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A Comparative Study Between Propofol And Etomidate In Patients Under General Anesthesia

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Abstract:
Background*: Induction of anesthesia is a critical part of anesthesia practice. Sudden hypotension, arrhythmias, and cardiovascular collapse are threatening complications following injection of induction agent in hemodynamically unstable patients. It is desirable to use a safe agent with fewer adverse effects for this purpose. Present prospective randomized study is designed to compare propofol and etomidate for their effect on hemodynamics and various adverse effects on patients in general anesthesia.*
Materials and Methods*: In this prospective randomised controlled study, 50 patients of ASA physical status I and II belonging to age group of 16-60 years undergoing general anesthesia were randomly allocated into 2 groups of 25 patients each, Group P (Propofol 2-2.5 mg/kg) and Group E (Etomidate 0.3 mg/kg).. The onset and duration of sensory and motor blockade, duration of postoperative analgesia, side-effects and haemodynamic parameters were compared between the groups.*
Results*: The mean age of patients in etomidate group was 32.6±8.48 years and in propofol group was 37.96±13.16 years. Mean heart rate, SBP, DBP, MAP was statistically significantly higher in etomidate group as compared to Propofol group. The proportion of side effects were higher in etomidate (group E) as compared to propofol (group P). The most common side effects were myoclonus, followed by nausea in etomidate group.*
Conclusion: *Etomidate provides better hemodynamic stability compare to propofol. Incidence of side effects are more common in etomidate as compare to Propofol. Myoclonus and vomiting were main side effects associated with use of etomidate.*
Key Word: *Propofol, Etomidate, General Anesthesia*

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I. Introduction

Ideal induction drugs for general anaesthesia must have stable hemodynamic profile, have a low risk of severe respiratory effects, & must be eliminated from body quickly. A reversible trinity of hypnosis, analgesia, & the cessation in reflex activity constitutes an effective global anaesthesia1. There has been an ongoing search for a more reliable and secure intravenous drug for a very long period. Etomidate and propofol are now the two most popular, fast-acting, and secure induction medications, however they have differing induction characteristics[1]. Etomidate, an inducing drug, was initially developed in 1964 and first used in therapeutic settings in 1972. It is also a fast-acting drug used to start and maintain anesthesia[2]. The Imidazole carboxylate etomidate is characterized by its distinguished hemodynamic stability. It somewhat protects the brain and just slightly slows breathing[3]. Due to its absence of effects on the sympathetic nervous system, baroreceptor reflex regulation system, and enhanced coronary perfusion, it is the recommended induction agent for cardiac patients[3,4]. It is the drug that is believed to have the lowest hemodynamic impact as comparing to other inducing drugs. In 1977, Propofol first time used in therapeutic context by Key & Rolly. Propofol is one of the drugs that is frequently used to induce general anaesthesia. This novel anaesthetic medication is distinguished by its quick onset of action, antiemesis, substantial inhibition of pharyngeal reflex, laryngeal reflex, & tracheal reflex, suitable depths of anaesthesia for intubation, with clear and painless recovery. It is a highly well-liked IV agent for induction nowadays[5]. The current study aims to compare hemodynamic & other effect of Etomidate and Propofol in adults under general anaesthesia.

II. Material And Methods

This prospective randomized interventional study was carried out on patients of Department of anaesthesiology, Katihar Medical College and hospital, Katihar, Bihar from March 2021 to March 2022. A total 50 adult subjects (both male and females) of aged ≥ 16, years were enrolled for in this study.

Study Design: Prospective randomized interventional study

Study Location: At Department of anaesthesiology, Katihar Medical College and hospital, Katihar, Bihar.

Study Duration: March 2021 to March 2022.

Sample size: 50 patients.

Subjects & selection method: The study population was drawn from patients undergoing general anesthesia. They were randomly allocated in two interventional groups as follows;
Propofol 2-2.5 mg/kg was administered to Group-P (n = 25).
Etomidate 0.3 mg/kg was administered to Group-E (n=25).

