Original Article

Comparison of Haemodynamic Stability of Etomidate versus Propofol for Induction of Anaesthesia in Patients undergoing Coronary Artery Bypass Graft Surgery

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Abstract:

Background: *Maintenance of hemodynamic stability during induction and obtundation of intubation stress response are the prime consideration of general anaesthesia.*

Aims: *The purpose of the study is to compare the hemodynamic effects of etomidate and propofol during induction and intubation in patients undergoing Coronary Artery Bypass Graft Surgery(CABG).*

Materials and Methods: *This prospective, double-blind randomized clinical trial, total eighty patients were randomly allocated and divided into two groups based on the induction agent used for anaesthesia (etomidate group or E group) and (propofol group or P group). Heart rate(HR), Mean Arteriolar Blood pressure(MAP), Cardiac Output (CO) & Cardiac Index(CI) were recorded at preoperative Baseline(T1), at premedication(T2), at induction(T3), at intubation (T4), 1 min after induction(T5), 3 min after induction(T6), 5 min after induction(T7). The use of vasopressors was also recorded, required for both the groups.*

Results: *Before induction, there was no significant difference in hemodynamics between the groups ($p > .05$). At induction, intubation & up to 5 min after induction thereafter all the hemodynamic parameters were significantly different from baseline value in both groups ($p < .001$). During the comparison between two group, it was noted that, in P group, propofol caused pronounced reduction of HR, MAP, CO & CI in comparison to E group, at induction(T3), at intubation (T4), 1 min after induction(T5), 3 min after induction(T6). The use of vasopressors was also in higher incidences in P group than E group.*

Conclusion: *This study confirms that Etomidate provides a stable hemodynamic condition in context with propofol during induction, intubation & immediate post induction period and this hemodynamic stability can improve the clinical outcomes in patients undergoing CABG.*

Key words: *CABG, Hemodynamic stability, Etomidate, Propofol, Induction*

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Introduction:

Maintenance of hemodynamic stability during induction and obtundation of intubation stress response are the main consideration of general anaesthesia for the patients undergoing CABG[1,2]. Because in case of the Cardiac surgery. patients are critically ill & cardiovascularly compromised [3,14]. Propofol, is widely used as induction agent because of its rapid onset of action, shorter duration action & minimal adverse effects. But it causes profound post-induction & pre-intubation hypotension & bradycardia due to the significant decrease of Systemic Vascular Resistance (SVR)[3] which is completely undesirable and detrimental in the cardiovascularly compromised patients[17]. Etomidate is an alternative induction agent which produces reliable & rapid onset of anaesthesia & is perceived as having a more stable hemodynamic

condition. So etomidate may be better choice for induction for the patients, where hypotension & bradycardia is undesirable. Etomidate may be a good alternative for induction of anaesthesia as it minimally releases histamine[4]. In the most previous studies the hemodynamic effects of both the agents are compared in abdominal, orthopedic and even in neurosurgical cases but not so much in case of cardiac surgery[5,6]. So this study was aimed to compare the hemodynamic effects of etomidate and propofol during induction and intubation in patients undergoing CABG and to test hypothesis that etomidate is superior propofol for induction & obtundation of intubation stress response in relation to hemodynamic stability.

Materials & Methods

This prospective, double-blind, randomized clinical trial was conducted in the department of Cardiac anesthesia of Combined Military Hospital, Dhaka from the period of January,2019 to December 2019. The study protocol was approved by the institutional Ethical Committee and with informed written consent,80 adult patients were selected in this study.

Inclusion Criteria

1. Adult patients age > 30 years
2. ASA grade III &IV
3. Scheduled to undergo elective off pump CABG
4. Patients with LVEF >50%

Exclusion Criteria

1. Patients with known history of allergy to study drugs
2. Patients with low LVEF < 50%
3. CABG with Cardiopulmonary Bypass (CPB)
4. TVCAD with Valvular Heart Disease (VHD)
5. Patients of > 65 years of age

