Original Research Article

A Comparative Study of Effect of Propofol, Etomidate Lipuro and Propofol-Etomidate Lipuro Admixture on Haemodyanamic Response and on BIS Values at Induction of General Anaesthesia- A RCT

Vipin Bansal[1], Ravindra Singh Sisodia[2], Deepak Tiwari[3], Saurabh Bhargava[4*]

[1]Department of Anesthesiology, MG Medical College, Jaipur, Rajasthan, India
[2]Department of Anesthesiology, MG Medical College, Jaipur, Rajasthan, India
[3]Department of Emergency Medicine, NIMS Medical College, Jaipur, Rajasthan, India
[4]Department of Emergency Medicine, NIMS Medical College, Jaipur, Rajasthan, India

Received: 18-06-2020 / Revised: 10-07-2020 / Accepted: 15-08-2020

Abstract

Background: Patients undergoing elective surgical procedures require an anesthetic agent which would provide a smooth, pleasant, rapid induction and recovery along with hemodynamic stability and minimal side effects. To achieve these goals Propofol, Etomidate and propofol – etomidate lipuro admixture may be the agents of choice. Bispectral index (BIS) monitoring has emerged as a convenient and versatile tool to titrate hypnotic agents**Aim**: 1. To compare the time of onset, of ,loss of consciousness and induction of anaesthesia using BIS index value among the propofol (1%), etomidate-lipuro (0.2%) and 50% (1:1) admixture of these agents (Etofol) in various procedures to choose the better induction agent. 2. To compare the hemodynamic changes caused by these agents**.Material and methods**:90 patients of either sex and of ASA physical status I or II scheduled for elective surgery under general anesthesia were selected for the study and were randomly placed into three groups. Group P was induced with intravenous Propofol 1%, Group E with intravenous Etomidate (2mg/ml) and Group PE with intravenous mixture of Propofol plus Etomidate (1:1) @ 400ml/hr till the BIS value reached 40. Patient was considered to be induced once the BIS value reached 40 and this time was noted for all three groups. BIS values and hemodynamic measurements were recorded before induction (T1), at induction (T2), before intubation (T3) after intubation (T4) and then after intubation, at 1 min (T5), at 3 min (T6), at 5 min (T7) and at 10 min (T8).**Results:** The Induction (time to reach BIS value of 40) was fastest in Etofol group. Induction dose of Etofol provided better control of BIS values after orotracheal intubation. It was also noted that Heart Rate remained near baseline in Etofol group at different time intervals. In the Post intubation period, a significant increase in the Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP), was noted in Group E. The increase in blood pressure at different intervals after intubation was found to be lowest in Group PE.**Conclusion:** We conclude that Etofol is associated with a shorter induction time and better haemodyanamic stability than Etomidate and Propofol alone. It also provides effective control of BIS values during induction, orotracheal intubation and thereafter.

Key words: Etomidate, Propofol, Etofol, bispectral index (BIS) and haemodyanamic stability.

**Correspondence*
Dr. Saurabh Bhargava,
Department of Emergency Medicine, NIMS Medical College, Jaipur, Rajasthan, India.
E-mail: drsaurabhb@gmail.com

Introduction

General anaesthesia is a medically induced coma with loss of protective reflexes. It is now a standard practice to induce general anaesthesia by using intravenous anaesthetic agents. Measurement of anaesthetic depth, though important, is a challenging task. There are several reasons for difficulty in evaluating dosages of anesthetic agents e.g. lack of a universally accepted definition of "consciousness", complex effects of anaesthesia on the human organism, increased use of combinations of anaesthetic agents rather than single drug, differences in the patient's response to anaesthesia over the course of the surgery, differences in responsiveness to specific anaesthetics related to age and sex and differences among individuals with regard to sensitivity to anaesthesia. During the evolution of modern anaesthesia practice, patient assessment has undergone a gradual change and refinement.Patients subjected to elective surgical procedures require an agent which provides smooth, pleasant and rapid induction and recovery, maintenance of hemodynamic stability, minimal respiratory depression and other side effects. To achieve these goals Propofol, Etomidate and propofol – etomidate lipuro admixture may be the agents of choice.Bispectral index (BIS) monitoring has emerged as convenient and versatile tool to titrate hypnotic agents[1-3]. BIS is a dimensionless number scaled from 100 to 0, with 100 representing an awake EEG and 0 representing electrical silence. Titrating anesthetic agents to a specific bispectral index during general anesthesia in adults allows the anaesthesiologist to adjust the amount of anesthetic agents according to the need of the patient, possibly resulting in reduced incidence of intraoperative awareness and a rapid emergence from anesthesia. There are various situations when BIS reading do not correlate clinically and to the expected depth of anaesthesia. According to the literature, different anaesthetic agents can also affect BIS differently[4]. The review of literature also suggests very few comparative studies available with these agents and and those that do, do not describe about their effects on BIS.