Inclusion criteria:
Patient posted for elective lower limb orthopaedic surgery

1. Age Group 16-60 years of Male and Female
2. ASA Grade I & II

Exclusion criteria:

1. Emergency surgeries
2. History of seizure disorder
3. Patient allergic to any study drugs
4. The use of steroids or the presence of confirmed primary or secondary adrenal insufficiency.
5. Presence of low blood pressure.
6. Patient suffering from epilepsy, COPD, and other co-morbid disorders.

Procedure methodology

Pre-anaesthetic examination was done with particular attention to the pulse rate. Blood pressures (systolic, diastolic and mean) recordings.

Apart from general physical and systemic examination, routine investigations, blood urea, serum creatinine, serum electrolytes, ECG and X- Ray chest were performed in all patients.

Upon arrival in the operation theatre, IV-line access was secured and lactate Ringer's infusion was started.

Monitoring included non-invasive blood pressure monitoring, Electrocardiogram and pulse oximeter.

Heart rate (HR), SYSTOLIC BLOOD PRESSURE (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded every minute for first three minutes, thereafter every 5 minutes till the completion of surgery.

Ten minutes prior to induction, the patients were premedicated with injections of fentanyl 2 mcg/kg IV, ondansetron 0.1 mg/kg IV,glycopyrrolate 0.2 mg IV, and midazolam 0.02 mg/kg IV. The end of induction was thought to be the loss of ocular reflexes. For three minutes, preoxygenation were performed with 100% oxygen.

Depending on group assignment, either propofol 2.0 mg/kg and etomidate 0.3 mg/kg was used to induce anaesthesia. Eye lash reflex loss was thought to be the final stage.

Propofol 2-2.5 mg/kg was administered to Group-P (n = 25).

Etomidate 0.3 mg/kg was administered to Group-E (n=25).

Prior to surgery, patients were informed to rate their discomfort during injections using the VAS scale. Myoclonus was also graded as well as its existence.

Endotracheal intubation was facilitated with inj. Vecuronium (0.1mg/kg body weight) after three minutes interval by same anaesthesiologist. The rate of breathing was kept under control at 12 to 14 cycles per minute, and the tidal volume was maintained at 8 ml/kg every breath. To keep the patient asleep, a 70:30 mixture of nitrous oxide & oxygen with 1% isoflurane was used. Vecuronium was given as needed at regular intervals.

Neostigmine 0.05 mg/kg and Glycopyrrolate 0.01 mg/kg were administered intravenously to reverse the residual neuromuscular block. Tracheal extubation was to follow after the patient had achieved adequate spontaneous tidal volume breathing and spontaneous eye opening. Vomiting and nausea after surgery were monitored for 24 hours in the patient.

Statistical analysis

The statistical analysis was performed using SPSS version 20.
To evaluate the significance of a difference between continuous data, an unpaired t test was used.

The format for continuous data was Mean+-standard deviation. Number and percentage were used to present categorical data. The significance of the difference between groups of categorical data was used to determine the chi square or fisher exact test.

III. Result

All 50 patients with ASA physical status I/II involved in the study who satisfied all inclusion criteria were randomly separated into two groups in the Department of Anaesthesiology, Katihar Medical College & Hospital, Katihar , Bihar. All the patients completed the study without any exclusion. The collected data were analyzed. The following observations are as follows:

Table no 1

	group	N	Mean	Std. Deviation	Std. Error Mean	p-value
Age (Years)	Propofol	25	32.64	8.485	1.697	.096
	Etomidate	25	37.96	13.167	2.633	.097
Weight (Kg)	Propofol	25	58.40	9.979	1.996	1.000
	Etomidate	25	58.40	11.934	2.387	1.000

Table 1: Comparison of baseline characteristics of study participants

The mean age of patients in Propofol group was 32.6 years and in etomidate group was 37.9 years. The mean weight in both the groups was 58.4 kg. There was no difference between mean age and weight in both the groups. About half of the participants in Propofol group were males and half females. Two-thirds of participants in etomidate group were males.