Study Procedure

Randomization was done on basis of computer generated random number list. This randomization schedule facilitated patient disposition into two equal groups -Group P (propofol = 40) and Group E (etomidate = 40). The list was concealed in opaque sealed envelope that was numbered and opened sequentially after obtaining the patient's consent. All patients were advised to restrict solid per mouth at least 6 h before surgery along with tablet diazepam (5 mg) and ranitidine (150mg) on the night before surgery. On arrival to the operating room, an intravenous (IV) fluid (10 ml/kg) was started. An arterial line was placed into the radial artery and Edward CO sensor in cardiac monitor EV1000 was attached for measuring mean arterial pressure (MAP) and CO. All the preoperative baseline parameters were recorded. Fentanyl 2-4 μg/kg was administered intravenously just before induction. After pre-oxygenation with100% oxygen for 3 minutes, P group received propofol 1.5-2 mg/kg and E group received etomidate 0.2mg /kg. IV over 30-60 sec rocuronium 0.6 mg/kg was administered and the patient was oro-tracheally intubated by the main examiner. The main examiner was unaware about the type of induction agent. After intubation, the patient was mechanically ventilated with a mixture of oxygen and medical air (1:1) with addition of isoflurane which was included into the gas mixture immediately after intubation The tidal volume was 6 ml/kg, the breathing frequency was 10-14 /min and fresh gas flow was 2 litre/min with maintaining end tidal CO2 value 35 - 40 mmHg. No surgical intervention was allowed until 5 minutes after induction. HR, MAP, CO and CI values all were recorded before premedication, immediately before and after induction of anesthesia, at intubation and1, 3, and 5 min after intubation. The study was ended at that point and thereafter all the vitals were monitored throughout the surgery. Data were stored in an IBM-compatible computer. Any adverse effect like bradycardia, hypotension, pain on injection cough, laryngospasm, bronchospasm, apnoea and any involuntary movement was also noted. Injection Vecuronium infusion started to maintain relaxation. All complications were treated after 1 min of their duration. Hypotension (MAP d" 55 mm Hg) was treated with IV bolus dose of phenylephrine and intravenous infusion of Inj. Adrenaline, Noradrenaline and Dobutamine, until the desired clinical effect was achieved. Hypertension (MAP ≥100 mm Hg) was treated with fentanyl 1 μg/ kg up to three times and afterwards with a nitroglycerine infusion (10 - 100 μg/ min). Bradycardia (HR ≤40/min) was treated with atropine 0.3 mg. Tachycardia (HR ≥90/min) was treated with fentanyl 1 μg/kg. Data were analyzed with the IBM SPSS Statistics 22 statistical software. Data were summarized by routine descriptive

statistics namely mean and standard deviation (SD) for numerical variables and counts and percentages for categorical variables. Numerical data were compared between groups by Student's independent t-test as data were normally distributed. The Chi-square test was employed for intergroup comparison of categorical variables. All analysis was two tailed and $p < 0.05$ were considered statistically significant.

Result

In this study total 80 patients were randomly selected & all the demographic variables like age, sex, height 7 body weight were comparable between two groups (Table 1). Baseline haemodynamic parameters in both groups were also comparable ($p<0.05$). Each intubation was successful at the first attempt & took < 20 sec. In table 3, it was shown that, P group, immediately after induction MAP was decreased (90.42 ± 6.69) from baseline value (103.63 ± 8.42) up to intubation. Just after intubation, MAP was increased transiently (92.78 ± 6.62) and then it again gradually came down to basal level at the end of study (98.84 ± 3.42). Whereas, in E group after induction MAP was decreased to some extent (96.69 ± 3.93) from baseline value (102.82 ± 3.82), but it was increased after intubation (101.77 ± 5.04) and remained stable to the end of study period (102.23 ± 4.41). After induction, in both the groups MAP significantly differed from base line value during intragroup comparison. At all-time intervals ($p < 0.01$), it was shown that, during intubation, MAP did not significantly increase in two groups. During intergroup comparison, MAP was significantly lower in P group than E group at 1, 3 and 5 minutes after intubation ($p = 0.000$) (Table 3). 4 out of 40 patients in E group required rescue IV fentanyl (2 mcg/kg) and infusion nitroglycerine (10 - 100 mcg/kg/min) to control BP. Similar to MAP, HR, CO and CI all parameters were decreased from their baseline value just after induction in both the groups and increased transiently just after intubation. During intubation, HR, CO and CI was not significantly different between two groups. HR, CO and CI came down to its baseline value in E group at end of study, but in P group their value remained significantly at lower level than baseline value. During intragroup comparison parameters were significantly differ from their baseline values ($p < 0.01$). During intergroup comparison their values were significantly lower in P group than E group at 1, 3 and 5 min after intubation ($p = 0.000$) (Table IV-VI).

