Original Research Article

A comparative study of the effect of propofol and etomidate as an induction agent on haemodynamic changes during induction and endotracheal intubation

ABSTRACT:

Presently Propofol and Etomidate are popular as rapid acting inducing agents.]. Direct laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation. this study is conducted to compare the effects of these two drugs on hemodynamic responses during induction and endotracheal intubation,to compare time of induction to choose the better induction agent andto study adverse effects of the two drugs, if any.**METHOD-:** This is prospective randomized double-blind study. 60 ASA I and II patients randomly divided into two groups group P and group Eof 30 each of either sex in age group of 18-65 years posted for elective surgery under general anesthesia.Group P:(n-30) received 2.5mg/kg Propofol and Group E:(n-30) received 0.3mg/kg Etomidate for induction.vital parameters such as HR, SBP, DBP, MAP, and SPO2 recorded at baseline(T0),before induction(T1), after induction(T2), during laryngoscopy(T3) ,after intubation at 1min, 2min, 3min, 5min and at 10 min.Time of induction was taken as period between time of start of study drug till loss of eyelash reflex**Results:** Induction time between the two study groups was statistically insignificant. ($p>0.05$) The fall in heart rate at post induction(T2), at 1 min, 2 min after intubation in Group P as compared to Group E was statistically significant, fall in SBP, DBP and MAP at post induction(T2), at 1 min, 2 min, 3 min and 5 min after intubation in Group P as compared to Group E was statistically significant. Pain on injection was more with propofol. However, myoclonus was more with etomidate

KEYWORDS : Propofol, Etomidate, Laryngoscopy, endotracheal intubation.

INTRODUCTION: Endotracheal intubation and laryngoscopy are very essential tools in the hands of anesthesiologists in maintaining airway.Endotracheal intubation has become an

integral part of the anesthetic management and critical care of the patient and has been practiced following its description by Rawbothem and Magill in 1921[1].In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and tracheal intubation[2]Direct laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation. This response is transient, occurs 30 secs after laryngoscopy and intubation and lasts for less than 10 minutes[3]An ideal induction agent for general anesthesia should have hemodynamic stability, minimal respiratory side effects and rapid clearance. Presently Propofol and Etomidate are popular as rapid acting inducing agentscharacteristics of rapid and smooth induction and recovery, Propofol, 2,6 diisopropylphenyl, is the most popular induction agent decreases blood pressure, cardiac output, and systemic vascular resistance[4,5] due to inhibition of sympathetic vasoconstriction andimpairment of baroreceptor reflex regulatory system [6,7]. .Etomidate is a carboxylate imidazole-containing compound 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[8,9]. Considering the common use of Propofol and Etomidate as an induction agent, this study is conducted to compare the effects of these two drugs on hemodynamic responses during induction and endotracheal intubation in a patient undergoing elective surgery under general anesthesia.

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- **METHOD** After approval from medical ethics committee, Dr D Y Patil Medical College and Hospital, Pune, written informed consent taken from all the patients participating in the study. The study was carried out on sixty (60) patients ASA I and II undergoing elective surgeries under standard general anaesthesia.Unwilling patients, pregnant patients, patients with heart diseases were excluded from studies. The patients were divided into two groups of 30 each. Randomized, double blinded method was used for grouping the patients. The patients and investigator were not aware of the drugs given. Drugs were prepared and administered by the theatre anaesthesiologist who was not part of data collection or analysis.

- Group P:(n-30) received 2.5mg/kg Propofol ivgiven slowly for induction
- Group E:(n-30) received 0.3mg/kg Etomidate iv given slowly for induction

- The patients were kept nil per orally for 8 hrs. prior to surgery. On arrival in operation theatre standard anesthesia monitors including pulse oximeter, NIBP, ECG, etc. connected to the patient. Baseline vital parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and SPO2 recorded. (T0)

PREMEDICATION**:** Patient was premedicated with Ondansetron 0.1 mg/kg i.v., inj. Midazolam 0.02 mg/kg i.v. and inj. Fentanyl 2 mcg/kg i.vPREOXYGENATION Patient was pre-oxygenated with 100% oxygen for 3 minutes. All vital parameters were recorded again(T1).

