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Original Research Article

A Prospective Randomized Study of Etomidate and Propofol Induction on Hemodynamic Response in Patients Undergoing Short Surgical Procedures with Laryngeal Mask Airway

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Conflict of interest: Nil

Abstract:

Objective: This study was done to compare Etomidate and Propofol as inducing agent in general anaesthesia for laryngeal mask airway with following objectives. To evaluate and compare haemodynamic parameters between the two groups and compare the ease of insertion of laryngeal mask airway.

Methods: Prospective randomized single blind controlled study was conducted in 90 patients of either sex in the age group of 20-60 years of ASA grade I or II scheduled for short surgical procedures with LMA insertion under general anaesthesia. Patients were randomly divided into two groups of 45 patients each. Group P Propofol (P) (n=45) Group E: Etomidate (E) (n=45).Total sample size-90. Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation and end-tidal carbon dioxide (ETCO2;) baseline and then every minute after the induction until ten minutes. Duration and number of attempts for LMA insertion, side effects such as pain on injection, myoclonus and postoperative nausea & vomiting if any were recorded.

Results: Demographic variables were comparable in both the groups. Patients in etomidate group showed little change in mean arterial pressure (MAP) and heart rate (HR) as compared to propofol ($p > 0.05$) from baseline value. Pain on injection was more in propofol group while myoclonus activity was higher in etomidate group.

Conclusion: This study concludes that etomidate is a better agent for induction than propofol in view of hemodynamic stability and less pain on injection.

Keywords: Etomidate anesthesia, propofol, Induction of anesthesia; Myoclonus; Hemodynamic stability; Mean arterial pressure.

Introduction

Induction is an important step, while conducting general anaesthesia (GA). Patients are susceptible to hemodynamic instability at the time of induction. Thus, an agent with least effect on hemodynamics would be the agent of choice. Supraglottic airway devices have become a standard fixture in airway management, filling a niche between the face mask and tracheal tube'. Dr. Archie J Brain a British Anaesthesiologist at London Royal Hospital in 1981 developed this novel device.

The increased speed and reliability of placement, improved hemodynamic stability at induction, reduced anaesthesia requirement for airway tolerance, lower frequency of coughing during insertion and lower incidence of sore throat are the main advantages of Laryngeal Mask Airway (LMA) over endotracheal tube. The LMA is now being used in more than 50% of general anaesthetics administered in many centres. The LMA is inserted blindly into the pharynx forming a low-pressure seal around the laryngeal inlet and permitting gentle positive pressure ventilation. It is also useful in management of difficult and failed intubation.

It has been included in the difficult airway algorithm of American Society of Anaesthesiologist (ASA). Successful insertion of the LMA requires adequate mouth opening and sufficient depth of anaesthesia to suppress the upper airway reflexes to prevent untoward events such as coughing, gagging and laryngeal spasm" Different induction agents both intravenous and inhalational have been used to facilitate insertion of LMA. Propofol is the most

popular induction agent for LMA insertion in current anaesthesia practice however its cardiovascular side effects, especially hypotension, has been questioned its routine use for LMA insertion in high-risk cardiovascular patients. It has got rapid and smooth recovery with no hangover effect, minimal nausea and vomiting but it is also associated with adverse effects like pain on site of injection, apnoea, haemodynamic disturbances and involuntary movements". It causes a dose dependent decrease in blood pressure primarily through decrease in cardiac output and systemic vascular resistance".

Etomidate which produces less hypotension can be considered as an alternative agent for LMA insertion. Etomidate is a hypnotic agent with minimal histamine release and very stable hemodynamic profile. However, pain on injection and myoclonus are the most common side effects. Pain on injection, venous irritation and hemolysis has been abolished by new- fat emulsion of etomidate (medium chain triglycerides and soyabean named etomidate-lipuro) but the incidence of myoclonus was not reduced with the new preparation". Etomidate is considered primarily for elderly patients and patients who have cardiovascular compromise". Etomidate has less inhibitory effect on the upper airway reflexes which may make it difficult to insert laryngeal mask airways. Concurrent use of opioids has been found to improve the conditions for LMA insertion, without the need of concomitant muscle relaxant.

