

Original Research Article

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A comparison of propofol and etomidate as anaesthetic agents for elective non-cardiac surgery

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ABSTRACT

Background: To compare propofol and etomidate as anaesthetic agents for elective non-cardiac surgery with respect to stability of haemodynamic parameters, systemic side effects and quality of induction.

Methods: Randomised, blinded study of 100 patients posted for elective non-cardiac surgery under general anaesthesia, divided into two groups. In group P (n=50) induction was achieved with injection Propofol 1mg/kg, whereas in group E (n=50), it was achieved with injection etomidate 0.3mg/kg after premedication with injection midazolam 0.04mg/kg and fentanyl 2μg/kg in both the groups. Hemodynamic parameters like, heart rate, systolic BP, diastolic BP, Mean BP and induction time in seconds, pain on injection, myoclonus, post-operative nausea, vomiting were recorded at different time intervals (base line, at induction, immediately after intubation and 1, 3, 5 and 15 min after intubation).

Results: There was no statistically difference was found in demographic profile and baseline hemodynamic parameters but significant difference was found in intraoperative mean HR, SBP, DBP, MBP at various time intervals, and our result was more in favour of E group as compare to P, in which above recorded vital parameters were decreased more than E and induction time was also faster in E as compare to P. Pain on injection and post-operative nausea, vomiting was more in group P as compare to E, however the myoclonus movements was more in E group as compare to P but statistically not significant.

Conclusions: Etomidate is a better intravenous induction agent of anaesthesia than Propofol in hemodynamically unstable patient also as it has faster onset of action with less pain and post-operative nausea, vomiting with good hemodynamic stability.

Keywords: Etomidate, Hemodynamic parameters, Induction, Propofol, Postoperative

INTRODUCTION

The goal of inducing anaesthesia with minimum significant side effects continues to occupy the minds of anaesthesiologist. Authors prefer intravenous anaesthetic agents to induce anaesthesia, as induction is usually smoother and more rapid than that associated with most of the inhalational agents. Other uses of Intravenous (IV) induction agents other than induction of general

anaesthesia (GA) are to provide sedation in critical care unit and along with various type of peripheral nerve block and neuroaxial block, (TIVA) total intravenous anaesthetic agents to maintain anaesthesia, sole drug in day care anaesthesia and also along with local infiltration. IV induction agents are selected on the basis of following quality including, smooth and rapid induction, minimum effect on heart rate and blood pressure and effectively suppress intubation response. Over the years there has

been a continuous search for better and safer intravenous induction agent. The ideal IV anaesthetic agent has a rapid onset of action, quickly cleared from the bloodstream and CNS, protects vital tissues, has other desirable pharmacologic effects (e.g., an antiemetic effect), minimum effect on hemodynamic parameters, with minimum adverse effects and cost effective also. Propofol is most widely used IV anaesthetic agent for induction of anaesthesia, is alkylphenol derivative, with rapid onset, smooth induction and short duration of action, though can cause pain at the injection site. It produces unconsciousness within less than one minute. It is rapidly and extensively metabolized in the liver and at extrahepatic sites, leads to its high rate of total body clearance.¹

The drug has direct antiemetic effect through an unknown mechanism. It is euphorogenic, but unlike ketamine does not have residual psychotic effects. Propofol cause more hypotension because it reduces systemic vascular resistance.¹ Etomidate is carboxylated imidazole derivative. New lipid emulsion preparation of etomidate associated with less pain and minimum venous irritation with provide better sedation and can be consider as induction agents of choice in respiratory disease patient because it has minimum histamine release and no respiratory depression and also it may be induction agent of choice in cardiac and neuro anaesthesia because minimum effect on sympathetic nervous system and baroreceptor reflex regulatory system, increased coronary perfusion.²⁻⁵ But the incidence of myoclonus was persist with new preparation also.

The aim of present study was to select a better and safer induction agent in between propofol and etomidate by comparing certain parameters such as change in blood pressure and heart rate at various time interval and induction time, pain on injection, myoclonic movements, and post-operative nausea and vomiting.

