

# To Evaluate and Compare the Efficacy of Propofol, Etomidate as Induction Agent in Maintaining Haemodynamic Stability in Elective Surgery Under General Anaesthesia

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DOI: 10.29322/IJSRP.10.03.2020.p9906

<http://dx.doi.org/10.29322/IJSRP.10.03.2020.p9906>

## **ABSTRACT**

Hemodynamic stability at the time of induction of anaesthesia and during surgery has been major concern for the anaesthetist of both ancient and modern era's .Induction agent's causes vasodilatation, myoclonic seizures, nausea and vomiting and attenuation of axis thereby decreasing blood pressure. The aim and objective of this study is to evaluate the hemodynamic effect of etomidate and propofol and as induction agents in elective surgeries under general anaesthesia.

To observe any postoperative adverse effects such

To observe any postoperative adverse effects such as nausea , vomiting or seizures with propofol and etomidate as induction agent.

## **INTRODUCTION**

Hemodynamic stability at the time of induction of anaesthesia and during surgery has been a major concern for the anaesthetist of both Ancient and modern eras. The maintenance of hemodynamic stability during induction of anaesthesia is dependent on both basal tone of the autonomic nervous system and also importantly influenced by baroreceptor reflex regulation of autonomic outflow influencing cardiac function and peripheral vascular resistance.<sup>(1)</sup>

Direct laryngoscopy and intubation produces marked circulatory effects known as pressor response, characterised by a sudden increase in heart rate and altered rhythm. Pressor response to laryngoscopy and intubation is documented fact in patients, under a variety of anaesthetic techniques. <sup>(2-3)</sup>

The effects of laryngoscopes and intubation on the cardiovascular system were noted early that the cardiac reflex could originate in the trachea, larynx and bronchi. These reflexes were named vasovagal since both the afferent and efferent paths of the reflex were assumed to the vagus nerve, however In 1990 concluded that these changes could be attributed to the stimulation of cardio accelerator nerves implying an increase in the cardiac sympathetic tone rather than vagal stimulation .This response is due to an increase in cardiac output rather than an increase in systemic vascular resistance. <sup>(4)</sup>

It is proposed that the mechanism of hemodynamic and catecholamine response to or tracheal intubation is that of somato-visceral reflex. Direct laryngoscopy activates proprioceptors at the base of the tongue which leads to hypertension, tachycardia and other

arrhythmia in proportion of magnitude of stimulus. Subsequent intubation stimulates the receptors in larynx and trachea with enhancement of hemodynamic and epinephrine response<sup>(5)</sup>

The mean increase in arterial pressure due to laryngoscopy and intubation may be upto 20-25 mmHg. This peak response occurs approximately 30-35 sec after laryngoscopy. These cardiovascular changes due to direct laryngoscopy and intubation are transient, variable and unpredictable and usually well tolerated by healthy individuals, however these changes may be fatal in patients with hypertension, coronary artery disease or raised intracranial tensions.

It was also demonstrated that there is an increase in concentration of catecholamines like adrenaline and non adrenaline in response to the stimulus of laryngoscopy and intubation<sup>(6)</sup>

Wide range of intravenous induction agents of anaesthesia is now available. Thiopentone, propofol, etomidate, ketamine are used for induction to lower the stress response to laryngoscopy and intubation and to maintain better hemodynamic stability at the time of induction and during surgery.

Induction agents cause vasodilatation, myoclonic seizures, nausea, vomiting and attenuation of Autonomic Nervous System thereby decreasing blood pressure. Each intravenous anaesthetic induction agent affects hemodynamic changes differently. Thiopental is a commonly used induction agent.

In this study, we aim to evaluate the hemodynamic effects of propofol and etomidate in order to find the better hemodynamic stability during induction, laryngoscopy, intubation and during surgery under general anaesthesia in elective surgeries.