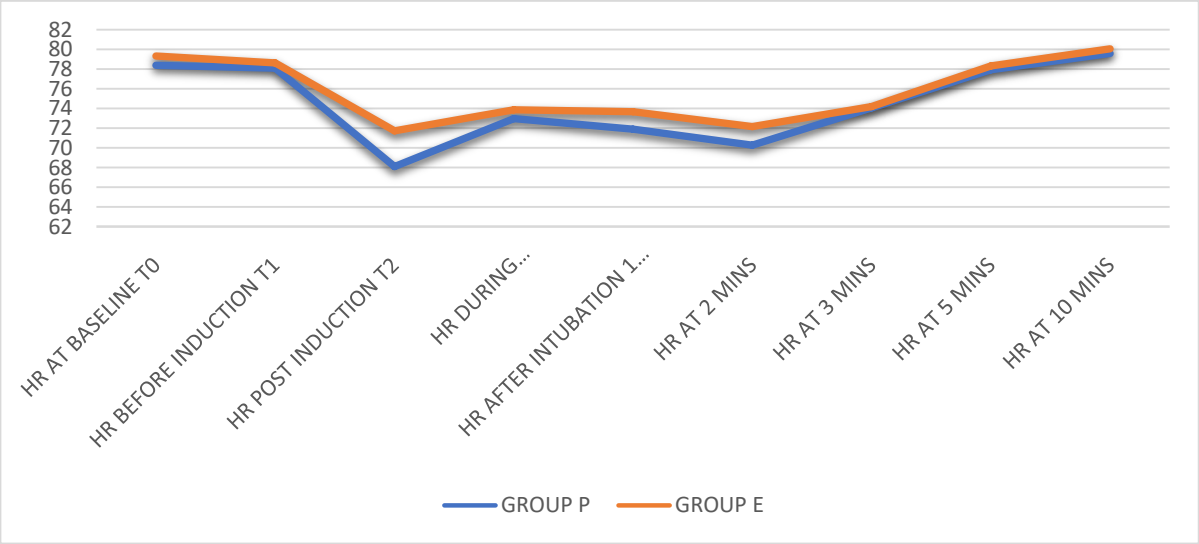
For induction - group P received Inj. Propofol 2.5mg/kg i.v and group E received Inj. Etomidate 0.3mg/kg i.v. given over 30 sec. After induction of anesthesia hemodynamic parameters were recorded(T2). Time of induction was taken as period between time of start of study drug till loss of eyelash reflex. The choice of muscle relaxant will be Inj. succinylcholine(2mg/kg) given after administering induction agent. Laryngoscopy and tracheal intubation attempted with appropriate size of endotracheal tube. All vital parameters will be recorded again during Laryngoscopy. (T3) Proper placement of endotracheal tube was confirmed by capnography and bilateral auscultation of chest. Periodic monitoring of vital parameters carried out at 1, 2, 3, 5 and 10 minute intervals post intubation.Anesthesia maintained with Oxygen, Nitrous oxide (33:66) and Isoflurane, along with intermittent boluses of muscle relaxant inj. vecuronium i.v. 0.1mg/kg as and when required throughout the surgery. At the end of surgery, patient will be reversed with inj. Glycopyrrolate 0.008 mg/kg i.v. along with Inj. Neostigmine methyl sulphate 0.05mg/kg intravenously.

RESULTS

TABLE NO. 1HEART RATE

VARIABLE	GROUP P MEAN ± SD	GROUP E MEAN ± SD	P VALUE
HR AT BASELINE T0	78.4 ± 2.74	79.33 ± 1.918	0.133
HR BEFORE INDUCTION T1	78.1 ± 2.59	78.63 ± 1.847	0.362

