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Comparison of haemodynamic response to induction with propofol versus etomidate in patients scheduled for elective surgery

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***Abstract*---**Introduction: Laryngoscopy and endotracheal intubation are harmful stimuli that can produce adverse response in the cardiovascular, respiratory and other physiological systems. These changes are reflected in haemodynamic parameters which can be fatal for patients with low cardiac reserve and may alter the balance between myocardial oxygen supply and demand and as a result, myocardial ischemia can be precipitated. This observational comparative study was conducted to compare the haemodynamic effects of Propofol and Etomidate during induction of general

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anaesthesia in patients scheduled for elective surgery. Materials and Methods: 58 patients of American Society of Anaesthesiologists (ASA) physical status I and II of age group 18-60 years scheduled for elective surgeries under general anaesthesia were randomly assigned in two groups (n=28). Group P received injection Propofol (2.5mg/kg) and group E received injection Etomidate (0.3mg/kg) during induction. Hemodynamic parameters were recorded at various time intervals. Statistical analysis was done using software (MedCalc Version 20.014). P value was considered significant if $p \leq 0.05$. Results: Demographic profile was comparable in both the groups. Hemodynamic parameters at baseline and after premedication were comparable. Patients in propofol group showed significant changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) compared to etomidate ($P<0.05$). Conclusion: Our study concludes that, the magnitude of haemodynamic changes that occur during induction with injection propofol were far more greater when compared with injection etomidate. Injection etomidate provides better haemodynamic stability during induction and intubation.

***Keywords*---**etomidate, haemodynamic changes, induction agent, propofol.

Introduction

Laryngoscopy and endotracheal intubation precipitate harmful stimuli that can cause adverse response such as increase in heart rate, blood pressure and arrhythmias, which can be dangerous for patients with limited cardiovascular reserve. These hemodynamic changes may disrupt the balance between myocardial oxygen supply and demand, increasing the likelihood of ischemia in patients (Choudhary et al., 2020).

Propofol, 2,6-diisopropylphenol, a phenol group of drug with sedative and hypnotic properties, is the most commonly used induction agent due to its advantages of rapid and smooth induction and recovery, as well as a lower incidence of nausea and vomiting. On the other hand, the principal disadvantages include decreased blood pressure, dose-dependent cardiorespiratory depression, pain on injection, and lack of analgesia (Langley & Heel, 1988).

Etomidate, carboxylated imidazole is characterized by hemodynamic stability, minimal respiratory depression and cerebral protective effects. Its lack of effect on sympathetic nervous system, baroreceptor reflex regulatory system and its effect of increased coronary perfusion even on patients with moderate cardiac dysfunction makes it an induction agent of choice in cardiac disease patients. However, pain on injection, thrombophlebitis, myoclonus and adrenocortical insufficiency are some undesirable adverse effects (Forman & Warner, 2011). This randomized observational study was conducted to compare the effects of Propofol and Etomidate on heart rate, blood pressure, and oxygen saturation during induction and intubation, so that we can choose a safer induction agent.

Materials and Methods

After obtaining ethical committee's approval, an observational study was conducted in the department of anaesthesiology of Dhiraj Hospital. All the patients aged between 18 to 60 years old of either gender belonging to American Society of Anaesthesiologists (ASA) grade I or II undergoing elective surgical procedures under general anaesthesia were considered for study. All patients were explained the purpose and nature of the study in their own language and were included in the study only after obtaining written and informed consent. The patients were randomly divided into two equal groups by chit method, 28 patients in each group. Group P received injection Propofol (2.5 mg/kg) I.V. as an induction agent of anaesthesia, whereas Group E received injection Etomidate (0.3 mg/kg) I.V.