## **MATERIAL AND METHODS**

This randomized double blind clinical study was conducted in the department of anaesthesia National institute of medical sciences Rajasthan jaipur, after approval from Institutional Ethical Committee ,on 60 patients aged between 18 to 60 years of either sex , ASA physical status I and II undergoing elective surgery lasting for approximately 2 hrs under general anaesthesia. Written informed consent was taken from all patients. The patients were randomly divided into three groups. Randomization was done by computer generated random numbers tables.

Group I induction with inj.propofol (2mg/kg IV)

Group II induction with inj.etomidate (0.3mg/kg IV)

Patient having following criteria were excluded from the study

- 1) Cardiac, hepatic and renal disease
- 2) Respiratory diseases
- 3) Known hypertensive
- 4) Known diabetic
- 5) Epilepsy
- 6) Pregnant patients
- 7) Known case of difficult airway (MP grade III and IV)

Baseline heart rate (preoperative) systolic blood pressure (SBP) diastolic blood pressure (DBP) mean blood pressure (MBP) and oxygen saturation (SPO2) and end tidal carbon dioxide (ETCO2) were noted.

The patients were kept nil per oral for 8 hours prior to the surgery. All patients were premedicated with tab.alprazolam 0.25mg; tab Ranitidine 150mg at night before surgery and in the morning. All patients received inj.glycopyrolate 0.2mg i.v.In preoperative ward prior to the surgery. On arrival at operation theatre standard anaesthesia monitors including pulse oxymetry, electrocardiogram, non invasive blood pressure (NIBP) was attached and hemodynamic parameters were recorded. A 18 G intravenous cannula was secured and ringer lactate infusion was started. Inj midazolam 0.025 mg/kg iv and inj. Nalbuphine 0.1mg/kg was given 2 minutes before

induction. Group I received inj. Propofol 2mg/kg iv and group II etomidate 0.3mg/kg iv. All study drugs were prepared by an anaesthesiologist who was blinded to the details of the study. Volume of medication and speed of injection were equal in all three groups. After induction of anesthesia, hemodynamic variables were recorded. Inj rocuronium 1-2mg/mg given. Laryngoscopy and endotracheal intubation was done by experienced anaesthesiologist. Duration of laryngoscopy was kept less than 10 seconds. Trachea was intubated with adequate size of endotracheal tube. Proper placement of ETT was confirmed by capnography and bilateral auscultation of chest. Following successful placement of ET tube anesthesia was maintained by isoflurane 1-1.5% and equal mixture of oxygen-nitrous oxide (4 L/min) along with intermittent bolus of rocuronium as required throughout the surgery. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and oxygen saturation were continuously monitored and recorded before induction and after induction at 1 minute, 2 minute, 5 minutes, 10 minutes, 20 minutes, 30 minutes, 60 minute by the anaesthesiologist who is blinded to the study.