HR POST INDUCTION T2	68.10 ± 6.48	71.73 ± 2.016	*0.005
HR DURING LARYNGOSCOPY T3	72.97 ± 1.99	73.87 ± 3.181	0.194
HR AFTER INTUBATION 1 MIN	71.90 ± 1.32	73.67 ± 3.315	*0.009
HR AT 2 MINS	70.27 ± 1.23	72.17 ± 1.683	*0.001
HR AT 3 MINS	74.07 ± 3.07	74.20 ± 3.022	0.866
HR AT 5 MINS	77.93 ± 1.23	78.33 ± 1.493	0.262
HR AT 10 MINS	79.60 ± 1.30	80.07 ± 1.337	0.176



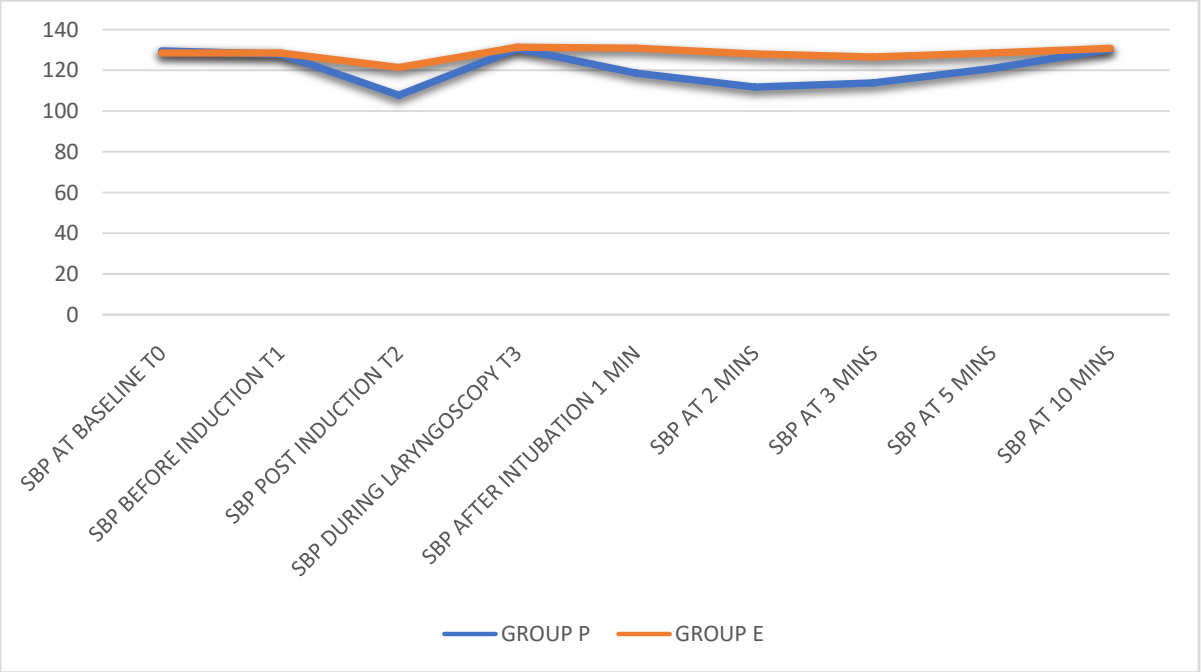
Graph1: comparison of heart rate between two groups

Table 1 and graph 1 show comparison of heart rate between two groups.. In group P, HR decreased at post induction(T2) (68.10±6.48), at post intubation 1min (71.90±1.32) and at 2 min (70.27±1.23) as compared to group E. It was statistically significant.

TABLE NO. 2SBP

VARIABLE	GROUP P MEAN ± SD	GROUP E MEAN ± SD	P VALUE
SBP AT BASELINE T0	129.53 ± 3.048	128.53 ± 1.961	0.136

SBP BEFORE INDUCTION T1	128.00 ± 1.742	128.33 ± 1.900	0.482
SBP POST INDUCTION T2	107.80 ± 2.483	121.43 ± 1.960	*0.001
SBP DURING LARYNGOSCOPY T3	130.70 ± 1.119	131.40 ± 1.673	0.062
SBP AFTER INTUBATION 1 MIN	118.67 ± 1.988	130.93 ± 1.143	*0.001
SBP AT 2 MINS	111.80 ± 3.078	128.07 ± 3.542	*0.001
SBP AT 3 MINS	113.87 ± 3.598	126.60 ± 1.499	*0.001
SBP AT 5 MINS	120.90 ± 1.125	128.53 ± 1.479	*0.001
SBP AT 10 MINS	130.33 ± 0.922	130.80 ± 1.126	0.084