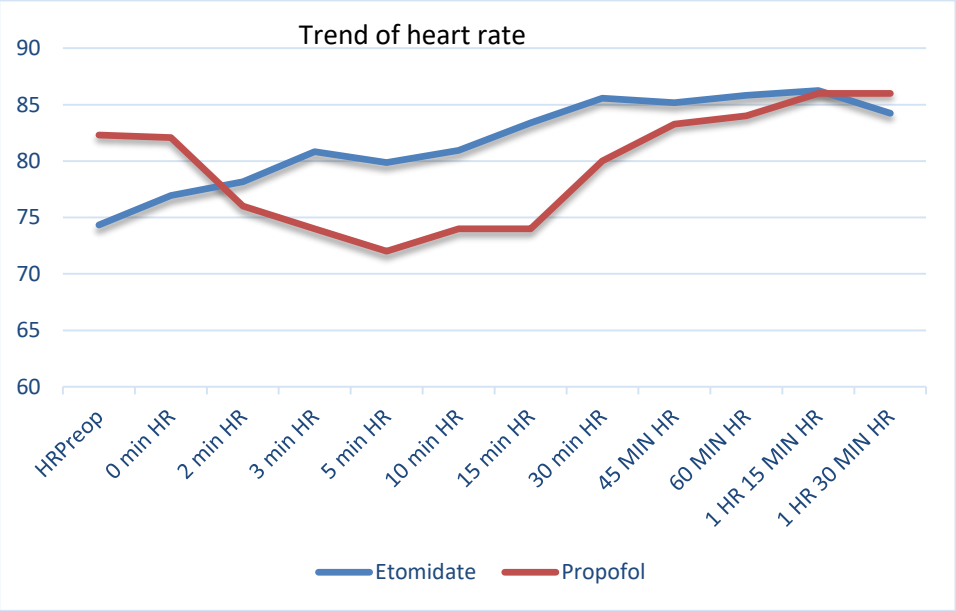

Figure 1: Line diagram showing trend of heart rate (mean) in both groups over 1.5 hours.

Mean heart rate was statistically significantly higher in etomidate group as compared to Propofol group during preoperative period and at 3 minutes. However at 15 minutes, 30 minutes, 60 minutes and 90 minutes, the mean heart rate of etomidate group was lower than Propofol group (p-value<0.05). Moreover, the heart rate was within physiological range at all points in the study. (Figure 1).

