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To Evaluate the Hemodynamic Effects of Induction doses of Propofol and Etomidate under Entropy Guidance: A Prospective, Observational Study

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Abstract

Context: Entropy monitoring enables us to administer the anaesthetic doses of induction agents with precision so as to avoid intraoperative awareness, light planes of anaesthesia on one hand and delayed recovery, haemodynamic instability on the other. *Aims:* To evaluate the haemodynamic effects of induction doses of propofol and etomidate under entropy guidance, in patients undergoing under general anaesthesia. *Study design*: A prospective, observational study. *Methodology*: This study was conducted on 100 patients of ASA I and II between the age group 18-60 years. The patients in group A, were induced with etomidate and group B, with propofol till entropy reached a value of 40. Haemodynamic parameters at and after induction were noted. *Results*: All statistical calculations were done using SPSS 21 version. The mean of mean arterial pressure at 1 minute after induction in group A and B was 85.9±10 and 75.5±8 respectively (p=0.00) and after laryngoscopy, in group A and B was 98.4±8.1 and 105.3±9.1 respectively (p=0.00). Significant rise in the heart rate was seen with propofol after laryngoscopy and intubation. (p=0.018) *Conclusion*: On induction doses under entropy guidance, the haemodynamic effects observed with propofol were more pronounced than that of etomidate. Propofol caused more hypotension than etomidate after induction, whereas, there was statistically significant rise in heart rate after laryngoscopy and intubation.

Keywords: Intravenous; Propofol; Etomidate; Induction; Haemodynamic Parameters; And Entropy.

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Introduction

With the advances in technology soaring high, the depth of anaesthesia can be assessed with newer monitors, which help in preventing awareness from inadequate doses of anaesthetics and side effectsfrom higher doses.

Spectral entropy, bispectral index and narcotrend enable us to determine the depth of anaesthesia [1,2] and are currently in vogue. Entropy monitoring adopts a scale from 0 to 100. The readings between 40 and 60 represent satisfactory level of anaesthesia. Using lower doses of anaesthetics, the side effects of induction agents may be reduced but may lead to inadequate anaesthesia and awareness. The advantage of entropy monitoring is that it enables to administer the dose of induction agent with precision.

Propofol, has achieved popularity, partially because of its short half- life, rapid recovery profile and less sedative effect [3]. The fall in blood pressure is seen more with higher doses of propofol, fast speed on injection [4,5] and is dose dependent. Etomidate

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has a rapid onset of action with a greater cardio stability.

In this study, we aim to evaluate the hemodynamic effects of induction doses of etomidate and propofol using entropy guidance for laryngoscopy and intubation.

Aims and Objectives

- To evaluate the hemodynamic effects of induction doses of etomidate and propofol using entropy guidance for laryngoscopy and intubation as a primary outcome measure.
- To observe the side effects, if any, of the induction agents as a secondary outcome measure.

Materials and Methods

This study was conducted in the department of anaesthesiology after obtaining approval from the Institutional Ethical Committee and a written informed consent from all the patients. This prospective, observational study was conducted for two years on 100 patients, aged 18-60 years, of ASA grade I & II, who were scheduled to undergo elective surgical procedure under general anaesthesia.

Patients with associated comorbidities, extremes of age, pregnant patients and anticipateddifficult airway (MP grade III and IV) were excluded from the study.

Allocation of Groups

100 healthy patients were randomly allocated in two groups.

Group A: (n=50) Induction dose of IV etomidate (0.2 mg/Kg -0.3mg/Kg) was given till entropy of 40 was achieved.

Group B: (n=50) Induction dose of IV propofol (2mg/Kg-3mg/Kg) was given till entropy of 40 was achieved.

