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PROSPECTIVE RANDOMISED STUDY COMPARING THE HAEMODYNAMIC AND ENDOCRINE RESPONSE TO INDUCTION WITH ETOMIDATE AND PROPOFOL IN PATIENTS UNDERGOING CARDIAC SURGERY ON CARDIOPULMONARY BYPASS

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ABSTRACT Haemodynamic status must be stable during induction for cardiac surgeries to avoid further myocardial deterioration. Compared to induction agents like Thiopentone , Propofol, Ketamine and Midazolam , Etomidate is found to have a more stable hemodynamic profile even though it causes a short term adrenocortical suppression.This study compares the haemodynamic profile and the hormonal alteration between Etomidate and Propofol following induction in cardiac surgery particularly in patients undergoing coronary artery bypass surgery on cardiopulmonary bypass.

KEYWORDS : Etomidate, Propofol, hemodynamic variables , serum cortisol levels

INTRODUCTION

In Cardiac anaesthesia, to achieve the objectives of hemodynamic stability, amelioration of stress response to intubation and continued maintenanace of the balance between myocardial oxygen demand and supply, variety of induction agents have been tried . This study aims to compare the hemodynamic profile and hormonal alteration between etomidate and propofol when used for inducing patients undergoing coronary artery bypass surgery on cardiopulmonary bypass. The comparison is with respect to,

1. Induction hemodynamics
2. Induction, post bypass and 24 hr serum cortisol levels

Propofol is an alkyl phenol having hypnotic properties(2,6, diisoprophylphenol).Its cardiovascular effects are of importance in this study.The most prominent effect of propofol is a decrease in the arterial blood pressure. Induction produces a 25-40% decrease in Systolic Blood pressure , mean and diastolic pressure. Also, it is associated with decrease in cardiac output /cardiac index(±15%), stroke volume index(±20%) and systemic vascular resistance(15-25%) It causes a decrease in the slope of the right ventricular end systolic pressure volume relationship curve. Left ventricular stroke work index is also reduced by 30%. Peripheral vascular actions of propofol are due to an inhibition of sympathetic vasoconstrictor nerve activity rather than direct vasodilation . Its negative inotropic effect on the heart is reversible with adrenergic stimulation.In clinical concentrations the net effect of propofol on contractility is insignificant because of a simultaneous increase in the sensitivity of the myofilaments to activator calcium.Both vasodilatation and myocardial depressant effect seem to be dose dependant and plasma concentration dependant.

Heart rate does not change significantly after an induction dose of propofol.It inhibits the baroreflex and reduces tachycardic response to hypotension.It preserves the global myocardial oxygen demand supply ratio. It has minimal effect on SA node or on AV conduction or accessory pathway conduction. Propofol suppresses atrial (supra ventricular) tachycardias.

Propofol after a single dose or a prolonged infusion does not affect corticosteroid synthesis or alter the normal response to adrenocorticotropic hormone stimulation.

Etomidate is an imidazole derivative and exists as 2 isomers(+ isomer being active as a hypnotic).It is water insoluble. Induction dose is 0.2 - 0.6 mg/kg I.v.

Dosage is reduced by concomitant administration of an opioid or benzodiazepine.

In CVS, an induction doe of 0.3mg/kg results in almost no change in heart rate, MAP, Mean pulmonary artery pressure, pulmonary capillary wedge pressure, central cenous pressure, stroke volume, cardiac index and pulmonary and systemic vascular resistance.Produces 50% decreases in myocardial blood flow and oxygen consumption.Increases coronary sinus blood oxygen saturation by 20-30%.Myocardial supply demand ratio is well maintained.These effects are due to lack of effect on sympathetic nervous system and baroreceptor function.Haemodynamic stability could be due to in vivo alpha2B- receptor mediated increase in blood pressure.

Endocrine effects :There is dose dependent reversible inhibition of the enzyme 11 beta hydroxylase which converts 11 deoxycortisol to cortisol and a relatively minor effect on 17 alpha hydroxylase.This effect is due to free imidazole radical of Etomidate binding to cytoxhrome P 450 resulting in inhibition of ascorbic acid sysnthesis required for cortisol synthesis.Long term etomidate infusions produced adrenocortical suppression.

Due to the properties of haemodynamic stability, minimal respiratory depression, cerebral protection and rapid recovery profile, after either a single dose or a continuous infusion.,it is used for induction in patients with a compromised cardiovascular system like, patients undergoing CABG, PTCA, Aortic aneurysm repair and thoracic surgery.

MATERIALS AND METHODS

Thirty American Society of Anaesthesiologists Grade II and III patients undergoing elective Coronary Artery Bypass Surgery with the use of Cardiopulmonary Bypass were randomized to receive anaesthetic induction agent etomidate in Etomidate Group (0.2 mg /kg) or propofol in Propofol Group (2 mg/kg) .

