0.2 mg/kg etomidate is superior than propofol (2.5 mg/kg) in terms of hemodynamic stability and the occurrence of discomfort during injection. The only disadvantage was the occurrence of myoclonus. As a result, we believe that etomidate is a superior alternative for patients with uncontrolled hypertension, septic shock, the critically sick, and patients with coronary artery disease who are prone to hemodynamic fluctuations during induction.

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