



Comparision of Etomidate versus Propofol for Anaesthesia in Short Case Surgical Procedures

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ABSTRACT

Background: *Etomidate and Propofol are two ultra short-acting IV induction agents. Studies for long duration surgeries found that etomidate provides effective, reliable anaesthesia, rapid recovery and minimal side effect but very less studies are available for short duration surgical procedures. A present study was aimed to evaluate hemodynamic changes, compare duration of recovery from anaesthesia and compare safety of both drugs.*

Material and Methods: *We conducted single centred, open labelled, parallel group Randomised Control Trial on 60 patients between 18 to 60 years age, having physical status ASA I, II or III undergoing elective or emergency short (less than or equal to 30 minutes) surgical procedures. Patients who met inclusion criteria were randomly divided into two groups of 30 each based on computer generated software after taking written and informed consent. Patients were given premedication and IV induction agent (loading dose) followed by i.v. infusion according to their group.*

Results: *Mean of Modified Aldrete Score and Modified Observer's Assessment of Alertness Score were 9.06 & 9.87, 4.25 & 4.9; Group P and E respectively. Mean variation of HR and MAP after 5 mins of induction was less significant. But SPO2 was 2.57 and 0.17, in group P & E respectively (P value=0.026). Recovery duration from anaesthesia was much rapid and faster in Group E. Fewer side effects were observed in group E.*

Conclusions: *Etomidate was haemodynamically more stable and showed rapid recovery and lesser side-effects in comparison to propofol. But both were equally efficacious.*

Keywords: *Propofol, Etomidate, TIVA.*

Introduction:

Propofol has an onset of action of approximately 45 seconds and begins to redistribute from the blood to fat and muscle in 3 to 5 minutes, with a rapidly resolving clinical effect. Propofol provides reliable amnesia and rapid recovery. Etomidate has an onset of action of approximately 1 minute and duration of action of 5 to 15 minutes. It is

considered to have the least hemodynamic effects. TIVA has become popular, practical and possible only in recent times because of pharmacokinetics and pharmacodynamics of newer anesthetic agent and also modern techniques.

Now days, day care surgeries, short surgical procedures are frequently performed in which patients require relative amnesia, short and

effective anesthesia, rapid recovery, early post operative discharge and mobilization. We evaluated hemodynamic changes, duration of recovery from anaesthesia and side effects of both drugs.

Material and Methods

After obtaining approval by institutional human ethics research committee, written and informed consent were obtained. We conducted single centred, open labelled, parallel group Randomised Control Trial on 60 patients between 18 to 60 years age, having physical status American Society of Anaesthesia I, II or III undergoing elective or emergency short (less than or equal to 30 minutes) surgical procedures. Patients were randomly divided into two groups of 30 each based on computer generated software. Patients having allergy to these drugs, pregnancy and epilepsy were excluded from study.

Detailed history, clinical examination, routine and specific investigations were done as per protocols. Airway assessment like mouth opening, mallampati grading, dentition, neck flexion and extension of all patients was done. Patients were kept NBM 8 hours prior to procedure for solids. In the preoperative room i.v.access was established. Vital parameters like, heart rate, systolic blood pressure diastolic blood pressure, mean arterial pressure, oxygen saturation were recorded as a base line value. Volume of medication and speed of injection were equal in both groups. All patients were given Inj. Ranitidine 1mg/kg i.v. and Inj. Metochlopramide 0.2 mg/kg i.v. 30-45 minutes prior to procedure. Then patient was shifted to operation theatre. ECG, pulse oxymeter, blood pressure monitor were applied and vital parameters were recorded. All patients were given Inj. Midazolam 0.02 mg/kg i.v. and Inj. Fentanyl 2mcg/kg i.v. before the induction. For re-establishment of fluid balance, ringer's solution or normal saline was infused and continued at rate of 5ml/kg/hr during surgery. Routine vitals and arterial saturation monitoring were done every 5 minutes. After that, anesthesia was induced with

Inj. Propofol 2 mg/kg i.v. bolus followed by i.v. infusion 100 mcg/kg/min or Inj. Etomidate 0.3 mg/kg i.v. bolus followed by i.v. infusion 10mcg/kg/min. Continuous O2 supply was given by O2 mask at 4-6L/min.