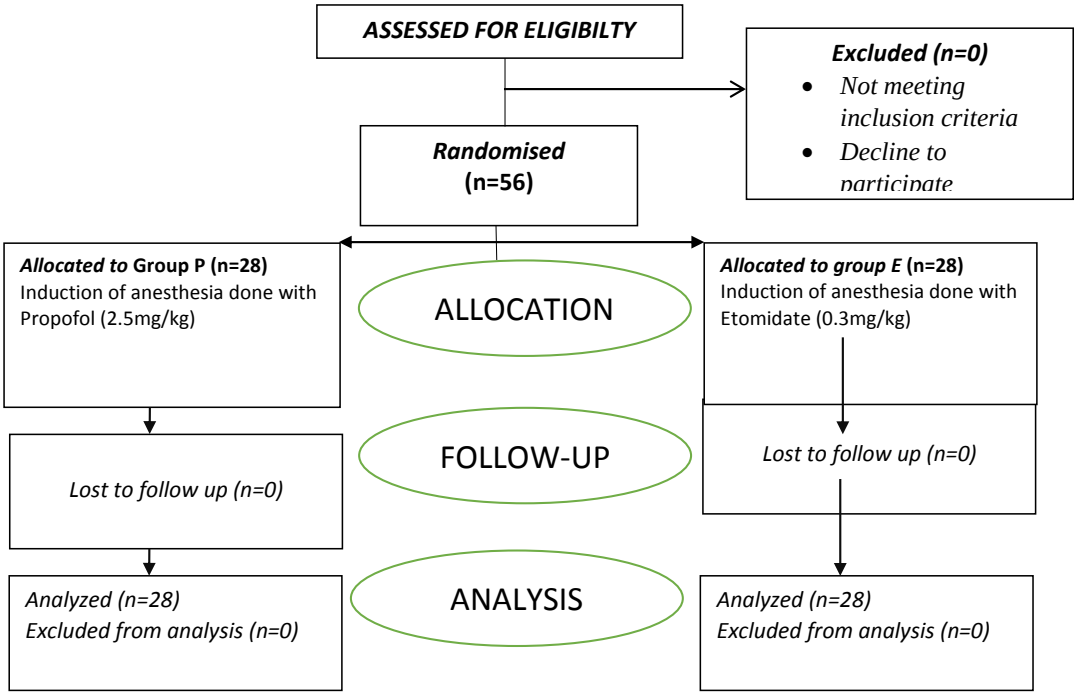
Patient aged between 18-60 years of either gender, who are scheduled to undergo elective surgical procedure under general anesthesia, belonging to ASA physical status I and II and who are willing to sign the written and informed consent were included in this study. Patients who refuse for the study, with a history of hypersensitivity to Propofol / Etomidate, with uncontrolled comorbidities, on steroid since last 6 months and with any condition which may increase the risk of a full stomach were excluded from the study.

1. Study Site: Dhiraj Hospital, S.B.K.S M.I.R.C
2. Study Design: Observational Comparative study
3. Duration of Study: 18 MONTHS
4. Sample Size: 56 Patients
5. Statistical Analysis: The data was expressed as mean ± standard deviation (SD). The mean value for each parameter was calculated using the formula, mean= $\sum Xi/n$ and SD was calculated using the formula $\sqrt{1/n\sum(Xi - X)^2}$. The unpaired Student's *t*-test for equality of means was employed for inter group comparison after obtaining the mean values and the SD and the two-tailed significance (*P*) was calculated. The paired *t*-test was utilized for intra group comparison. The statistical analysis was done using software (MedCalc Version 20.014).

P value was considered significant if $p \leq 0.05$, very significant if $p \leq 0.01$, highly significant if $p \leq 0.001$ and not significant if $p > 0.05$. All the patients satisfying inclusion and exclusion criteria were considered for the study. Written and informed consent was taken. Patients were shifted into the operation theatre, intra venous access was established with 18G cannula and infusion of lactated Ringer's solution started at 5 ml/kg. Multiparameter monitors were attached. All the patients were given premedication with inj. glycopyrrolate 0.004 mg/kg , injection ondansetron 0.08 mg/kg, injection midazolam 0.02mg/kg, injection tramadol 1mg/kg intravenously and then preoxygenated with 100% oxygen for 5 minutes. Induction of anesthesia done either with Propofol or Etomidate, as per their respective pre-decided group, until loss of eyelash reflex occurs. After check ventilation, injection succinylcholine 2mg/kg i.v. given. Laryngoscopy and intubation with appropriate endotracheal tube was done by an experienced anaesthesiologist. Depth of anesthesia maintained with oxygen (O_2), nitrous oxide (N_2O) (50:50), isoflurane and with injection atracurium (loading dose 0.5mg/kg