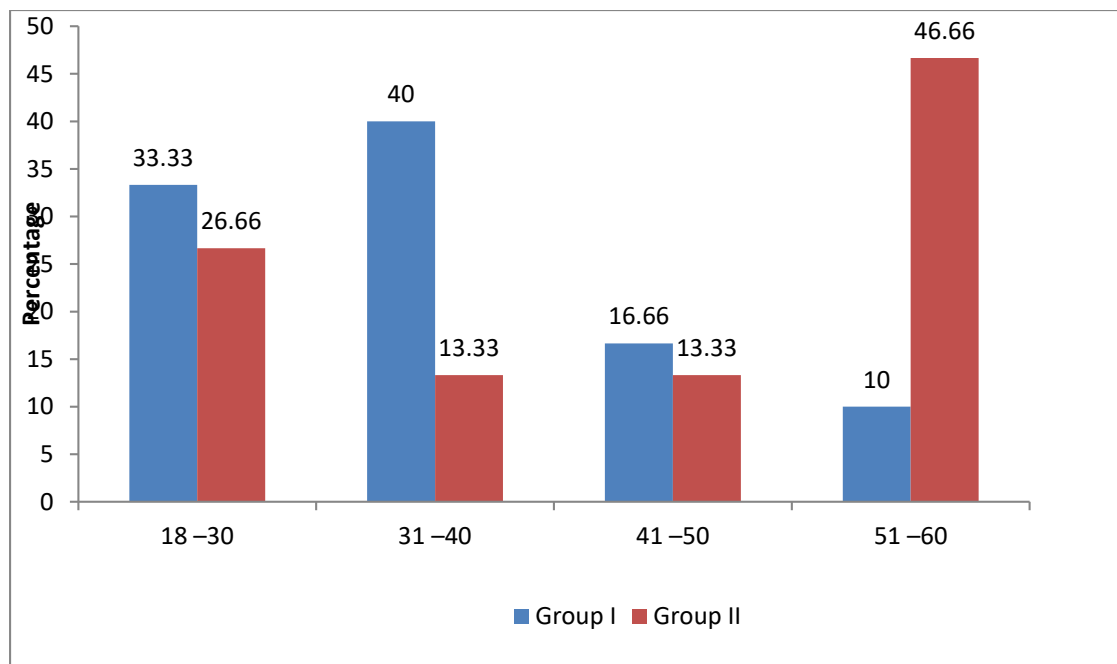
**OBSERVATIONS AND RESULTS**

This prospective randomized double blind study was carried out on 60 patients between the age group 18-60 years at MIMS, Rajasthan Jaipur to evaluate the hemodynamic effects of etomidate and propofol as induction agent in elective surgeries.

**Age distribution of patients in different groups**(Table 1)

Age(in years)	N	Group I (n-30)		Group II (n-30)		x <sup>2</sup>	p-value
		F	%	F	%		
18 –30	10	33.33	8	26.66	8	11.45	0.009
31 –40	12	40	4	13.33	4		
41 –50	5	16.66	4	13.33	4		
51 –60	3	10	14	46.66	14		

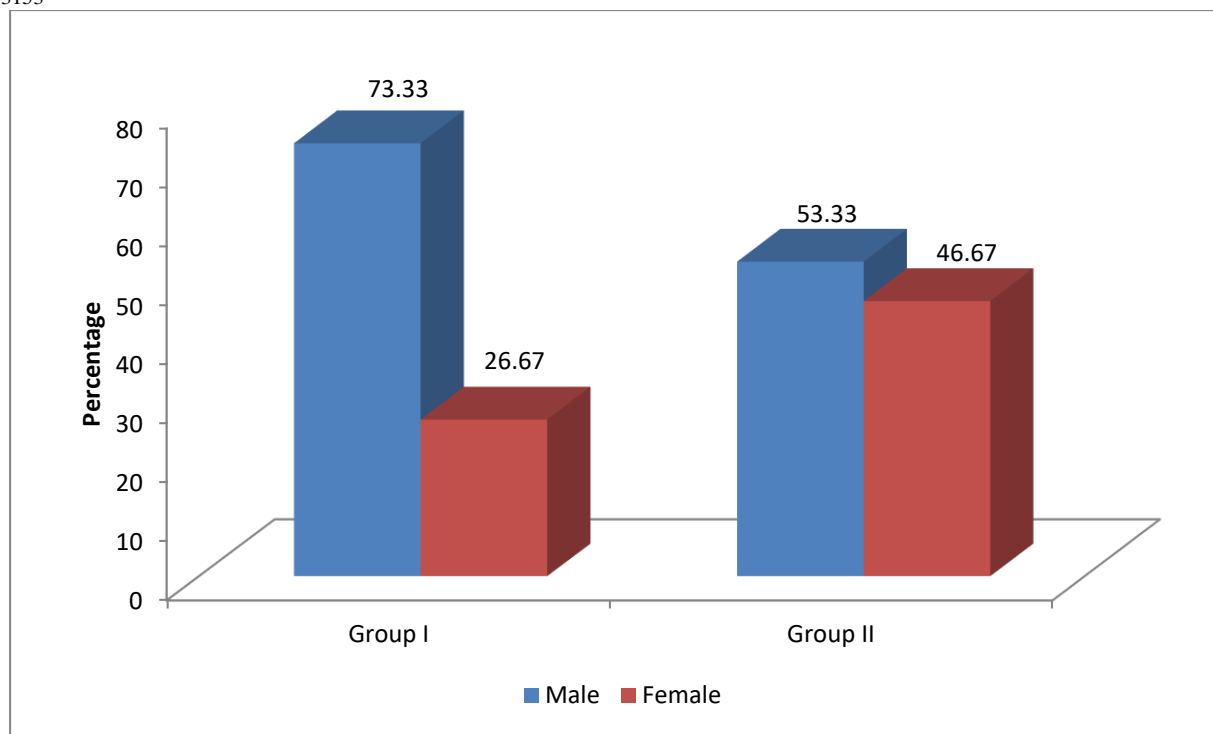
As evident from the table age of the patients was comparable both the groups.(p=0.990). The minimum numbers of patients were in the age group of 41- 50 years.