Material and Methods

This was a single center, prospective, Block randomized controlled study conducted at a Tertiary care level, Medical college Hospital, after due clearance from the institutional ethics committee. Written informed consent was taken from all the patients.90 healthy patients aged between 18 to 60 yrs and ASA grade I and II scheduled for elective lumbar spine surgeries under general anaesthesia were enrolled. The patients were divided randomly into three groups, each group comprising of thirty patients.

Inclusion criteria

1. Patients with ASA grade I and II
2. Patients of age group 18 to 60 yrs of either sex undergoing elective lumbar spine surgery under general anesthesia
3. Patients willing to give written and informed consent

Exclusion criteria

1. Patients refusal
2. Patients having Sensory or motor deficit
3. Patients having compromised renal, pulmonary and cardiac status
4. Patients on medications like hypnotics, narcotic analgesics or sedatives
5. Patients having known allergy to anesthetic agents used in study
6. Presence of hypotension or any vascular disease
7. Presence of primary or secondary steroid deficiency or patients on steroid medications
8. History of any seizure disorders
9. Patients with anticipated difficult intubation.
10. Patients with ASA grade 3,4 and 5

The patients were divided into three groups of 30 each according to drugs used.

Group P: Propofol 1% was given for induction.

Group E: Etomidate (0.2%) was given for induction.

Group PE: Etofol (1:1 admixture of propofol 1% and etomidate 0.2%) was given for induction.

Randomization was done by chit in box method (Simple Random Sampling method). According to the randomization, syringes were prefilled and loaded on syringe pumps with 20 ml of the induction agent by an anaesthesiology resident. All syringes were look alike and containing, either 20 ml of propofol or 20 ml of etomidate or 20 ml of 1:1 mixture of propofol and etomidate.On arrival in the operation theatre, fasting status, consent and preanaesthetic check up sheet were checked. Standard monitors (NIBP, Pulse Oxymetry and ECG leads) were attached to the patients for recording baseline parameters (SpO_2, pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and Mean arterial blood pressure (MBP)).Two peripheral intra-venous (I.V.) lines with 18/20G Cannula were secured and ringer lactate was started through one I.V. cannula at rate of 120ml\hr.BIS leads were applied to the patient. The BIS score was measured by means of an Aspect VISTA BIS monitor with frontal assemblage. The quality index of the signal automatically calculated by the Aspect-VISTA was

used to evaluate the quality of the measured signal considering only those measurement in which the SQI (Signal Quality Index) was between 80 to100. After this base line measurement of BIS was taken(T1). All groups of patients received I.V. premedication inj. glycopyrolate (0.004 mg/kg), inj. fentanyl (2 μg /kg) and inj. medazolam (0.02 mg/kg) before the induction with either propofol, etomidate or etofol.Patients were preoxygenated with 100% oxygen. Hemodynamic parameters were recorded just before induction. Inducing agent was delivered as an infusion using a syringe pump @ 400ml/hr, upto a BIS value of 40 was achieved (T1). The patients were kept ventilated by Bag and face mask with 100% oxygen. This induction time (time taken in seconds from the commencement of inj. of the drug till BIS value 40) was noted. This was followed by inj. Vecuronium 0.1 mg/kg I.V. Hemodynamic parameters were measured just after induction (at BIS 40) and just before intubation.Using direct laryngoscopy, Patient was intubated with an endotracheal tube of appropriate size, 3 Minutes after the administration of Inj Vecuronium. Tube position was confirmed by auscultation. BIS values and hemodynamic measurements were recorded after intubation at 1 min (T5), 3 min (T6), 5 min (T7) and at 10 min (T8). During this period of 10 min, anesthesia was maintained with 50% oxygen and air and sevoflurane 2%.

