

A Comparative Evaluation of Propofol, Etomidate and Admixture of Propofol - Etomidate for Induction during General Anaesthesia

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Abstract: ***Background:** Propofol and Etomidate are non barbiturate inducing agents. These drugs have different induction characteristics and recovery profile. Propofol causes pain at injection site, hypotension but has clear headed recovery whereas Etomidate is cardiostable but can cause myoclonus. Propofol & Etomidate group both used to decrease side effects. **Objective:** our study we compare Propofol, Etomidate and admixture of Propofol - Etomidate on induction characteristic i.e loss of eyelash reflex, pain at injection site, myoclonus, hemodynamic parameters and recovery profile. **Methods:** Total no. of patients in our study was 90 with ASA grade I and II, age 18-55 years included for surgical procedure under general anesthesia were randomly divided into three groups of 30 patients each. Patients in group -I was induced with inj. Propofol (3mg/kg) i.v and patient of group -II were induced with inj. Etomidate (0.3 mg/kg) i.v and patients of group -III were induced with Combination of inj. Propofol and inj. Etomidate in the ratio of 1:1 by volume. Onset time i.e time to disappearance of eyelash reflex, pain at injection site and myoclonus, were noted. Continuous hemodynamic monitoring i.e HR, SBP, DBP, MAP and recovery profile was done. All the result were tabulated and statistically analysed. **Result:** In patients of admixture Propofol-Etomidate Group, loss of eye lash reflex are earlier than Propofol and Etomidate group. In Propofol group have pain at injection site and patient in Etomidate group have some incidence of myoclonus. **Conclusion:** Admixture of Propofol-Etomidate is hemodynamically more stable with less side effect and early recovery.*

Keywords: Propofol; Etomidate; Mean arterial pressure; Heart rate; Pain ;myoclonus; loss of eye lash reflex ;recovery profile

1. Introduction

No ideal induction agent has yet been discovered in term of providing a stable haemodynamics during endotracheal intubation. In all methods used for induction of anaesthesia, it is aimed to preserve the haemodynamic balance and to provide optimal conditions for the patient by reducing side effects.

Traditionally anaesthesia was induced by inhalational anaesthetic agents i.e. Ether, Chloroform, later some other inhalation agents were also introduced i.e Halothane, Isoflurane and Sevoflurane. Inhalational agents have slower onset and longer residual effect⁽¹⁾. Some causes irritation to respiratory mucosa, coughing, bronchospasm and marked haemodynamic changes⁽²⁾.

These effects can be overcome by using intravenous anaesthetic agents. The introduction of intravenous anaesthetic agents in the 1930s caused a major shift in the concept of anaesthesia by replacing the inhalation anaesthetic agents by intravenous anaesthetic agents⁽³⁾⁽⁴⁾.

Thiopentone sodium was the leading inducing agent of choice for the next 50 years. It causes bronchospasm and apnea. For these reasons Thiopental is less commonly used nowadays.⁽⁵⁾

Gradually newer intravenous anaesthetic induction agents were introduced such as Ketamine, Propofol and Etomidate.⁽⁶⁾

Ketamine is good analgesic but it is not safe in patients of cardiovascular and neurological disease because it increases intracranial, intraocular, intragastric pressure and also increases cardiac workload.

Propofol and Etomidate are non-barbiturates and are most popular, rapid acting and smooth intravenous inducing agents.⁽⁷⁾

Propofol (2, 6-diisopropylphenol) is most commonly used induction agent in general anaesthesia. Propofol decreases blood pressure, cardiac output and systemic vascular resistance due to inhibition of sympathetic vasoconstriction and impairment of baroreceptor reflex regulatory system. Hypotension and pain on injection are the major drawbacks.^(8,9)

Etomidate is a carboxylated imidazole containing compound characterized by minimal respiratory depression, haemodynamic stability, and cerebral protective effects. Its lack of effect on sympathetic nervous system, baroreceptor reflex regulatory system and increase in coronary perfusion rate.⁽¹⁰⁾

2. Material and Method

Our study was carried out in the department of Anaesthesia, S.S. Medical College and associated Sanjay Gandhi and Gandhi Memorial Hospitals, Rewa (MP) from April 2016 to March 2017. After institutional ethical committee approval, our study was conducted on patients of ASA grade I and II between 18 to 55 yrs of age with both sex posted for elective surgery under general anaesthesia.

