

ORIGINAL RESEARCH**A Prospective Randomized Comparative Study of Hemodynamic Effects of Etomidate vs Propofol During Induction and Intubation Under General Anaesthesia****Sarpatwar Sailesh¹, Boini Chiranjeevi²**¹Assistant Professor, Department of Anesthesiology, RIMS, Adilabad, Telangana, India.²Assistant Professor, Department of Anesthesiology, Govt Medical College, Siddipet, Telangana, India.**ABSTRACT**

Background:The aim of the study is to compare induction with etomidate and propofol on hemodynamic response to laryngoscopy and intubation.

Materials and Methods: The study was conducted in 60 ASA I & II patients in the age group of 18 to 60 years who were posted for elective surgeries under general anaesthesia. Their baseline heart rate, systolic blood pressure, diastolic blood pressure, SpO₂ and ETCO₂ were recorded. Both the groups were premedicated with iv glycopyrrolate 5mcg/kg, iv midazolam 0.025mg/Kg, iv fentanyl 2mcg/Kg. Following premedication, the above variables were again recorded. Group P patients were induced with iv propofol at the dose of 2 mg/Kg and Group E patients received iv etomidate at 0.4mg/Kg. In both the groups, Injection vecuronium was given at the dose 0.08mg/Kg and they were maintained with O₂:N₂O =33%:66% and Isoflurane 1% dial concentration. Laryngoscopy was performed by trained anesthesiologists after 5 mins. Duration of laryngoscopy was kept at a maximum of 10 seconds. Trachea was intubated with appropriate size endotracheal tube. The variables (HR, SBP, DBP, MAP, SpO₂) were measured during induction, intubation and post intubation at intervals of 1,2,3,5 and 10 mins.

Results: On comparing the two groups, the following results were obtained – Age, Sex, Weight and ASA status were comparable in both the groups. Propofol was found to produce hypotension in more or less 20%- 30% of patients irrespective of the underlying condition. Etomidate was found to maintain hemodynamic stability though there were no significant difference in heart rate variability in both the groups during laryngoscopy and intubation. Myoclonus was seen in 4 out of 30 patients induced with Etomidate, pain on injection was more common with Propofol. Apnea occurred in 12 out of 30 patients induced with Etomidate, 28 patients out of 30 in propofol group, vomiting and nausea are more with Etomidate than propofol but the difference was statistically insignificant.

Conclusion: As per the results of the study, Propofol produced more hemodynamic changes than Etomidate. Thus, we conclude that Etomidate is more stable in terms of hemodynamic stability.

Keywords: Etomidate, Propofol, Apnea, Myoclonus, vecuronium, laryngoscopy, Intubation.

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INTRODUCTION

The introduction of general anesthetics into clinical practice date back to 150 years. It stands as one of the pioneering innovations of medicine that lead to the development of modern

surgery and spawned the specialty of anaesthesiology. General anaesthesia can broadly be defined as a drug- induced reversible depression of the central nervous system resulting in the loss of perception to all external stimuli. It is usually defined as a triad of amnesia, analgesia, and muscle relaxation.

Since introduction of general anaesthesia, no ideal induction agent has been discovered which provides stable hemodynamic conditions during endotracheal intubation.

Airway management and patient safety is the most important aspect of patient management in general anaesthesia. Safest and gold standard method of protecting airway, delivering anaesthetic gases and protection against aspiration is securing airway with endotracheal tube.^[1,2]

An ideal induction agent should have hemodynamic stability and minimal intubation stress response, minimal respiratory side effects, rapid clearance. The laryngoscopy and intubation causes stress response leading to changes in hemodynamic parameters which can be detrimental to patients who are at cardiac risk.^[3]

These hemodynamic responses can affect myocardial perfusion in a negative way by increasing the myocardial oxygen demand and cardiac work load which can lead to ischemia. During intubation, stimulation of laryngeal and tracheal tissues causes catecholamine discharge which can cause an increase in sympathetico adrenergic activity causing an increase in heart rate and systemic arterial pressure. Uses of general anaesthetic agent with intravenous induction can often cause hypotension by many mechanisms. Most important are suppressive effects of these agents on myocardial contractility, baroreceptor activity, sympathetic activity and central nervous activity.

Propofol is most commonly used agent for induction in general anaesthesia. It is a short acting IV anesthetic agent but it causes hemodynamic instability by causing profound hypotension. It also causes pain on injection. Allergic reactions are also being documented.

Etomidate is recently added drug to induction agent and being used in common practice in recent days due to its cardio stable nature.