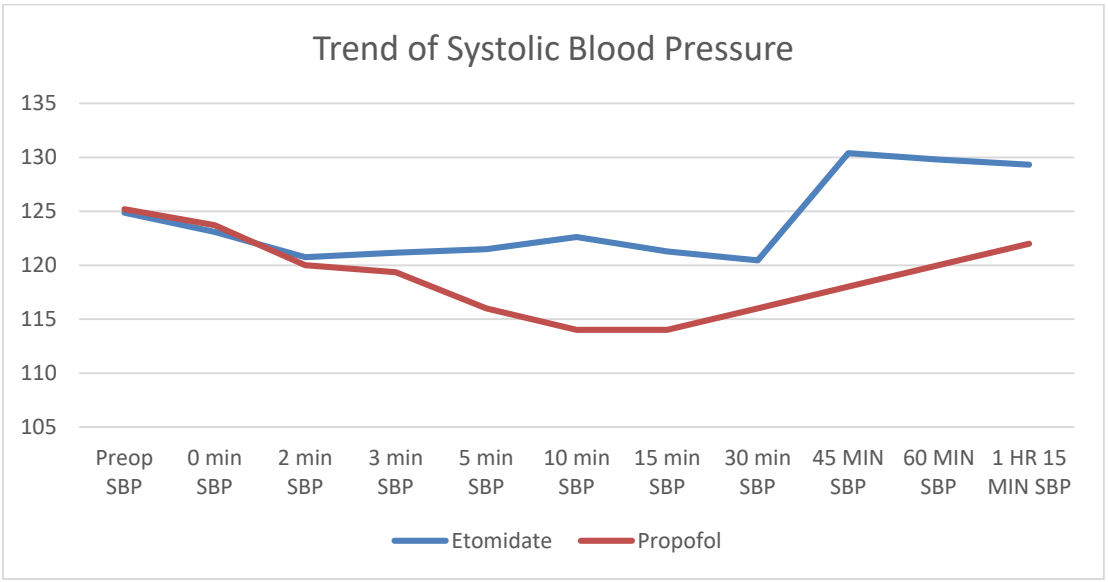

Figure 2: Line diagram showing trend of Systolic blood pressure (mean) in both groups over 2 hours.

The systolic blood pressure was lower in etomidate group as compared to Propofol group from 2 min, 5 minutes, 10 minutes till 90 minutes postoperatively (Figure 2).

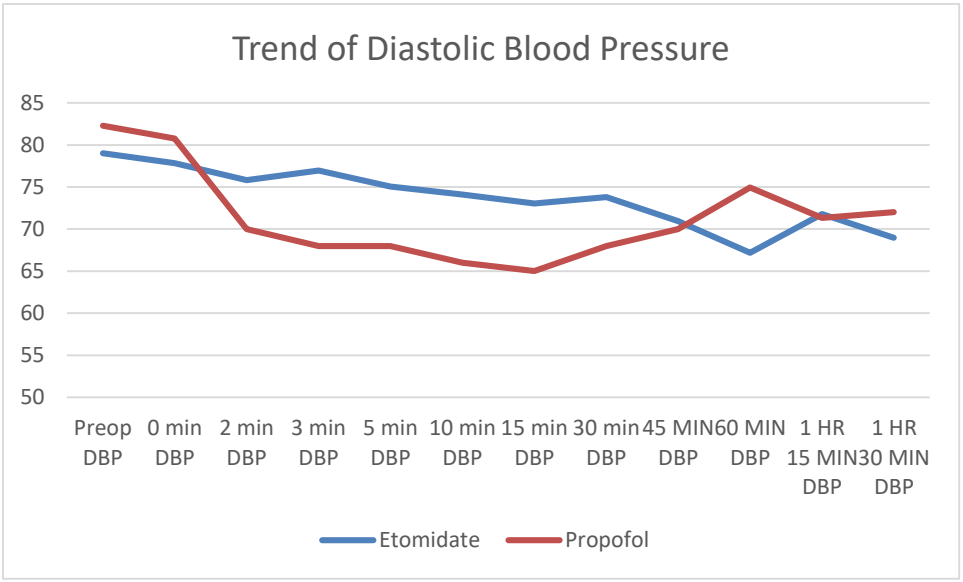

Figure 3: Line diagram showing trend of Diastolic blood pressure (mean) in both groups over 2 hours.

The diastolic blood pressure was within physiological limits throughout the study period. However, diastolic blood pressure in etomidate group was statistically lower than Propofol group at 15 minutes and 30 minute (Figure 3).