METHODS

After obtaining approval from the Hospital Ethical Committee, hundred patients who posted for non-cardiac surgery were included in present study after obtaining written informed consent from each patient. The study period was for one year from December 2014 to November 2015 and study conducted in tertiary care hospital of new Delhi. Patients of American Society of Anaesthesiologists (ASA) Grade I, II, with 18 to 60 years age of either sex included in this study and patients of, ASA grade III or above, age more than 60 years and less than 18 years of either sex, allergic to study drugs, history of seizures, presence of known primary or secondary adrenal insufficiency, patients on steroid medications in past six months, pregnancy and lactating mothers and patients refusal were excluded from the present study.

Randomization of posted patients were done by computer generated random numbers into two groups of 50 each.

- Group P (n = 50) and
- Group E (n=50)

Preanesthetic checkup was carried out in every posted patient with airway assessment and any difficult airway was mentioned in record file. Day before surgery all the posted patients were instructed for nil by mouth (NBM) for 8 hour and tablet alprazolam 0.25mg and tablet ranitidine 150mg given orally at bed time, than in morning 8 am patients shifted to preoperative room, vitals were recorded than antibiotic injection was given and shifted to operation theatre (OT), taken on OT table, all monitor were attached including ECG, non-invasive blood pressure (NIBP), pulse oximeter and baseline blood pressure (systolic, diastolic and mean), heart rate, SPO₂, respiratory rate were recorded in every patient in each group than after 18G intravenous cannula was secured and ringer lactate was started at rate of 20ml/hour, than injection midazolam 0.04mg/kg as anxiolytic agent and injection fentanyl 2 μ g/kg as an analgesic was given to every patient in both group 10min before induction. Then every patient was preoxygenated with 100% oxygen for 3 minute by bag and mask ventilation and injection propofol (1.0mg/kg) and injection etomidate (0.3mg/kg) body weight intravenously given to patient by attending anaesthetist for induction of GA in respectively P and E group over 30-60sec, induction time was recorded in each group by observing anaesthetist. Injection vecuronium 0.1mg IV used as relaxant agent to facilitated endotracheal intubation with appropriate cuffed endotracheal tube (ETT) size 7, 7.5, and 8 was used. Than ETT was fixed after checking bilateral air-entry by use of stethoscope and put on closed circuit ventilation system and isoflurane, nitrous (60%) and oxygen (40%) was used to maintain anaesthesia, and minimum alveolar concentration (MAC) was kept 1-2, end tidal CO₂ was maintained between 30-35mmHg. Intraoperative analgesia and relaxant agents was repeated with injection fentanyl 1 μ g/kg and vecuronium 0.015mg/kg if surgery prolonged more than an hour, isoflurane was discontinued at the time of closure or suturing of incision site and then reversal was prepared with injection neostigmine 0.05mg/kg and injection glycopyrrolate 0.01mg/kg than nitrous was stopped and slowly reversal was given than extubation was done after proper oropharyngeal suction with red rubber catheter after extubation 100% oxygen was given by face mask, after checking for cough and swallowing reflux and patient was fully conscious following all the verbal command, vital parameters were stable, shifted to recovery room where asked for rescue analgesic requirement and injection ondansetron 4mg given as antiemetic agents.

Following parameters were recorded in each group intraoperatively at various time intervals and reading was mentioned in record form by observing anaesthetist

- Base line heart rate (HR) and systolic, diastolic, mean blood pressure (SBP, DBP, MBP), SPO₂, ECG, respiratory rate

- Above hemodynamic parameters were recorded after induction, after intubation, than 1, 3, 5, 15min after intubation
- Induction time (in second) was recorded for both the group - administration of drug to loss of eyelash reflex
- Pain on injection of induction agents
- Myoclonus movements intraoperatively
- Post-operative nausea, vomiting (PONV).