Methodology

Pre anaesthetic evaluation was done a day prior to surgery and all the investigations were carried out. All patients were kept fasting for 8 hours. In operation theatre, IV line was secured with 18 G cannula and normal saline was started. Baseline vitals parameters systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), heart rate (HR), oxygen saturation (SpO2), end tidal carbon dioxide ($EtCO_2$) were noted. Study drug was prepared according to the groups allocated randomly by a computer generated randomization. Patients were premedicated with IV glycopyrrolate 0.2mg/kg, IVmidazolam (0.05 mg/Kg) and IV fentanyl 2μg/kg and pre oxygenated with 100% oxygen via facemask. Anaesthesia was induced with IV induction agents (propofol/etomidate), as per the study group, while observing entropy. Induction dose at entropy 40 was observed. After ensuring adequate mask ventilation, neuromuscular blockade was achieved with IV vecuronium 0.1mg/kg. Patient was ventilated via facemask for four minutes followed bylaryngoscopy and endotracheal intubation. After confirming position of endotracheal tube, anaesthesia was maintained with oxygen and nitrous oxide (40:60), sevoflurane (0.5-1%) and intermittent top ups of IV vecuronium (0.02mg/kg) with controlled ventilation. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), heart rate(HR), oxygen saturation (SpO_2), end tidal carbon dioxide ($EtCO_2$) were noted at induction and 1, 2, 3, 4, 5, 10 min thereafter. On conclusion of surgery, patients were reversed with IV neostigmine 0.05 mg/Kg and IV glycopyrrolate 0.02mg/Kg and extubated after fulfillment of extubation criteria.

Any intraoperative side effects such as hypotension, bradycardia, hypertension, tachycardia, myoclonic jerks, seizures, pain on injection, bronchospasm or laryngospasm were noted.

