

Haemodynamic Responses to Tracheal Intubation using Propofol, Etomidate, and Etomidate –Propofol Combination in Anaesthesia Induction

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Conflict of interest: Nil

Abstract:

Background: Haemodynamic changes during laryngoscopy and intubation are the major concern during induction under general anaesthesia. This study aims to compare the effects between inj PROPOFOL, inj ETOMIDATE and inj ETOFOL (etomidate and propofol) during induction and intubation in elective surgeries.

Objectives: To evaluate and assess the effects of the 3 different induction agents, on the variation in heart rate (HR) and mean arterial pressure (MAP) were noted. They are baseline (T1), after induction (T2), before intubation (T3) and immediately after the intubation (T4) and T5, T6, T7, T8, T9 & T10 at 1st, 2nd, 3rd, 4th, 5th and 10th minutes after intubation.

Material And Method: After obtaining Ethical committee clearance taken, 90 patients aged 15 to 60 years of either sex and ASA physical status I and II scheduled for elective surgery under general anaesthesia were taken up for the study. Written and informed consent was obtained from the patient. Design of this study was a prospective randomised control study. The patients were randomly placed into three groups, of each 30 in number. Group P induced with Inj. Propofol (2.5 mg/kg IV), Group E with Inj. Etomidate (0.3 mg/kg IV) and Group PE with Inj. Propofol (1.25mg/kg iv) and Inj. Etomidate (0.15mg/kg iv). Heart rate (HR), mean arterial blood pressure (MAP) were noted at different time interval (T1- baseline, T2-after induction, T3- before intubation, T4-immediately after intubation, T5-T10 represent 1,2,3,4,5,10 mins after intubation and it was compared.

Results: Stata version 17.0 software were used for analysis of the data. Anova test used for analysing HR, MAP and AGE whereas fishers exact test done for gender. In the results demographic data were comparable. On comparing, MAP mean arterial pressure in all 3 groups with their baseline value, there was a significant fall in group P ($p < 0.000$) was noted at T4, T5 time interval when compared to group E, and group PE. MAP of group PE ($p < 0.000$) at T4, T5 time interval was noted higher when compared to other two groups.

Conclusion: The combination of etomidate and propofol (etofol group PE) has better hemodynamic stability with minimal changes compared to Etomidate and Propofol alone. It is would be recommended that (Etofol) the combination of Etomidate and Propofol can be used in situation where haemodynamic stability warranted.

Keywords: Haemodynamics, Induction, Intubation, Etomidate, Propofol, Etofol..

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Introduction

General anaesthesia is 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 loss of reflex response.

In all methods used for anaesthesia induction, it is aimed to preserve the haemodynamic balance. Laryngoscopy leads to sympathetic responses leading to tachyarrhythmia, raise in blood pressure (hypertension), increased intracranial tension and greater myocardial workload (myocardial infarc-

tion). Various drugs have been tried to minimize intubation response. Induction agents have a major role in mitigating intubation response. Etomidate is a hypnotic agent with minimal effect on cardiovascular system (cardio stable nature) but it lacks analgesic property. Cardiovascular stability is characteristic of Etomidate when it is used for induction of anaesthesia with 0.3 mg/kg IV. Propofol is a good agent to reduce airway reflexes, but can cause hemodynamic fluctuations.

The hypothesis of this study was that combination

of Etomidate and Propofol together as Etofol, given as induction agent, would maintain the stable haemodynamics during induction and intubation than they are given separately.

Aim of the Study

To compare the haemodynamic response (heart rate and mean arterial pressure) to tracheal intubation using propofol, etomidate and combination of propofol and etomidate [etofol].

Objectives of the Study

Primary objective: To assess the effect of the induction agent on the variation in heart rate (HR) and mean arterial pressure (MAP) after induction, before intubation and immediately after the intubation from 1 minute - 10 minutes.

Secondary objective: To assess the variation of the Rate Pressure Product (RPP) after induction and before the induction and immediately after the intubation from 1 minute to 10 minutes.