Table I: *Basic demographic characteristics.*

	Values in mean (SD). BSA=body surface area.		
Parameter	Etomidate (n=40)	Propofol (n=40)	P-value
Age(yrs)	43.62±9.92	42.74±8.84	0.59
Height(cm)	149.199±5.45	150.139±4.58	0.08
Weight(kg)	64.98±2.08	65.62±1.98	0.88
BSA(m^2)	1.63±0.21	1.62±0.118	0.31
Mean EURO score	1.8±1.4	2.4±1.6	0.48
Mean Hematocrit(%)	41.2±4.2	40.8±4.4	0.53
Mean LVEF(%)	58.8±10.80	60.2±11.7	0.32

Table-II: *ASA Physical Status & Co-Morbid Conditions*

Parameters	Etomidate(n=40)	Propofol(n=40)
ASA physical status		
ASA III	28	32
ASAIV	12	08
Co-morbid Conditions		
Hypertension	26	27
IHD	30	24
DM	18	15
Hypothyroidism	06	05

Table III: Comparison of effect of propofol and etomidate on mean arterial pressure (mmHg). Values in mean ±SD.

Mean Arteriolar Pressure(MAP)	Etomidate(n=40)	Propofol(n=40)	P-value
Pre op baseline(T1)	102.80±3.42	103.63±8.42	0.59
Premed(T2)	100.78±4.20	96.78±6.68	0.42
Induction(T3)	96.69±3.93	90.42±6.69	0.35
Intubation(T4)	101.77±5.04	92.78±6.62	0.09
After 1 min(T5)	99.88±4.88	93.88±5.59	0.004
After 3 min(T6)	100.85±3.82	96.64±6.74	0.000
After 5 min(T7)	102.23±4.41	98.84±3.42	0.000

Table IV: *Comparison of effects of propofol and etomidate on heart rate (HR). Values in mean ±SD*

Heart Rate(HR)	Etomidate(n=40)	Propofol(n=40)	P-value
Pre op Baseline(T1)	88.26±8.68	90.20±6.70	0.85
Premed(T2)	86.88±4.85	88.04±5.44	0.45
Induction(T3)	86.24±5.78	82.08±4.50	0.21
Intubation(T4)	92.35±6.04	88.68±8.81	0.15
After 1 min(T5)	90±4.38	87.05±7.78	0.001
After 3 min(T6)	89.89±3.80	84.82±4.75	0.000
After 5 min(T7)	88.78±2.98	85.70±5.50	0.000

Table V: *Comparison of effects of propofol and etomidate on Cardiac Output (CO). Values in mean± SD.*

Cardiac Output(CO)	Etomidate(n=40)	Propofol(n=40)	P-value
Pre op baseline(T1)	5.41±0.04	5.34±0.34	0.07
Premed(T2)	5.38±0.03	5.28±0.25	0.06
at induction(T3)	5.22±0.34	4.38±0.18	0.24
at intubation(T4)	5.20±0.08	4.98±0.20	0.79
after 1min(T5)	5.40±0.18	5.18±0.27	0.52
after 3 min(T6)	5.5±0.24	5.28±0.38	0.000
after 5 min(T7)	5.4±0.25	5.28±0.21	0.001

Table VI: *Comparison of effects of propofol and etomidate on Cardiac Index (CI). Values in mean ±SD.*

Cardiac Index(CI)	Etomidate((n=40)	Propofol(n=40)	P-value
Pre op baseline(T1)	4±0.10	4.1±.08	0.19
Premed(T2)	4.2±0.2	4.0±0.07	0.08
induction(T3)	4.1±0.08	3.7±0.04	0.06
intubation(T4)	4.0±0.06	3.8±0.04	0.08
after 1 min(T5)	4.1±0.10	4.0±0.08	0.004
after 3 min(T6)	4.3±0.05	4.2±0.02	0.002
after 5 min(T7)	4.3±0.15	4.2±0.06	0.001

During the study period, there was no pain on injection, cough, laryngospasm, bronchospasm, apnoea and any involuntary movements in either group of patients without any hypotension or bradycardia.

Discussion

In this study, we compared the haemodynamic effects of propofol and etomidate during induction, intubation and 5 minutes thereafter in patients undergoing CABG under general anaesthesia. It was found that in both group hypertension and tachycardia occurred during induction & intubation, but the degree and duration of haemodynamic alternation (hypertension and tachycardia) were more profound in propofol than etomidate group. It was also shown that, during induction, propofol caused significant hypotension & bradycardia. Anaesthetic induction, is also associated with significant haemodynamic suppression due to peripheral vasodilatation, reduction in preload and venous return and to a lesser extent, decreased myocardial contractility[7]. On the other hand, stress response during laryngoscopy and intubation leads to various haemodynamic changes like hypertension, tachycardia, dysrrhythmia, myocardial infarction and increase in intracranial and intraocular pressure. These changes are due to increase in plasma concentrations of epinephrine, norepinephrine and vasopressin[8]. The undesirable haemodynamic effects of laryngoscopy and tracheal intubation, are not only detrimental for intraoperative safety, but also prudent in post-operative recovery, long term survival and health care costs[9]. Maintaining adequate depth of anaesthesia is essential for stable hemodynamics during induction and intubation. it is a challenging task for anaesthesiologist.