There is also reduction in myoclonic movements when etomidate is used in conjugation with midazolam or fentanyl or a combination of both .The aim of this study was to evaluate and compare etomidate with propofol for haemodynamic effects, ease of insertion and occurrence of adverse effects on induction and insertion of LMA using propofol and etomidate as induction agents in patients posted for short surgical procedures.

Materials and Methods

This prospective randomized single blind controlled study was carried out in the Department of Anesthesiology at Santokba Durlabhji Memorial Hospital, Jaipur after approval from the institutional ethics committee and review board and written informed patient consent. This study was conducted in 90 patients of either sex in the age group of 20-60 years of ASA grade I or II scheduled for short surgical procedures with LMA insertion under general anaesthesia. Patients were randomly divided into two groups of 45 patients each.

- Group P Propofol (P) (n=45)
- Group E : Etomidate (E) (n=45).
- Total sample size-90

Inclusion Criteria:

- All patients with ASA I and II aged between 20-60 years of either sex scheduled for short elective (urogenital) surgeries lasting not more than 30 minutes requiring GA with LMA were eligible for our study.
- Patients who gave informed written consent.

Exclusion Criteria:

- Patients with history of epilepsy/seizure disorders.
- Patients with gastroesophageal reflux disease.
- Any allergy/hypersensitivity to propofol and etomidate.
- Patients with cardiovascular and respiratory diseases
- Patients with hepatic and renal diseases.
- Patients with BMI>30

Data Collection Methods:

Demographic data like age, weight, height, body mass index, diagnosis and duration of surgery was noted.

Sampling Method:

After obtaining informed written consent from patients, patients were randomly divided into two groups and were unaware of group allocation:

Group 'P': Propofol group - 45 patients
Group 'E': Etomidate group - 45 patients

Preanesthetic Checkup: All patients were visited on the day prior to surgery and explained about the anaesthetic technique and perioperative course. Each patient had a preanaesthetic checkup.

Groups: Patients were randomly allocated to 2 groups (45 patients in each group)

Group P received Propofol IV 2.5mg/kg.
Group E received Etomidate-lipuro IV 0.3mg/kg.

Procedure: Patients were fasted for over 6 hours preoperatively. Patients consent and PAC was checked. In the operation room standard monitoring i.e. heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP). And mean arterial pressure (MAP) and oxygen saturation (SPO2) were applied and baseline readings were recorded. All patients were preoxygenated for 3 minutes with oxygen flow rate 6 lit. /min on circle breathing system. Patients were premedicated with intravenous fentanyl 2 µg/kg and Glycopyrrolate 0.2mg. After this patient were induced either with propofol or etomidate-lipuro according to randomization.

Group P received IV 2.5mg/kg of propofol while group E received IV etomidate 0.3 mg/kg over 30 seconds. A pre-deflated and well-lubricated LMA was placed by pushing it along the hard palate up to the point of maximum resistance, LMA size was selected according to the weight of the patient and

inserted after the commencement of apnea and loss of eye lash reflex. To determine the proper location of LMA, placement was checked and confirmed by observing bilateral chest movement, ETCO2 -O2 saturation and listening to breathing sounds with a stethoscope.

When LMA insertion failed 0.5mg/kg of succinylcholine was given. The insertion time started from picking up of LMA till effective airway was achieved. The effective airway was considered by achieving bilateral synchronized chest movement, square waveform capnograph and no audible leak. The number of attempts of LMA insertion was noted as 1 and 2. An insertion attempt was defined as placement of LMA in mouth. In case of apnea mechanical ventilation was continued. Maintenance of anaesthesia was achieved with oxygen (O2), nitrous oxide (N,O) in 1:2 ratio and sevoflurane in 2-3% with spontaneous ventilation on circle breathing system.

