

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

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Abstract : Many anaesthetic drugs have been used as induction agent. Propofol, although most commonly used induction agent, causes significant reduction in arterial pressure. Another agent, etomidate, has advantage of minimizing hypotension. **Materials and Methods:** A total of fifty patients posted for surgery under general anaesthesia were taken up for the study and were randomly allocated into two groups. All patients received intravenous fentanyl citrate (2µg/kg) followed by a study drug over 30-60 seconds. Propofol group (Gr P) received 2.5 mg/kg dose of propofol, and etomidate group (Gr E) received etomidate at 0.2 mg/kg. Heart Rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and SpO₂ were noted at the following time intervals: before induction, at the end of induction (loss of eyelash reflex), at the end of intubation and after 5 minutes of intubation. Adverse effects such as pain on injection and myoclonus were also recorded. **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.

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I. Introduction

Propofol, 2, 6 - diisopropylphenol, a non-barbiturate anaesthetic agent has been accepted in recent times as an effective alternative to the time tested thiopentone sodium for intravenous induction of anaesthesia because of smooth and rapid induction, better intubating condition by maintaining upper airway integrity and most importantly rapid recovery from anaesthesia. [1,2] The most important side-effects of this drug are hemodynamic instability and cardiovascular complications, such as hypotension. Systolic blood pressure has been found to be reduced by 26-28%, diastolic blood pressure by 19% and the mean arterial pressure by 11% from the baseline, without significant changes in stroke volume and cardiac output when anaesthesia was induced with 2 mg/kg body weight of propofol. [3,4] It can also lead to bradycardia by increasing the production and releasing of nitrous oxide which has been seen in 4.2% of patients. [5]

Etomidate was first introduced in early 1970s with the advantage of minimizing hypotension. Its lack of effects on sympathetic nervous system, baroreceptor reflex regulatory system and its effects of increased coronary perfusion even on patients with moderate cardiac dysfunction makes it an induction agent of choice in cardiac disease patients.[6] One of the important side effects of this drug is suppression of adrenocortical function by blocking 11β-hydroxylase enzyme and myoclonic movements in 30-40% of the patients.[7]

Considering the common use of propofol and etomidate for induction of anaesthesia and the importance of patients' hemodynamic stability during induction, this study was conducted to compare the effects of these two drugs on the cardiovascular responses of patients undergoing surgeries with general anaesthesia.

II. Materials & Methods

After obtaining approval from research ethics board, RIMS, Imphal, Manipur, this randomized interventional study was conducted on patients with ASA grade I and II, age of 18-65 years, belonging to either sex posted for procedure under general anaesthesia. The patients were explained about the purpose and procedure of the study and were enrolled after getting their written informed consent. Preanaesthetic evaluation

were done in all patients scheduled for elective surgeries. Detailed history, physical examination and basic investigation were performed in all patients a day prior to the surgery for anaesthesia fitness. History was taken to rule out any major systemic illness. All patients were kept overnight fasting and received alprazolam 0.25-0.5 mg and ranitidine 300 mg orally on night before surgery.

On the day of surgery, patients in all the groups were premedicated with inj. glycopyrolate 0.2 mg intravenously (IV) and inj. ondansetron 4mg IV just before induction. On the operation table, routine standard monitoring (ECG, pulse oximetry, NIBP) were fixed and baseline vital parameters like heart rate (HR), blood pressure (BP) and arterial oxygen saturation (SpO₂) were recorded. Intravenous line was established with 18G cannula in the non dominant hand and intravenous fluid was started.

Using a computer generated random number table, patients were allocated to one of the two groups i.e. either propofol group (Gr P) or etomidate group (Gr E). The study drugs were prepared by an anaesthesiologist blinded to the study. Inj. fentanyl citrate 2µg/kg was given intravenously to all the patients and were preoxygenated with 100% oxygen for 3 minutes. Two minutes after fentanyl administration, induction agent (study drug) was given over 30-60 seconds. Endotracheal intubation was facilitated with inj. rocuronium bromide 0.9 mg/kg at 90 seconds and anaesthesia was maintained by using oxygen, nitrous oxide, isoflurane and intermittent dose of inj. rocuronium bromide. Residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrolate 0.008 mg/kg. Endotracheal extubation was carried out after getting protective airway reflex.