In Cardiac surgery, acute alternation of MAP is detrimental, as sudden hypotension during induction may hamper cardiac perfusion and on the other hand marked hypertension during intubation may lead to irreversible damage to myocardial perfusion due to the imbalance between the O2 demand and supply of which is already severely compromised. So tight control of MAP is prime concern during cardiac surgery[2]. Invasive haemodynamic monitoring, especially beat to beat measurements of arterial blood pressure and cardiac output, are useful for accurate monitoring and management of perioperative haemodynamic changes. Monitoring of Cardiac Output (CO) & Cardiac Index(CI) are also essential to ensure adequate myocardial tissue perfusion in the perioperative period[10]. There was less study in the available literature which compares the haemodynamic of effects propofol and etomidate on cardiac output before and after intubation in cardiac surgery. We decided to use Edward CO sensor in our study because it only requires a standard radial arterial line and we were interested in trends of CO & CI. In our study, it was found that after induction HR, MAP, CO & CI all were decreased from baseline value in both groups, but 1 minute after intubation they were increased. These changes in MAP, HR, CO & CI were more pronounced in P Group. At the end of study period, in E group MAP, HR, CO & CI all the parameters reached to their basal level, but in P group their values decreased in lower level. In one study, Larsen and colleagues compared the haemodynamic effects of propofol and etomidate induction in geriatric patients undergoing major upper abdominal surgery[10]. They found that after induction MAP and HR were decreased in both groups to the same extent, but at intubation the haemodynamic stress response was more prominent in etomidate group. In another study, Kaushal RP., et al. observed the effect of propofol and etomidate induction in patients undergoing CABG or mitral/aortic valve replacement under CPB. They found that after induction decrease in HR from baseline values in P group, but not in E group. After intubation HR raised in both P and E group, but after 5 minutes HR became normal in P group, but in E group it remained at higher level[11]. In another study, Singh and colleagues compared the induction effect of etomidate (0.2 mg/kg) and propofol (1.5/mg kg) in patients with coronary artery disease and left ventricular dysfunction[12]. They found that MAP, cardiac index (CI) and HR were significantly decreased after induction and increased after intubation in comparison with the baseline with no significant differences between the groups. Similar to our study, Haessler and colleagues found that propofol induced severe hypotension predominantly in patients with severe triple-vessel disease. Similarly, McCollum JSC and Dundee JW, when compared

the efficacy of IV boluses propofol and etomidate as induction agent in elective surgeries under GA, they found that hypotension was more with propofol 2.0 and 2.5 mg/kg than etomidate 0.3 mg/kg[13]. In our study, as both the induction agent was administered through bolus doses, no such haemodynamic alternation was occurred in E group.In another study, Bendel and colleagues compared the haemodynamic effects of propofol and etomidate after slow bolus administration(titrating to BIS 60 or less) in patients with aortic stenosis[14]. They found that propofol is more likely to cause hypotension thanetomidate, which is due to aortic stenosis. Shivanna S., et al. in 2015 conducted a study to compare haemodynamic stability of propofol and etomidate in patients undergoing CABG with CPB. They observed that after induction, mean MAP reduced by 30% in group P and 22% in group E[15].

In a another study by Shah SB., et al. in cardiac surgery (2017), they used State and Response Entropy for induction and intubation. The fall in MAP was much sharper for Group-P (24.3% and 28.66%) as compared with Group-E (15.87% and 16.6%)[16]. The above studies were supporting from our study in respect to cardiac compromise patients. In our study on patient undergoing cardiac surgery, the haemodynamic variation was more pronounced and prolonged in P group than E group. In some recent studies also the same haemodynamic variations like our study were noted with etomidate induction[17,18]].

Limitations: The study had its limitations. Firstly, it was a single centre study with small sample size. Secondly, serum cortisol level could not be measured in our study. To evaluate the haemodynamic effects of both drugs in higher risk group like in elderly and severely cardiac compromised patients were not included. So, further studies are needed.

Conclusion

From this study it can be showed that though propofol is a popular induction agent, but etomidate induction is more ideal for CABG, as better haemodynamic is maintained with less hypotension and bradycardia at inducton and after intubation. On the other hand, in cardiac Anaesthesia, use of propofol was not associated with stable haemodynamics because of its inability to prevent a profound decrease in HR and blood pressure at and after induction. We can therefore conclude that, when used for induction of anaesthesia, etomidate provides superior haemodynamic stability to propofol as well as better outcome in patients undergoing CABG.

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