Materials and Methods

It is a prospective randomized controlled trial conducted in Thanjavur medical college and hospital from January 2023 to January 2024 in patients scheduled for elective surgeries under general anaesthesia.

Inclusion criteria:

1. Patient undergoing elective surgery with endotracheal intubation under general anaesthesia
2. Age between 18-65 years of both genders
3. ASA Class I and II

Exclusion criteria:

1. Allergy to drugs
2. Uncooperative patients
3. Chronic use of analgesia or sedatives
4. BMI >25kg/M²
5. Anticipated difficult intubation (Mallampatti III & IV)
6. Hypertension and Cardiovascular disease

Sample size:

Patients were randomly assigned to three groups, 30 each with 1:1 allocation using computer generated random numbers. GROUP P was to receive Propofol and GROUP E was to receive Etomidate, GROUP PE was to receive Propofol and Etomidate. Keeping alpha error = 0.05, beta error = 0.2, mean difference of SBP between E & P GROUP observed in previous study with MD = 7.23, sample size calculated was 30 per group.

The following pre-operative assessments were done for each subject who was selected after application of inclusion and exclusion criteria.

- Blood hemoglobin
- Blood sugar
- RFT
- ECG
- Chest X ray
- Blood pressure
- Heart rate
- SpO₂

Procedure

After getting Institutional Ethical Committee approval, this prospective randomized, controlled study was being conducted on ninety patients of the American Society of Anesthesiologist. Physical Status I and II aged between 18 and 65 years of either sex.

The patients who were admitted under the department of Surgery /Anesthesia for the day care surgery at Thanjavur Medical College Hospital, Thanjavur were approached. After the selection of subjects as per inclusion and exclusion criteria with pre-operative assessments, the patients were provided with a full informed consent form and information sheet. Thorough pre-anaesthetic check-up of all patients including all routine investigations was done. The procedure was explained to the patient and written informed consent was taken. Patients were administered with premedication drugs and on admission to the operating room, electrocardiography (ECG), non-invasive blood pressure, peripheral Oxygen saturation (SpO₂) Preoperatively, pulse rate and non-invasive systolic and diastolic blood pressure of the patients were recorded.

Lactated Ringer's solution infusion was started at 10 mL kg⁻¹ via an 18 G venous cannula in the back of the non-dominant hand. Patients were randomly allocated into three equal study groups. The randomization sequence was concealed in opaque sealed envelopes that were kept by the senior anaesthesia staff. The envelope was opened before induction. After obtaining written informed consent from the patients.

They were randomly divided into 3 groups: Group P (n = 30) was administered Propofol, group E (n = 30) was administered Etomidate and group PE (n = 30) was administered Etomidate - Propofol (Etofol) combination for anaesthesia induction. After administration of 1 mcg/kg Fentanyl to all patients in anaesthesia induction, patients in group P were administered 2.5mgkg⁻¹ Propofol, group E received 0.3mgkg⁻¹ Etomidate, group PE received 1.25 mgkg⁻¹ Propofol and 0.15 mgkg⁻¹ Etomidate in separate injectors. The medications were given at the rate of 1 mL/sec and in group PE, the venous cannula will be washed out with saline for 5 seconds between medications. When loss of consciousness is obtained (eye lash reflex loss), 0.6 mg/kg inj. Rocuronium muscle relaxant was given.

The patient was intubated by the orotracheal route (single attempt). After intubation, the cuff of the endotracheal tube was inflated. Following the intubation, the patients were ventilated to preserve end-tidal CO₂ pressure between 35-40 mm Hg and anaesthesia was maintained with 2% sevoflurane in a 50% O₂/N₂O mixture. After the completion of the surgery patient extubated after reversing with inj. neostigmine 50 mcg/kg and inj. Glycopyrrolate 10mcg/kg. During induction and intubation, the effect of the induction agent on the variation of the heart rate, mean blood pressure and rate pressure product were observed and noted in defined time period, T 1 baseline, T 2 after induction, T 3 before the intubation and T4 immediately after the intubation and T5, T 6, T7, T 8, T 9, T 10 at 1, 2, 3, 4, 5, 10 minutes after intubation.