The depth of anesthesia was checked by loss of eyelash reflex, regular smooth respiratory movement and no movement on painful stimuli. Patients were maintained on spontaneous respiration if respiratory depression was detected then; increase in supplemental oxygenation was done, assisted respiration by using manual resuscitation was given or usage of oropharyngeal/nasopharyngeal airway if required.

Patients were observed for any side effects of etomidate or propofol. Infusion technique would decrease incidence of pain on injection and myoclonus. Anaesthesia was continued till surgical dressing. After the surgery, any side effect experienced by the patients was noted. The time to recovery from anesthesia was recorded just after completion of surgery by response to painful stimuli and response to following verbal commands.

In case of Bradycardia (HR less than 50/min) Inj. Atropine 0.6 mg i.v. (may repeat up to maximum dose of 3 mg) was given and if hypotension(fall in systolic BP more than 20%of base line) fast fluids (ringer's solution/normal saline/colloid solution) and Inj. Mephentermine 6 mg i.v. in incremental doses were given. Once patient responds to painful stimuli and verbal command, he/she was shifted to post-op recovery room. In the post operative recovery room patients were assessed by Modified Aldrete Criteria, Modified Observer's Assessment of Alertness score to note the recovery from anesthesia every 10 mins.

In our study, sample size was calculated in respect of hemodynamic parameter (MAP at baseline and five minute of induction). A 20% difference could be determined between the group at 80% power and 5% significance ($\alpha=0.05$, $\beta=0.80$). Analysis was performed by descriptive statistics. STATA was used to analyses the data. Descriptive statistics mean (SD) and Frequency were used for

analysis. Independent T test was used to compare groups. P value <0.05 was significant for comparisons in both groups.

Results

Total 80-100 patients were explained about type of study, methodology, drug usage and their side-

effets. Out of these, 72 patients were assessed for eligibility and among them 60 patients fulfil all required inclusion criteria. They had given informed consent for the same from March 2015 to June 2016. [Figure1]

