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A Study on Hemodynamic Response During Induction with Etomidate, Propofol or Combination of Etomidate and Propofol in General Anaesthesia

Vasantha Kumar J[1], Lubna[2]

[1]Associate Professor [2]Post Graduate Student, Department of Anaesthesiology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka 560002, India.

Abstract

*Introduction***:** Patient's safety is the most important aspect of patient management in general anesthesia. Stress response during laryngoscopy and intubation leads to hemodynamic changes. In all the methods used for induction of anesthesia, it is aimed to preserve the hemodynamic balance and to provide optimal conditions by reducing the side effects. The purpose of this study was to compare hemodynamic response during induction with propofol, etomidate or combination of propofol and etomidate with special reference to pain on injection and myoclonus in patients requiring endotracheal intubation in elective surgeries. *Materials and Methods:* It is a prospective randomized comparative study. After getting ethical committee clearance, a group of ninety patients aged 18 to 65 years of either sex and ASA physical status I or II scheduled for elective surgery under general anesthesia were assigned randomly to Three Groups Group (P) was induced with Injection. Propofol (2 mg/kg) intravenously Group (E) with Injection. Etomidate (0.3 mg/kg) intravenously and Group (P + E) with Injection. Propofol (1 mg/kg) plus Injection. Etomidate (0.15 mg/kg) intravenously. Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Blood Pressure (MAP) and Oxygen Saturation (SpO_2) were noted at different time intervals. Presence of pain on injection and myoclonus were also observed. *Statistical Analysis:* Data will be analyzed by descriptive Statistics. Student's *t*-test was used to compare the significant difference between two means. ANOVA for three groups. The Chi-square test was used for categorical data such as gender, American Society of Anesthesiologist physical status, injection pain and myoclonus. A value of $p < 0.05$ is considered as statistically significant. *Results:* There was significant difference in mean HR ($p < 0.001$) between the 3 groups within 1–5 minutes of induction. MAP among all three groups decreases after induction and it was more in Group P than in Group E and Group P + E. The incidence of myoclonus in Group E was 80% while in Group P + E was 1.3% and none in Group P. The incidence of pain on injection in Group P was 86.7%, Group E was 10% and none in Group P + E. *Conclusion:* The incidence of hemodynamic instability, pain on injection, myoclonus is less with E + P group. Therefore, we concluded that combination of etomidate & propofol can be considered as valuable alternative as an induction agent.

Keywords: Etomidate; Propofol; Hemodynamics; Injection Pain; Myoclonus.

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Corresponding Author: Vasantha Kumar J, Associate Professor, Department of Anaesthesiology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka 560002, India.
E-mail: drvjk.yash@gmail.com

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Introduction

Anesthesia induction is commonly initiated by intravenous administration of induction agents. Anideal induction agent should have properties such as hemodynamic stability, minimal respiratory side effects, rapidclearance, minimal drug interactions etc. Over the years, there has been a continuous search for better and safer intravenous induction agents.

Propofol, an alkyl phenol derivative is one of the most widely used induction agents with rapid onset and short duration of action.[1] But it is associated with significant blood pressure reduction and decrease in systemic vascular resistance especially in volume depleted and cardiac patients.[2] A significant decrease in heart rate is also observed with this agent.[3] Many patients also report some degree of pain and discomfort with intravenous administration.[4] Etomidate is a hypnotic agent with minimal effect on cardiovascular system having a very stable hemodynamic profile.[5] But it has side effects like pain on injection and also myoclonus.[6] Rarely it can inhibit enzymatic synthesis if adrenal steroids which can last up to 6–8 hours even after single induction dose.[7] Patient's safety is the most important aspect of patient management in general anesthesia. Stress response during laryngoscopy and intubation leads to hemodynamic changes. In all the methods used for induction of anesthesia, it is aimed to preserve the hemodynamic balance and to provide optimal conditions by reducing the side effects.

With this background, we hypothesize that, with the use of average doses of combination of etomidate and propofol would reduce the hemodynamic deterioration. Therefore, the present study was designed to evaluate the effect of combination of both these drugs while used and the primary objective was to compare the hemodynamic parameters associated with etomidate propofol combination and sole use of each drugs. Secondary objective was defined as incidence of myoclonus and injection pain.