INCLUSION CRITERIA

- Elective surgery patients of age between 18-60 yrs with Mallalmpatti scores I and II.
- Patients who have given written and informed consent.
- Patients posted for Coronary artery bypass graft surgery with normal Left Ventricular function.
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EXCLUSION CREITERIA

- Patients posted for emergency surgery
- Patients with LV dysfunction
- Preexisting arrhythmias
- Congestive cardiac failure.
- Mechanical ventilation
- On steroid therapy
- Preexisting Bleeding and coagulation abnormalities
- Renal dysfunction (creatinine >2 mg /dl)
- Patients with difficult airway
- Poor lung compliance such as pulmonary fibrosis
- Patients with any other comorbidities other than diabetes or hypertension.

After inserting the Arterial line and central venous line, cardiac output monitor was connected to the radial arterial cannula. This monitor measures cardiac output, cardiac index, stroke volume, stroke volume variation, stroke volume index by processing the digitalized arterial pressure waveform.By connecting the central venous pressure to the monitor, we get the values of Systemic vascular resistance and

systemic vascular resistance index(SVRI).

Statistical analysis was performed from the data obtained and a P value of < 0.05 was considered significant .

Period of study: 2012-2013.

RESULTS AND DISCUSSION

Baseline hemodynamic variables were comparable in both the groups.

Heart Rate : Reduces following induction in both groups and increases above baseline 1 minute after intubation.

Systolic Blood Pressure: There was no statistically significant difference between the two groups in the baseline systolic pressure.

There was a statistically significant decrease from the baseline,1,2,3minutes after induction in propofol group as compared to etomidate.

There was a statistically significant difference in systolic blood pressure 5 minutes after intubation with a much lower systolic BP in propofol group as compared to etomidate (Table – 1).

This was comparable with the study done by A.K. Pandey et al[1], Hassler et al[4] and Tulay Hosten[7].

Diastolic Blood Pressure: No statistically significant difference between the two groups in Diastolic BP.

Cardiac Index: There was a significant reduction in Cardiac Index from the baseline following induction with Propofol in the second and third minute. No statistically significant difference between the two groups 1 minute after intubation and 5 minutes after intubation.(Table – 2).
This was similar to the study done by Bendel[2] and colleagues where there was a reduction in the cardiac index following induction more with Propofol in patients undergoing surgery on aortic stenosis.

TABLE – 1
SYSTOLIC BLOOD PRESSURE

Systolic BP	Etomidate	Propofol	P value
Baseline(sbp 0)	123±12.25	130.60±8.59	0.59
1 min after induction(sbp1)	115.1±11.27	105.00±9.64	**0.013**
2 minutes after induction(sbp2)	111.9±10.34	98.80±9.65	**0.001**
3 minutes after induction(sbp3)	106.46±8.53	92.34±6.60	**0.00**
1 minute after intubation(sbp4)	128.46±8.24	125±7.31	**0.261**
5 minutesafter induction(sbp5)	117.47±9.45	104.74±11.67	**0.003**

Stroke Volume Index : There was no statistically significant difference in stroke volume index between the two groups following induction and intubation.

From the above data, Etomidate was found to be more hemodynamically stable as compared to Propofol.

TABLE – 2 CARDIAC INDEX

Caardiac index	Etomidate	Propofol	P value
Baseline(ci 0)	3.97±0.54	4.37±0.56	0.06
1 min after induction(ci1)	3.56±0.42	3.45±0.55	0.485
2 minutes after induction(ci2)	3.42±10.34	3.04±0.54	0.026
3 minutes after induction(ci3)	3.23±0.33	2.74±0.50	0.005
1 minute after intubation(ci4)	4.17±80.47	4.25±0.69	0.716
5 minutes after intubation(ci5)	3.60±0.36	3.42±0.76	0.420

Cortisol levels
Baseline cortisol levels between the two groups was comparable.

In Etomidate group serum cortisol levels reduce to almost half after initiation of cardiopulmonary bypass(p value< 0.05)

In Propofol group, serum cortisol levels almost double following initiation of cardiopulmonary bypass(p value < 0.05)

From the above data,it is observed that serum cortisol levels do reduce with etomidate but this is transient and the cortisol levels return to normal with in 24 hours.

In both the groups serum cortisol levels increase 24 hours later above baseline and much above normal limits. But the increase in Etomidate is less than that of Propofol(p value < 0.05).(Table – 3).

This transient reduction in cortisol levels during Cardiopulmonary bypass may be beneficial as it is a high stress state for the body. The above results correlate well with the study done by A.K.Pandey[1] et al. at AIIMS, New Delhi, and study done by Crozier[3] and colleagues.

TABLE – 3 SERUM CORTISOL LEVELS

Cortisol level	Etomidate	Propofol	P value
Baseline	14.33±2.30	15.60±2.46	0.158
After CPB	8.62±1.21	29.06±4.73	0.000
24 hrs later	27.05±5.95	37.08±3.6	0.000

CONCLUSION:

Induction with Etomidate provided more hemodynamic stability as compared to Propofol. Etomidate does cause a reduction in serum cortisol levels but it is transient and returns to normal within 2 hours. There is no inhibition of serum cortisol by propofol. Etomidate can therefore be safely used as an anaesthetic induction agent in patients with good LV function for CABG on CPB without serious cortisol suppression lasting more than twenty four hours.

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