Inclusion criteria: All the surgical patients of ASA grade I and II between 18 to 55 years of age of either sex posted for elective surgery under general anaesthesia.

Exclusion criteria: Patients with Mallampatti grade III-IV, known hypersensitivity to inj. Propofol or Etomidate, Cardiovascular dysfunction, were excluded from the study

Group division

Group I (Propofol)	(n-30) were given Inj. Propofol 2.5mg/kg body weight I.V.
Group II (Etomidate)	(n-30) were given Inj. Etomidate 0.3mg/kg body weight I.V.
Group III (Propofol-Etomidate)	(n-30) were given combination of drug dose of Inj. Propofol and Inj. Etomidate in the ratio of 1:1 by volume I.V. for induction

All the patients were uniformly premedicated with inj Glycopyrrolate 0.01mg/kg body weight, Inj. Midazolam 0.3mg/kg body weight, Inj. Fentanyl 2mcg/kg body weight and injection ondansetron 0.08mg/kg body weight intravenously 15 min prior to induction.

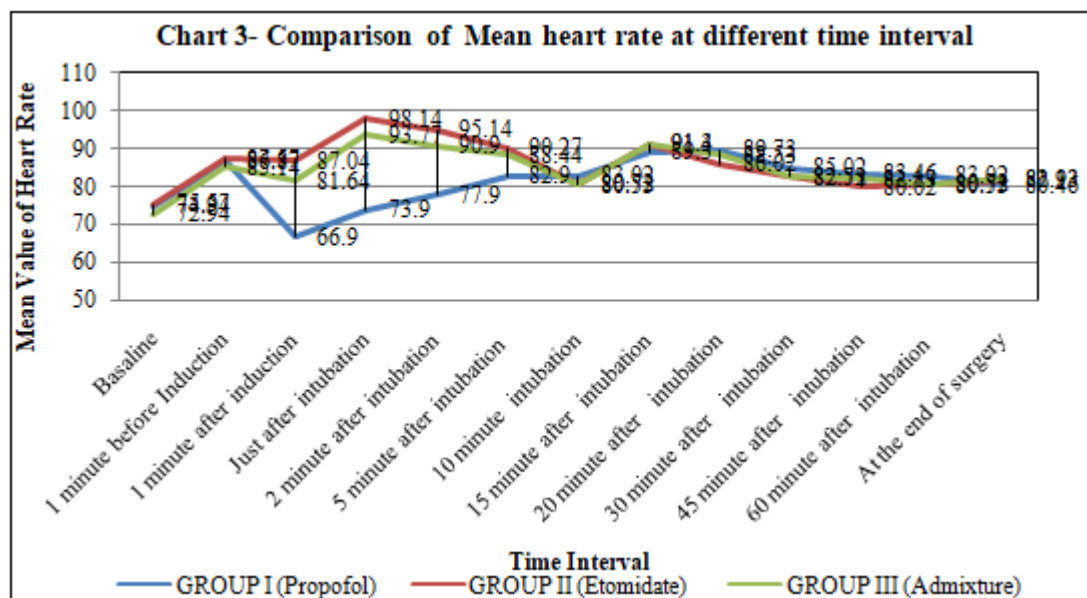
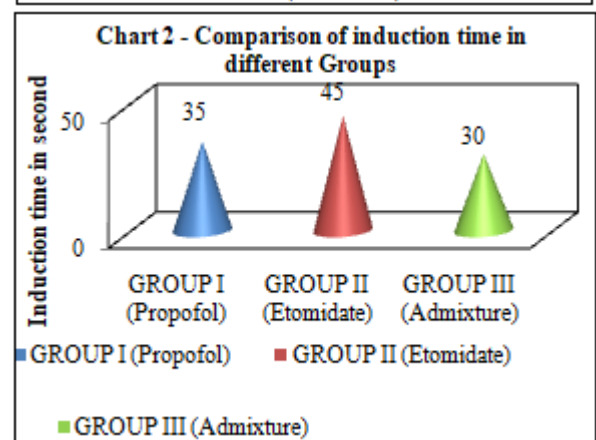
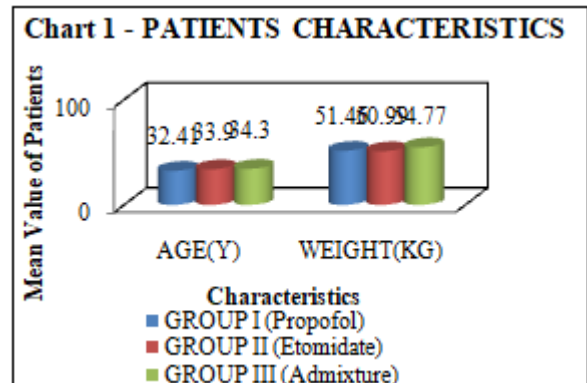
Heart rate, blood Pressure (SBP, DBP, MAP) were recorded at 1 min before induction and 1min after induction, just after intubation and at 2 min, 5min, 10min, 15min, 20min, 30min, 45min, 60min at end of surgery.