Materials and Methods

After obtaining approval from institutional ethical committee and informed written consent from each patient. 90 patients scheduled for elective surgery under general anesthesia in hospitals attached to Bangalore Medical College and Research Institute during the period from February 2019 to June 2019.

Patients aged 18–65 years, scheduled for elective surgeries under general anesthesia with endotracheal intubation, and patients belong to ASA class 1 & 2 were included in the study. Patient refusing to participate in the study, Patients with preexisting hypertension, IHD, on beta blockers, ASA physical status III and IV, patient with history of hypersensitivity to Propofol /Etomidate were excluded from the study.

Based on previous study, Meena K, et al.,[8] heart rate after two minutes of induction is taken in Group E was 96.37 ± 6.031 and and in Group P + E was 91.17 ± 6.747. To detect a minimum of difference of 5.22 beats/min.

Sample size is calculated using the formula,

$n = 2 (Z\alpha + Z_{1-\beta})^2 \sigma^2/d^2$

Where Zα = standard table value for 95% CI = 1.96

$Z_{1-\beta}$ = Standard table value for 80% Power = 0.84

σ = Standard Deviation = 40.8d = Effect Size = 5.22

$n = 26.4$

A minimum of 30 patients would be required in each group, keeping confidence interval (α) at 95% and power of study (β) at 80%.

Patients were randomly allocated into one of the Three Groups comprising 30 each, using numbers generated from www.random.org.

For induction, *Group P* received Injection. Propofol 2 mg/kg IV, *Group E* received Injection. Etomidate 0.3 mg/kg IV and Group *P + E* received Injection Propofol 1 mg/kg plus Injection. Etomidate 0.15 mg/kg IV.

A prior preanesthetic evaluation was done on the previous day of surgery. On arrival at Operation Theater, a 18G/20G intravenous (IV) cannula was secured in the nondominant hand and suitable intravenous fluid was started. Standard anesthesia care monitors were attached and baseline hemodynamic parameters were noted. Patients were premedicated with Inj. Glycopyrrolate 4 mcg/kg, Inj. Midazolam 0.03 mg/kg and Fentany l2 mcg/kg 2 minutes prior to induction and were preoxygenated with 100% oxygen for 3 minutes.

For induction Group P received Injection. Propofol 2 mg/kg IV, Group E received Injection. Etomidate 0.3 mg/kg IV, Group P + E received Injection Propofol 1 mg/kg plus Injection. Etomidate 0.15 mg/kg IV.

After induction, hemodynamic variables were recorded. One minute after loss of consciousness & inability to respond to verbal commands, Injection

Vecuronium (0.1 mg/kg) was given after which patient was ventilated with bag and mask. 3 minutes after the administration of muscle relaxant, laryngoscopy and endotracheal intubation was done using an adequately sized endotracheal tube. Depth of anesthesia was further maintained by isoflurane 1-1.5% and equal mixtures of oxygen-nitrous oxide (3–4 L/ min) along with intermittent bolus of vecuronium (0.02 mg/kg) as required throughout the surgery.

Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Blood Bressure (MAP) and Oxygen Saturation (SpO_2) were continuously monitored. Hemodynamic parameters before induction, after induction and at 1 minutes, 2 minutes, 3 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes after induction were recorded.

Statistical Analysis:

Data was entered in Microsoft excel and was exported into SPSS Version 21.0. Data was analyzed by descriptive Statistics; Student's *t*-test was used to compare the significant difference between two means. ANOVA was e used to compare the significant difference between three or more groups. The Chi-square test was used for categorical data such as gender, American Society of Anesthesiologist physical status, injection pain and myoclonus. A value of $p \leq 0.05$ is considered as statistically significant.