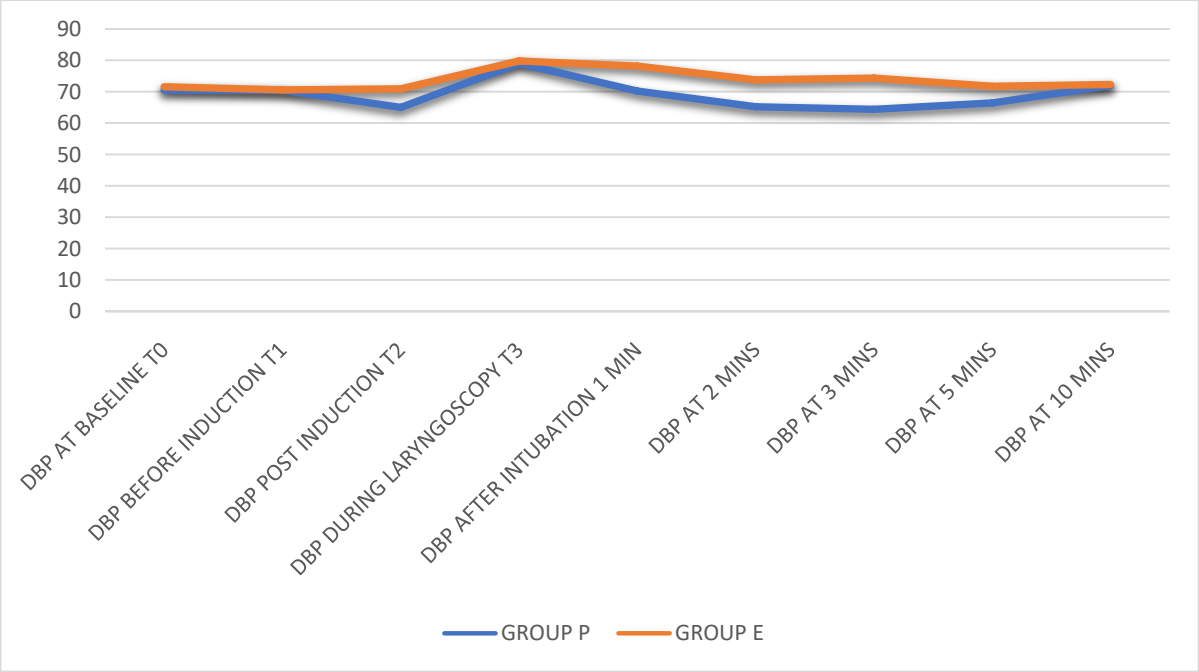


Graph 2: comparison in systolic blood pressure between two groups

Table no 2& Graph 2 show comparison in systolic blood pressure between two groups.In Group P, SBP decreased at post induction (T2) (107.80±2.483), after intubation at 1 min (118.67±1.988), at 2 mins (111.80±3.078), at 3 mins (113.87±3.598) & at 5 min (120.90±1.125).as compared to group E. It was statistically significant.

TABLE NO. 3DBP

VARIABLE	GROUP P MEAN ± SD	GROUP E MEAN ± SD	P VALUE
DBP AT BASELINE T0	70.53 ± 3.319	71.60 ± 2.749	0.180
DBP BEFORE INDUCTION T1	70.47 ± 2.813	70.60 ± 2.978	0.859
DBP POST INDUCTION T2	65.00 ± 2.393	70.93 ± 3.051	*0.001
DBP DURING LARYNGOSCOPY T3	79.07 ± 2.227	79.80 ± 2.941	0.281
DBP AFTER INTUBATION 1 MIN	70.20 ± 2.592	78.20 ± 2.483	*0.001
DBP AT 2 MINS	65.20 ± 2.821	73.80 ± 2.295	*0.001
DBP AT 3 MINS	64.40 ± 2.660	74.37 ± 2.076	*0.001
DBP AT 5 MINS	66.47 ± 2.837	71.77 ± 3.126	*0.001
DBP AT 10 MINS	72.00 ± 2.913	72.30 ± 3.042	0.698