After surgery patients were reversed with Inj. Glycopyrrolate 0.5 mg and Inj. Neostigmine 2.5 mg and were extubated.

Recovery profile: To assess recovery characteristic after intubation in Propofol, Etomidate and admixture Groups, we

observed for drowsiness, excitement, PONV and cough and we observation were decoded, tabulated and statistically analysed by using mean, standard deviation, p value, ANOVA test Chi-square test and student t test.

3. Observation



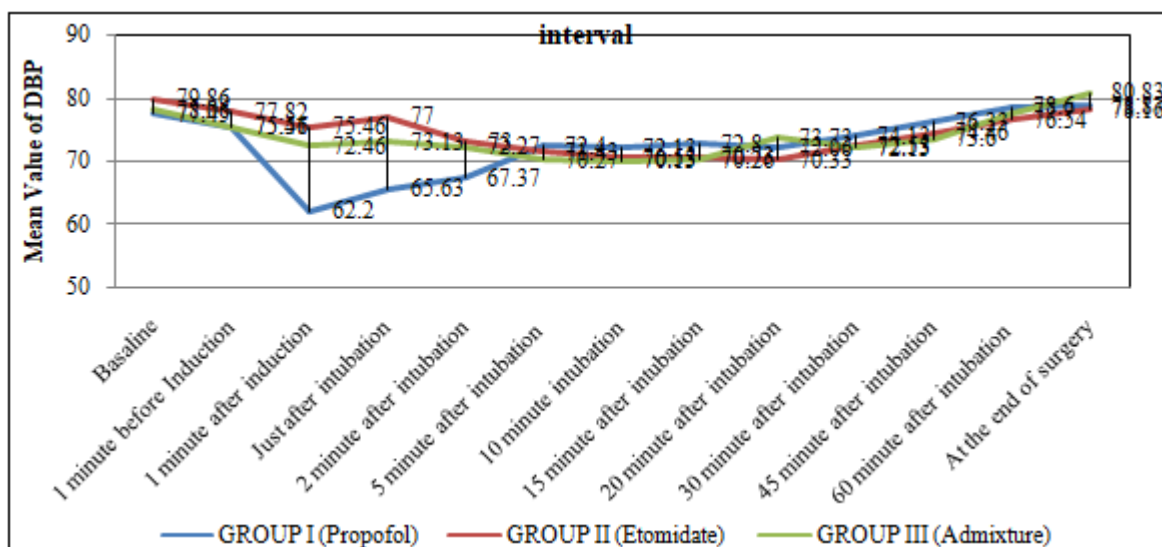
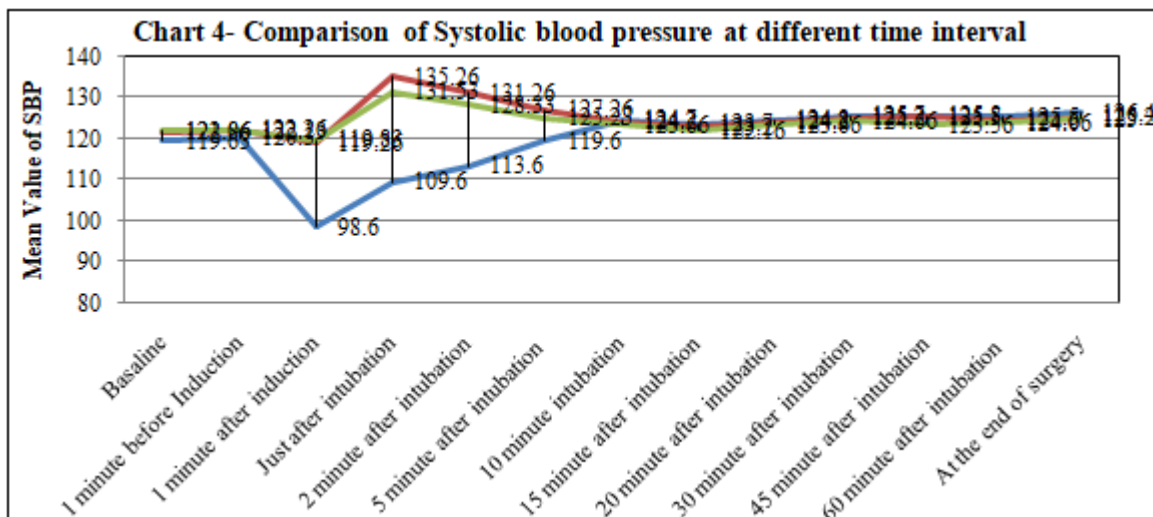