Results

The demographic features of the patients recruited in the three groups were comparable regarding age, sex and BMI ($p > 0.05$), Table 1. There is a statistically significant fall in heart rate in Group P at 2 minutes, 3 minutes and 5 minutes postinduction compared to other Two Groups ($p < 0.05$), Fig. 1. There is a significant fall in systolic blood pressure in Group P from 1 minute to 10-minute postinduction compared to others given ($p < 0.05$), Fig. 2.

There is a significant fall in diastolic blood pressure in group P from 3 minutes post induction which sustained up to 30 minutes ($p < 0.05$), (Fig. 3).

There is a significant fall in mean Arterial Blood Pressure (MAP) in Group P which started at 3 minutes and persisted upto 30 minutes when compared to other groups ($p < 0.05$), Fig. 4. The incidence of pain on injectionin Group P was 86.7% of total patients in that group, while it was 10% of patients in Group E and none in Group P + E (Fig. 5).

There was 80% incidence of myoclonus in Group E compared with Group P and Group P + E which were 0% and 1.3%, respectively, (Fig. 6).

Table 1: Demographic details of patients recruited in the present study

Demographic data	Group P	Group E	Group P + E
Age (years)	34.5	33.63	35.48
Gender (male/female)	14/16	15/15	13/17
BMI (Kg/M2)	21.76	21.95	21.43

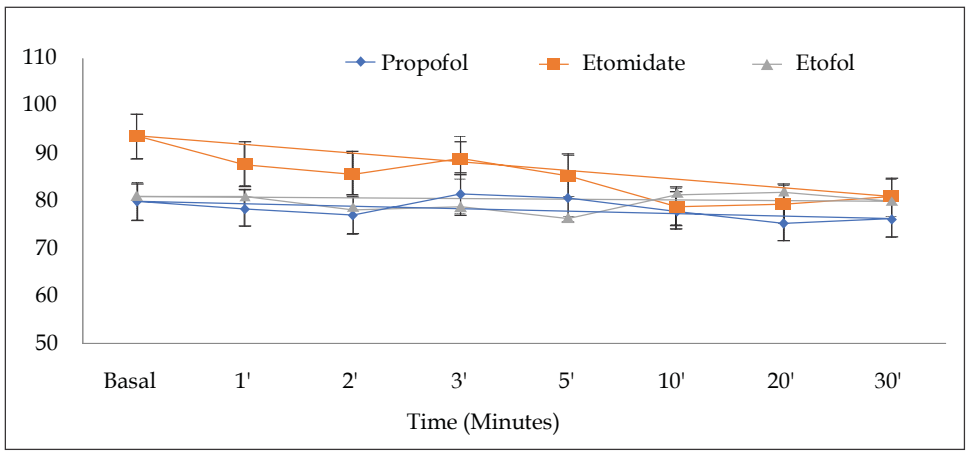

Fig. 1: Comparison of heart rate at different time interval in patients belongs to different groups

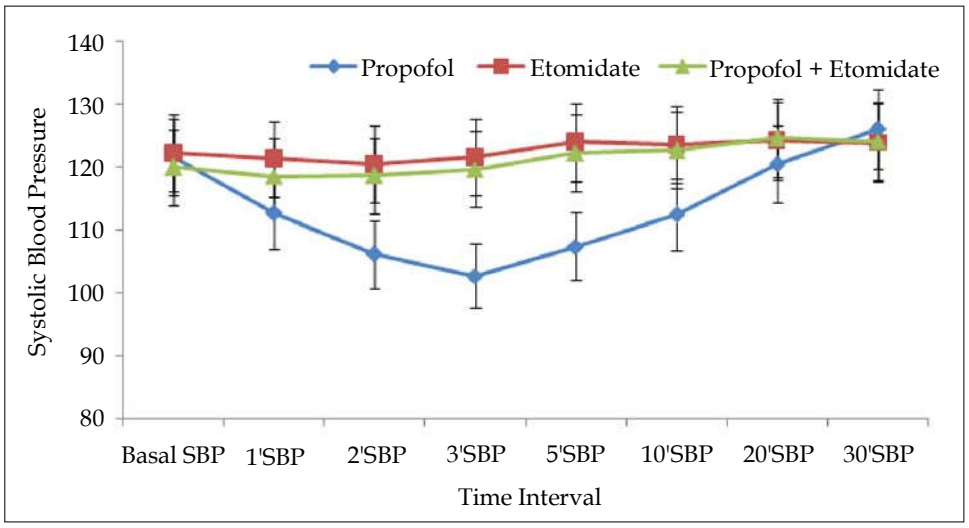

Fig. 2: Comparison of systolic blood pressure at different time interval of postinduction in patients belongs to different groups