Statistical Analysis: The observations recorded in all three groups were tabulated and statistical analysis was done using one way analysis of variance (ANOVA) for the findings and p value< 0.05 was taken as statistically significant

Results

In the present study it was found that the mean age of all the patients in E, PE, P, groups were 35.93 ± 13.33 years, 36.93 ± 12.64 years, 42.23 ± 12.10 years respectively, did not show statistically significant difference. There were no significant difference found in demographic data in all the groups as patients were between 35.93 to 42.23 years of age and 54.03 to 61.56 kg of Weight of both sexes.The mean HR (rate/min) for the three groups at different times of observation is depicted in Figure 1. In all three groups, baseline heart rate values and that after administration of study drugs were insignificant. The HR values after intubation at time intervals 1, 3, 5 and 10 min had p value <0.05 and was statistically significant.

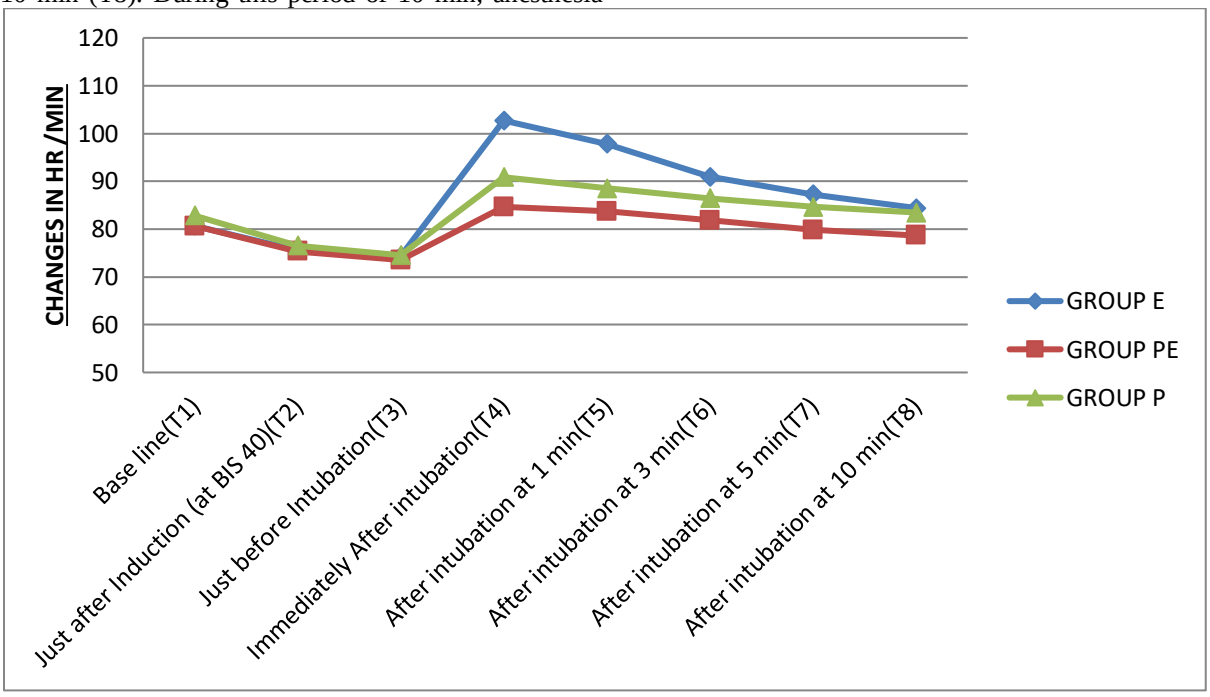

Fig 1:Changes in heart rate in groups

During the current study it was also found that the SBP (mm/hg) of the three groups at different times of observation; the baseline SBP values were statistically insignificant. The SBP values at BIS 40, before intubation, after intubation and at time intervals 1,3,5 and 10 min had p value <0.05 and were statistically significant And for the DBP (mm/hg) of the three groups at different times of observation; the baseline DBP values were statistically insignificant. The DBP values at BIS 40, before intubation, after intubation and at time intervals 1, 3, 5 and 10 min had p value <0.05 and were statistically significant