and maintenance dose 0.1mg/kg i.v. intermittently). Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and oxygen saturation(SPO_2) were recorded before premedication as baseline values. These parameters were measured after premedication and after induction at 1 min, 3 mins, 5 mins, 10 mins, 15 mins and 20 mins. when the patient fulfils extubation criteria, residual neuro muscular blockade was antagonised with intravenous injection of glycopyrrolate 0.008mg/kg and injection neostigmine 0.05mg/kg. Extubation done as per the standard protocol.

Study Flow Diagram

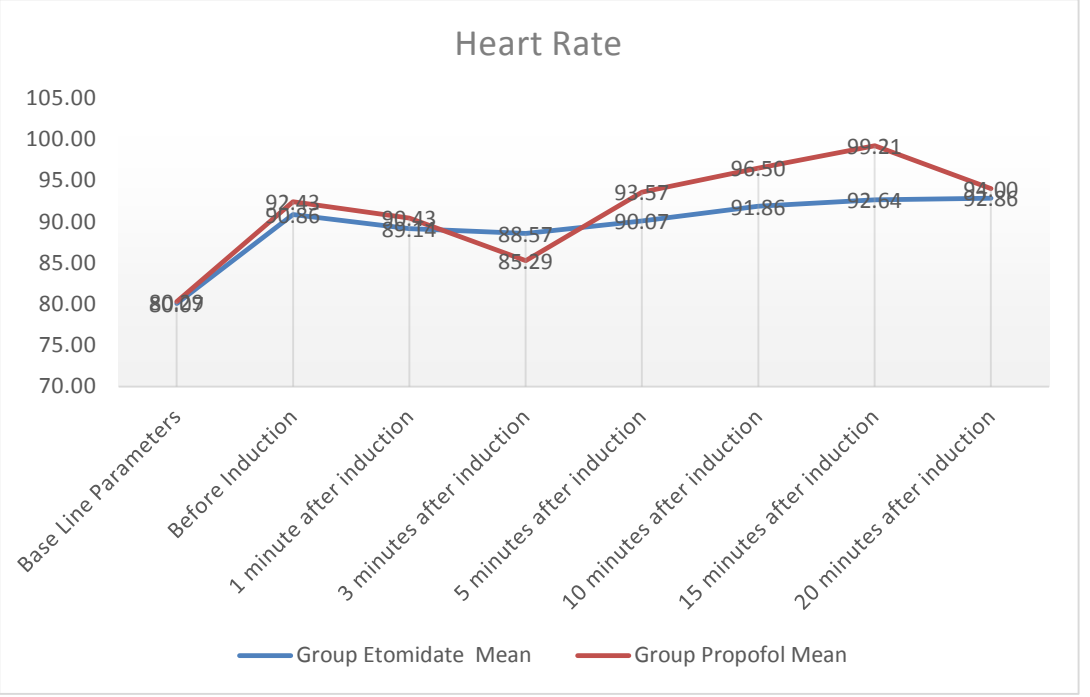


Results

Table I: Demographic Profile

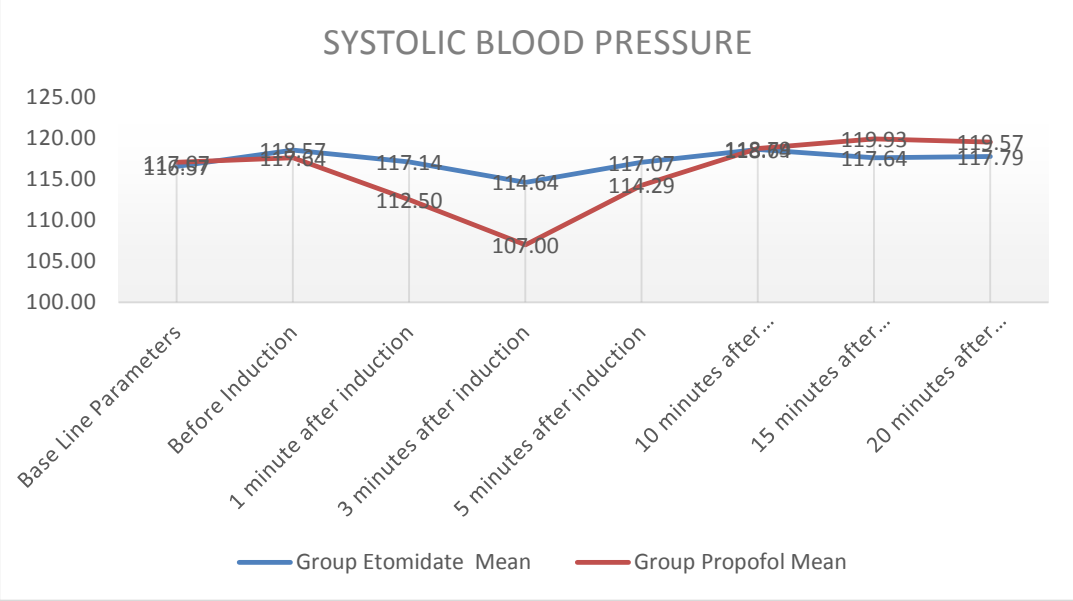
Demographic profile	Group Etomidate (n=28)	Group Propofol (n=28)	P-value
Mean age (years) ± SD	35.89 ±11.01	36.18 ±12.56	0.9271
Mean weight (kg) ± SD	62.75 ±9.41	61.86 ±10.54	0.7402
Gender Male (Total, percentage)	13, 46.43%	13, 46.43%	
Female (Total, percentage)	15, 53.57%	15, 53.57%	