Power of analysis

It was calculated based upon the hemodynamic parameters in previous study report (MAP at the first

minute of intubation was taken as the main result), a 10% difference could be determined between the group, then the power of the study found to be 80% and significance was 5% ($\alpha=0.05, \beta=0.80$).

Statistical Analysis

The data were coded and entered into the Microsoft excel sheet (MS Office 2019). The data were then entered into the Stata version 17.0 for statistical analyses. Descriptive statistics were stated as mean \pm standard deviation for continuous variables and as number and percentage for nominal variables. Age, HR, MAP and RPP were evaluated with one-way analysis of variance (ANOVA) and post-hoc tests with Bonferroni correction. The chi-square test was used for categorical data such as gender. p value <0.05 was considered statistically significant.

Observation and Results

Heart Rate

Table 1: Comparison of mean heart rate in various time interval

Heart Rate	Group-P Mean \pm SD	Group-E Mean \pm SD	Group-PE Mean \pm SD	F value	p value	Statistical test
T1	87.8 \pm 10.9934	82.23 \pm 8.041	93.66 \pm 11.127	9.510	0.000	S
T2	97.26 \pm 8.905	84.36 \pm 6.860	91.26 \pm 8.764	18.457	0.000	S
T3	106.03 \pm 8.352	87.9 \pm 5.58	89.63 \pm 4.701	73.233	0.000	S
T4	119.466 \pm 9.372	91.53 \pm 6.480	91.96 \pm 3.50	161.018	0.000	S
T5	124.23 \pm 9.065	92.66 \pm 11.630	93.56 \pm 6.33	112.848	0.000	S
T6	119.03 \pm 4.9304	92.6 \pm 10.584	92.23 \pm 4.91	132.466	0.000	S
T7	111.46 \pm 4.232	91.93 \pm 8.717	93.03 \pm 5.41	87.985	0.000	S
T8	105.33 \pm 3.790	90.66 \pm 6.588	92.23 \pm 7.195	53.292	0.000	S
T9	98.9 \pm 3.907	89.26 \pm 5.595	91.26 \pm 6.219	27.283	0.000	S
T10	94.03 \pm 4.156	89.46 \pm 5.799	89.76 \pm 4.994	7.742	0.001	S

(T1-Baseline, T2-after induction, T3-before intubation, T4-after intubation, T5-1st minute after intubation, T6-2nd minute after intubation, T7-3rd minute after intubation, T8-4th minute after intubation, T9-5th minute after intubation, T10- 10th minute after intubation.)