After thorough scrutiny and checking of the data, statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS), 21 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.

III. 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).

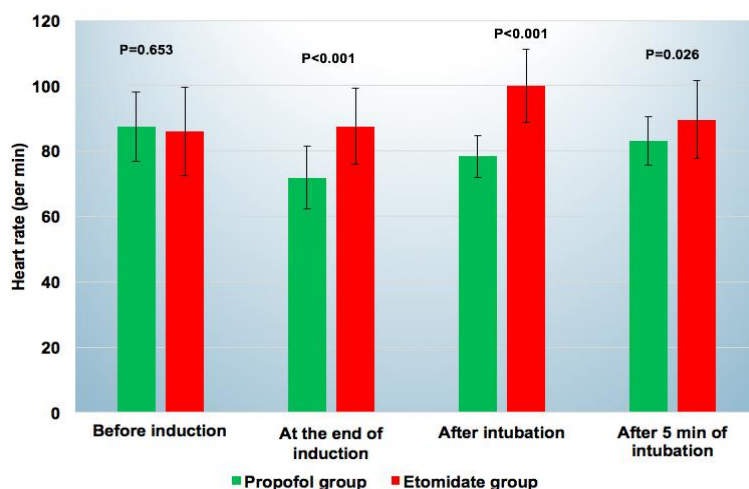


Fig. 1 showing comparison of heart rate between the groups

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).

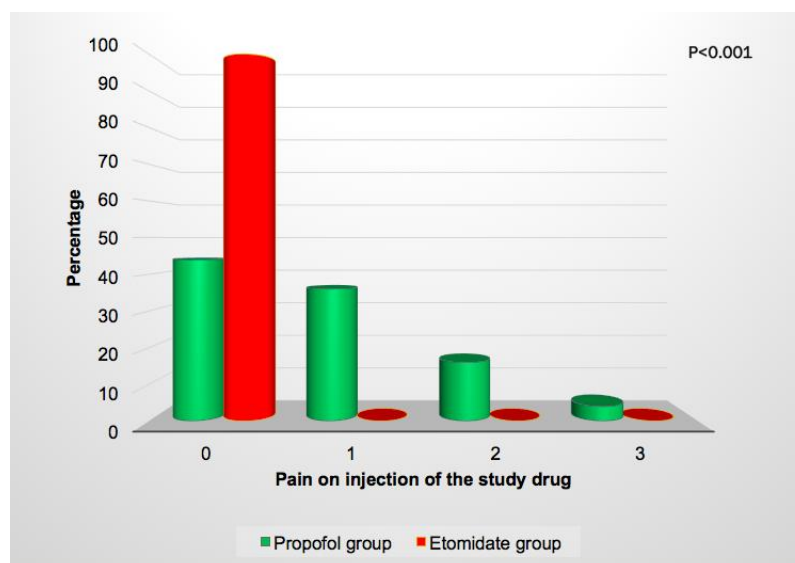


Fig. 2 Pain on injection of the study drugs

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).

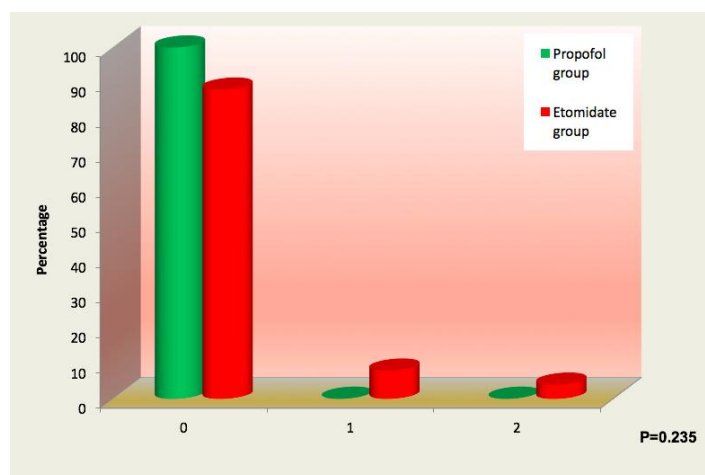


Fig. 3 Incidence of myoclonus observed with study drugs

IV. Discussion

This was a comparative study, carried out in 50 patients, of ASA I and II undergoing surgery under general anaesthesia using either propofol or etomidate as inducing agent. Group P (n=25) received 2.5 mg/kg of inj. propofol and group E (n=25) received inj. etomidate of dose 0.2 mg/kg intravenously.