As shown in table 1 both the groups were comparable and statistically not significant in terms of sample size, gender distribution, mean age, and mean weight.



Graph I: Graphical representation of changes in mean heart rate

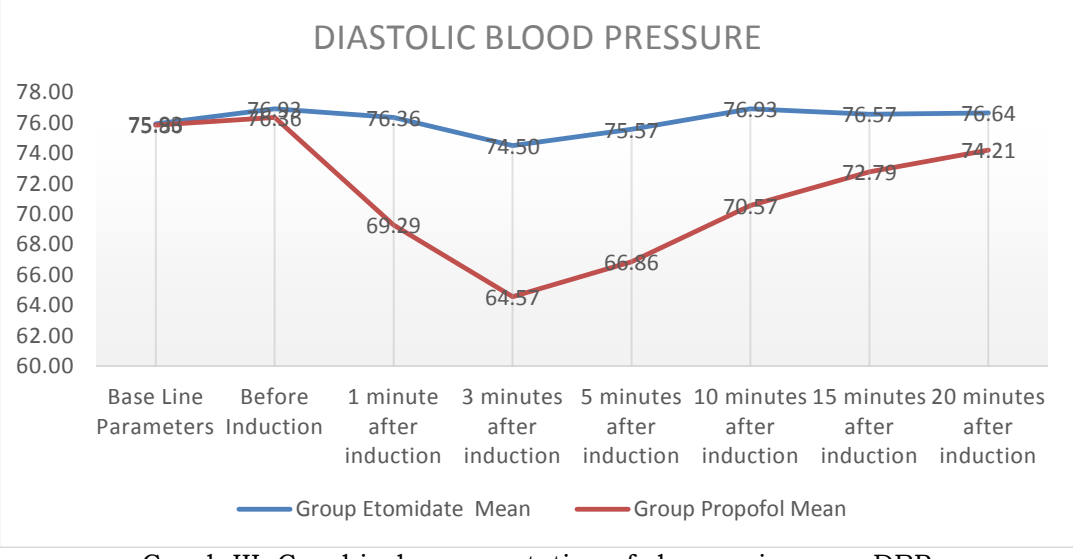
Mean heart rate noted at baseline, after premedication, and 1 minute after the induction were comparable and statistically not significantly. After 3 minutes of induction, decrease in mean heart rate noted in group Propofol when compared with group Etomidate. The change is statistically significant ($p < 0.05$). Significant increase in mean heart rate observed 5 minutes after induction in group when compared with group Etomidate ($p < 0.05$). Increase in mean heart rate observed at 10 minutes and 15 minutes after induction in group Propofol when compared with group Etomidate. ($p \leq 0.01$ very significant and $p \leq 0.001$ highly significant respectively). Twenty minutes after induction mean heart rate of both the groups was comparable and was statistically not significant ($p > 0.05$).