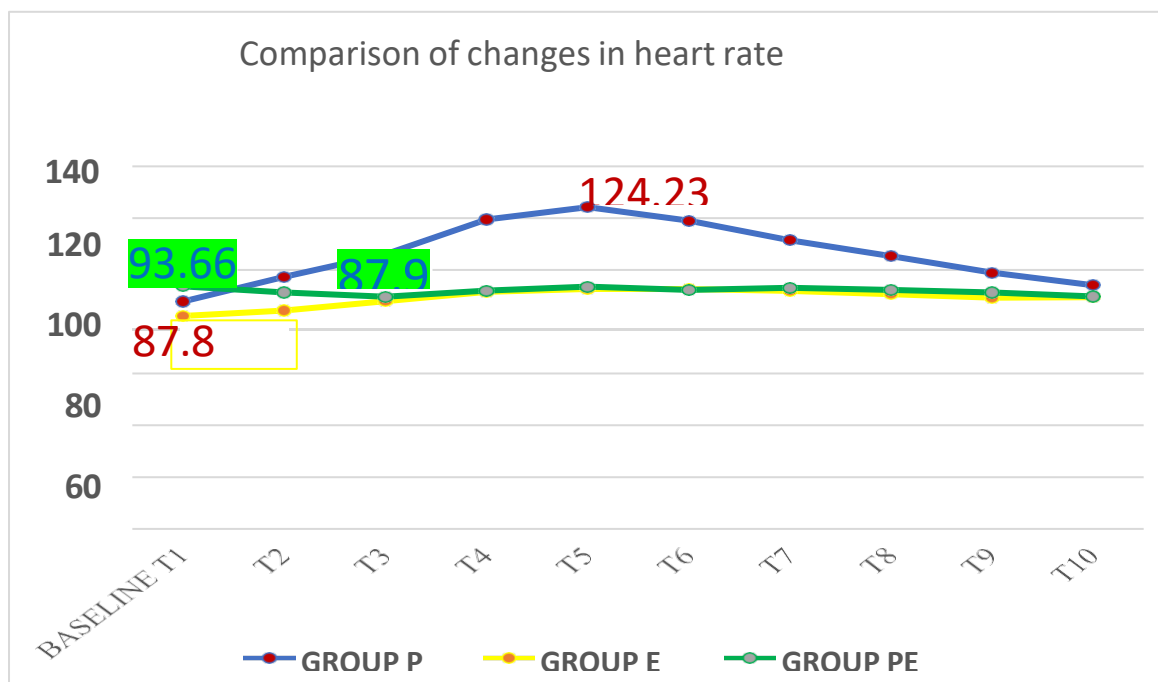


Figure 1: Comparison of changes in heart rate (bpm) between the 3 groups at various times

Interpretation

Baseline and pre-induction, intubation and post intubation and T5-T10 minutes HR were comparable among all three groups with statistical significant differences ($p < 0.05$) by using ANOVA TEST shown in the Table (5). At T5 time period there was a significant increase in heart rate in Group P when compared to Group E and Group PE. Group P produces significant tachycardia 41% rise in HR from baseline.

Systolic Blood Pressure

Table (2): Systolic Blood Pressure in various time interval

Interpretation

On comparison of changes in SBP between 3 groups it was found to be statistically significant during after induction, after intubation, 1st min to 10th min after intubation (T2-T10) time period.

Table 2: Systolic Blood Pressure in various time interval

Systolic BP	Group-P Mean±SD p value	Group-E Mean±SD p value	Group-PE Mean±SD p value	F value	p value	Statistical test
T1	123±7.080	121.93±6.93	121.83±4.69	0.313	0.732	NS
T2	107.23±6.61	116.86±5.29	123.46±4.39	65.882	0.000	S
	0.000	0.013	1.000			
T3	95.4±6.52	122.53±5.06	117.06±3.95	221.130	0.000	S
	0.000	1.000	0.01			
T4	89.46±6.57	125.73±5.47	110.26±3.99	3334.107	0.000	S
	0.000	0.283	0.000			
T5	88.46±6.67	126.76±7.11	112.6±3.970	304.4887	0.000	S
	0.000	0.024	0.000			
T6	94.166±3.56	124.66±3.83	119.93±3.84	575.129	0.000	S
	0.000	1.000	1.000			
T7	101.66±4.49	124.53±4.89	118.46±6.02	156.807	0.000	S
	0.000	1.000	0.422			
T8	108.9±5.89	121.53±4.74	119.66±5.96	45.037	0.000	S
	0.000	1.000	1.000			
T9	114.46±6.25	122.06±5.644	122.33±6.10	16.595	0.000	S
	0.000	1.000	1.000			
T10	118.9±6.42	122.86±6.93	123.33±5.99	5.998	0.004	S
	0.471	1.000	1.000			