**Distribution of patients in different groups according to gender** (Table 2)

Gender	Group I (n-30)		Group II (n-30)		x <sup>2</sup>	p-value
	F	%	F	%		
Male	22	73.33	16	53.33	2.58	0.107
Female	8	26.67	14	46.67		

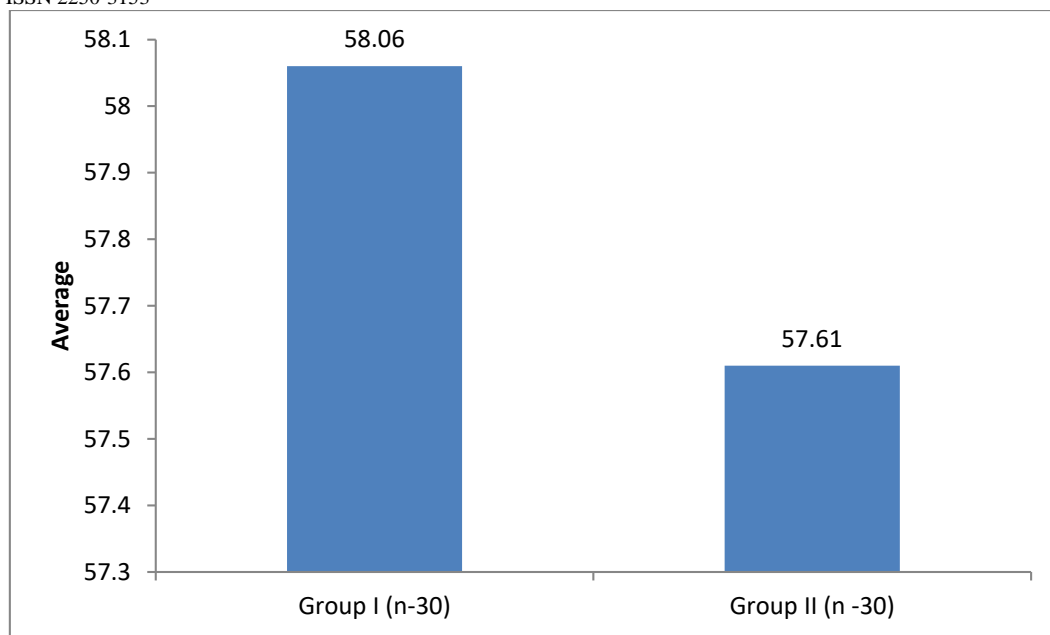
As evident from the table there were 38 males and 22 females in our study. Gender comparison was comparable among both groups. (p =0.107)



**Mean distribution of weight in different groups**(Table 3)

	Weight(in Kg) Mean $\pm$ SD	F	P-value
Group I (n-30)	58.06 $\pm$ 1.76	0.241	0.308
Group II (n -30)	57.61 $\pm$ 1.61		

As evident from the table mean weight (kg) in group I was 58.06  $\pm$  1.76, in group II was 57.61 $\pm$  1.61 which was statistically non significant. (p=0.308)