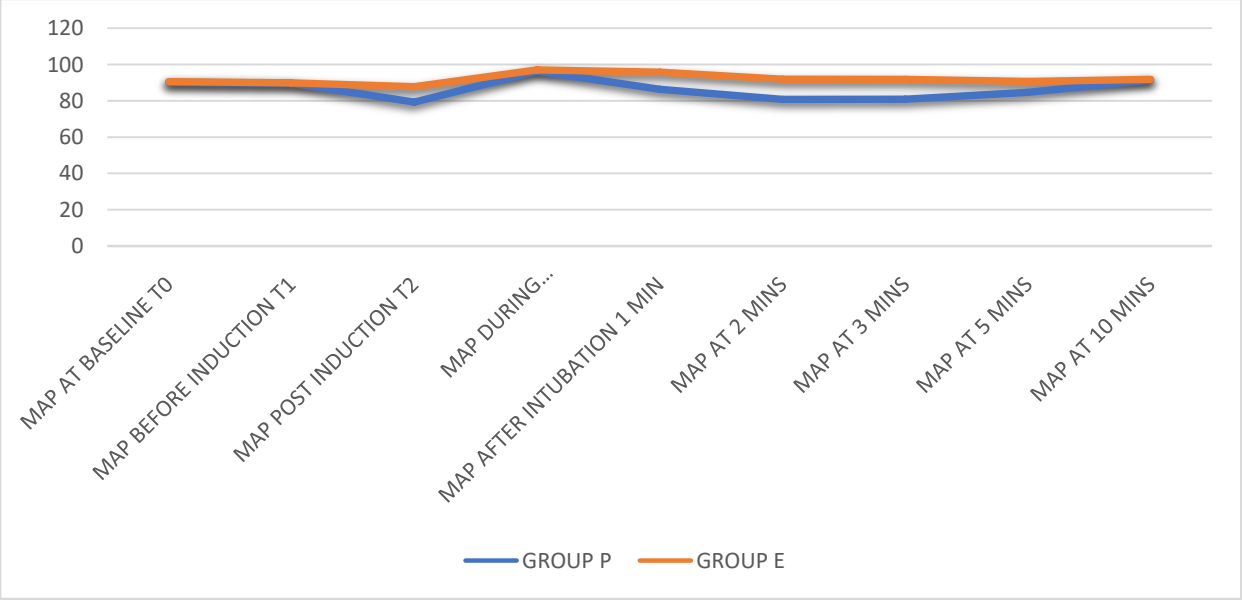


Graph 3: comparison of Diastolic Blood Pressure between two groups

Table no 3& Graph 3 show comparison of Diastolic Blood Pressure between two groups. In Group P, DBP decreased at post induction (T2) (65.10±2.393), after intubation at 1 min (70.20±2.592), 2 mins (65.20±2.821), 3 mins (64.40±2.660), and 5 mins (66.47±2.837) as compared to group E. It was statistically significant.

TABLE NO. 4MAP

VARIABLE	GROUP P MEAN ± SD	GROUP E MEAN ± SD	P VALUE
MAP AT BASELINE T0	90.20 ± 2.33	90.57 ± 1.87	0.492
MAP BEFORE INDUCTION T1	89.64 ± 1.91	89.84 ± 2.01	0.695
MAP POST INDUCTION T2	79.26 ± 1.77	87.76 ± 2.04	*0.001
MAP DURING LARYNGOSCOPY T3	96.27 ± 1.57	97.00 ± 1.88	0.113
MAP AFTER INTUBATION 1 MIN	86.35 ± 1.85	95.77 ± 1.69	**TABLE NO. 8 MAP** *0.001
MAP AT 2 MINS	80.73 ± 2.08	91.88 ± 2.00	*0.001
MAP AT 3 MINS	80.88 ± 2.00	91.77 ± 1.38	*0.001
MAP AT 5 MINS	84.61 ± 1.94	90.68 ± 2.16	*0.001
MAP AT 10 MINS	91.44 ± 1.99	91.80 ± 2.05	0.499



Graph 4:comparison of Mean Arterial Pressure between two groups

Table 4& Graph 4 show comparison of Mean Arterial Pressure between two groups.In Group P - MAP decreased at post induction (T2) (79.26±1.77), after intubation at 1 min

(86.35±1.85), 2 mins (80.73±2.08), 3 mins (80.88±2), and 5 mins (84.61±1.94) as compared to group E. It was statistically significant.