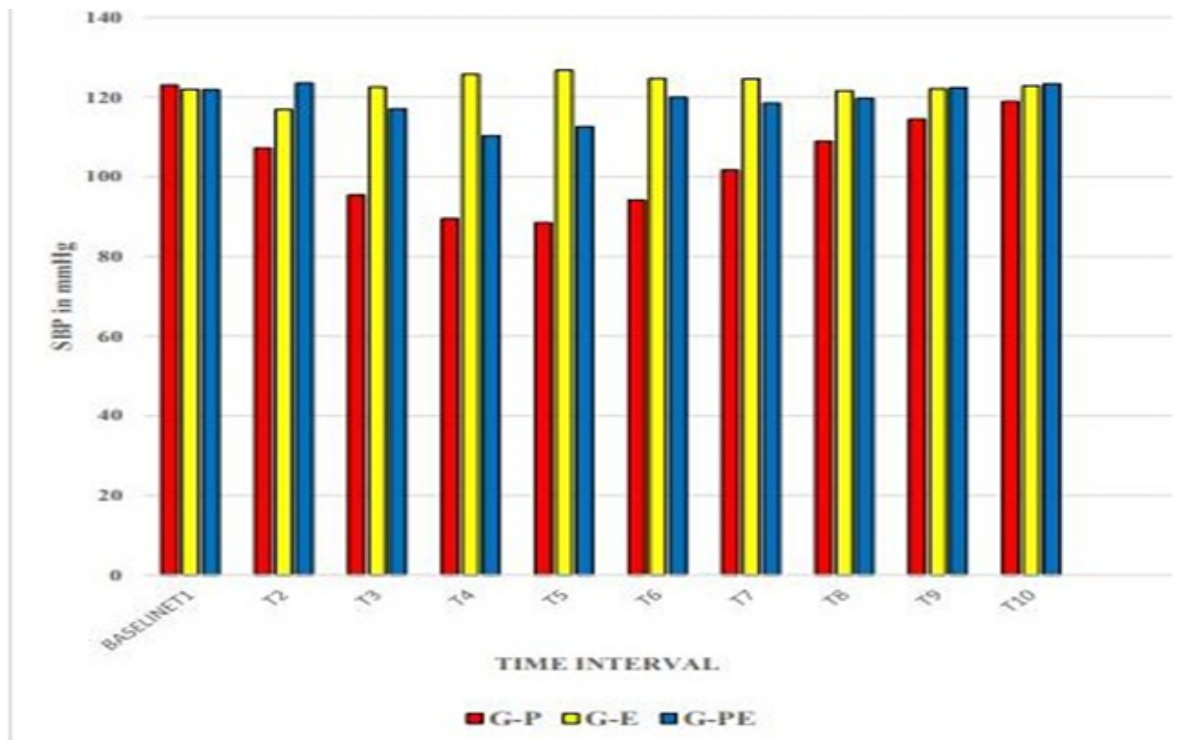


Figure (2): Comparison of changes in SBP (mmhg) between the 3 groups at various time intervals Diastolic Blood Pressure

Table 3: Diastolic BP in various time interval between 3 groups

Diastolic BP	Group-P Mean± SD p value	Group-E Mean± SD p value	Group-PE Mean± SD p value	F value	p value	Statistical Test
T1	74.93±6.25	73.4±5.84	76.9±7.25	2.201	0.117	NS
T2	64.4±5.73 0.000	72.53±5.17 1.000	77±5.27 1.000	41.990	0.000	S
T3	55.13±6.25 0.000	74.73±4.11 1.000	72.86±3.58 0.074	152.802	0.000	S
T4	49.33±7.68 0.000	78.06±5.90 0.028	67.46±3.748 0.000	175.942	0.000	S
T5	46.3±6.84 0.000	79.4±6.97 0.001	70.73±2.99 0.000	254.001	0.000	S
T6	55.26±5.69 0.000	76.13±4.86 1.000	74.66±4.21 1.000	165.294	0.000	S
T7	61.3±5.05 0.000	77.2±4.68 0.235	74.2±5.01 1.000	88.287	0.000	S
T8	66.26±3.62 0.000	75.6±4.59 1.000	75.06±50.3 1.000	41.521	0.000	S
T9	70.73±5.18 0.267	75.36±5.13 1.000	76.16±5.11 1.000	9.743	0.000	S
10	73.06±5.42 1.000	77.13±4.35 0.272	76.3±5.57 1.000	5.224	0.007	S

On comparing DBP in Propofol, Etomidate and Etofol group shows statistically significant in all 3 group in all time period from (T2) after induction to 10 mins after intubation (T10) except baseline.