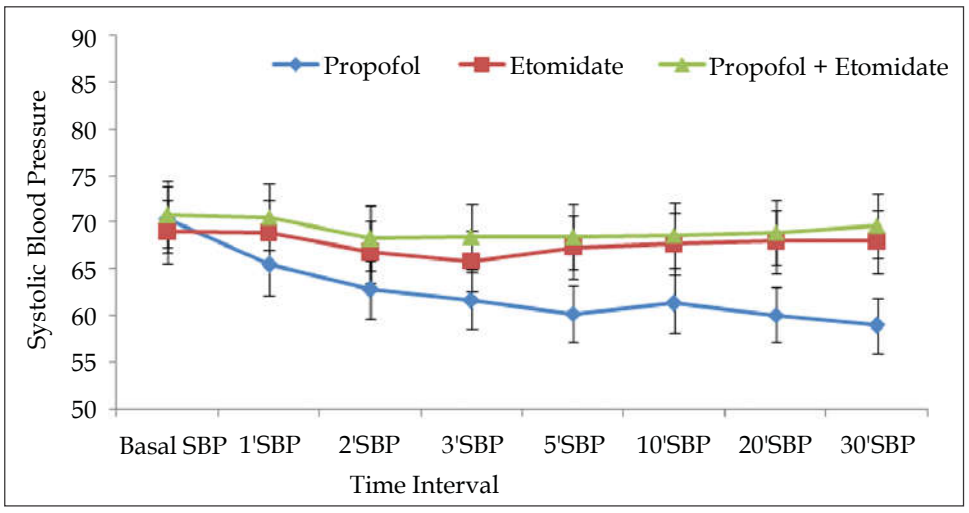

Fig. 3: Comparison of diastolic blood pressure at different time interval of postinduction in patients belongs to different groups

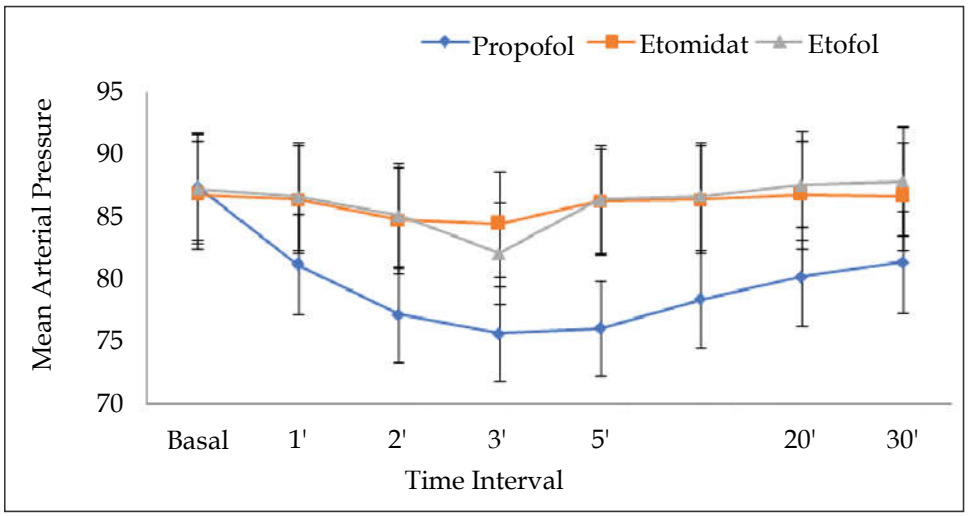

Fig. 4: Comparison of mean arterial blood pressure at different time interval of postinduction in patients belongs to different groups