**HEART RATE (Table 5.1)**

Time	Group I (n-30)	Group II (n-30)	F	p-value
Baseline	81.53±12.29	84.53±9.81	2.79	0.300
At 0 minute	73.03±11.37	76.73±8.33	4.32	0.156
At 1 minute	69.03±10.65	74.83±8.65	2.68	0.024
At 2 minute	79±8.53	80.76±10.22	0.000	0.471
At 5 minute	75.90±8.26	79.13±9.19	0.185	0.157
At 10 minute	74.86±9.11	78.60±8.70	0.572	0.110
At 30 minute	73.43±9.79	78.53±10.14	0.266	0.052
At 60 minute	74.23±9.52	79.06±10.05	0.000	0.061

As evident from the table the baseline heart rate was comparable among the groups. Mean HR in Group I was 81.53±12.29, in group II was 84.53±9. The F value was 2.792 and p value was 0.300. Statistically significant fall in heart rate was seen at 1 minute of induction (p<0.05)

**Systolic blood pressure (SBP) (Table 6.1)**

Time	Group I (n-30)	Group II (n-30)	F	p-value
Baseline	139.16±9.39	135.13±8.71	1.07	0.090
At 0 minute	101.86±7.94	118.56±14.44	18.10	0.000
At 1 minute	94.10±9.38	112.93±17.06	14.30	0.000
At 2 minute	94.76±7.37	127.26±10.97	3.44	0.000
At 5 minute	96.40±8.70	125.60±9.34	0.60	0.000
At 10 minute	97.33±6.37	120.26±13.42	9.35	0.000
At 30 minute	99.13±6.53	125.23±7.84	0.21	0.000
At 60 minute	99.76±5.65	125.30±8.01	1.36	0.000

As evident from the table base line SBP was comparable among the groups. Mean SBP in Group I was  $139.16 \pm 9.39$ , in group II was  $135.13 \pm 8.71$ . The F value was 1.07 and p value was 0.090. Statistically significant fall in SBP was observed in group I at 0min which persisted till 60 minutes.

**Diastolic blood pressure** (Table 7.1)

Time	Group I (n-30)	Group II (n-30)	F	p-value
Baseline	87.43±4.04	86.40±4.53	0.799	0.355
At 0 minute	58.06±6.17	74.66±10.63	7.74	0.000
At 1 minute	56.23±5.70	69.73±11.97	13.73	0.000
At 2 minute	57.86±5.37	80.36±7.55	3.37	0.000
At 5 minute	58.56±7.69	80.20±6.25	0.06	0.000
At 10 minute	56.93±5.81	79.63±6.17	0.80	0.000
At 30 minute	61.30±9.21	80.43±5.82	1.95	0.000
At 60 minute	58.23±6.32	80.56±7.33	4.97	0.000

As evident from the table base line DBP was comparable among the groups .Mean DBP in Group I was  $87.43 \pm 4.04$ , in group II was  $86.40 \pm 4.53$ . The F value was 0.799 and p value was 0.355. Statistically significant fall in DBP was observed throughout the procedure

**Mean blood pressure** (Table 8.1)

Time	Group I (n-30)	Group II (n-30)	F	p-value
Baseline	104.33±3.86	98.83±17.24	2.64	0.094
At 0 minute	72.36±6.39	88.63±11.76	15.36	0.000
At 1 minute	68.36±6.29	84.20±13.40	18.92	0.000
At 2 minute	70.60±7.10	95.96±8.22	2.30	0.000
At 5 minute	70.83±8.14	95.03±6.78	0.01	0.000
At 10 minute	70.13±6.03	94.53±5.70	0.35	0.000
At 30 minute	70.46±4.56	95.73±5.86	0.31	0.000
At 60 minute	72.26±6.18	95.33±5.76	0.98	0.000

As evident from the table base line MBP was comparable among the groups .Mean MBP in Group I was  $104.33 \pm 3.86$ , in group II was  $98.83 \pm 17.24$ . The F value was 2.64 and p value was 0.094. Statistically significant fall in MBP was observed at 0min which persisted till 60 minutes.