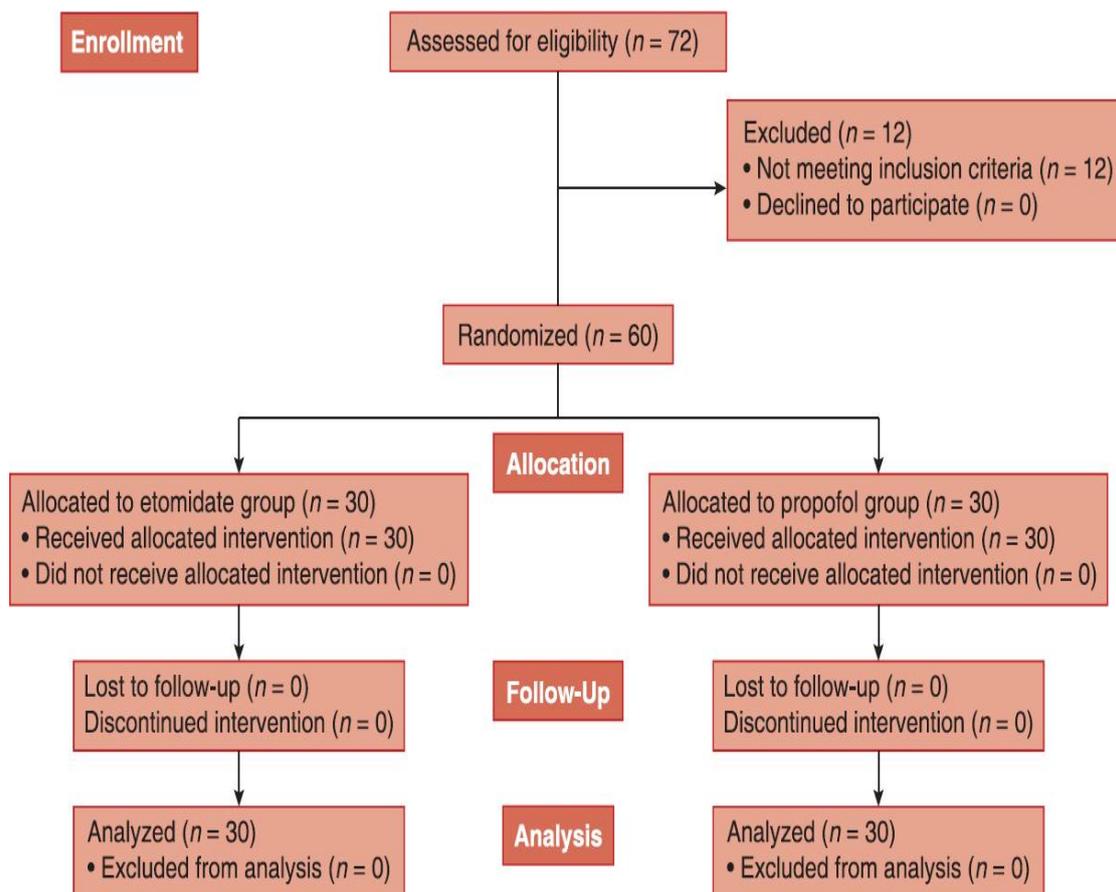


Figure 1: CONSORT flow diagram

In Group P 63.33% were male and 36.66% were female. In Group E 60% were male and 40% were female.

Perioperative heart rate and mean arterial pressure changes were observed in both group. Mean of baseline and mean of 5 min after induction were

compared for study evaluation. P value were 0.682 and 0.175 respectively, so statistically not significant. [Figure 2 and 3] mean of baseline spo2 and mean of 5 min after induction was compared for evaluation. P value was 0.0263, so statistically significant.[Figure 4]