It also has side effects like nausea, vomiting, increase in epileptogenic activity in patient with seizures, myoclonic activity. Rare but most important side effect of etomidate is decrease in serum cortisol by inhibition of 11 – beta–hydroxylase enzymes even after single dose for up to 24 hours but this decrease was found to be within physiological range.^[4]

The primary objective of this study was to compare the efficacy of two different induction agents (Inj. Propofol and Inj. Etomidate) in maintaining hemodynamic stability during induction and following endotracheal intubation in elective surgery.

Aim & Objectives

To compare the effect of intravenous induction agents propofol and etomidate in maintaining hemodynamic stability during and after endotracheal intubation.

Objectives

- To assess the effect of the induction agent on the variation in heart rate during laryngoscopy and intubation.
- To assess the variation of blood pressure during laryngoscopy and intubation.

MATERIALS & METHODS

Study Centre: Osmania medical college, government ent hospital, koti. Osmania general hospital, afzalgunz, hyderabad. Mnj cancer hospital, lakidikapul and government maternity hospital, petlaburz.

All the hospitals affiliated to Osmania Medical college, with ethical committee approval and consent from patient.

Duration of the Study: December 2017 – September 2019.

Study design: Randomized double blinded controlled interventional study.

Method: After institutional ethical committee approval, study was conducted in sixty patients between 18-60 years of age, of either sex, weighing 40 to 80 kg and ASA grade I or II scheduled for elective surgeries under general anaesthesia after obtaining informed consent from the patients.

Sample Size: Based on a previous study by Masoudifar et al, it was seen that patients who received propofol (26%) had hypotension following intubation compared to etomidate (8%). Based on this study, the sample size was calculated using n Master 2.0 software with an alpha error of 5% and power of 80%. Sample size was found to be 76, rounded off to 30 per group to account for dropouts. over all sample size is 60 with etomidate group 30 and propofol group 30.

Analysis Plan: Collected data were analyzed using statistical package SPSS version 21.0

Inclusion Criteria

- 18 – 60 years of either sex
- Weight 40 to 80kgs.
- ASA grade I and II.
- Mallampati grade I and II.
- Elective surgeries

Exclusion Criteria

- Patient refusal.
- Emergency surgeries.
- Patients with cardiovascular diseases like ischemic heart disease (IHD) and hypertension.
- ASA grade 3 and above
- Pregnant lactating and menstruating women
- Existence of considerable pathology in pharynx/larynx.
- Patients on beta blockers and antihypertensive medication.
- Diabetic patients.
- Known history of allergy to propofol or etomidate.
- History of seizure disorder

Preoperative Preparation

All the patients were subjected to basic haematological and biochemical investigations which included hemoglobin, total count, differential count, platelet count, renal and liver function tests, random blood sugar. 12 lead ECG, chest x ray and USG abdomen were also taken for all the patients.

The patients were kept nil per oral for 8 hours before surgery. All the patients were given tablet Alprazolam 0.25 mg and tab Metoclopramide 10 mg on the night before the surgery. Tab Pantoprazole 40 mg and tab metoclopramide 10 mg on the morning of surgery given at 6 am with sips of water.

On arrival to the preoperative room, informed consent was obtained for the participation of the patient in the study. The patients were randomly allocated into two groups by sealed envelope technique into:

GROUP P–Propofol 30 patients

GROUP E- Etomidate 30 patients

Patient was shifted to the operation theatre by trained personnel on a trolley.

RESULTS

The data collected was analyzed using SPSS software version 21 (statistical package for social science). Continuous variables were given by means with standard deviation. Categorical variables were given by frequency and percentages. Student t-test was used for testing the significance of all the variables, means and standard deviation. Chi – square test was used to compare the proportions. All the statistical results were considered significant at the p value of less than 0.05.

Table 1: Gender Distribution

	Propofol		Etomidate		Total	
	No	%	No	%	No	%
Male	15	50.00	16	53.33	31	51.67
Female	15	50.00	14	46.67	29	48.33
Total	30	100	30	100	60	100
Sex Ratio(Male: Female)	15: 15		16: 14		31: 29	
p-value	0.80* (Not Significant)					

*P value >0.05 Not Significant

Propofol and Etomidate groups were comparable with respect to gender distribution. Male and female were more or less equally distributed in both the groups. There were 15 males and 15 females in the propofol group and 16 males and 14 females in the etomidate group. The P value was 0.08 therefore statistically not significant.