Steward score of recovery was used to assess the recovery of patient in both the group after anaesthesia, its content are conscious level, intact airway, motor power⁶

- Conscious level: 2 for fully awake, 1 for responding to stimuli, 0 - not responding to stimuli
- Airway maintenance: 2 for coughing on command, 1 for maintaining a good airway, 0 - airway needs maintenance
- Movement of limbs: 2 - moving limbs purposefully, 1 - non purposeful movements, 0 - not moving limbs. Patients of score 2 in conscious level, 2, or 1 for airway, 2 for limb movements are considered to shift in postoperative ward.

Sample size and statistical methods

Sample size was calculated keeping in view at the most 5% risk, with minimum 80% power and 5% significance level (significant at 95% confidence level). However, consider the past data, which gives idea of variation in the variables, play important role in calculating the sample size. If follow up was included in the study, the sample size should be 50 in each group for safer side and normality of the data.

To analyse the data we used SPSS version 18.0, alpha value (significance value) is less than 0.05. To compare mean values between the two groups, t-test was used for normal data, for nominal data chi-square test was used. If significance value (p-value) is less than 0.05, than we can say that there is significant mean change in the observations at different time points at 95% confidence level and if p-value is less than 0.01 in that case the significance level will be 99%, otherwise (p-value greater than 0.05) mean change is considered as nonsignificant.

RESULTS

Data were collected and statistically analysed as explained above. Both the group was comparable in demographic characters, age, sex, weight, and ASA grade. The mean age was (mean \pm SD) 41.64 \pm 11.43 and 42.68 \pm 11.20 years and mean weight was 63.78 \pm 7.55, and 62.92 \pm 7.95kg in group P and E respectively. In both the group female preponderance was found, this was because more female patients admitted for surgery and male to female ratio was 1:2.84 and 1:2.33 in P and E group respectively. In both the group ASA grade I patients was

admitted more than ASA II physical status and ratio was 2.1:1 and 1.94:1 in group P and E respectively. No statistically significant difference was found amongst the two groups in above recorded data (p value =>0.05) (Table 1).

Table 1: Distribution of demographic characteristics in both the group.

Parameters	Group P	Group E	P value
Age (years) (mean \pm SD)	41.64 \pm 11.43	42.62 \pm 11.20	0.323 (NS)
Weight (kg) (mean \pm SD)	63.78 \pm 7.55	62.92 \pm 7.95	0.290 (NS)
Male/Female ratio	13/37	15/35	0.328 (NS)
ASA grade I/II	34/16	33/17	0.416 (NS)

Base line hemodynamic parameters were comparable in both the groups (Table 2 showed variation in base line blood pressure and heart rate) but no significant different was noted. The duration of surgery and type of surgery was also comparable in both the groups (Table 3 and Figure 1).

Table 2: Base line hemodynamic parameters in both the groups.

Base line mean parameters	Group P (mean \pm SD)	Group E (mean \pm SD)	P value
HR (beat/min)	82.20 \pm 6.80	81.96 \pm 6.81	0.430
SBP (mm Hg)	130.22 \pm 9.69	130.98 \pm 8.91	0.342
DBP (mm Hg)	81.68 \pm 7.37	82.60 \pm 7.14	0.264
MBP (mm Hg)	97.86 \pm 8.6	98.73 \pm 7.33	0.284

Table 3: Duration of surgery (SX) in both groups.

Type of SX	Duration in group P (mean \pm SD) minute	Duration in group E (mean \pm SD) minute	P value
Lap choli	82 \pm 20	80 \pm 24	0.652
Lap appendicectomy	78 \pm 12	74 \pm 9.96	0.073
Lap epigastric hernia	124 \pm 18.56	126 \pm 20.2	0.607
Lap ventral hernia	124 \pm 18.65	128 \pm 18.78	0.287
Mastoid	186 \pm 19.56	180 \pm 19.86	0.131
Tonsillectomy	62 \pm 8.78	64 \pm 8.98	0.263
FESS	220 \pm 20.56	224 \pm 20.78	0.336
Radius# ORIF	64 \pm 10.56	62 \pm 9.98	0.333