Table 6: Comparison of pain at injection site & myoclonic movement on different Groups

Grades	Pain at injection site				myoclonic movement			
	Group I (Propofol)	Group II (Etomidate)	Group III (Admixture)	P value	Group I (Propofol)	Group II (Etomidate)	Group III (Admixture)	P value
Grade 0	15	30	30	0.0003	30	14	28	0.0001
Grade I	09	01	02		0	10	01	
Grade II	05	00	01		0	5	01	
Grade III	01	00	00		0	1	00	

4. Discussion

To find out a better inducing agent for general anaesthesia. We compare Propofol, Etomidate and admixture of Propofol-Etomidate with regard to the induction characteristics, haemodynamic parameters and recovery profile.

After giving the study drug, induction time (from the start of Injection to the loss of eyelash reflex), pain at Injection site, myoclonus, haemodynamic parameter and recovery profile were noted in all the patients.

Heart rate and blood pressure (SBP, DBP, MAP) were recorded at regular interval. All data were recorded; tabulated and statistically analysed using ANOVA, t-test and chi-square test which ever applicable.

Demographic profile:- sex distribution in all three groups in which propofol group M/F 12/18, Etomidate group M/F 14/16, and admixture group M/F 13/17 patients.

Induction characteristic

Induction time- Our study shows the mean induction time of Group I is 35 ± 10 second, Group II 45 ± 9 second and III shows 30 ± 8 second. The difference in the induction time was statistically significant in Group III as compared to I & II groups. The induction time is faster in (III > I > II) groups

The induction is faster in admixture group than Propofol and Etomidate Group due to both Etomidate and Propofol are known to have short duration of action that will cause rapid induction.

Pain at Injection site:- Our study we observed pain at Injection in fifteen patients in Group I, one patient in Group

II and three patients in Group III. The incidence of pain at injection site was more in Group I as compared to Group II and Group III. The difference in pain at Injection site was clinically as well as statistically significant ($p < 0.0003$)

The cause of pain at Injection site with Inj Propofol is due to activation of kininogens. Pain incidence at Injection site was lower in the admixture group because of the decrease in the release of kinins and decrease Propofol concentration.

Similar results were found by Saricaoglu F et al⁽¹¹⁾(2011) who compared Propofol, Etomidate and admixture Group for anaesthesia induction. They found that the incidence of Injection pain was lowest in the admixture group among all the Groups (83.8% in the Propofol Group and 63.2% in the Etomidate Group and concluded that Etofol (Propofol plus Etomidate) is a valuable agent for induction because it is associated with less pain on Injection maintains better haemodynamic stability than Etomidate-lipuro and Propofol.