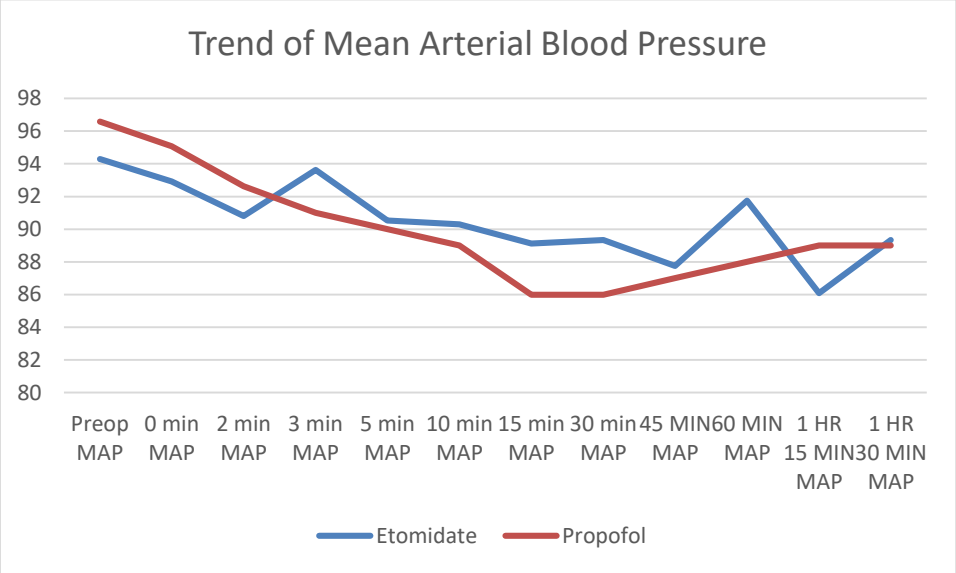

Figure 4: Line diagram showing trend of mean arterial blood pressure (mean) in both groups over 2 hours.

The mean arterial pressure was statistically lower in Propofol group at 10 minutes and till 1.30 hours in the study (Figure 4).

Table 2: Distribution of side effects in both the study groups

Side Effects	Group A	Group B	p-value
Myoclonus	9 (36%)	0	.00
Thrombophlebitis	3 (12%)	0	.23
Nausea	7 (28%)	2 (8%)	.066
Vomiting	3 (12%)	1 (4%)	.297
VAS for pain	6 (24%)	8 (32%)	.396

Table 2 shows that the proportion of side effects were higher in Propofol group as compared to Etomidate group. The most common side effects were myoclonus, followed by nausea in Propofol group. Among etomidate group, nausea was most common side effects. Myoclonus and thrombophlebitis was not observed in Etomidate group..

IV. Discussion

The current study was conducted on 50 patients with Propofol and etomidate as interventions. The objective of our study was to compare hemodynamic responses during induction and intubation with intravenous etomidate and Propofol and compare any side effects which occur thereafter. Patients from Department of Anaesthesia, Katihar Medical College were enrolled in the study and were divided into 2 groups based on the intervention received. Propofol (2,6-diisopropylphenol) has proven to be an excellent intravenous anesthetic because of its faster onset and rapid recovery, better intubation conditions, and minimal postoperative complications. The main disadvantage of induction with propofol is the decrease in systemic blood pressure and pain during injections. Another induction agent, etomidate, was introduced into clinical practice in 1972. It provides greater cardiac stability and a faster onset of action and rapid recovery. The main drawback was adrenal insufficiency and this drug was banned. A literature search of showed no evidence of adrenal insufficiency after single doses of etomidate. This revived interest in the drug. Therefore, the constant search for an ideal general anesthesia induction agent has continued. We conducted this study to compare the hemodynamic characteristics and side effects of both drugs during induction to choose a better induction agent for general anesthesia. In our study, demographic data in terms of age, weight, gender and nature of surgery were comparable in both the propofol and etomidate groups. In our study, the mean age of patients in Propofol group was 32.6 years and in etomidate group was 37.9 years. The mean weight in both the groups was 58.4 kg. There was no difference between mean age and weight in both the groups. About half of the participants in Propofol group were males and half females. Two-thirds of participants in etomidate group were males. Mean heart rate was statistically significantly higher in etomidate group as compared to Propofol group during preoperative period and at 3