OBSERVATIONS AND RESULTS The demographic profile was comparable. There was no statistically considerable difference between the study groups with respect to baseline parameters of HR, SBP, DBP, MAP and SpO2.The fall in heart rate at post induction(T2), at 1 min, 2 min after intubation in Group P as compared to Group E was statistically significant with P value (<0.05). The fall in SBP,DBP and MAP at post induction(T2), at 1 min, 2 min, 3 min and 5 min after intubation in Group P as compared to Group E was statistically significant with P value (<0.05).

Induction Time:According to our study the mean induction time in group P was 35.03 ±2.498 sec whereas in Group E was 35.33±2.218sec, which was statistically insignificant.Pain on injection was more in group P 26 out of 30 than group E, myoclonus was more in group E 23 patients out of 30 compared to group P

DISCUSSIONThe maintenance of hemodynamic stability during induction of anesthesia is dependent on basal tone of the autonomic nervous system and baroreceptor reflex regulation of autonomic outflow influencing cardiac function and peripheral vascular resistance.

Propofol is an intravenous induction agent which combines the desirable characteristics of smooth induction and rapid recovery from anesthesia.Propofol also reduces preload, afterload and contractility which directly effects on vascular smooth muscle and has venous dilating properties. It causes reduction in tonic levels of sympathetic activity.

The salient properties of etomidate like hemodynamic stability, minimal respiratory depression, and favourable pharmacokinetics enable rapid recovery after a single dose. Etomidate causes reduction in myocardial function and basal sympathetic tone. It maintains hemodynamic stability by preserving or augmenting baroreflex mechanisms.

In the present study, there was no significant difference in demographic data between the two groups in relation to Age, weight, gender, and ASA grades.Induction Time:In our study the mean induction time in group P was 35.03 ±2.498 sec whereas in Group E was 35.33±2.218sec, which was statistically insignificant.Results of our study similar with study

results of Dr Supriya Agarwal et al[10] in 2020showed that mean duration of time to loss of consciousness between etomidate and propofol group was statistically insignificant

. In group P, HR decreased at post induction(T2) (68.10±6.48), at post intubation 1min (71.90±1.32) and at 2 min (70.27±1.23) as compared to group E, was statistically significant.Results of our study similar with study results of Djordjević B et al[11]conducted a study in 1999,in Group P showed that slowing down of radial pulse was more marked in propofol, than in etomidate or thiopentone group at 2 min, 5 min,10 min after induction of anesthesia.

SBP decreased at post induction (T2) (107.80±2.483), after intubation at 1 min (118.67±1.988), at 2 mins (111.80±3.078), at 3 mins (113.87±3.598) & at 5 min (120.90±1.125).as compared to group E, was statistically significant.In Group P - MAP decreased at post induction (T2) (79.26±1.77), after intubation at 1 min (86.35±1.85), 2 mins (80.73±2.08), 3 mins (80.88±2), and 5 mins (84.61±1.94) as compared to group E, was statistically significant.results of our study similar with results obtained in studyShahJigna, et al. [12]study conducted in 1999,greater decrease in blood pressure was in propofol group than etomidate after induction at 2,5 and 10 min after induction

.DBP decreased at post induction (T2) (65.10±2.393), after intubation at 1 min (70.20±2.592), 2 mins (65.20±2.821), 3 mins (64.40±2.660), and 5 mins (66.47±2.837) as compared to group E. It was statistically significant..results of our study similar with results obtained in studyShahJigna, et al. [12]in 2018 fall mean in DBP in group P from baseline compered to group E was statistically significant at 1min ,3 min ,5 min and 10 min after induction.