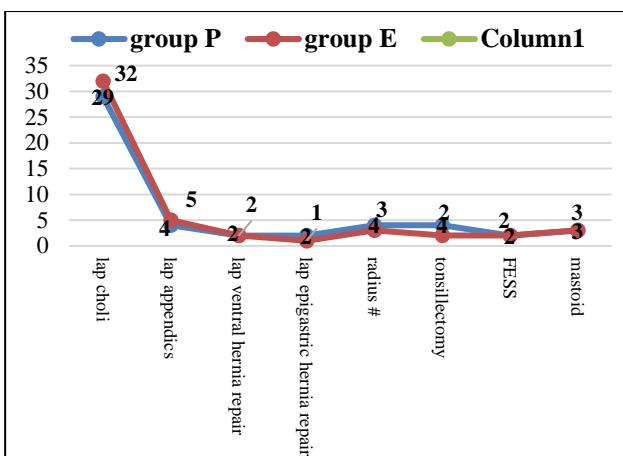


Figure 1: Distribution of various type of surgery in both groups.

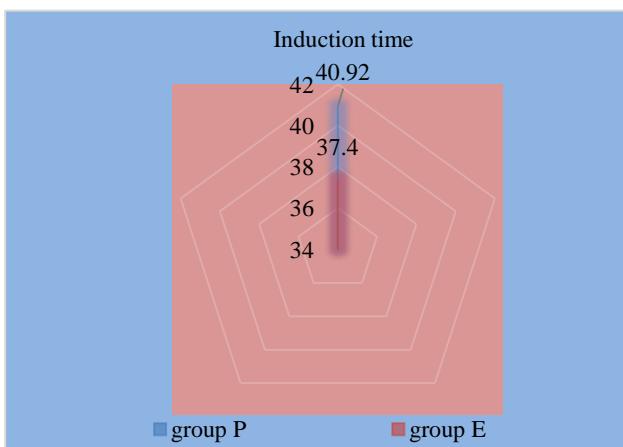


Figure 2: Induction time in seconds in both the groups.

Figure 2 showing distribution of induction time in both the group which is the time of injection of study drug to loss of eyelash reflexes and recorded in seconds, it was shorter in E (37.40 ± 7.28 s) as compare to group P (40.92 ± 7.74 s), statistically significant difference was noted (P value=0.011). Figure 4 showed variation in systolic blood pressure (SBP).

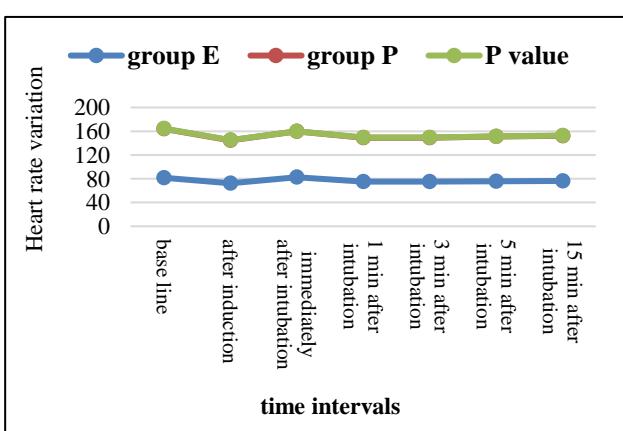


Figure 3: Mean heart at various time intervals.

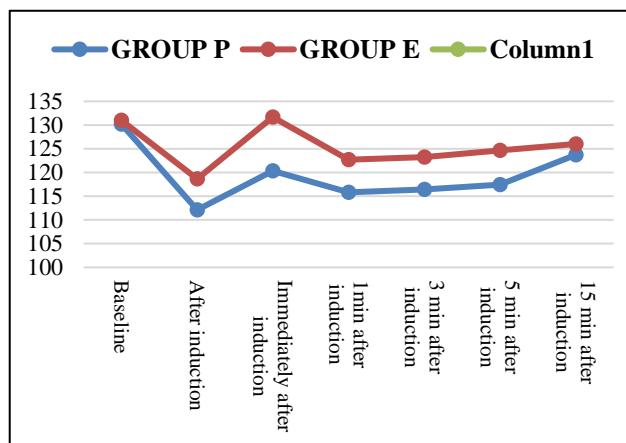


Figure 4: Mean SBP at various time intervals.