minutes. However at 15 minutes, 30 minutes, 60 minutes and 90 minutes, the mean heart rate of etomidate group was lower than Propofol group (p-value<0.05). Moreover, the heart rate was within physiological range at all points in the study. The SBP was lower in etomidate group as compared to Propofol group from 2 min, 5 minutes, 10 minutes till 90 minutes postoperatively. The DBP was within physiological limits throughout the study period. However, diastolic blood pressure in etomidate group was statistically lower than Propofol group at 15 minutes and 30 minute. The mean arterial pressure was statistically lower at 10 minutes and till 1.30 hours in the study. The mean Spo2 was similar across both the study group within the study period. The mean respiratory rate lower in Propofol group as compared to etomidate group at 2 minutes till study end. The proportion of side effects were higher in Propofol group as compared to Etomidate group. The most common side effects were myoclonus, followed by nausea in Propofol group. Among etomidate group, nausea was most common side effects. Myoclonus and thrombophlebitis was not observed in Etomidate group. Our study findings we compared cross existing studies and many findings validate the findings of this study.

Most of the studies have enrolled patients with age group 30-45 years of age[6-9,12] including our study.

Similarly, the weight of participants were between 55-65 kg in many studies35,[7,8] including our study except Miner[9] and Ding T et al[10] who had enrolled heavier patients in their study. Propofol is currently the most popular intravenous general anesthetic with smooth induction, pleasant sleep, rapid recovery and minimal nausea and vomiting. Despite these positive properties, it also has adverse effects, such as injection pain, which can cause discomfort when anesthesia is induced. It was previously hypothesized that propofol may directly or indirectly interact with sensory nerve fibers located in the venous adventitia.

Many factors seem to influence the incidence of pain after propofol administration, few of which are vessel size, injection site, drug injection rate, propofol concentration in the aqueous phase, and blood buffering effects. The degree of pain also depends on the volume injected and the blood flow through the vein[11].

In the etomidate group, the addition of propylene glycol diluent to etomidate caused pain, which can be minimized by administration of etomidate and before use. of lignocaine or lignocaine. opioid through a large vein with a rapid intravenous infusion rate, as shown by Mayer et al[12] in 1996. Miner JR[13] found that 20% of 110 patients randomized to the etomidate group had myoclonic movements, indicating that myoclonus was much more frequently observed in patients receiving etomidate. Our results also correlate with those of Fatma S et al[14] which indicated that the prevalence of myoclonic activity was higher in the etomidate group. A study was conducted by Aggarwal S et al[15] also showed that myoclonic movements were observed only in the etomidate group and that propofol-induced patients did not show signs of myoclonus.

The hemodynamic stability observed with etomidate is due to its unique lack of effects on both sympathetic nervous system[54] and baroreceptor function, and its ability to bind and stimulate peripheral α-2B adrenergic receptors with subsequent vasoconstriction. There is a possibility. The reduction in systemic blood pressure after propofol bolus injection is dependent on both vasodilation with reduced preload and afterload and myocardial depression (negative cardiotonic effect)[16]

The neurological mechanism of myoclonus is unclear. There are only a few theories that suggest that this represents some kind of seizure activity, while other theories suggest that it is an inhibitory phenomenon, probably because high doses of etomidate reduce cortical activity before reducing subcortical activity[17].

Propofol-induced hypotension is mediated by inhibition of the sympathetic nervous system and impairment of baroreflex regulatory mechanisms. Conversely, etomidate maintains hemodynamic stability by maintaining both sympathetic outflow and autonomic reflexes[18].

Limitations of our study

Our results may not be applicable to other age groups in the population. Patients with severe comorbidities, hemodynamically compromised patients or patients with low cardiac reserve were not included in our study. However, based on the drug profile of etomidate, it is expected to show similar hemodynamic stability in such patients. Thus, it would be interesting to evaluate the effect of etomidate induction on hemodynamic parameters in these patients.

V. Conclusion

Our study shows that etomidate provides better hemodynamic stability than propofol when used as an induction agent in patients. Propofol causes more injection site pain than etomidate. . Incidence of side effects are more common in etomidate as compare to Propofol. Myoclonus and vomiting were main side effects associated with use of etomidate.

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