Pain on administration of drug was noted as none, mild, moderate, and severe. None was considered as negative response to questioning. Mild pain was considered as pain reported only in response to questioning without any behavioral sign. Moderate pain was considered as pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning include withdrawal of arm. Severe pain was considered as a strong vocal response or pain accompanied by arm withdrawal.

Myoclonus on administration of drug was noted as none, mild, moderate and severe. None was considered as no myoclonic movements. Mild myoclonus was considered as short movement of a body segment (e.g. a finger or wrist). Moderate myoclonus was considered as mild movement of two different muscle groups e.g. face and arm. Severe myoclonus was considered as intense myoclonic movements in two or more muscle groups, fast adduction of limb. Nausea and Vomiting were evaluated postoperatively as early (0 to 6) hrs) and late (6 to 12hrs).Patients with vomiting in the post-operative period received inj. Ondansetron 4mg intravenously as rescue antiemetics.

The hemodynamic parameters including HR, SBP, DBP, MAP, $ETCO_2$ and oxygen saturation (SPO2) were measured every one minute after induction for ten minutes. The haemodynamic parameters were maintained at 25% of baseline systolic blood pressure. A decrease in systolic blood pressure of more than 25% of baseline was treated by decreasing the concentration of sevoflurane and increasing the Ringer's lactate infusion and if required 3mg increments of inj. Ephedrine. Tachycardia was defined as HR>100/min. and if there was an increase in systolic blood pressure more than 25% of baseline value it was treated by deepening the level of anaesthesia and by increasing the concentration of sevoflurane. Bradycardia was defined as HR<60/min. and was treated if the heart rate was less than 45/min with inj. Atropine 0.3mg increments. Total time and number of attempts of LMA insertion were recorded along with the side effects such as pain on injection, myoclonus and postoperative nausea and vomiting.

PARAMETERS MEASURED: Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation and end tidal carbon dioxide (ETCO2;) baseline and then every minute after the induction until ten minutes. Duration and number of attempts for LMA insertion, side effects such as pain on injection, myoclonus and postoperative nausea & vomiting if any.