**SpO<sub>2</sub>** (Table 9.1)

Time	Group I (n-30)	Group II (n-30)	F	p-value
Baseline	99.10±0.80	99.13±0.86	0.76	0.877
At 0 minute	99.10±0.80	98.83±2.03	1.47	0.507
At 1 minute	96.10±16.28	99.13±0.86	3.30	0.312
At 2 minute	99.10±0.80	99.13±0.86	0.07	0.877
At 5 minute	96.10±16.47	99.23±0.77	3.35	0.302
At 10 minute	99.13±0.81	99.16±0.74	0.58	0.870
At 30 minute	96.16±16.48	98.93±0.82	3.40	0.362
At 60 minute	99±0.78	99.36±0.71	0.09	0.065

No significant change was seen in SPO2 among both the groups at various time intervals (p>0.05)

**ETCO<sub>2</sub>** (Table 10.1)

Time	Group I (n-30)	Group II (n-30)	F	p-value
Baseline	37.23±3.09	38.23±3.96	2.19	0.280
At 0 minute	34.83±1.17	34.83±1.20	0.08	1.000
At 1 minute	36.73±0.84	38.16±6.63	1.82	0.246
At 2 minute	34.56±1.07	34.80±1.06	0.02	0.401
At 5 minute	34.23±1.65	34.73±1.28	3.34	0.196
At 10 minute	36±1.48	32.93±1.96	0.28	0.000
At 30 minute	32.96±0.76	33.20±0.80	0.99	0.255

At 60 minute	39.60±1.45	39.56±1.65	0.07	0.934
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Base line ETCO<sub>2</sub> was comparable at 0 min among both the groups. Statistically significant rise was seen at 1 min which persisted up to 60 minutes. (p <0.05)

## DISCUSSION

General anesthetic induction agents may decrease arterial blood pressure via cardio vascular depression and attenuation of autonomic nervous system activity. On the other hand laryngoscopy and endotracheal intubation elicit vasopressor responses such as hypertension and tachycardia. Various attempts have been made to overcome and attenuate hemodynamic instability during induction, laryngoscopy, and intubation. In many studies induction agents, either alone or in combination have been used to achieve minimum cardiovascular. Although many studies used thiopentol sodium as sole induction agent, it was found unsatisfactory as it does not suppress airway reflexes. Propofol has been advocated as a preferred i.v induction agent but induction with propofol alone causes remarkable reduction in blood pressure. Various studies shows that etomidate provide better hemodynamic profile but for its adverse effect like myoclonus and adrenal suppression. Recently Hacettepe University, studied propofol and etomidate for availability of admixture and reported that etofol (admixture of etomidate and propofol) can be used for induction agent.

After approval from institutional ethical committee we conducted a randomized double blind study in the department of anesthesia NIMS during the period of 20-02-2018 to 10-04-2018, comprising 60 patients of ASA grade I and II, age between 18-60 who were randomly selected and divided into two groups 30 each.

Informed consent were taken from all the patients were induced in Group I Induction with Propofol 2mg/kg, Group II induction with etomidate 0.3mg/kg and the patient was intubated and maintain on oxygen and nitrous (50-50%), isofluraine

Hemodynamic parameters and adverse effects if any were noted at various time intervals. The data obtained from this study was organised and analysed statistically. Observation was made and results were drawn.

### **Demographic profile**

In our study out of total (60) number of male patients was 38 and female patients were 22. No significant difference (p=0.107 and  $X^2=2.58$ ) was observed in gender distribution between the groups (table 2).

Demographic profile of the study done by **K Meena et al** also had comparable age group (p=0.178) and comparable gender distribution (p=0.241).<sup>7</sup>

### **Heart rate (HR)**

In our study baseline heart rate was comparable among the groups. Mean HR in Group I was  $81.53 \pm 1.76$ , in group II was  $84.5 \pm 9.8$ . The F value was 2.792 and p value was 0.300. Statistically significant fall in heart rate was seen at 1 minute of induction (p<0.05) (table 5.1)

**Masoudifar M et al** concluded there were no significant difference among groups I (Propofol) and II (Etomidate) in terms of HR (P = 0.47).<sup>(8)</sup>