Myoclonus:-Our study sixteen patients in Group II and two patients patients in Group III and none of the patients in Group I, has myoclonus. The incidence of myoclonus was (Group II>I>III). The difference in myoclonus movement was clinically as well as statistically significant ($p < 0.0001$)

Incidence of myoclonus can be decreased by preinduction priming with subanaesthetic dose of Etomidate. The Propofol in the admixture can act as preinduction priming in our study.

Similar results were found with Saricaoglu F et al⁽¹¹⁾(2011) compared Propofol, Etomidate and Etofol in anaesthesia induction. They found the highest incidence of myoclonus in the Etomidate Group (93.4%) as compared with Propofol Group (0%) and Etofol (14.3%) ($p < 0.0001$).

Heart Rate: The baseline MHR in all three groups were 74.94 ± 5.78 , 75.57 ± 4.47 and 72.94 ± 4.83 respectively. Which is almost equal in all three groups.. ($P>0.05$)

After induction, the MHR in all three groups were 66.9 ± 5.76 , 87.04 ± 4.40 and 81.64 ± 5.98 respectively. The HR was decrease from baseline value in patients of all three Groups. The decrease in HR was more in propofol as compared to etomidate and Etofol ($P<0.05$)

Just after intubation and after 2 min. of intubation, the MHR was 73.9 ± 5.76 , 98.14 ± 4.20 and 93.77 ± 7.394 just after intubation and 77.9 ± 5.762 , 95.14 ± 4.20 , 80.53 ± 6.33 at 2 min after intubation in propofol, etomidate and admixture group respectively. Here HR increase in all three Groups from baseline.but this increase HR was more in etomidate as compare to propofol and Etofol. ($p < 0.05$).

After 5 min of intubation, mean HR was 82.9 ± 5.78 , 90.27 ± 4.21 and 88.44 ± 4.96 in Propofol, Etomidate and Etofol respectively. Here HR increase in all three Propofol, Etomidate and Etofol Groups from baseline. Comparison in all 3 groups shows the difference of HR increase was statistically significant between Propofol & Etomidate and Propofol& Etofol ($p < 0.05$). But it was statistically

insignificant between Group II & III ($p > 0.05$). At the end of surgery ($p > 0.05$).

Similar results seen by Yağan Ö et al⁽¹²⁾ They found MHR decrease in all the three Groups after induction. This decrease was more in the Propofol than the Etomidate and the Etofol. Just after intubation HR was increased in all the three Groups but this increase was more in the Etomidate Group than the Propofol and the Etofol Groups.

Systolic blood pressure:-The baseline mean SBP was 120.3 ± 6.12 mmHg, 122.26 ± 4.48 mmHg and 122.13 ± 4.47 mmHg in Propofol, Etomidate and Etofol respectively. The baseline SBP of Propofol, Etomidate and Etofol are almost equal and the difference in SBP.($P> 0.05$).

After induction, mean SBP was 98.6 ± 6.12 mmHg, 119.26 ± 4.48 mmHg and 119.83 ± 5.07 mmHg in Propofol, Etomidate and Etofol respectively. The SBP in all three Groups was decreased in patients of from baseline. The decrease in SBP was more in Propofol Group as compared to Etomidate Group and Etofol Group. The inter Group comparision shows the difference of decrease in SBP was statistically significant between Group I & II and Group I & III ($p < 0.05$). But it was statistically insignificant between Group II & III ($P>0.05$).

After intubation, mean SBP was 109.6 ± 6.13 mmHg, 135.26 ± 4.4 mmHg and 131.53 ± 4.71 mmHg in Group I, II and III respectively. There was increase in SBP in all three Groups from baseline value. But this increase in SBP was more in Group II as compare to Group I and Group III. The inter Group comparision shows the difference of increase in SBP was statistically significant in all three Groups.($p < 0.05$).

After 2min as well as after 5 min of intubation, the mean SBP was 113.6 ± 6.12 mmHg, 131.26 ± 5.48 mmHg and 128.33 ± 6.85 mmHg at 2min after intubation and 119.6 ± 6.14 , 127.26 ± 4.48 mmHg, and 125.23 ± 7.08 mmHg at 5 min after intubation in Group I, Group II, Group III respectively. There was slight increase in SBP in all three Groups from baseline value. The inter Group comparison shows the difference of increase in SBP was statistically significant in Group I & II and Group I & III ($p < 0.05$) but it was statistically insignificant between Group II & III ($p > 0.05$).