Observation Chart

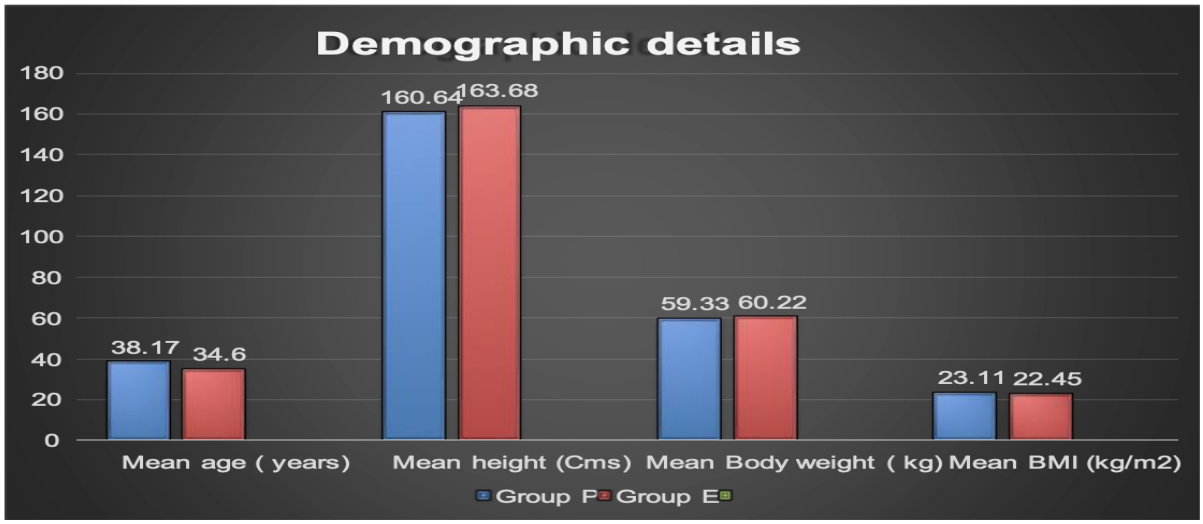

Figure 1: DEMOGRAPHIC DETAILS

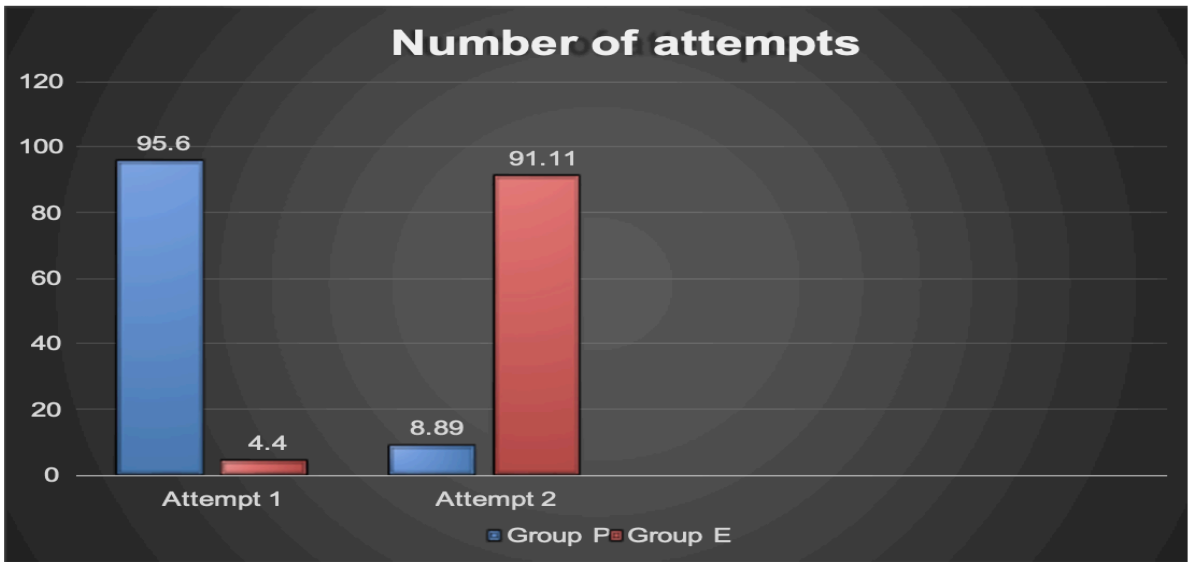

Figure 2: NUMBER OF ATTEMPTS OF LMA INSERTION

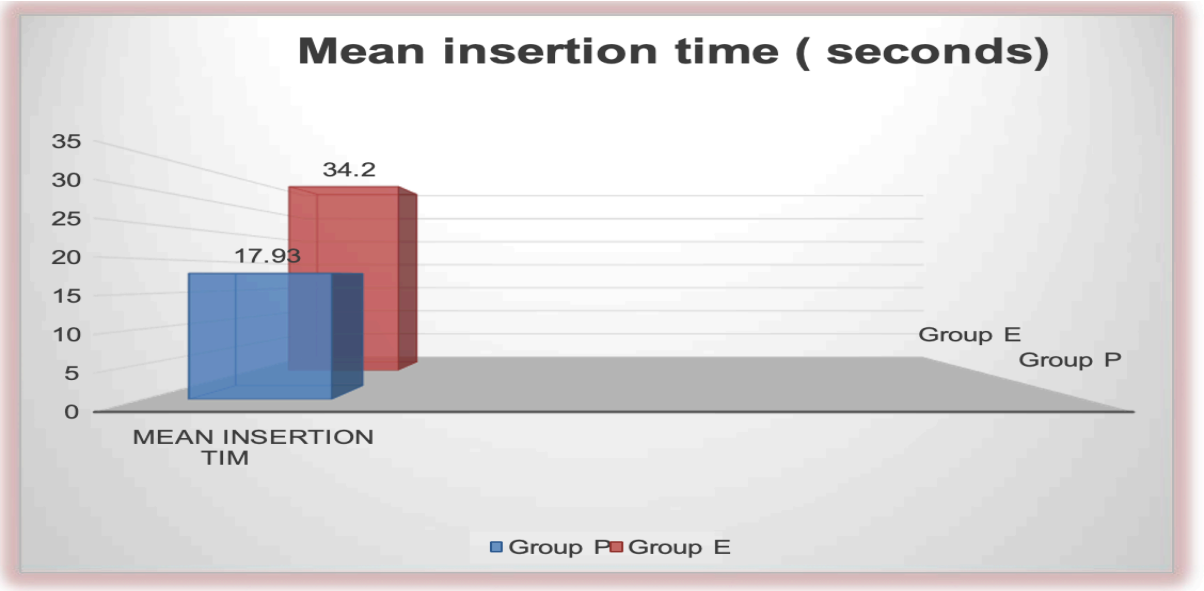

Figure 3: MEAN INSERTION TIME OF LMA

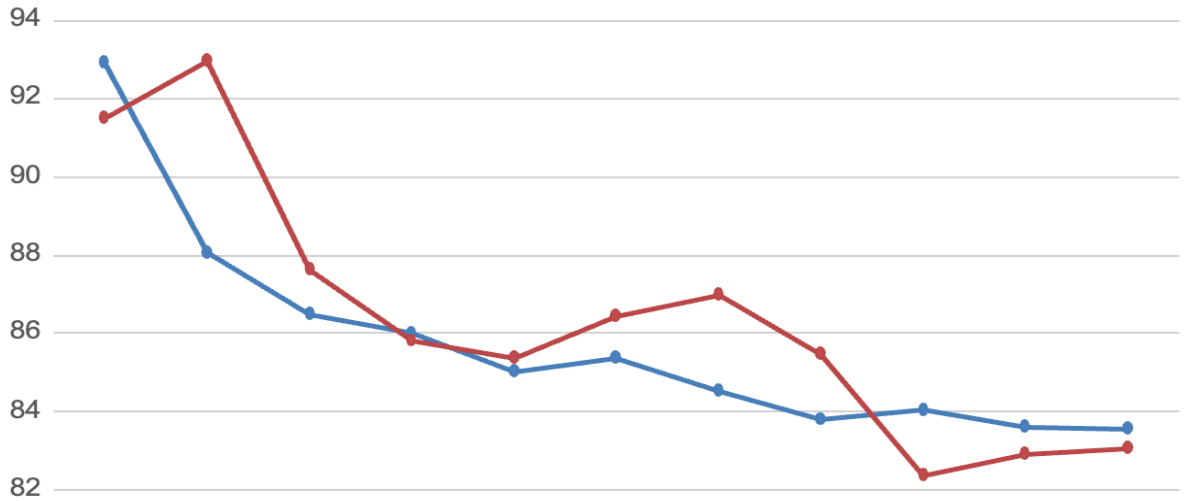

Figure 4: MEAN HEART RATE

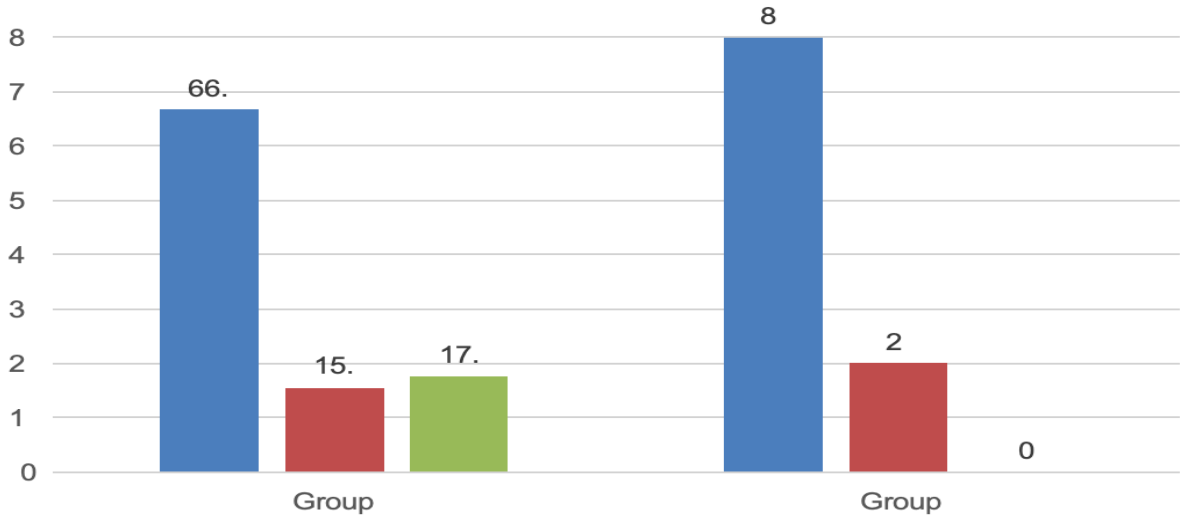

Figure 5: PAIN ON INJECTION

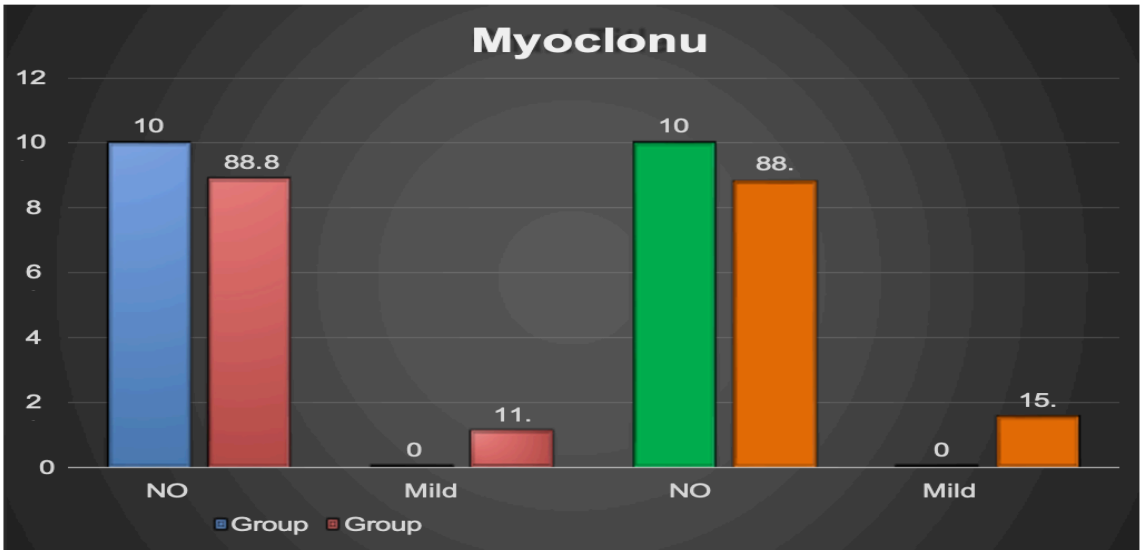

Figure 6: MYOCLONUS

Results

- Both of study group were comparable for demographic and ASA grading.
- LMA insertion was done in first attempt in 95.6% patient in group P and 8.89% in group E that shows propofol to be a better agent for LMA insertion.
- Etomidate is a good agent for induction of GA in elderly and cardiac patient but has lesser inhibitory effect on laryngeal reflexes as compared to propofol.
- Mean insertion time for LMA was more in group E (34.2 sec.) as compared to group P (17.93 sec.)Succinylcholine was used in 95.6% of group E as compared to only 2.2% in group P making it evident that propofol is better in inhibiting airway reflexes.
- There was significant fall in heart rate in both groups after induction but it was comparable. There was fall in mean SBP and DBP in both group after 10 minutes of induction but it was more in propofol group, however it was not clinically significant.
- Etomidate has better hemodynamic stability because of its lack of effect on sympathetic nervous system and baroreceptor, but the stimulating effect on alpha and beta adrenergic receptor
- 76% of group P and 100% of group E patients did not have any pain on injection.
- 44% in group E showed myoclonus but none in group P.Etomidate had shown favorable outcome for pain but not for myoclonus. End tidal CO2 and SPO2 were found to be statistically insignificant in both groups.
- There was no nausea in group P but 12 patient had nausea in group E