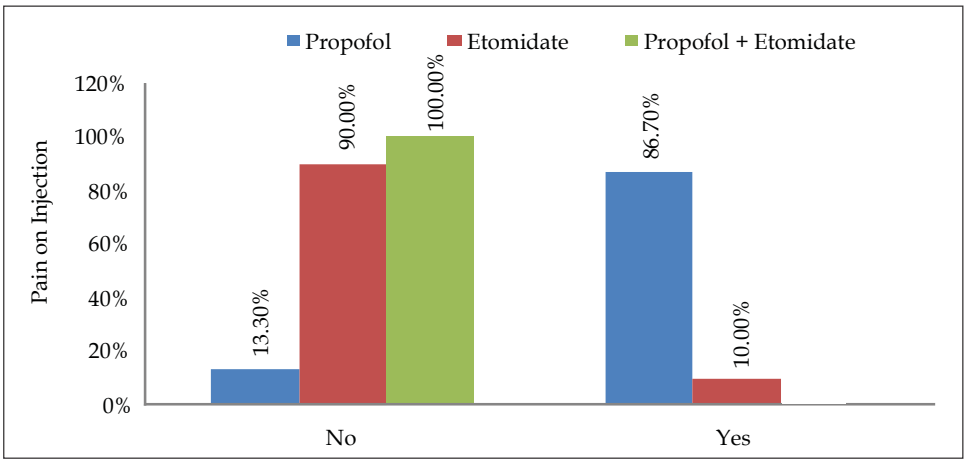

Fig. 5: Comparison of pain on injection at different time interval of postinduction in patients belongs to different groups

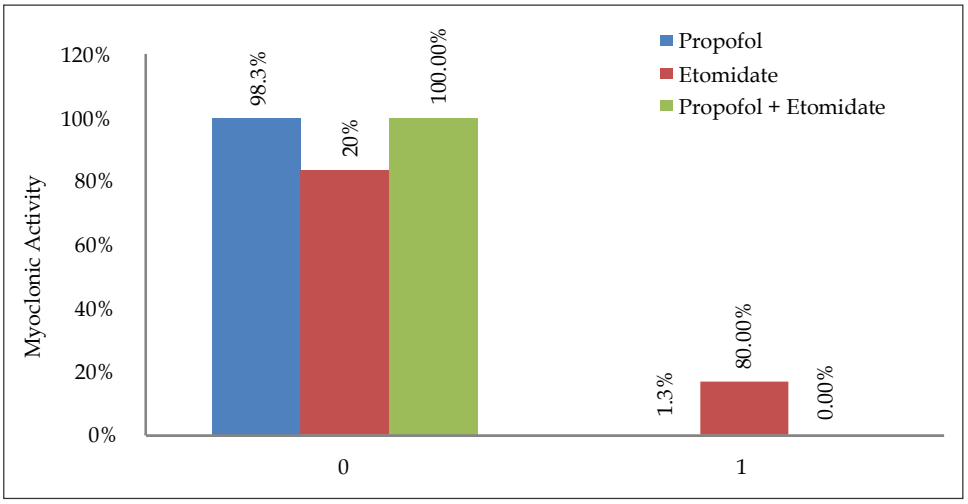

Fig. 6: Comparison of myoclonic activityat different time interval of postinduction in patients belongs to different groups

Discussion

Hemodynamic changes during perioperative period have become greater concern in modern day anesthesia. Hence, combinations of various anesthetic agents have been used for better hemodynamic stability and lesser adverse effects. In this study, we compared the hemodynamic effects of using combination of propofol & etomidate with each agent used separately for intravenous induction for general anesthesia. Pain on injection and presence of myoclonus were also observed.

Etomidate is an imidazoline group derivative known for its hemodynamic stability, had been widely used in various cardiac surgeries. It also causes pain on injection due to a solvent present in it. Propofol on the other hand is one of the commonest induction agents used in day care surgeries which also has pain on injection as a common side effect.

These two drugs were studied at Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Technology for availability for admixture. They reported that these drugs can be mixed and physically available for an admixture, which they named this admixture etofopol.[9] In our study, we included 90 patients of ASA 1 & 2 physical status who were to undergo general anesthesia and divided into three groups of 30 each as described above.