Table 1: Changes in Mean Arterial Pressure (mm Hg) (MEAN ± SD)

	GROUP E	GROUP PE	GROUP P	P –value
Base line(T1)	91.15±7.90	90.54±8.26	90.74±7.88	E Vs PE=>0.05 E Vs P=>0.05 PE Vs P=>0.05 Non Significant
Just after Induction (at BIS 40) (T2)	81.84±6.75	85.70±8.10	76.96±8.17	E Vs PE=<0.05 E Vs P=<0.01 PE Vs P=<0.001 Significant
Just before Intubation (T3)	78.25±9.58	82.15±6.94	67.80±7.66	E Vs PE=<0.05 E Vs P=<0.01 PE Vs P=<0.001 Significant
Immediately After intubation (T4)	105.21±7.03	96.54±10.73	91.96±9.57	E Vs PE=<0.01 E Vs P=<0.001 PE Vs P=<0.05 Significant
After intubation at 1 min. (T5)	100.53±6.86	93.67±8.70	88.35±7.39	E Vs PE=<0.01 E Vs P=<0.001 PE Vs P=<0.05 Significant
After intubation at 3 min (T6)	98.55±5.89	91.50±8.56	84.60±6.43	E Vs PE=<0.05 E Vs P=<0.01 PE Vs P=<0.05 Significant
After intubation at 5 min (T7)	96.30±5.19	89.50±6.50	82.06±5.56	E Vs PE=<0.05 E Vs P=<0.01 PE Vs P=<0.05 Significant
After intubation at 10 min (T8)	93.21±5.09	88.45.±7.50	80.43±5.61	E Vs PE=<0.05 E Vs P=<0.001 PE Vs P=<0.01 Significant

Above table shows the MAP (mm/hg) of the 3 groups at different times of observation; the baseline MAP values were statistically insignificant. The MAP values at BIS 40, before intubation, after intubation and at time intervals 1,3,5 and 10 min had p value <0.05 and was statistically significant.

Table 2: Intra-Operative Changes in BIS (Mean ± S.D.)

	GROUP E	GROUP PE	GROUP P	P –value
Base line (T1)	97.31±1.41	96.90±1.54	97.09±1.89	E Vs PE=>0.05 E Vs P=>0.05 PE Vs P=>0.05 Non Significant
Just after Induction (at BIS 40) (T2)	43.87±6.55	42.93±6.15	46.52±4.77	E Vs PE=>0.05 E Vs P=>0.05 PE Vs P=>0.05 Non Significant
Just before Intubation (T3)	43.71±4.97	43.46±3.55	45.75±3.65	E Vs PE=>0.05 E Vs P=>0.05 PE Vs P=>0.05 Non Significant
Immediately After intubation (T4)	50.21±6.23	44.56±5.52	65.21±6.08	E Vs PE, P= <0.01,S E Vs P, P=<0.001,S PE Vs P, P= <0.001,S
After intubation at 1 min. (T5)	46.18±5.77	40.87±9.26	53.87±5.42	E Vs PE, P = <0.01,S E Vs P, P=<0.001,S PE Vs P, P= <0.001,S
After intubation at 3 min (T6)	42.81±4.67	38.59±3.04	50.15±6.85	E Vs PE, P = <0.01,S E Vs P, P=<0.001,S PE Vs P, P= <0.001,S
After intubation at 5 min (T7)	41.28±4.89	38±2.54	47.71±5.43	E Vs PE, P =<0.05,S E Vs P, P=<0.001,S PE Vs P, P= <0.001,S
After intubation at 10 min (T8)	40.25±5.24	36.77±2.41	46.76±7.25	E Vs PE, P =<0.05,S E Vs P, P=<0.001,S PE Vs P, P= <0.001,S

The above table shows the BIS of the three groups at different times of observation; the base line BIS values just after administration of study drugs were insignificant. The BIS values, after intubation, at time interval 1, 3, 5, and 10 min had p value <0.05 and were statistically significant.