Table 2: Age Distribution

Age	Propofol		Etomidate	
	Number	%	Number	%
20 – 30	17	56.67	9	30
30 – 40	7	23.33	9	30
40 – 50	6	20	12	40
Total	30	100	30	100
Mean ± SD	32.03±14.07		33.07±10.01	
p-value	0.074*(NotSignificant)			

*P value >0.05 Not Significant

Patient in the age group of 20 to 50 years were included in the study. Propofol group had a mean age of 32.03 ±14.07 years and Etomidate group with the mean age of 33.07± 10.01 years. The mean age was comparable in both the groups with a P value of 0.074.

Table 3: Weight

Propofol		Etomidate		p-value
Mean	SD	Mean	SD	
60.03	6.52	61.67	6.98	0.06*

*P value >0.05 Not Significant

With respect to weight both the groups were comparable with each other. Mean weight of propofol group is 60.03±6.52 and etomidate 61.67±6.98 the p value is 0.06 which is statistically not significant.

Table 4: Asa Grade

ASA grade	Propofol		Etomidate	
	No.	%	No.	%
1	12	70.00	11	36.67
2	18	30.00	19	63.33
Total	30	100	30	100
p-value	0.79* (Not Significant)			

*P value >0.05 Not Significant

American society of Anaesthesiologist physical status were comparable in both the groups with the p value of 0.79. Thus statistically not significant.

Table 5: Heart Rate

Variables	Propofol		Etomidate		p- value
	Mean HR	SD	Mean	SD	
Pre-op	76.50	10.04	80.33	9.42	0.13*
Pre-Medication	73.37	9.35	78.27	9.29	0.05
Induction	79.47	11.62	79.23	9.64	0.93*
Intubation	85.83	20.14	86.07	8.71	0.95*
1 Min	91.43	13.17	85.33	7.93	0.03
2 Min	90.20	12.73	82.40	9.48	0.01
3 Min	89.67	9.46	82.40	9.92	0.01
5 Min	88.07	9.47	82.23	10.40	0.03
10 Min	85.27	11.84	80.70	8.95	0.10*

.p value < 0.05: Significant * p value > 0.05 : Not Significant

Heart rate in both propofol and etomidate group increased after intubation compared to the values at induction. In the propofol group, the heart rate increased by seven to twelve beats per minute. In the etomidate group the heart rate increased by three to seven beats per minute, which was measured during intubation and 1,2,3, and 5 mins after intubation. The difference was statistically significant.

Table 6: Systolic Bloodpressure

Variables	Propofol		Etomidate		p- value
	Mean SBP	SD	Mean SBP	SD	
Pre-Op	126.20	9.07	128.40	7.67	0.32*
Pre-Medication	121.13	9.93	123.43	7.31	0.31*
Induction	111.17	9.05	122.27	6.36	0.001
Intubation	114.77	12.09	128.07	7.75	0.001
1 Min	107.57	18.03	123.20	7.36	0.001
2 Min	97.03	8.34	119.03	8.60	0.001
3 Min	95.43	6.71	116.20	6.66	0.001
5 Min	94.57	5.35	116.37	7.37	0.001
10 Min	97.70	7.95	116.60	7.18	0.001

.p value < 0.05: Significant * p value > 0.05 : Not Significant

When compared with systolic blood pressure values at the induction, there was a greater change in the propofol group at intubation as well as 1, 2, 3, 5 and 10 mins after intubation. The difference was statistically significant with respect to the etomidate group during the same period with a p value of <0.05.

Table 7: Diastolic Blood Pressure

Variables	Propofol		Etomidate		p- value
	Mean DBP	SD	Mean DBP	SD	
Pre-Op	75.30	10.38	80.23	10.27	0.07*
Pre-Medication	72.80	9.83	77.10	8.86	0.08*
Induction	67.03	7.65	74.33	8.52	0.001
Intubation	65.57	15.27	79.87	10.87	0.001
1 Min	63.17	7.00	75.93	9.66	0.001
2 Min	60.30	5.60	73.87	8.46	0.001
3 Min	58.53	5.26	71.90	7.10	0.001
5 Min	60.10	6.31	71.83	6.37	0.001
10 Min	62.10	4.91	71.17	5.94	0.001

.p value < 0.05: Significant * p value > 0.05: Not Significant.

Following intubation the change in diastolic blood pressure was more in propofol group compared to etomidate group with respect to the values at induction. The difference between the two groups was statistically significant with the p value of < 0.05.