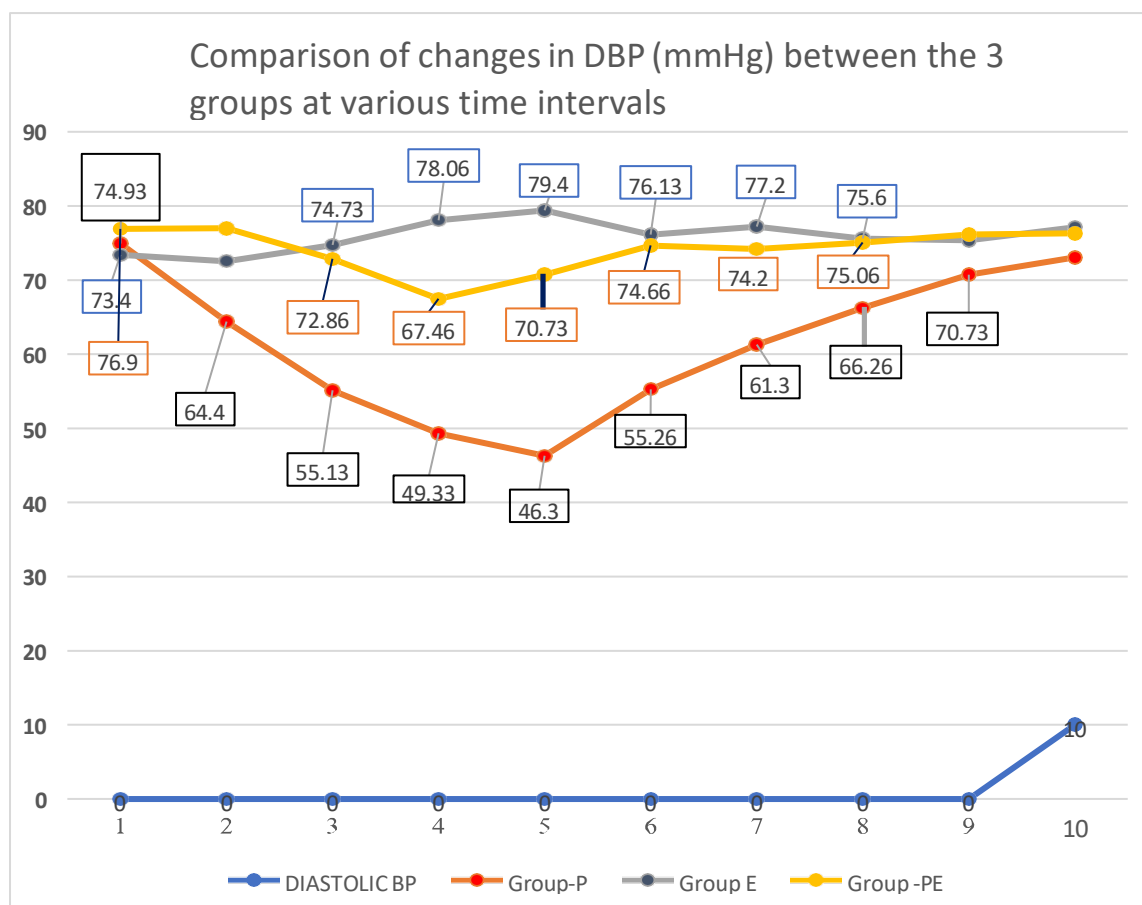


Figure 3: Comparison of changes in DBP between the 3 groups at various time intervals