Table 3: Time To Reach BIS to 40 (Induction Times Of Groups) (Mean ± SD)

GROUP E	GROUP PE	GROUP P
170(±28.8)sec	158.5 (±22.4)sec	194.2(±33.5)sec

This table shows induction time (time to reach BIS to 40), which is faster in Etofol group (158.5 (±22.4)sec) than propofol (194.2(±33.5)sec) (p<0.001) and etomidate group (170(±28.8)sec) and is statistically significant (p<0.05) as depicted in the figure below.

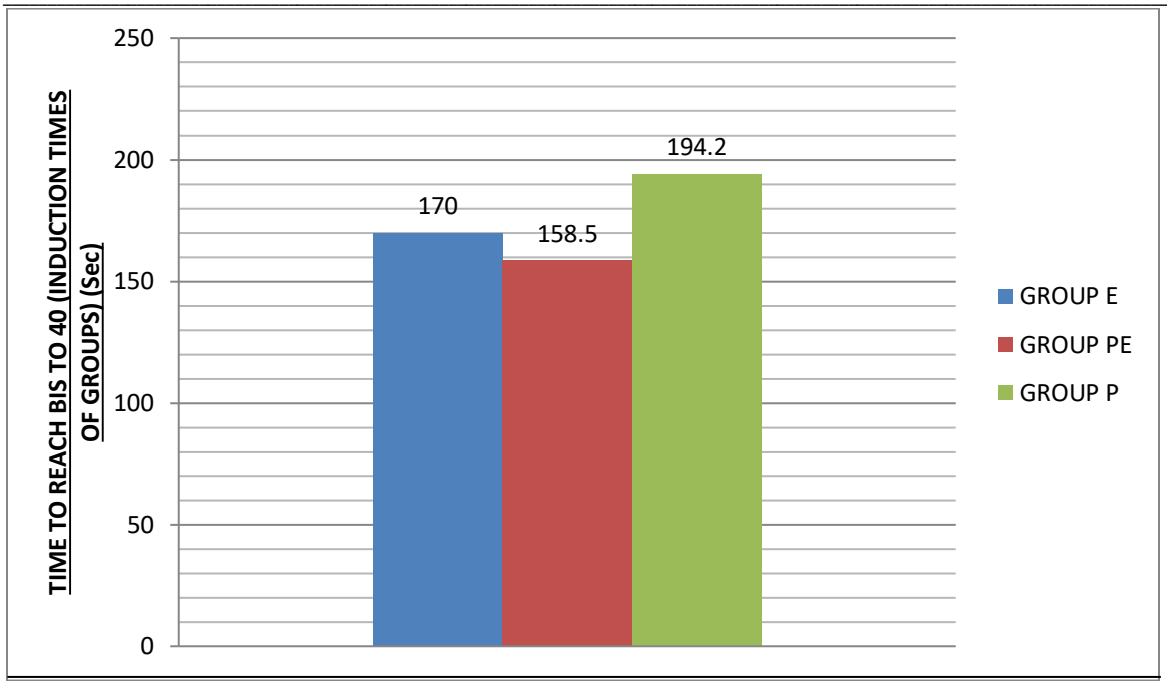

Fig 2: Induction Time

Discussion

With the evolution of modern anaesthesia practice, patient assessment has undergone gradual change and refinement. BIS index offers a direct and accurate method for continuous brain status monitoring and provides a measurement of hypnotic effect of anaesthetic agents.The results from the present study indicate that Induction (time to reach BIS to 40) was faster in etofol group than propofol and etomidate group. Baseline Heart rate was almost similar in all three groups. Heart Rate remained near baseline in etofol group compared to propofol and etomidate groups at different time intervals. Baseline SBP, DBP and MAP were almost similar in all three groups. But after intubation, significant increase was found in group E that was significantly greater than group PE and P. The increase in blood pressure at different intervals after intubation was found lower in Etofol group than Etomidate group, which was significant. It suggests that Etofol had more protective effect than Propofol and Etomidate against haemodynamic responses.After intubation, there was a significant increase in BIS value in Etomidate group and Propofol group compared to Etofol group. It proved that induction dose of Etofol provides better control of BIS values after orotracheal intubation. There was no significant difference in SpO_2 in all three groups.The results of the current study are found to be similar to the following studies:Hyun-Mok et al. (2012) found that as compared to BIS, Spectral entropy did not decrease in patients with myoclonus, at the time of loss of consciousness, suggesting that BIS may evaluate hypnotic levels better than spectral entropy during induction of anesthesia with etomidate[5].Although, BIS monitoring is not a substitute for clinical judgment it may enable the anesthetist to make informed decision about the dosing and balance of anaesthetic agents.In another clinical trial conducted by Huibao Zheng et al. (2019) comparing propofol and etomidate, it was found that patients who received etomidate as induction agent had fewer side effects on the hemodynamic profile and the BIS value was lower at LOC[6].In another BIS guided comparative study between propofol and etomidate published by M. Kamenik & A. Moller Petrun, (2013) [7]it was concluded that while there was no significant difference in terms of hemodynamics before intubation, incidence of hypotension and tachycardia was more in propofol group while incidence of hypertension was more in etomidate group in the post intubation period. The results of our study were similar to the results of a study by Fatma Saricaoglu et al. (2011) in terms of time of induction with etofol as compare to propofol and