Graph II: Graphical representation of changes in mean SBP

Mean systolic blood pressure of both the groups was comparable at baseline and after premedication, and is statistically not significant ($p > 0.05$). At 1 minute and 3 minutes after induction mean systolic blood pressure of group Propofol decreased when compared to group Etomidate. ($p < 0.01$ and $p < 0.001$ respectively) The parameters were statistically very significant and highly significant respectively.

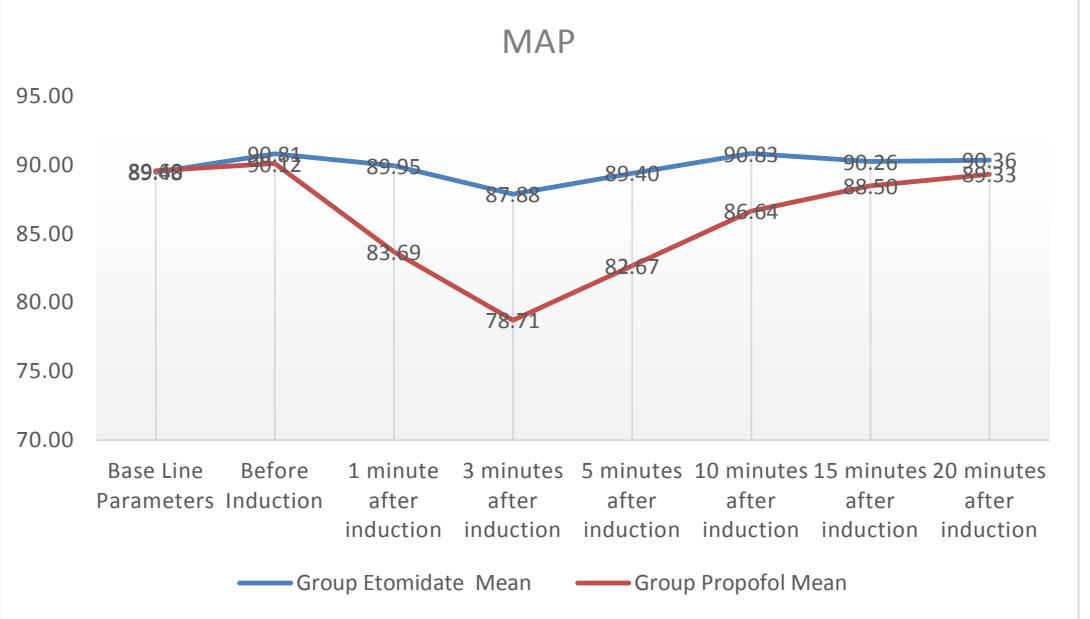
Further after 5 minutes of induction the changes in both groups were comparable and holds no statistical significance ($p > 0.05$).



Graph III: Graphical representation of changes in mean DBP

Mean diastolic blood pressure of both groups noted at baseline and after premedication was comparable and not statistically significant. ($p > 0.05$).