Table 4: Rate Pressure Product at various time interval between the 3 groups

Rate Pressure (RPP)	Group-P Mean±SD p value	Group-E Mean ±SD p value	Group-PE Mean ±SD p value	F value	p value	Statistical Test
T1	10762.8 ±1613.647	10050.8±1233.93	11426.7±1534.09	6.576	0.002	S
T2	10436.93±1052.782	9865.4±749.18	11264.26±1108.27	13.498	0.000	S
T3	10088.267±733.460	10779±928.37	10489.4±595.06	6.174	0.003	S
T4	10508.733±1029.794	11533.6±1251.09	10138.4±484.80	16.434	0.000	S
T5	10896.2±547.566	11805.2±2054.54	10566.53±764.36	7.255	0.001	S
T6	11202.53±487.843	11566.53±1542.53	11098.13±632.44	158.994	0.000	S
T7	11134±960.689	11458.13±1266.43	11026.2±1054.52	1.250	0.292	NS
T8	11459.167±531.09	11014.267±852.128	11054.73±1213.9	2.195	0.118	NS
T9	11309.8±582.11	10892.4±784.68	11176.33±1091.85	1.905	0.155	NS
T10	11187.73±583.566	10991.6±749.18	11075.73±880.93	0.519	0.597	NS

On comparing RPP in Propofol, Etomidate and Etofol groups on various time period. Fig 5 shows that Etofol was statistically significant from baseline to 2nd min after intubation.