Statistical Analysis: All the data were entered on Excel Sheet Analyzed in SPSS, Quantitative data were summarized in the form of Mean and S.D. The difference in the means of both the groups was analyzed using two Independent Sample. The

collected data was summarized by using frequency, percentage, mean & S.D. To compare the qualitative outcome measures Chi-square test or Fisher's exact test was used. To compare the quantitative outcome measures independent t test was used. If data was not following normal distribution, Mann Whitney U test was used. SPSS version 22 software was used to analyse the collected data. p value of <0.05 was statistically significant.

Discussion

Induction of anesthesia is a critical part of anesthesia practice. Sudden hypotension, arrhythmias, and cardiovascular collapse are threatening complications following injection of induction agent in hemodynamically unstable patients. It is desirable to use a safe agent with fewer adverse effects for this purpose. Propofol may result in hypotension and respiratory depression, while etomidate is considered to be a safe induction agent for haemodynamically unstable patients because of its low risk of hypotension.

Etomidate is frequently selected over propofol for induction of anaesthesia because of a putatively favourable haemodynamic profile, but data confirming this perception was limited.Song JC et al did a randomized clinical trial and found out that etomidate anesthesia during ERCP caused more stable haemodynamic responses compared with propofol.

The primary endpoint was to compare the haemodynamic effects of etomidate vs. propofol in ERCP cases. The secondary endpoint was overall survival. MBP values in the etomidate group decreased significantly less than those in the propofol group (P<0.05). The ERCP duration and recovery time in both groups was similar. There was no significant difference in the survival rates between groups (p = 0.942). Etomidate anesthesia during ERCP caused more stable haemodynamic responses compared with propofol.

Baradari, A.G et al did a randomized clinical trial comparing hemodynamic responses to ketamine-propofol combination (ketofol) versus etomidate during anesthesia induction in patients with left ventricular dysfunction undergoing coronary artery bypass graft surgery. Hannam JA et al too studied haemodynamic profiles of etomidate vs propofol for induction of anaesthesia in a randomised controlled trial in patients undergoing cardiac surgery. Mean arterial blood pressure (MAP) and boluses of vasopressor administered after induction were recorded. Groups were compared using regression models with phase and anaesthetist as factors. Propofol caused a 34% greater reduction in MAP-time integral from baseline after induction of anaesthesia than etomidate, despite more frequent use of vasopressors with propofol, confirming the superior haemodynamic profile of etomidate in this context.

Aggarwal S et al did a comparative study between propofol and etomidate in patients under general anesthesia. This prospective randomized study is designed to compare propofol and etomidate for their effect on hemodynamics and various adverse effects on patients in general anesthesia. Demographic variables were comparable in both the groups. Patients in etomidate group showed little change in mean arterial pressure (MAP) and heart rate (HR) compared to propofol (p > 0.05) from baseline value. Pain on injection was more in propofol group while myoclonus activity was higher in etomidate group. This study concludes that etomidate is a better agent for induction than propofol in view of hemodynamic stability and less pain on injection.

Contrary to our study, Alipour M et al did a study to evaluate the effects of propofol, etomidate, and thiopental administered during phacoemulsification (PE) cataract extraction on intraocular pressure (IOP) and hemodynamic responses with insertion of laryngeal mask airway (LMA). Blood pressure (BP) and HR of patients during the surgery were monitored and registered before and after induction and intubation. BP declined remarkably after induction (P<0.001) and rose significantly after LMA insertion in all groups, except in the propofol group. The HR was decreased significantly after induction, except in thiopental. Propofol prevented IOP increase after induction compared with other drugs. Decrease in BP and HR after induction and LMA insertion was remarkable. Thiopental seemed to be the best drug for controlling cardiovascular parameters, especially HR, and it also prevents IOP rise.