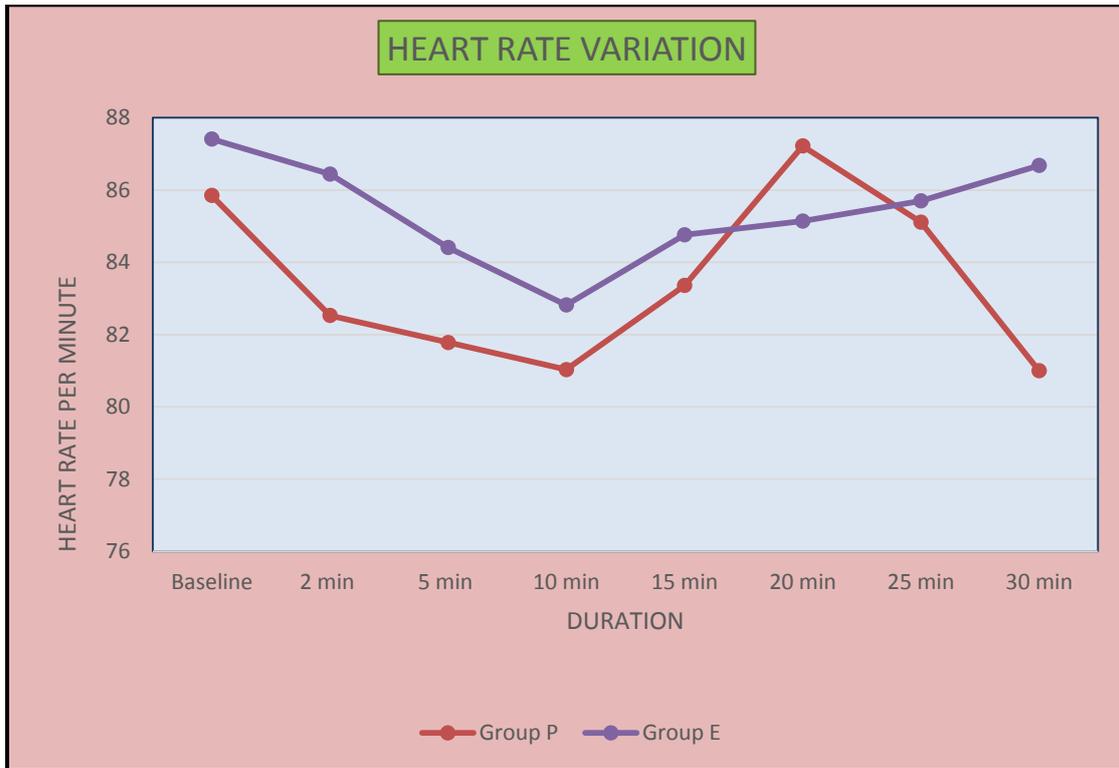


Figure 2: Perioperative HR variation

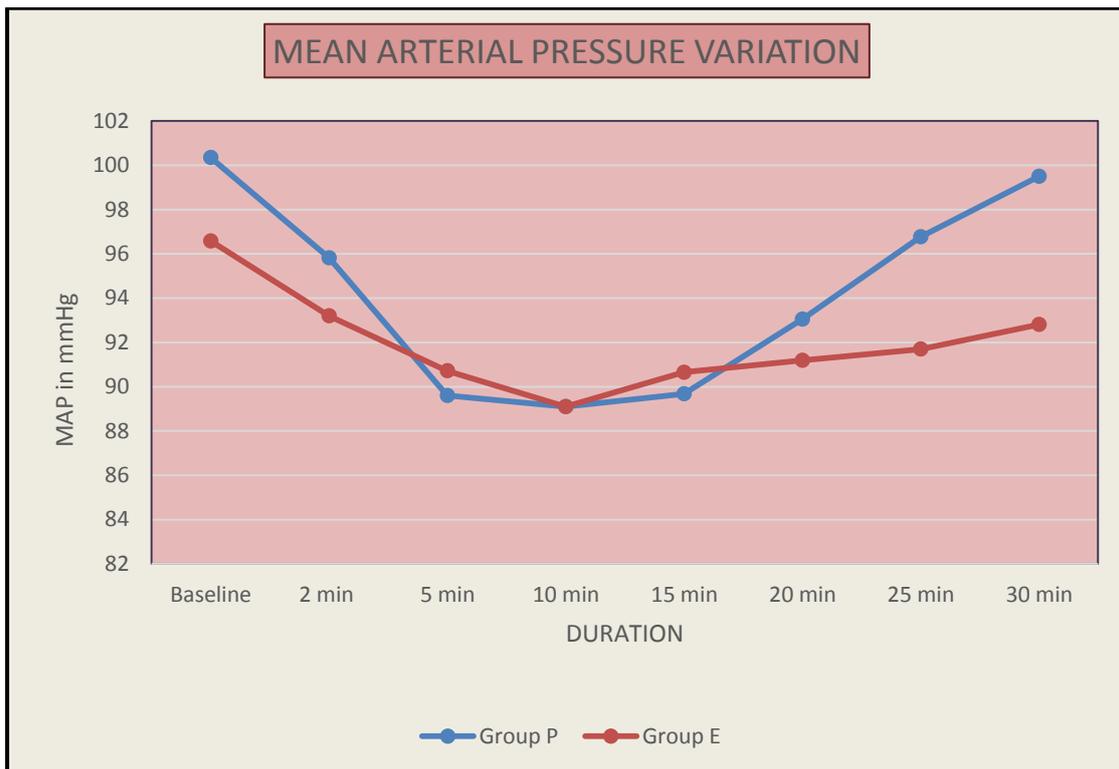


Figure 3: Perioperative MAP variation

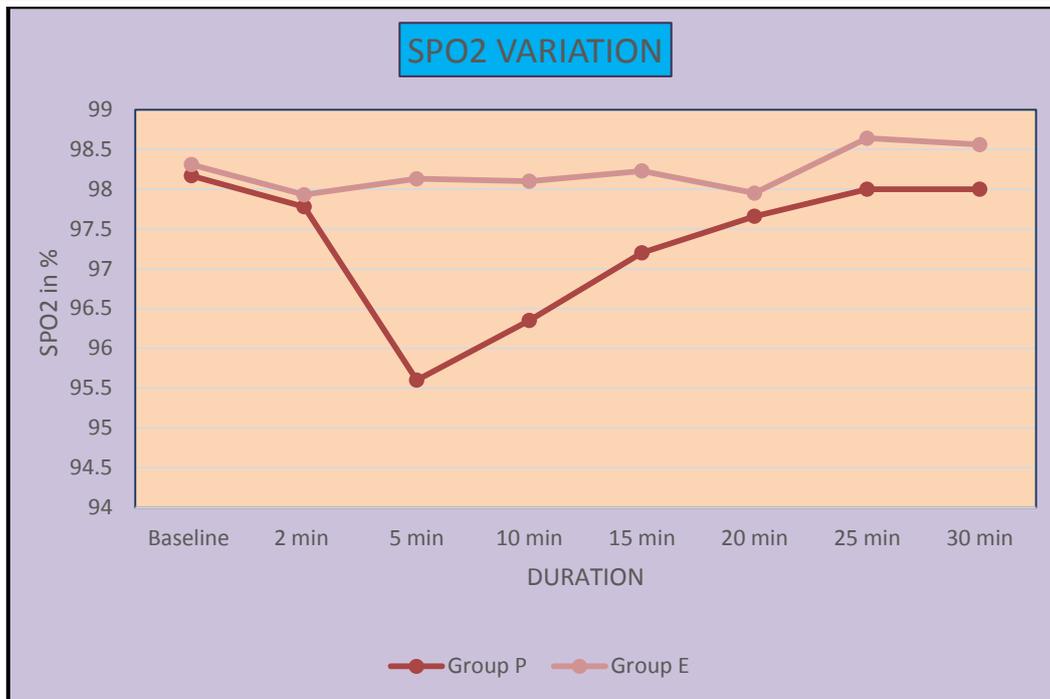


Figure 4: Perioperative SPO2 variation

In Group P 56.66% patients having side effect compare to Group E 36.66% patients having side effect. So, Propofol has more number of side

effects than Etomidate. Bradycardia, apnoea and allergic reaction were only present in Propofol group.[Figure 5]'