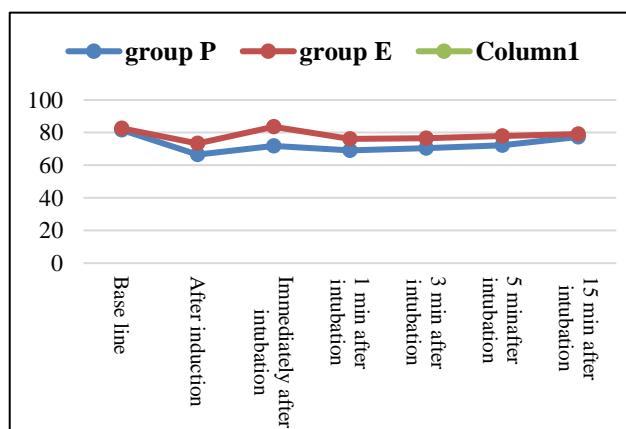


Figure 5: DBP at various time intervals.

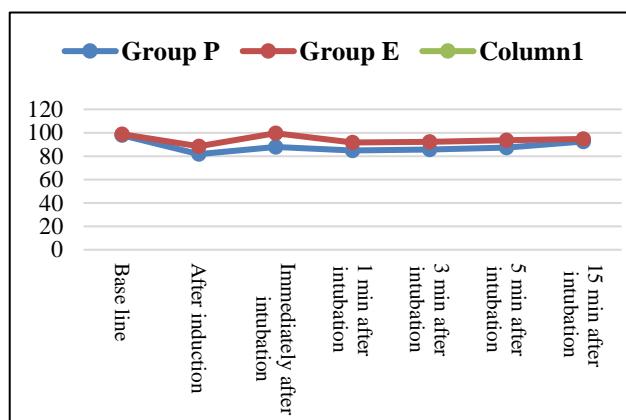


Figure 6: MBP (mean blood pressure) at various time intervals.

Figure 5 showed variation in diastolic bold pressure (DBP), and Figure 6 showed variation in mean blood pressure (MBP) at various time interval started from base line, immediately after induction, and intubation and 1, 3, 5, 15min after intubation. SBP, DBP, and MBP was decreased in both the group except immediately after

intubation all three blood pressure was increased in both the group because of intubation stress response, and in group E, this stress response was noted minimum as compare to baseline parameters (p value=0.134), and this fall in mentioned blood pressure was more in group P as compare to E at 1, 3, and 5min after intubation and difference was statistically significant (p value <0.001) but after 15min of intubation all the vital parameters including SBP, DBP, MBP, was comparable in both the groups (p=0.098).

Table 4: Side effects in both the group.

Side effects	Group P (n=50)	Group E (n=50)	P value
Pain on injection	25 (50%)	9 (18%)	<0.001
Myoclonus	0 (0%)	3 (6%)	0.039
PONV	15 (30%)	11 (22%)	0.181

Table 4 showed systemic and local side effects in both groups. Local side effect like pain on injection was more with Propofol as compare to etomidate, and the difference was statically significant (p value <0.001), authors know that propofol cause more irritation of vein and other side effects like myoclonus was more in group E (6%) of cases as compare to P group in which none of the patient showed myoclonus movements. PONV were more in group P 15 (30%) cases as compare to 11 (22%) of cases in group E.