In our study in group Pout of30 patients, 26 patients had pain on injection (86.7%) where asin group E- 7 patients out of 30 had pain on injection (23.3%),Our findings in consistent with finding of Agarwal S et al[13]in 2016 who did a comparive study between etomidate and propofol 100 patients undergoing general anesthesia

Out of30 patients 2 patients in group Phad myoclonus activity (6.7%). In group E 23 patients out of 30 had myoclonus activity (76.7%.)Fatma Saricaoglu et al[14] 2011 in his study comparison of etomidate-lipuro,propofol and admixture at induction. 90 patients assigned into three groups;higher incidence of myoclonus seen in etomidate-lipuro group

CONCLUSION: Both, Propofol and etomidate are safe induction agents.Etomidate maintains better haemodynamic stability than propofol as induction agent.Pain on injection was more with propofol. However, myoclonus was more with etomidate. Both drugs were associated with no significant side effects/complication.

REFERENCE

1. Magill, Endotracheal Anesthesia: Proceedings of the Royal Society of Medicine. 1928;22(2): p985-989.
2. Ried IC, Brace DE - Irritation of the respiratory tract and its reflex effect upon heart; SurgGynaec and Obst; 1940:70: pg 157-162.
3. Stoelting RK, Circulatory changes during laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without lidocaine. Anesthesiology:1977; 47 pg 381-841
4. Hugo Van Aken H, Meinshausen E, Prien T, et al. The influence of fentanyl and tracheal intubation on the hemodynamic effects of anesthesia induction with propofol/N2O in humans. Anesthesiology 1988; 68: pg 157-163.
5. Stoelting, Roberta L. Hinges, Katherine E. Marschall. Stoelting'sAnesthesia and Co-existing Disease. 5th Edition. Philadelphia: Churchill Livingstone, 2009.
6. Paris A, Philipp M. Tonner PH, et al. Activation of alpha 2B-adrenoceptors mediates the cardiovascular effects of etomidate. Anesthesiology. 2003:99:889-895.
7. Morel J. Salard M, Castelain C, et al. Haemodynamic consequences of etomidate administration in elective cardiac surgery: a randomized double-blinded study. Br J Anesthesh. 2011; 107:503-509.
8. Snell RS. The Respiratory System in the Head and Neck. In: Clinical Anatomy by regions. 9th edition. Taylor C, editor. Lippincott Williams and Wilkins; Philadelphia: 2012;639-649.
9. Bishop MJ, Bedford RF, Kil HK. Physiologic and Pathophysiologic responses to intubation. In: Benumof JL. Airway Management – Principles and Practise. 1st edition. Mosby; New York: 1996;102-118
10. Dr. Agarwal Supriya, Sharma Vidushi et al A comparative study between Etomidate and Propofol as an induction agent during induction, laryngoscopy and intubation, International Journal of Medical and Biomedical Studies, 2020; Volume 4(12):165-167.
11. Djordjević B, Stojiljković MP, Loncar-Stojiljković D, Krivokapić D, Vojnosanit et al A clinical comparison of Cardiovascular effects of induction doses of the intravenous

anesthetic, propofol, etomidate and thiopentone]. Pregl. 1999 Jan-Feb;56(1):15-19. Serbian.

12. ShahJigna, et al. Comparative study of propofol vs etomidate as an induction agent to evaluatehemodynamicchanges during induction of anesthesia in controlled hypertensive patients.Anesthesia, Pain & Intensive Care: An international journal of anesthesiology, pain management, intensive care & resuscitation, 2018; 22(3): 361-367.
13. Aggarwal S, Goyal VK, Chaturvedi SK, Mathur V, Baj B, Kumar A. A comparative study between propofol and etomidate in patients under general anesthesia. Braz J Anesthesiol. 2016 May-Jun;66(3):237-241.
14. Fatma Saricoaglu, SennurUzun, Oguzhan Arun, Funda Arun, UlkuAypar, et al. A clinical comparison of etomidate –lipuro and admixture at induction. Saudi journal of anesthesia 2011; 5:62-66.