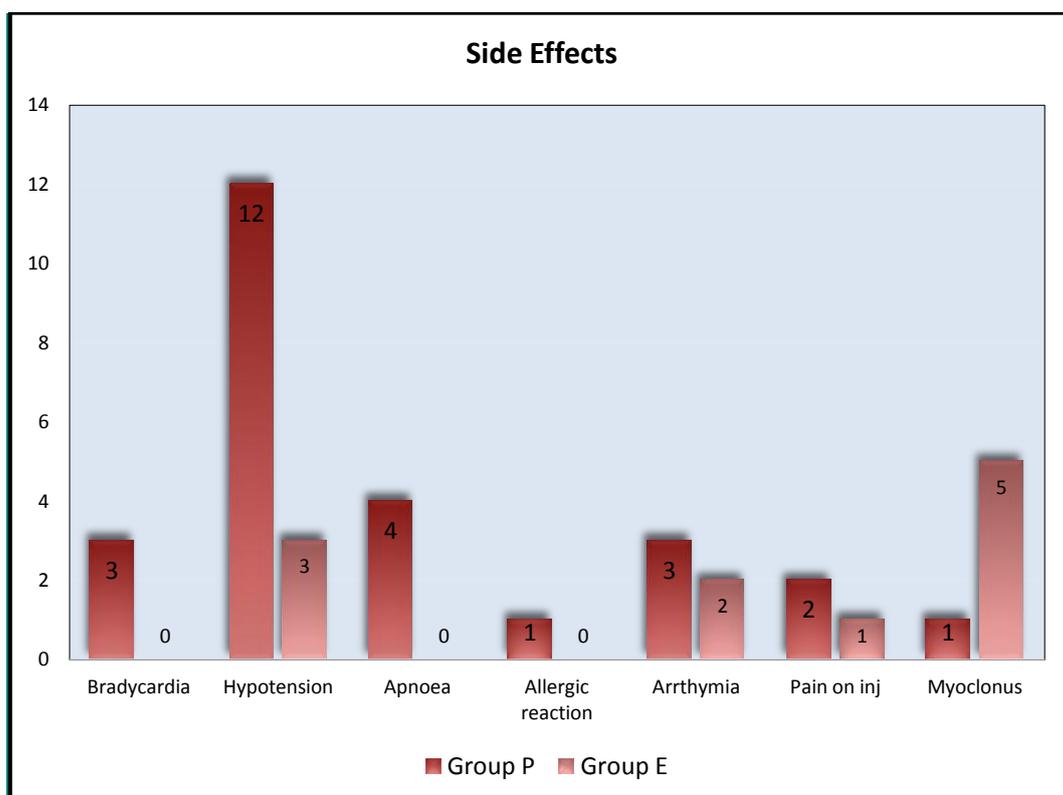


Figure 5: Side-effects

Mean of Modified Aldrete Score (out of 10) and Modified Observer's Assessment of Alertness Score(out of 5) are 9.06 & 9.87, 4.25 & 4.9 ;

Group P and Group E respectively. These both scores are measured after response to verbal command.

There was statistically significant difference for Response to painful stimuli and verbal commands in both groups. P value were 0.0003 and 0.0001 respectively.[Table 1] After all these parameters and statistic value remark that recovery duration from anesthesia was much rapid and faster in Etomidate group than Propofol group.

Table1: Recovery duration from anaesthesia

	Group P	Group E
Response to painful stimuli	2.25	1.02
Response to verbal command	5.64	2.68

Discussion

As a being anaesthetic, Selection of the anesthetic agent and dose most appropriate for the clinical scenario is most important. There is a requirement of a deeper plane of anesthesia while avoiding any airway compromise which is a necessity for conduction and successful outcome of any surgery.

A depth of anesthesia monitor is said to be the "Holy Grail" of anesthesia. Induction of anesthesia is associated with hemodynamic variation of mild to moderate degree depending upon many factors. The rapid induction without any side effect is a valuable characteristic that wanted from an ideal induction agent. Both etomidate and propofol are known to allow rapid induction. They are short acting IV induction agents, commonly used for short surgical procedures done under TIVA.

A standardized pre-medication, induction, maintenance and recovery duration were followed and noted in all the cases. In our study, comparison of both groups by means of hemodynamics (Heart Rate, Mean Arterial Pressure, SPO₂), recovery from anesthesia (response to painful stimuli, response to verbal command, Modified Aldrete Score, Modified Observer's Assessment of Alertness score) and any side effect due to usage of both drugs were assessed.

In our study, there were 3 cases of bradycardia in group P in which a drop of HR from 90's to 50's. Out of 3, two cases were needed Inj. Atropine 0.6 mg as a vagolytic agent. There were clinically and

statistically significant drop of HR after induction of 5 min, 10 min in group P. There were 12 cases of clinically significant hypotension in group P and 3 cases in group E in which >20% drop of blood pressure from baseline value. A drop was significantly present at 5 min, 10 min after induction which recovered gradually at the end of surgery. These cases were managed with fluids pushed fast (crystalloid/colloid) and cardiac stimulant drug. There was no need of cardiac stimulant drug in group E.

In a study by Hosseinzadeh et al.¹, comparing hemodynamic changes during placement of laryngeal mask airway (LMA) using propofol or etomidate, after the administration of premedication. His main finding of the study was that more stable hemodynamic was provided by etomidate than propofol. In a study by Möller et al.² which used propofol and etomidate in general anesthesia induction accompanied by BIS monitoring, the Mean Arterial Pressure (MAP), cardiac index (CI) and systemic vascular resistance index (SVRI) values of 48 patients were compared. A significantly high level of hypotension incidence was found in the propofol group than etomidate group.

Weisenberg M et al. found in their study that the mechanisms of arterial hypotension following IV anesthetic induction were multifactorial. The hemodynamic stability seen with etomidate may be due to its unique lack of effect on both the sympathetic nervous system and baroreceptor function and capacity to bind and stimulate peripheral alpha-2B adrenergic receptors with a subsequent vasoconstriction³. Decrease in systemic blood pressure after bolus injection of propofol is dependent on both vasodilation with reduced preload and after load and myocardial depression (negative inotropic action).⁴ Wu et al.⁵ also concluded that etomidate preserve hemodynamic stability during anesthesia.