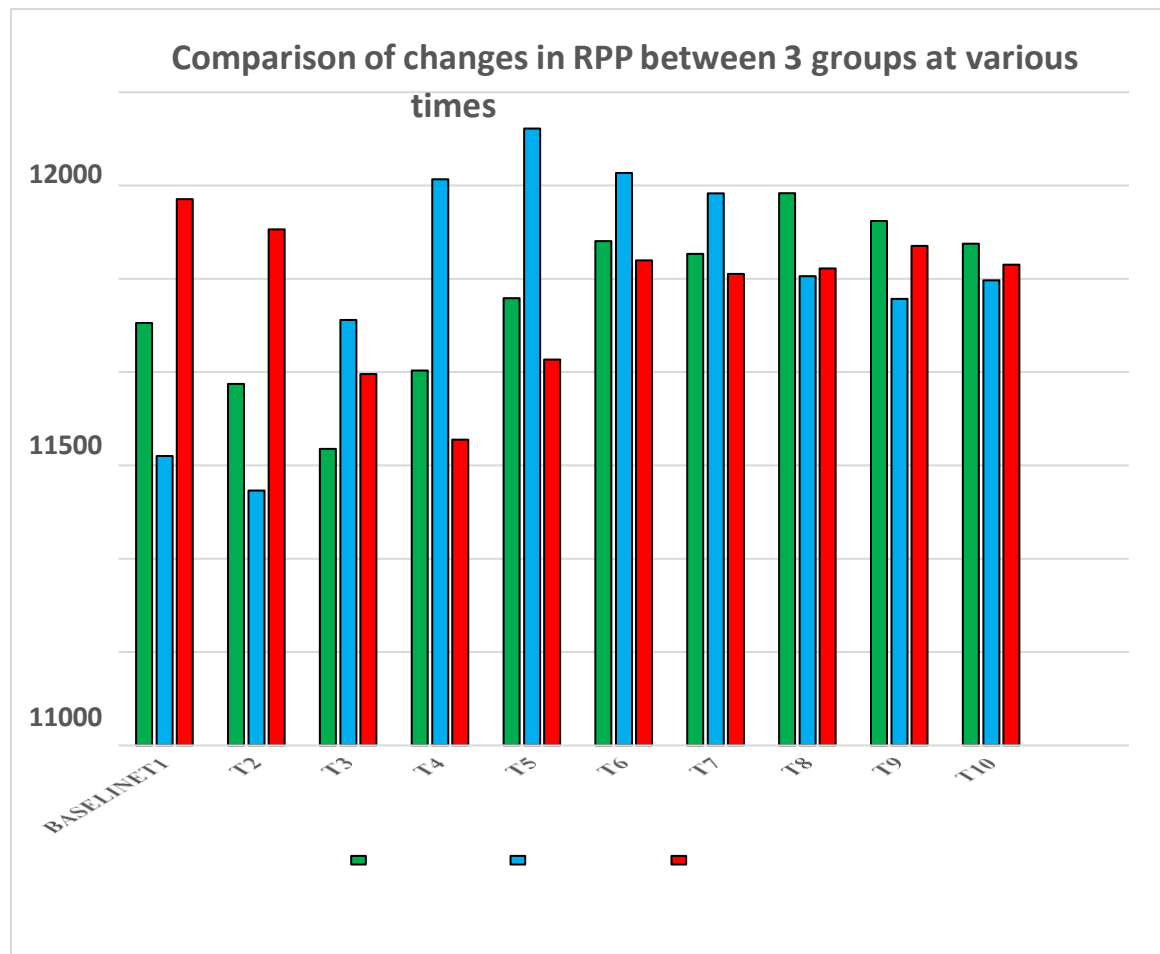


Figure 4: Comparison of changes in RPP between 3 groups at various time intervals

In this study five time periods are showing non normal distributions they are

- baseline rate pressure product,
- after induction MAP (T2),
- after induction RPP,
- before intubation RPP
- after intubation RPP to 10 mins after intubation in rate product pressure

For parametric independent variable, Kruskal wallis test was done. It showed, there were a statistically significant difference between Propofol, Etomidate, Etofol groups in baseline RPP $H(2) = 13.361$, $P = 0.001$, with mean rank of 45.75 for Propofol group, 33.05 for Etomidate group, 57.70 for Etofol group.

T2 MAP - after induction, there was a statistically significant difference between Propofol, Etomidate, Etofol groups. $H(2) = 51.207$, $P = 0.000$ mean rank for Propofol 20.73, 46.87 for Etomidate, 68.90 for Etofol.

Results

- Demographic data were comparable between 3 groups.
- A significant increase in heart rate from baseline was noted in Group P than compared to Group E and Group PE. It showed that Group P

produces significant tachycardia with 41% rise in HR at T 5 interval ($p < 0.05$).

- When comparing to Group P and group E, a significant reduction in HR from baseline was noted in Group PE, only at T3 interval.
- On comparing 3 groups, Group P showed 33% significant decrease in MAP from baseline at T5 interval whereas Group PE (10.07%) and Group E (2.96%). Group P produces significant tachycardia and hypotension when compared to other 2 groups ($p < 0.05$).
- Group E showed significant increase in MAP from baseline at T 5 time period ($p < 0.05$) when compared to other two groups.
- Group PE showed significant decrease in oxygen consumption at T4 time period when compared to other two groups.

Discussion

This study was carried out to compare Etomidate, Propofol and a 50% admixture of Etomidate and Propofol on the haemodynamic responses prior to and following tracheal intubation. In this study we got the result that Etofol group is haemodynamically more stable than Etomidate and propofol group. This result was supported by studies listed in Bibliography.

The etofol is an alternative to Etomidate alone in patients where laryngoscopic response to hemodynamic parameters is a concern. Combination of Etomidate and propofol had better hemodynamic stability than Etomidate alone at 1 minute after intubation. Etofol is associated with a shorter induction time and better hemodynamic stability and has less side effects and early recovery time. Etofol is an effective alternative for facilitating insertion of LMA with added advantage of lack of cardiovascular depression.

Conclusion

- We concluded that the ETOFOL (combination of Etomidate and Propofol) had better haemodynamic response with MAP and HR than Etomidate or Propofol alone at 1 min after intubation.
- Etomidate was better than Propofol in all points of time i.e from before intubation and after intubation from 1min -10 mins.
- The ETOFOL proved to be significantly better in maintaining uniform hemodynamic stability without any extremes than either Propofol or Etomidate.

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