**Singh R et al** studied there was a significant increase from baseline in heart rate (P = 0.001) at 1 minute after intubation. This statistically significant difference can be due to ASA grade III patients with coronary artery disease and left ventricular dysfunction.<sup>(9)</sup>

**Mulier JP et al** studied cardiovascular effects of propofol in comparison with thiopental and observed no statistically significant difference in heart rate and cardiac index.<sup>(10)</sup>

## SYSTOLIC BLOOD PRESSURE

In our study base line SBP was comparable both the groups. Mean SBP in Group I was  $139.16 \pm 9.39$ , in group II was  $135.13 \pm 87.1$ . The F value was 1.07 and p value was 0.090. Statistically significant fall in SBP was observed in group I at 0min which persisted till 60 minutes (table 6.1).

Findings of our study are comparable with the studies of **Masoudifar M et al**<sup>8</sup>, **Geeta Karki et al**<sup>11</sup>, **Kalogridaki M et al**<sup>12</sup> and **Meena et al**<sup>7</sup>.

**Masoudifar M et al** concluded that changes of SBP in the group B (Propofol) was statistically significantly ( $P = 0.019$ ), clinically significant hypotension was seen in 26.1% of patients in group B (Propofol) and 8% of patients in group A (Etomidate). Patients of group A (Etomidate) had more stable hemodynamic parameters.<sup>(8)</sup>

**Geeta Karki et al** concluded that Etomidate offers superior hemodynamic stability during induction compared to thiopentone and propofol, similar to our study.<sup>(9)</sup>

**Kalogridaki M et al** found statistically significant drop in systolic blood pressure in group P (Propofol) when compared with the baseline value (mean decrease 15.2 mmHg, 95% CI 5.6-24.8 mmHg,  $p=0.001$ ).<sup>(10)</sup>

**Meena et al** observed significant fall in systolic blood pressure in group I (Propofol) as compared to group II (etomidate) Systolic blood pressure prior to induction was non significant ( $p=0.536$ ). There was significant fall in blood pressure in group I at induction which persisted till 5 minutes after intubation ( $p=0.000$ ). The combination of etomidate plus propofol had better hemodynamic stability than etomidate or propofol alone.<sup>(7)</sup>

## DIASTOLIC BLOOD PRESSURE

In our study base line DBP was comparable among the groups. Mean DBP in Group I was  $87.43 \pm 4.04$ , in group II was  $86.40 \pm 4.53$ . The F value was 7.99 and p value was 0.355. Statistically significant fall in DBP was observed throughout the procedure (table 7.1).

**Masoudifar M et al** found that changes of the DBP was significantly higher in the group B (Propofol) ( $P = 0.001$ ) at various time intervals, which is comparable with our study.<sup>(8)</sup>

## MEAN BLOOD PRESSURE

In our study base line MBP was comparable among the groups. Mean MBP in Group I was  $104.3 \pm 3.86$ , in group II was  $98.83 \pm 17.24$ . The F value was 2.64 and p value was 0.94. Statistically significant fall in MBP was observed at 0min which persisted till 60 minutes. (table 8.1)

**Masoudifar M et al** found that changes in MBP was statistically significant in group B ( $P = 0.008$ ). Hypotension happened in 26.1% of group B and 8% of group A ( $P = 0.09$ ).<sup>(8)</sup>

**Moller et al** used propofol and etomidate in general anesthesia induction and found that MBP values after induction in the propofol group were significantly lower than those of the other group. Following intubation, the MBP values in the etomidate group were statistically significantly higher than those of the propofol groups.<sup>(13)</sup>

## SPO2

In our study no significant change was seen in SPO2 in both groups ( p value  $>0.05$ ). (Table 9.1)

## ETCO2

In our study ETCO<sub>2</sub> varies from minimum 30mmHg to 45mmHg maximum. This is statistically significant at various time intervals but changes in ETCO<sub>2</sub> are not clinically significant and therefore no clinical intervention was required. (Table 10.1)

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