DISCUSSION

All the surgical procedures are performed under anaesthesia, which is categorized in to general anaesthesia (GA), regional anaesthesia (RA) and local infiltration, depends on patient general condition, and type of surgery. Induction of GA can be done by intravenous (IV) and inhalational anaesthetic agents but in most of the cases IV agents are preferred over inhalational because of rapid and smooth induction with minimal systemic effects. Recently various type of IV agents are used e.g. thiopentone, midazolam, Propofol and etomidate, opioid etc. During induction of anaesthesia many complications are noted like sudden fall in blood pressure, arrhythmias, cardiac arrest, hypoxia so it is desirable to use a safe agent with minimum systemic side effects. In present study we compared the Propofol and etomidate as induction agents of GA for their effect on hemodynamic parameters and various adverse effects on patients and we found that there was no significant difference in both groups in view of demographic profile, duration and type of surgery and baseline hemodynamic parameters. The main findings of the present study showed that pain on injection and induction time was less, but myoclonus was more with the use of etomidate as compared to Propofol. Patients who received etomidate as induction agent showed more stable haemodynamic in comparison to Propofol. There was no statistically significant difference in two groups regarding

postoperative nausea and vomiting. Present study was favoured by a study conducted by Zhang et al, and Saricaoglu F et al, they observed faster induction with etomidate in comparison to Propofol.^{7,8} Hemodynamic parameters were more stable with etomidate as compare to Propofol and our results were agreement with Skinner et al.⁹ In a study done by Singh R et al, they observed that the etomidate was the least effective in minimizing stress response of intubation among other compared induction agents and mean heart rate and blood pressure was significantly increased from baseline etomidate group and present study results also showed that etomidate minimally decrease intubation stress response.¹⁰ Propofol significantly decreased blood pressure and heart rate immediately after induction, it is because it inhibits sympathetic nervous system stimulation and impair baroreceptor reflex also.

Another study also in favour of etomidate conducted by Prasad R et al, found that Propofol significantly decreased blood pressure at various time interval after induction.¹¹ Etomidate is better induction agents as compare to Propofol as it preserves sympathetic outflow and autonomic reflexes also, so minimum changes in vital parameters after introducing of drug.^{12,13} Local side effect like pain on injection was more in P group as compared to group E, and the difference was found statistically significant in our study. Other study which favour present result are the studies conducted by Altmayer P et al, Nyman et al, and Saricaoglu et al, they all found same result that pain was more severe with propofol with added lidocaine as compare to etomidate as induction agent.^{10,14,15} Myoclonic movements during induction was observed in etomidate group only in our study but difference was not significant. Preent result was favoured by, Aggarwal S et al, also found that incidence of myoclonus was more in the etomidate group (20% patients) as compared to propofol group (1.8% patients).¹⁶

Similarly, Schwarzkopf KR et al, Isitemiz et al, concluded that midazolam and fentanyl is use as premedication, both are effective in reducing etomidate-induced myoclonic muscle movements in comparison to those who received no premedication.^{17,18} Fifteen patients in the group P and eleven patients in the group E had nausea and vomiting in the post-operative period and difference was statistically nonsignificant (P =0.181). In studies done by Mayer M et al, and Pierre M et al, they observed that induction of anaesthesia with etomidate does not increases PONV and incidence of PONV is comparable after induction of anaesthesia with Propofol and etomidate.^{19,20} Results of our study are also consistent with these studies.

In the present study, authors did not analyse, the changes in serum cortisol levels during the post-operative period in etomidate group and did not studied the incidence of thrombo-phlebitis, which may occur after injection of etomidate and propofol.

Further studies are needed to establish safety of etomidate in patients with poor ventricular functions and in patients with hypotension and shock and needed to search for better agents to suppress pressor response of laryngoscopy in patients receiving etomidate as induction agent.

CONCLUSION

Intravenous induction agent are choose by anaesthesiologist on the consideration of rapid and smooth induction of general anaesthesia with minimum effect on cardiovascular respiratory, and central nervous system, with minimum local side effect like pain on injection and with less incidence of postoperative nausea and vomiting and with intrinsic pharmacological desired properties like antiemetic, analgesic, and muscle relaxation and must be cerebral protective and no major systemic side like myoclonus movements. In the present study authors conclude that etomidate is better induction agents as compare to propofol as it is nearly fulfilling above mentioned requirement.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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