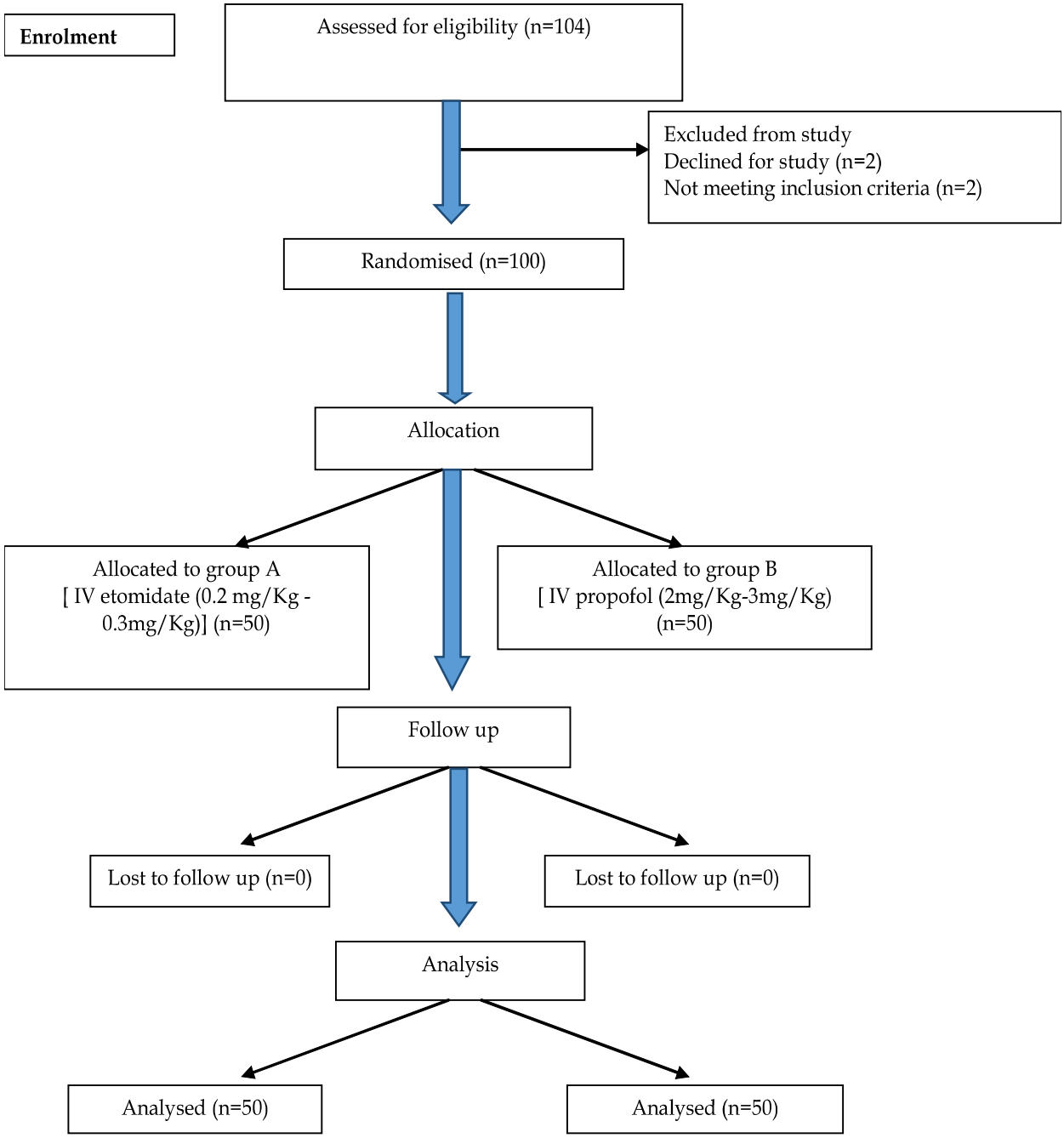
Parameters Observed were

- Baseline vitals [SBP, DBP, MAP, HR, SpO_2, $EtCO_2$] at induction and 1, 2, 3, 4, 5, 10 minutes after intubation.
- Adverse effects

The data from the above study was systematically collected, compiled and statistically analyzed to draw relevant conclusions. Data were described in terms of range, mean±SD,and percentages as appropriate. Comparison of quantitative variables between study groups was done using Students t test and Mann Whitney U test for independent samples for parametricand non parametric data respectively. A p value of <0.05 was considered to be significant. SPSS 21 version was used for calculations for Microsoft windows.

This study did not impose any financial burden to participants.

Consort 2010 Flow Diagram



Observations and Results

This prospective randomized comparative study was conducted on 100 healthy adult patients, aged 18-60, in MMIMSR to evaluate the haemodynamic effects of induction doses of etomidate and propofol using entropy monitor and determine their side effects, if any, intraoperatively.

All patients were evaluated for demographic data, haemodynamic parameters at baseline, before and after induction and intubation, side effects and complications.

The following observations were made and results were analysed statistically using appropriate statistical tests.

Patients in both the groups were comparable with respect toage, sex, ASA grade and MP grading. ($p>0.05$)

The mean dose of induction agent, according to entropy (DE) in group A was 16.7±2.4 and mean dose according to entropy (DE) in group B was 105.8±17.2.

As shown in Table 1, on comparison of systolic blood pressure in both groups at different time intervals, it was evident that in group B significant fall in SBP was observed compared to group A at T1, T2 and T3 ($p<0.005$). After laryngoscopy more rise in SBP in group B compared to Group A. ($p=0.004$)

As evident from the Table 2 above, in group B significant fall in DBP was observed compared to group A at T1, T2 and T3 ($p<0.005$). After laryngoscopy more rise in DBP in group B compared to Group A was observed. ($p=0.000$)

As depicted by Table 3, on comparison of mean arterial pressure in both the groups at different time intervals in group B significant fall in MAP was observed compared to Group A at T_1, T_2, and T_3 ($p<0.005$). After laryngoscopy more rise in MAP at T_5 in group B compared to group A. ($p=0.000$).

Time interval Group A (n-50) Table 4 shows, comparison of heart rate in both groups at different time intervals. As evident from the table above after laryngoscopy (T_5) significant rise in HR in group B (propofol) compared to group A (etomidate) was observed. ($p=0.018$).

Table 1: Systolic blood pressure of patients in both groups at different time period

Time interval	Group A (n-50) Mean	SD	Group B (n-50) Mean	SD	T	DF	p-value
T	121.2	14.6	123.4	14.2	-0.756	98	0.452^{NS}
T_0	125.3	12.9	128.2	12.4	-1.145	98	0.255^{NS}
T_1	116.2	14.2	100.6	10.8	6.174	98	0.000*
T_2	116.8	11.0	100.9	9.2	7.802	98	0.000*
T_3	118.7	9.5	109.5	7.5	5.343	98	0.000*
T_4	119.8	7.8	114.8	8.1	3.082	98	0.003*
T_5	131.3	9.9	137.2	10.2	-2.936	98	0.004*
T10	121.4	6.5	118.3	9.1	1.928	98	0.057^{NS}

*T0 - Baseline, T1 - 1 min after induction, T2 - 2 min after induction, T3 - Laryngoscopy time, T4- 1 min after laryngoscopy and intubation.