Table 8: Mean Arterial Blood Pressure

Variables	Propofol		Etomidate		p- value
	Mean MAP	SD	Mean MAP	SD	
Pre-Op	92.20	9.41	96.30	8.60	0.08*
Pre-Medication	88.87	9.02	93.07	7.30	0.05
Induction	80.20	11.28	90.60	7.21	0.001
Intubation	82.03	12.01	95.97	8.74	0.001
1 Min	78.33	8.10	91.63	7.94	0.001
2 Min	72.50	5.31	88.90	7.09	0.001
3 Min	70.87	4.81	86.70	5.37	0.001
5 Min	71.57	5.39	86.67	6.09	0.001
10 Min	73.93	4.76	86.37	5.14	0.001

.p value < 0.05 : Significant * p value > 0.05 : Not Significant

Mean arterial pressure is diastolic blood pressure + 1/3 of systolic blood pressure. The trend in Mean Arterial Pressure was similar to the trend in diastolic blood pressure. After intubation and 1, 2, 3, 5 and 10 mins afterwards the mean arterial pressure values were compared in etomidate as well as propofol groups. The mean arterial pressure decreased by maximum of 9 mm of Hg in propofol group, whereas the mean arterial pressure decreased by maximum of 4 mm of Hg in etomidate group. The difference between the two groups was statistically significant with p value of <0.05.

DISCUSSION

Rapid induction and hemodynamic stability with minimal side effects are the most important characteristics desired from an ideal induction agent.

In this study we compared the hemodynamic response to endotracheal intubation using etomidate and propofol as induction agents in 60 patients with 30 patients in each group, within the age group of 18- 60 years of either sex, weighing 40-80 Kg.

Regarding the underlying variables such as gender, age, weight and ASA physical status of the patients, there was no significant difference, thus the compounding effects of these variables had been neutralized. Regarding the weight, the propofol group had a mean of

60.03, and etomidate group had a mean of 61.03 but this difference between the groups, was not statistically significant.

The baseline and premedication values of systolic blood pressure, diastolic blood pressure, mean arterial pressure, were comparable in both the groups [Table6,7&8]. Following intubation with propofol, there were significant changes in systolic blood pressure, diastolic blood pressure and mean arterial pressure compared to etomidate group and p values at various time intervals remained significant (<0.05). This hypotension with propofol due to decrease in preload, was managed with fluids, and by decreasing concentration of inhalation agent.

Hug et al,^[5] conducted a study in 25,000 patients, he found out that propofol caused bradycardia in 4.2% patients and hypotension in 15.7% patients. In our study there was no incidence of bradycardia but significant hypotension occurred in 6 patients out of 30 patients which is around 20% which is comparable with the above study.

The effect of etomidate and propofol on heart rate is controversial. According to studies of Siedy J et al,^[6] Ghafor et al,^[7] and Kaur et al,^[8] Mean heart rate was comparable in both the groups. Heart rate may increase or decrease, or these changes can be minimal following induction with these agents. The reason for this difference is not clear.^[9,10]

Shah et al,^[11] reported sustained increase in heart rate with Propofol. In our study, the change in heart rate was not much significant at induction and intubation in both the groups but etomidate was found to maintain heart rate within range of 3-7 beats per minute at 1,2,3,5 mins following intubation [Table5].

In the study of Kahlon A et al,^[9] they found that etomidate caused myoclonus around 76% in placebo group, 44% in lignocaine group and 28% in midazolam group . In our study myoclonus was observed in 4 out of 30 patients (13.33%) who were induced with etomidate, while no equivalent signs were noted in propofol group. This finding correlates with the above study.

Picard P et al,^[10] did a study on 6264 patients which showed that on an average, 70% of patients complained, pain on injection. In our study, 22 patients out of 30 patients complained of pain on injection(73.33%).

Shah et al, Masoudifar and Beheshtian, Aggarwal et al, Meena Kumari, all the above studies showed that the changes in systolic blood pressure,^[11-14] diastolic blood pressure and mean arterial pressure were less in etomidate group compared to propofol group which is in total agreement with our study [Table 6,7 &8].

There was no statistically significant incidence of nausea and vomiting in both the groups. No other complications were noted in both etomidate and propofol group.

Limitation of the study

The study design had some limitation. We did not measure plasma cortisol and adrenocorticotrophic hormone level due to non-availability of the above tests in our institution.

CONCLUSION

As per the results of the study, Propofol produced more hemodynamic changes than Etomidate. Thus we conclude that Etomidate is more stable in terms of hemodynamic stability.

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