Larsen et al.⁶ examined the effects of propofol upon myocardial function by measuring changes in left ventricle function using transthoracic tissue-Doppler echocardiography and concluded

that a decrease in MAP with propofol is secondary to reduce cardiac filling or a consequence of a direct negative inotropic action of propofol.

In our study, we observed 4 cases of apnoea in group P compare to nil in group E. Out of 4 in one case there was drop from 98% on room air to 64% with supplemental oxygenation. There was need of manual assisted ventilation, oro-pharyngeal airway usage and increase in supplemental oxygenation in those cases. (P value=0.02) In our study, none of patients had required endotracheal intubation, ICU admission, prolonged hospital stay or mortality.

Kick O. et al.⁷ also observed that propofol produced more respiratory depression and apnoea interval but none of the patient required intubation. These observations are in concordance with our study. But Boysenet al.⁸ in their study concluded that there was no significant difference between two groups (propofol and etomidate) as regard to apnoea following induction.

In our study, we observed that recovery from anesthesia is much faster and quicker in group E than group P in terms of response to painful stimuli and response to verbal command. Deepa Kane et al.⁹ found delayed and prolonged sedation with propofol as compared to etomidate. This can be explained by the fact that the onset time after induction dose of propofol and etomidate is 40 s and 15–30 s, respectively while context sensitive half-life for propofol infusion up to 8 hrs is <40 min only. Toklu et al.¹⁰ compared recovery time of etomidate-ramifentanyl and propofol-ramifentanyl sedation in patients scheduled for colonoscopy and concluded that etomidate-ramifentanyl administration for sedation and analgesia during colonoscopy resulted in more stable hemodynamic response and shorter recovery and discharge times.

Pain during injection of anesthetic agent is a bad experience for patient while it quite embarrassing situation for an anesthesiologist. In our study, we had 2 cases in group P and 1 case in group E. Etomidate shown a favourable outcome and it was very well supported by other studies.

A serious problem with the use of propofol is the high incidence of pain on injection. The currently most common practice to reduce this problem is by adding lidocaine to the propofol solution but despite this the incidence of pain on injection remains unacceptably high (20%–39%).¹¹ It is already reported that etomidate is associated with significantly less pain on injection than propofol added lidocaine in children.¹²

The only negative characteristic noted with etomidate was high incidence of myoclonic jerks. Miner et al.¹³ was also concluded high incidence of myoclonus (20% vs. 1.8%) in etomidate and propofol group respectively.

Doenicke Wet al.¹⁴ found that fifty to eighty percent of unpremedicated patients may develop myoclonic movements after etomidate administration. Myoclonus is especially problematic in nonfasting patients, patients with open eye injuries, or those who have limited cardiovascular reserves.

The incidence of myoclonic movements can be reduced either by premedication with fentanyl or by preinduction priming with subanesthetic dose etomidate. Myoclonus was a common side effect of etomidate for procedural sedation, which occurred in 20% to 45% of the patients in the Falk review.¹⁵

Propofol has anti-emetic properties and studies have shown a lower incidence of postoperative nausea and vomiting (PONV) in patients receiving propofol as induction agent and more frequent nausea and vomiting during and after anesthesia in patients who received etomidate.¹³⁵

So, a number of studies have compared the efficacy of etomidate and propofol as an induction agent for long duration surgeries, rapid sequence intubation, cardiac surgery, cardio version, UGI and colonoscopy. In terms of efficacy every one found no significant difference, but hemodynamic stability and lesser side effects were shown by Etomidate. These results are similar to our study. Also, duration of recovery from anesthesia is rapid in etomidate than propofol.

Conclusion

We concluded that in terms of efficacy; propofol and etomidate were same. But hemodynamic stability and lesser side effect were shown by etomidate than propofol. Etomidate is far most good option than propofol in short case surgical procedures done under TIVA.

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