Induction of anaesthesia is associated with hemodynamic variation of mild to moderate degree depending upon many factors. In our study, we observed that propofol caused decrease in heart rate at induction in comparison to etomidate. The mean heart rate for propofol group at the time of induction is decreased (71.88 ± 9.51) as compared to the pre-induction (87.6 ± 10.61) in response to decrease in systolic blood pressure (Fig. 1). Our study corroborates with the findings of Das M et al [8] (pre induction heart rate of 82.2 ± 5.77 as compared to post induction heart rate of 75.93 ± 5.36). The probable mechanism of decrease in heart rate following propofol may be because it produces a resetting of the baroreflex mechanisms that enables a reduced HR to be sustained despite decreased 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].

Hypotension induced by propofol is mediated by inhibition of sympathetic nervous system and impairment of baroreflex regulatory mechanisms. Etomidate conversely maintains hemodynamic stability through preservation of both sympathetic outflow and autonomic reflexes.[12] Pensado A et al[3] did a study on haemodynamic effect of propofol during coronary artery bypass surgery. They showed that there was maximum decrease in systolic arterial pressure after 1 minute of administration of propofol. This finding correlates well with our study in which there was significant decrease in systolic blood pressure (113.88 ± 11.63 mmHg) from the baseline (135.12 ± 10.84 mmHg) after induction. Skinner et al[13] observed that there was a significant reduction in SBP following induction in the propofol group and a significant rise in SBP following intubation in the etomidate group which is similar to findings of the present study. 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 mean diastolic blood pressure (DBP) measured at various time intervals up to 5 min was on the lower side in the propofol group as compared to etomidate group in the present study. Clayes MA et al[4] showed that there were statistically significant decreases in diastolic arterial pressures 2 min after induction (19%) with propofol. This finding is consistent with present study, where statistically significant decrease in DBP of 15% was observed after induction with propofol. A study by Shah SB et al[14] found that in both propofol and etomidate group, there was a fall in DBP at 2 min and 3 min post induction. The fall in DBP was significant in propofol (27% and 30%) as compared to etomidate (17% and 16% respectively) which corroborates with the results 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. But in our study we found increase in DBP up to 5 minutes following induction. Colvin MP and colleagues[11] explained that the increased SBP and DBP with etomidate post induction might be due to its CNS stimulant action which maintains the BP directly or because of increased muscle tone which increases venous return and thus blood pressure. Recently, mechanism has been proposed that provides the basis for cardiovascular stability of etomidate. It is the capacity to bind and stimulate peripheral alpha-2B adrenergic receptors with a subsequent

vasoconstriction that is responsible for its stable haemodynamic profile. Alterations in the function or number of these receptors may account for abnormal responses during etomidate induction. [16]

The administration of propofol of 2.5mg/kg produced a maximum decrease in MAP after the induction (15%) ($p < 0.003$), which remained statistically significant throughout the entire study. Aggarwal S and colleagues [10] demonstrated a significant decrease in mean arterial pressure (MAP) from baseline at the time of induction with propofol as compared to etomidate where there was slight change in MAP. This finding is in correlation with our study where the MAP is lower than the baseline during induction in propofol group as compared to the etomidate group (Table 4). Our study is also comparable to Shivanna S et al [7] in which following induction there was a significant decrease in the variables compared to the baseline including mean arterial pressure (27 to 32%, $P = 0.001$). 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 $2 \mu\text{g}/\text{kg}$.

V. Conclusion

It can be concluded from the present study that 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. We therefore suggest that etomidate is a better option in patients particularly prone to hemodynamic fluctuation at induction like uncontrolled hypertension, septic, critically ill and patients with coronary artery disease.

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