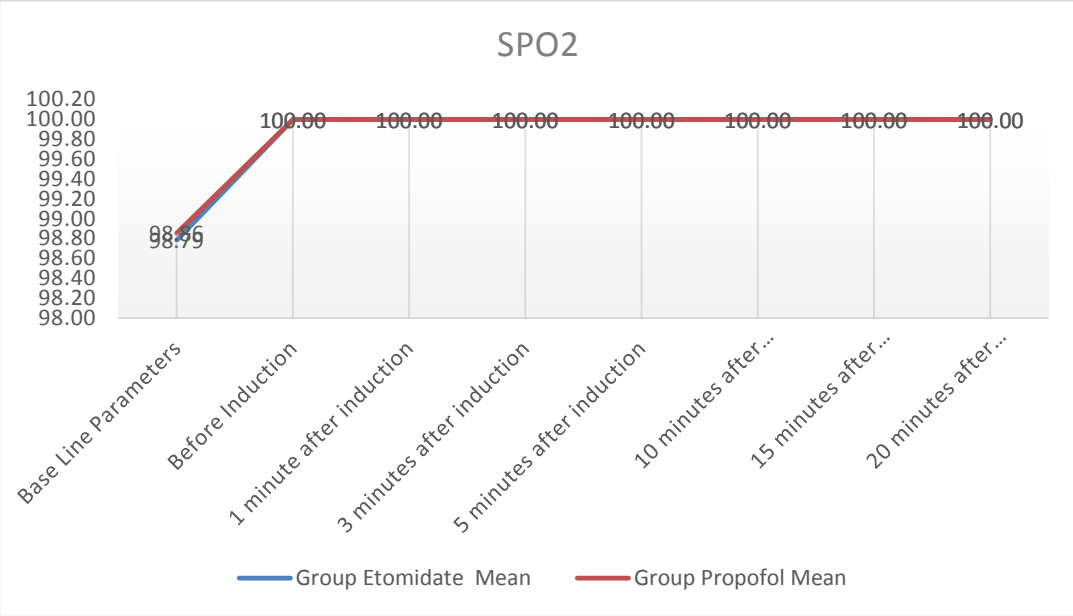
Decrease in mean diastolic blood pressure noted in group Propofol from 1 minute till 20 minutes post induction. When compared with group Etomidate, the fall in diastolic blood pressure was statistically highly significant ($p < 0.001$) till 15minutes after induction and significant ($p < 0.05$) at 20 mins post induction.



Graph IV: Graphical representation of changes in mean MAP

Mean arterial pressure of both groups noted at baseline and after premedication was comparable and not statistically significant. ($p > 0.05$).

There was a fall in Mean arterial pressure of group Propofol from 1 minute till 10 minutes after induction. When compared with group Etomidate the fall was highly significant ($p < 0.001$). There after the mean arterial pressure of both the groups was comparable and statistically not significant ($p > 0.05$)



Graph V: Graphical representation of changes in mean SPO_2

Baseline Mean oxygen saturation of both the group was comparable and statistically not significant ($p > 0.05$). Throughout the study there were no changes noted in oxygen saturation (SPO_2) in both the groups and thus holds no statistical significance.

Discussion

The stimulus in response to laryngoscopy and endotracheal intubation causes harmful effects on cardiovascular, respiratory and other physiological systems. Such effects are reflected as haemodynamic changes. These changes can be fatal for patients with low cardiac reserve as they alter the balance between myocardial oxygen supply and demand resulting in myocardial ischemia (Soleimani et al., 2017). Propofol and etomidate are one of the known anaesthetic agents which are routinely used for induction of anesthesia, with different clinical features.