Table 2: Diastolic blood pressure of patients in both groups at different time period

Time interval	Group A (n-50) Mean	SD	Group B (n-50) Mean	SD	T	DF	p-value
T	73.6	8.4	74.4	9.5	-0.498	98	0.620^{NS}
T_0	77.3	7.5	78.5	8.3	-0.783	98	0.435^{NS}
T_1	70.8	8.6	63.1	7.4	4.753	98	0.000*
T_2	70.8	6.9	64.6	5.5	4.844	98	0.000*
T_3	71.8	6.7	68.7	5.5	2.448	98	0.016*
T_4	72.5	5.4	73.1	7.2	-0.438	98	0.663^{NS}
T_5	82.5	8.9	89.3	8.9	-3.821	98	0.000*
T10	72.7	4.8	73.1	6.0	-0.401	98	0.689^{NS}

Table 3: MAP among patients in both groups at different time period

Time interval	Group A(n-50) Mean	SD	Group B (n-50) Mean	SD	t	DF	p-value
T	89.7	9.2	90.7	10.2	-0.552	98	0.582^{NS}
T_0	93.4	8.4	95.1	8.9	-1.012	98	0.314^{NS}
T_1	85.9	10.0	75.5	8.0	5.704	98	0.000*
T_2	86.2	7.8	76.6	6.1	6.798	98	0.000*
T_3	87.3	6.9	82.4	5.4	3.926	98	0.000*
T_4	88.2	5.5	86.9	6.7	1.031	98	0.305^{NS}
T_5	98.4	8.1	105.3	9.1	-4.006	98	0.000*
T10	89.0	4.3	88.2	6.4	0.707	98	0.481^{NS}

Table 4: Heart rate of patients in both groups at different time period

Time interval	Group A (n-50)		Group B (n-50)		t	DF	p-value
	Mean	SD	Mean	SD			
T	79.1	10.2	78.1	9.1	0.536	98	0.593^{NS}
T_0	83.2	8.9	85.0	10.3	-0.910	98	0.365^{NS}
T_1	83.6	9.1	84.9	10.5	-0.687	98	0.493^{NS}
T_2	83.8	9.1	84.7	9.6	-0.448	98	0.655^{NS}
T_3	84.0	8.6	85.6	8.9	-0.898	98	0.372^{NS}
T_4	83.6	7.8	86.2	7.9	-1.640	98	0.104^{NS}
T_5	94.1	10.2	99.7	13.0	-2.407	98	0.018*
T10	83.4	6.2	77.1	8.8	4.160	98	0.000*

Adverse Effects of Drugs

Incidence of pain on injection was 42% in group B and 0% in group A. Incidence of myoclonus was 16% in group A and 0% in group B. Adverse reaction was observed only in 2% patients in group B. Nausea vomiting was seen 6% in group A and 2% in group B.

Discussion

Monitoring of the level of consciousness of the patient under general anaesthesia, can be done most commonly by methods using EEG based indices [6]. Higher values of EEG are an indication of awake state and lower values are indication of sedation or loss of consciousness.

Datex Ohmeda has two sets of indices, state entropy (SE) and response entropy (RE). SE is has a frequency range of 0.8 to 32 Hz and it covers the hypnotic elements of EEG, while RE is has a frequency ranging from 0.8 to 47 Hz, which includes a significant amount of facial EMG. The EEG band that has lower frequency and denotes the cortical activity is the state entropy (SE). The response entropy (RE) is an indicator of analgesia [7].

The readings between 40 and 60 are considered as satisfactory level of anaesthesia. This is the point where awareness can be avoided and unnecessary prolongation of recovery is also prevented. The values of RE and SE differ more during intubation due to nociception and extubation because the effects of drugs on nervous system has diminished and the patient is regaining consciousness [8].