VS Rathore et al.[10] in 2019 compared etomidate, propofol and an admixture of etomidate and propofol (PE) as induction agents and noted

hemodynamic stability and side effects with each agent and admixture. They observed that there was a significant decrease in mean arterial pressure and diastolic blood pressure in propofol group postinduction which concurs with our study. However, the heart rate in all the three-group remained stable. Additional advantages like reduction in pain on injection and myoclonus were also observed with admixture.

In 2016, Meena K et al.[8] compared hemodynamic profile of etomidate, propofol and an admixture of etomidate and propofol (PE) as induction agents among 90 patients. They observed that Heart rate and mean arterial blood pressure in all study groups decreases after induction and it was more in Group I (Propofol Group) compared to Group II (Etomidate) and III (Etomidate + Propofol). However, there were increase in heart rate and mean arterial blood pressures after intubation in Group 11 and Group 111 which returned to baseline. In our study, there is a statistically significant fall in heart rate in Group P from 2 to 5 minutes postinduction. They concluded that combination proved to be significantly better than either propofol or etomidate alone.

In a study by Hosseinzadeh et al.,[11] comparing hemodynamic changes during placement of Laryngeal Mask Airway (LMA) using propofol, etomidate and etomidate-propofol combination where group one was given Inj. Propofol 2.5 mg/kg, Group Two received Inj Etomidate 0.3 mg/kg and Group Three 1 mg/kg Propofol + 0.2 mg/kg Etomidate. LMA placement was done after loss of eyelash reflex and no response to verbal command. The main finding of the study was that more stable hemodynamics was provided by combination of propofol and etomidate, even though the dose of both drugs is reduced in the combination which was similar to observations of our study.

In a study, performed by Yagan Ö et al.,[12] patients were randomly divided into three groups as Group P (n = 30, Propofol 2.5 mg/kg), Group E (n = 30, Etomidate 0.3 mg/kg) and Group PE (n = 30, Propofol 1.25 mg/kg + Etomidate 0.15 mg/kg). They found that Etomidate-propofol combination may be a valuable alternative when extremes of hypotensive and hypertensive responses due to propofol and etomidate are best to be avoided. There was no statistically significant difference between the groups with respect to injection pain. A significant difference was determined between Group P and Group E in terms of myoclonus incidence ($p < 0.05$). But in our study, we observed that there is statistically lower incidence on pain on injection with combination of etomidate and propofol with comparison to individual agents. The observation of incidence was comparable to their study.

In 2011, Fatma et al.[9] compared propofol etomidate, and combination of etomidate and propofol as induction agents and noted hemodynamic stability and side effects. They concluded that mean and SBP were significantly decreased in the propofol group compared to the etomidate and PE groups. The incidence of injection pain was significantly lower in the PE Group, although higher incidence of myoclonus activity was seen in etomidate group compared with propofol and PE Groups. In our study, pain upon injection with the admixture group was significantly lower than PE alone, and the incidence of myoclonus and changes in hemodynamic parameters were consistent with above study.

The combination reduces the pain on injection which can be attributed to the reduction in the lipid solvent and propofol concentration. It can also be attributed to bradykinin release which is reduced when combination is given.

Etomidate was found to be associated with higher incidence of myoclonic activity than any other induction agent. Certain agents like fentanyl, midazolam, dexmedetomidine as premedication have found to reduce the incidence of myoclonus. Even priming with etomidate before induction is also found to be useful in reducing incidence of myoclonus. There were only two patients in combination group who had myoclonus while induction.

In our study, it was concluded combination of etomidate and propofol causes less pain on injection compared with other two agents, and considerably reduced the incidence of myoclonus when compared with etomidate alone. The combination provides better hemodynamic stability and hence can be considered as valuable alternatives as an induction agent.

Conclusion

We concluded from our study that combination of etomidate and propofol can be considered as valuable alternative to other induction agents in view of hemodynamic stability and added advantages like decreases incidence of pain on injection and myoclonus

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Conflict of Interest: There is no conflict of interest.

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