The side effects of propofol include decrease in blood pressure, depression of ventilation in a dose dependent manner and pain on injection. It causes fall in arterial blood pressure and in turn leads to a decrease in cardiac output, stroke volume, and systemic vascular resistance. Further- more, propofol induces severe vasodilation while the effects of myocardial depression are not exactly clear (Kotani et al., 2008). Vasodilation of both arteries and veins leads to a decrease in preload and afterload. Propofol inhibits baroreflex response, so reflex tachycardia to hypotension is less. Drop in blood pressure after administration of propofol can be due to vasodilatation and reduced sympathetic activity (Kotani et al.,).

Etomidate does not inhibit sympathetic tone or myocardial function. It produces minimal change in heart rate and blood pressure at typical anaesthetic induction doses. It has the ability to cause minimal respiratory depression with cerebral

protective effects. It increases coronary perfusion and hence considered as induction agent of choice in cardiac patients (Forman & Warner, 2011). This study was conducted to evaluate the effects of Propofol and Etomidate by comparing change in heart rate, blood pressure and oxygen saturation, during induction and intubation, so that we can choose a safer induction agent.

Supriya Aggarwal el al (2014) evaluated the haemodynamic effects of propofol and etomidate during induction and intubation in their study. All the patients were premedicated with injection glycopyrrolate 0.2mg, injection midazolam 0.02mg/kg, and injection fentanyl 3mg/kg followed by induction with injection Propofol 2mg per kg in group I and injection etomidate 0.3 mg per kg in group II. It was noted that the changes in heart rate in both groups during induction and intubation were comparable. After induction fall in SBP, DBP and MAP noted in propofol group and the change was statistically significant when compared to etomidate. After laryngoscopy and intubation, the SBP, DBP and MAP increased but were not statistically significant. The magnitude of haemodynamic changes seen in propofol were more when compared to etomidate group (Aggarwal et al., 2016). Similar results were observed in our study, it was observed that there was more decrease in heart rate after induction with propofol than with etomidate. This may be due to the dose of propofol considered in our study. It was observed that, after 3 minutes post induction there was increase in mean heart rate. The increase was seen more in group propofol rather than group etomidate. The reason behind the increase in mean heart rate may be due to pressor response to laryngoscopy and intubation.

In the study conducted by Arvind Khare et al (2016) haemodynamic parameters were compared during induction of general anaesthesia with propofol 2.5mg/kg and etomidate 0.3mg/kg. It was observed that the magnitude of changes that occur in systolic blood pressure, diastolic blood pressure and mean arterial pressure following induction and intubation were statistically significant. The study concluded that etomidate provides more haemodynamic stability and less pain on injection when compared with propofol(Khare et al., 2016). Our study reflects similar results. It was observed that after induction there was significant fall in systolic blood pressure, diastolic blood pressure and mean arterial pressure, in both groups ($p<0.05$). The fall was more evident in group propofol whereas in group etomidate it was subtle. After intubation gradual raise in mean systolic blood pressure was noted in both groups. After laryngoscopy and intubation there was gradual increase in mean diastolic blood pressure and mean arterial pressure in group propofol and it holds statistical significance when compared with group etomidate ($p<0.05$). Throughout the time period observed, the magnitude of changes in mean systolic blood pressure in group propofol were more when compared to group etomidate.

The study conducted by Meena K et al (2016) used Propofol 2.5mg/kg, Etomidate 0.3mg/kg, and Propofol 1mg/kg plus Etomidate 0.2mg/kg as induction agents and compared haemodynamic effects respectively. Significant decrease in heart rate during induction was observed in propofol group. The data was statistically significant when compared to etomidate group. Changes in SBP, DBP, MAP of propofol group were statistically significant when compared with etomidate group. The study showed propofol caused more haemodynamic changes when compared

with etomidate. It also stated that the combination of propofol and etomidate gave better haemodynamic stability (Meena & Meena, 2016). Comparison between group propofol and group etomidate showed results which were similar to the results observed in our study.

Conclusion

Our study concludes that, the magnitude of haemodynamic changes that occur during induction with injection propofol were more when compared with injection etomidate. Etomidate provides better haemodynamic stability during induction and intubation.

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