In the present study, we have used entropy monitor to evaluate the hemodynamic effects of induction doses of propofol and etomidate under entropy guidance.

As shown in Table 5, in our study the baseline heart rate was comparable among groups,mean HR in group A was 79.16±10.241 and in group B was 78.12±9.115. (p value= 0.593). Statistically significant rise in HR was seen 1 minute after laryngoscopy and intubation in group B (mean 99.7±13.0) but no significant rise in group A (mean 94.1±10.2) p value was 0.018.

Kaushal RP et al. in 2015also studied hemodynamics of etomidate and propofol after induction in patients undergoing cardiac surgeries. Baseline HR in Etomidate and propofol group was 80.66±23.53 and 91.03±2.07 respectively. After intubation HR in etomidate group was 85.83±23.53 and in propofol group was 96.93±20.34 [9].

Table 5: Showing change in HR of both groups in different studies

Study author and year	Etomidate (A)					Propofol (B)				
	T_0	T_1	T2	T3	T4	T_0	T_1	T2	T_3	T4
Kaushal [9] RP et al 2015	80.66± 23.53	80.6± 12.92	-	-	85.83± 23.53	91.03± 2.07	88.53± 18.20	-	-	96.93± 20.34
Shah SB [10]et al 2015	77.1± 10.046	80.3± 8.819	80.32± 8.450	79.53± 16.305	78.6± 13.037	82.53± 11.40	87.69± 8.054	88.68+ 7.620	84.96± 8.181	85.49± 0.241
Present study	79.1± 10.2	83.6± 9.1	83.8± 9.1	83.6± 7.1	94.1± 10.2	78.1± 9.1	84.9± 10.5	84.7+ 9.6	86.2± 7.9	99.7± 13.0

Table 6: Showing changes in MAP of both groups in different studies

Study author and year	Group (A) T_0	T_1	T2	T3	T4	Group (B) T_0	T_1	T2	T_3	T4
Masoudifar M[11] et al 2013	97.2± 18	-	-	91.6± 30	121.4± 25.1	95.1± 16.7	-	-	84± 26.6	87.8± 22.2
Shah SB [10]et al 2015	98.03± 9.58	82.47± 8.23	81.77± 6.38	104.8± 9.06	97.10± 0.32	97.43± 5.69	73.10± 9.98	69.24± 8.3	91.17± 13.09	88.17± 9.58
Present study	89.7± 9.2	85.9± 10.0	86.2± 7.8	88.2± 5.5	98.4± 8.1	90.7± 10.2	75.5± 8.0	76.6± 6.1	86.9± 6.7	105.3± 9.1

Shah SB et al. also compared haemodynamic effects of propofol and etomidate after induction, laryngoscopy and intubation and concluded that propofol caused sustained increase in heart rate while etomidate keeps the heart rate stable. Baseline HR in etomidate group was 77.1±10.04 and in propofol group was 82.53±11.4 which was comparable. After intubation HR in etomidate group was 78.6±13.03 and in propofol group was 85.49±0.241 [10].

As shown in table 6, in our study baselin e MAP was comparable in both groups. Mean MAP in group A was 89.7±9.2 and in group B was 90.7±10.2. After induction there was fall in MAP in group B but no significant fall in group A. Mean MAP 1 min after induction in group A and B was 85.9±10 and 75.5±8 respectively. After laryngoscopy mean MAP in group A and B was 98.4±8.1 and 105.3±9.1 respectively.

Masoudifar M et al. found that baseline MAP in etomidate and propofol group was 97.2±18 and 95.1±16.7. After induction mean MAP in etomidate and propofol group was 91.6±30 and 84±26.6. Hypotension occurred in 26.1% of group B and 8% of group A (p = 0.09) [11].

Shah SB et al. [10] also compared haemodynamic effects of propofol and etomidate after induction, laryngoscopy and intubation and concluded that there was significant fall in MAP after induction with propofol compared to etomidate. Baseline MAP in etomidate and propofol group was 98.03±9.58 and 97.43±5.67 respectively. One min after induction the mean MAP in etomidate and propofol group was 82.47±8.23 and 73.10±9.98.