etomidate[8]. A RCT done on 90 patients, compared the Effect of Propofol, Etomidate and Propofol Plus Etomidate Induction on Hemodynamic Response to Endotracheal Intubation, concluded that Induction with propofol alone may cause hypotension in volume depleted patients, the combination of etomidate plus propofol provided better hemodynamic stability than etomidate alone at 1 min after intubation, though etomidate was equally stable at other points of time. The combination proved to be significantly better than either propofol or etomidate alone[9].

Conclusion

From the above study, it can be concluded that Etofol (1:1 admixture of etomidate-lipuro and propofol) is associated with decrease in induction time and better haemodyanamic stability than etomidate lipuro and propofol.In the current study it was found that Etofol provides effective control on BIS values during induction, orotracheal intubation and thereafter and we think it is a valuable agent for induction.

References

1. Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A-Bispectral index for improving anaesthetic delivery and postoperative recovery. Cochran Database Syst Rev, 2007;(4): CD003843.
2. M. Iannuzzi et al. Relationship between Bispectral Index, electroencephalographic state entropy and effect-site EC50 for propofol at different clinical endpoints British Journal of Anaesthesia.2005; 94 (5): 613–6.
3. Liu J, Harbhej S, White PF — Electro encephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. Anesth Analg, 1997;84:185-197.
4. Rev.Bras. Anestesiol. When the bispectral index (Bis) can give false results:.2009 ;59 (1):33.
5. Hyun-Mok et al. Effects of etomidate on bispectral index scale and spectral entropy during induction of anaesthesia by means of the raw electro-encephalographic and electromyographic charac - teristics. Korean J Anesthesiol. 2012; 62(3): 230–233.
6. Huibao Zheng et al.The effect of etomidate or propofol on brainstem function during anaesthesia induction: a bispectral index- guided study. Drug Des Devel Ther Drug Des 2019;13 :1941-1946.
7. M. Kamenik and A. Moller Petrun. Bisspectral Index-guided induction of general anaesthesia in patients undergoing major abdominal surgery using propofol or etomidate: Br J Anaesth 2013; 110(3): 388-96.
8. Fatma Saricaoglu et al. A clinical comparison of etomidate-lipro, propofol and admixture at induction. Saudi J Anaesth 2011;5(1): 62-66.
9. Kavita Meena , Rajesh Meena et al., A Comparative Study of Effect of Propofol, Etomidate and Propofol Plus Etomidate Induction on Hemodynamic Response to Endotracheal Intubation: J Anesth Clin Res 2016;7:5
10. Eric A Bruder et al. Single induction dose of etomidate versus other induction agents for endotracheal intubation in critically ill patients. Cochrane Database Syst Rev. 2015; 2(1): CD 010225.

Source of Support:Nil
Conflict of Interest: Nil