Ghafoor HB et al studied etomidate vs propofol for hemodynamic stability in general anesthesia with laryngeal mask airway, very similar to our study. There was no difference in the heart rate between the two groups. A significant drop was found for systolic blood pressure (SBP) in propofol group while diastolic blood pressure (DBP) was decreased in both the groups. In propofol group, successful in-sertion of LMA was achieved on the first attempt in 93.3% of patient as compared to 36.7% in etomidate group. Conclusion: Use of etomidate for induction of laryngeal mask anesthesia can prevent the hypotension following induction; however it may delay the insertion of laryngeal mask airway.

The purpose of this study by Hosseinzadeh H et al is comparing three methods of induction of anesthesia (Propofol, Etomidate, Propofol+Etomidate) in the hemodynamic stability after LMA insertion in elective surgeries.Heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were measured before induction and 30 seconds

after induction. Apnea time is recorded in all patients. Number of attempts to laryngeal mask insertion, ease of placement, was compared in three groups. Etomidate plus propofol is an effective and alternative to propofol and etomidate for facilitating LMA insertion with the added advantage of lack of cardio-vascular depression.

Rathore VS et al did clinical analysis of propofol, etomidate and an admixture of etomidate and propofol for induction of general anaesthesia. In this prospective, randomised, double-blind controlled study, a decrease in systemic haemodynamics from baseline following induction in group P compared to groups E and PE. Using an admixture of etomidate and propofol as the induction agent reduced the incidence of side effects observed with use of either drug alone such as pain upon injection, myoclonus and haemodynamic instability

Anandh V et al studied hemodynamic changes on LMA insertion with same dose of etomidate and varying doses of propofol. Double blinded randomized clinical trial study design was adopted. Hemodynamic parameters like Blood pressure (systolic, diastolic and mean arterial pressure). There was no statistical significant difference between demographic data. There was statistical significant difference in hemodynamic (Systolic, diastolic and mean arterial pressure) and mean pulse rate changes over time between the three groups. There was no statistical significant difference found in terms of oxygen saturation, number of LMA attempts and duration of LMA insertion. This study results suggest that Group A and Group B regimens provides desirable hemodynamic stability following insertion of LMA than Group C.

In addition to the favourable side effect profile, airway maintenance and respiratory depression was similar in all three groups. Abidin ZU et al did comparative study of hemodynamic response using laryngeal mask airway (LMA) versus endotracheal tube (ETT) in controlled hypertension patients. The hemodynamic response was noted, recording pulse rate, Systolic BP, Diastolic BP, and MAP immediately after 1,3,5 minute of laryngoscopy & intubation or LMA insertion.

The study revealed attenuated hemodynamic response to LMA insertion with improved hemodynamic; stability compared to laryngoscopy & intubation. The results advocate using supraglottic airway devices, especially LMA merits, in selected patients & circumstances. Laryngoscopy and tracheal intubation can cause serious cardiovascular responses in patients such as hypertension, tachycardia, and arrhythmias. Alternative airway maintenance techniques may attenuate these hemodynamic stress responses. Jarineshin H established better hemodynamic profile of laryngeal mask airway insertion compared to laryngoscopy and tracheal intubation.

There were no differences in the mean SBP and DBPs between the three groups at the other time points. Maintaining the airway using laryngeal mask airway is associated with less cardiovascular responses compared to direct laryngoscopy and tracheal intubation

Conclusion

Success rate of LMA insertion is high in propofol group as compared to etomidate group. Both induction agents cause statistically significant decrease in haemodynamic parameters during induction but decrease is more in propofol group and haemodynamic stability was more in etomidate group. Propofol has lesser side effects like nausea, vomiting and myoclonus than Etomidate group.

Declarations:

Availability of data and material: Department of Anesthesiology at Santokba Durlabhji Memorial Hospital, Jaipur **Code availability**: Not applicable **Consent to participate**: Consent taken **Ethical Consideration**: There are no ethical conflicts related to this study. **Consent for publication**: Consent taken

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