Few adverse effects of etomidate and propofol were noted in our study. Myoclonus was observed in 16% patients with etomidate and none with propofol. Pain on injection was observed in 42% patients receiving propofol and 0% with etomidate. Nausea and vomiting was seen in 6% patients with etomidate and only 2% with propofol. Kaushal RP et al. [9] observed no incidence of nausea vomiting, adverse reaction, myoclonus and pain on injection in both groups

Miner et al also concluded higher incidence of myoclonus (20% vs. 1.8%) in etomidate and propofol groups respectively. Pain on injection was observed only in propofol group [12]. Aggarwal S et al. concluded that pain on injection was seen in 50% patients with propofol and 4% patients with etomidate [13].

Conclusion

The haemodynamic effects observed after induction doses of propofol were more pronounced than that of etomidate. Propofol caused more hypotension than etomidate after induction, whereas there was statistically significant rise in heart rate after laryngoscopy and intubation.

Pain on injection was observed to be more in patients receiving propofol than etomidate. Nausea and vomiting was commoner with etomidate than propofol.

Thus, etomidate may be a better alternative induction agent to maintain cardio stability under entropy monitoring.

Acknowledgement

Nil

Conflict of Interest

Nil

Key Messages

On induction of anaesthesia with entropy monitoring, haemodynamic effects of propofol were more pronounced than that of etomidate

References

1. Kreuer S, Beidler A, Larsen R. The Narcotrend- A new EEG monitor designed to measure depth of anaesthesia. A comparison with bispectral index in monitoring during propofol- remifentanil- anaesthesia. Anaesthesist. 2001;50:921-5.
2. Ellerkmann RK, Soehle M, Alves TM. Spectral entropy and bispectral index as the measure of electroencephalographic effects of propofol. Anaesth Analg. 2006;102:1456-62.
3. Kondo U, Kim SO, Murray PA. Propofol selectively attenuates endothelium- dependant pulmonary vasodilation in chronically instrumented dogs. Anaesthesiology. 2000;93:437-46.
4. Schmidt C, Roosen C, Struys M. Contractility in humans after coronary artery surgery. Anaesthesiology. 1999;91:58-70.
5. Morgan GE, Mikhail MS, Murray MJ. Clinical Anaesthesiology. Fourth edition. McGraw Hill. 2006:200-2.
6. Brown EN, Solt K, Purdon PL. Monitoring Brain State During General Anaesthesia and Sedation. Miller's Anesthesia. Eighth edition. Elseiver. 2015:1525-30.
7. Balci C, Karabekir H, Sivaci R. Determining entropy valuesequivalent to the bispectral index during sevoflurane anaesthesia.Arch Med Sci. 2010;6(3): 370-4.
8. Grover VK, Bhart N. Measuring Depth of Anaesthesia- An Overview on the Currently Available Monitoring Systems. 2014.
9. Kaushal RP, Vatal A, Pathak R. Effect of Etomidate and propofol induction on haemodynamic and endocrine response in patients undergoing coronary artery bypass grafting or mitral valve and aortic valve replacement on cardiopulmonary bypass. Annals of CardiacAnaesthesia. 2015;18(2):172-8.
10. Shah SB, Chowdhury I, Bhargava AK. Comparision of haemodynamic effects of intravenous etomidate versus propofol during induction and intubation using entropy guided hypnosis levels. J Anaesthesiol Clin Pharmacol. 2015;31:180-5.
11. Masoudifar M, Beheshtian E. Comparision of cardiovascular response to laryngoscopy and tracheal intubation after induction of anaesthesia by Propofol and Etomidate. Journal of Research in Medical Sciences. 2013;18(10):870-4.
12. Miner JR, Danahy M, Moch A. Randomized clinical trial of etomidate versus propofol for procedural sedation in emergency department. Ann Emerg Med.2007;49:5-22.
13. Aggarwal S, Goyal VK, Chaturvedi SK. A comparative study between propofol and etomidate in patients under general anaesthesia. Revista Brasileira De Anestesiologia. 2016;66(3):237-41.