After 10 min of intubation up to the end of surgery, the changes in mean SBP were statistically insignificant ($p > 0.05$).

Similar results were seen in study by Meena K at al⁽¹³⁾(2016) studied the effects of Inj Propofol 2.5 mg/kg BW, Inj Etomidate 0.3 mg/kg BW and Inj Propofol 1 mg plus Inj Etomidate 0.2 mg /kg BW on haemodynamic effects. They found decrease in SBP after induction, in all three groups this decrease was more in Propofol Group than Etomidate Group and Propofol plus Etomidate Group. Just after intubation SBP was increased in all three Groups but this increase was more in Etomidate Group than Propofol Group and Propofol plus Etomidate Group. Admixture also provides better controle of haemodynamics.

Diastolic blood pressure

The baseline mean DBP was 77.45 ± 3.99 mmHg, 79.86 ± 5.38 mmHg, and 78.06 ± 5.84 mmHg, in Group I, II and III respectively. The baseline DBP of all the three Groups are almost equal and the difference in DBP was statistically insignificant in all the three Groups. ($P > 0.05$)

After induction, mean DBP was 62.2 ± 3.96 mmHg, 75.46 ± 7.08 mmHg and 72.46 ± 5.33 mmHg in Group I, II and III respectively. The DBP was decreased in patients of all three Groups from baseline value. The decrease in DBP was more in Group I as compared to Group II and Group III.

The inter Group comparison shows the difference of decrease in DBP was statistically significant between Group I & II and Group I & III ($p < 0.05$). But it was statistically insignificant between Group II & III ($P > 0.05$).

After intubation, mean DBP was 65.63 ± 3.728 mmHg, 77.00 ± 4.29 mmHg, 73.13 ± 4.18 mmHg respectively in Group I, II and III. There was increase in DBP in all three Groups from baseline value. But this increase in DBP was more in Group II as compare to Group I and Group III. The inter Group comparison the difference of increase in DBP was statistically significant in all three Groups. ($p < 0.05$).

After 2 minute of intubation, mean DBP was 67.37 ± 3.285 mmHg 73.00 ± 3.833 and 72.27 ± 3.80 mmHg in Group I, Group II, Group III respectively. There was slight increase in DBP in all three Groups from baseline value. The inter Group comparison shows the difference of increase in DBP was statistically significant in Group I & II and Group I & III ($p < 0.05$) but it was statistically insignificant between Group II & III ($p > 0.05$).

After 5 minute of intubation, mean DBP was 72.40 ± 2.95 mmHg, 71.43 ± 2.27 mmHg and 70.27 ± 4.093 mmHg in Group I, Group II, Group III respectively. There was slight increase in DBP in all three Groups from baseline value. The inter Group comparison shows the difference of increase in DBP was statistically significant in Group I & III ($p < 0.05$). But it was statistically insignificant between Group I & II and Group II and III ($p > 0.05$).

After 10 min of intubation up to the end of surgery, the changes in mean SBP were statistically insignificant in patients of all Groups. ($p > 0.05$).

Similar results were seen in the study of Meena K at al⁽¹³⁾ (2016) studied the effects of Inj Propofol 2.5 mg/kg BW, Inj Etomidate 0.3 mg/kg BW and Inj Propofol 1 mg plus Inj Etomidate 0.2 mg /kg BW on haemodynamic effects. They found decrease in DBP after induction, in all three groups this decrease was more in Propofol Group than Group Etomidate and Group Propofol plus Etomidate. Just after intubation DBP was increased in all three Groups but this increase was more in Etomidate Group than two other. Similar results were also found in our study.

Mean arterial pressure

The baseline mean MAP was 89.26 ± 4.71 , 88.2 ± 7.47 , 90.83 ± 3.83 mmHg in Group I, II and III respectively. The

baseline MAP of all the three Groups are almost equal and the difference in MAP was statistically insignificant in all the three Groups. ($P > 0.05$)

After induction mean MAP was 70.26 ± 4.12 mmHg, 83.7 ± 5.94 mmHg and 85.83 ± 3.14 mmHg in Group I, II and III respectively. The MAP was decreased in patients of all three Groups from baseline value. The decrease in MAP was more in Group I as compared to Group II and Group III. The inter Group comparison shows the difference of decrease in MAP was statistically significant between Group I & II and Group I & III ($p < 0.05$). But it was statistically insignificant between Group II & III ($P > 0.05$).

After intubation, mean MAP was 77.26 ± 4.71 mmHg, was 89.36 ± 6.57 mmHg, 93.83 ± 3.17 mmHg respectively in Group I, II and III respectively. There was increase in MAP in all three Groups from baseline value. But this increase in MAP was more in Group II as compare to Group I and Group III. The inter Group comparison shows the difference of increase in MAP was statistically significant in all three Groups. ($p < 0.05$).

After 2min as well as after 5 min of intubation, mean MAP was 77.12 ± 4.89 mmHg, 87.86 ± 6.63 , 91.83 ± 6.14 mmHg at 2min after intubation and 82 ± 4.89 mmHg, 86.36 ± 7.24 mmHg and 88.83 ± 4.46 mmHg at 5 min after intubation in Group I, Group II, Group III respectively. There was slight increase in MAP in all three Groups from baseline value. The inter Group comparison shows the difference of increase in MAP was statistically significant in Group I & II and Group I & III ($p < 0.05$) but it was statistically insignificant between Group II & III ($p > 0.05$).

After 10 min of intubation up to the end of surgery, the changes in mean SBP were statistically insignificant in patients of all Groups ($p > 0.05$).

Similar results were seen in study by Saricaoglu F at al⁽¹¹⁾ (2011): Etomidate-Propofol combination in that study was provided at a 1:1 ratio of 1% Propofol (20 mg /mL) and Etomidate (2 mg /mL). In the anaesthesia induction, the medications were applied by titration to provide at a target BIS value of 40. From the results of this study, it was reported that anaesthesia induction with a combination of Etomidate and Propofol provided a pain-free Injection, lower rate of myoclonus, and in comparison with Propofol and Etomidate used alone, achieved a quicker induction and better haemodynamic stability.

Meena K at al⁽¹³⁾ (2016) studied the effects of Inj Propofol 2.5 mg/kg BW, Inj Etomidate.3 mg/kg BW and Inj Propofol 1 mg plus Inj Etomidate 0.2 mg /kg BW on haemodynamic effects. They found decrease in MAP after induction, in all three groups this decrease was more in Propofol Group than Group Etomidate and Group Propofol plus Etomidate. Just after intubation MAP was increased in all three Groups but this increase was more in Etomidate Group than two other. Similar results were also found in our study.

Recovery characteristics

Our study, we observed a recovery characteristic after intubation. The incidence of drowsiness was found to be equal (3%) in patients of all three Groups i.e. Group I, II, III.

The incidence of excitement was found to be 3%, 6%, 0% in Group I, II and III respectively. PONV & cough / hiccups was found to be 3%, 3%, 0% in Group I, II and III respectively. The difference in recovery characteristics was clinically as well as statistically significant. ($p < 0.05$)

The admixture of Propofol-Etomidate had low incidence of excitement, PONV and cough / hiccups than Propofol and Etomidate alone at the time of recovery, so admixture was found to be better for smooth recovery. Our study, we found faster induction in admixture Group than Propofol and Etomidate Group.

Haemodynamic parameters (SBP, DBP, MAP, HR) were found to be more stable in admixture Group whereas decreased in haemodynamic parameters was more in Propofol Group at the time of induction and increased in haemodynamic parameters were found in Etomidate Group after intubation.

Incidence of Pain at injection site was found more in Propofol Group and myoclonus was found more in Etomidate Group whereas these complications were less in admixture Group (Propofol & Etomidate).

Recovery was smooth in admixture Group than two other Groups.

5. Conclusion

From ongoing discussion, following conclusion can be drawn:-

- 1) Admixture of Propofol and Etomidate provides rapid onset of action, stable haemodynamics and smoother recovery than Propofol and Etomidate alone.
- 2) Admixture is associated with less incidence of pain at injection site and myoclonus than Propofol and Etomidate alone.

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