

Hemodynamic Response and Dose Requirement during Induction and Intubation with Propofol and Pentothal Sodium in Patients Undergoing Elective Coronary Artery Bypass Surgery

Mangesh S. Gore¹, Lipika A. Baliarsingh², Deepika Teckchandani³

ABSTRACT

Introduction: The aim of the study was to observe haemodynamic changes during induction of patients undergoing CABG with Propofol and Pentothal. It was also intended to see if fixed dose combination of premedication with midazolam and fentanyl helps to reduce dose requirement of induction agents.

Material Methods: 60 ASA grade II patients posted for elective Coronary Artery Bypass Surgery (CABG) were divided into two groups. Group I (propofol group) and group II (pentothal Group). All patients received premedication as Inj. Midazolam 0.03 mg/kg and Inj. Fentanyl 4 µg/kg. With computer generated randomization patient was allotted to either propofol or Pentothal group. End point of induction taken as loss of eye-lash reflex or apnoea whichever appears first. Hemodynamic parameters were recorded from baseline till 7 minutes post intubation.

Results: In both the groups SBP, DPB, MAP, HR and RPP were found to be comparable. Both the drugs showed stable hemodynamic at various levels of observations. The mean dose required for induction was found to be 1.7 mg/kg with propofol and 1.07 mg/kg with Pentothal.

Conclusion: Both propofol and Pentothal are equally able to provide required stability even when standard doses of benzodiazepines and opioids are used in much lower doses than mentioned in literature.

Keywords: Hemodynamic Response, Induction, Intubation, Coronary Artery Bypass Surgery, Reduction in Doses of Induction Agents

but with obvious risk of myocardial insult in perioperative period.⁵ When midazolam is used for induction it shows lot of side effects in the form of fall in MAP, fall in Cardiac index and delayed recovery as the dose needs to be very high.¹⁰ Fentanyl in induction doses 4µg/kg onwards causes tight-chest syndrome, and needs some hypnotic agents along with.¹¹

Many of the centres and institutions are still using propofol and Pentothal sodium for induction as etomidate is either not available or due to cost constraints.

It has also been seen that use of these agents in conventional doses (pentothal 5 mg/kg & propofol 1.5 mg/kg) causes severe haemodynamic disturbances warranting use of vasopressors or inotropes around the time of induction in patients with left ventricular dysfunction.⁸ Use of adjuvants as premedication in the form of benzodiazepines and opioids help in reduction of total doses of induction agents and also help to manage stress response during laryngoscopy and intubation.¹¹

Therefore it is a common practice to use combination of opioids and benzodiazepines for either induction or as adjuvants with conventional induction agents.

Hence we designed a study to observe haemodynamic effects during induction with Pentothal or Propofol along with fixed dose combination of Midazolam and fentanyl given as premedication in CAD patients.

The basic/primary aim of the study was to observe haemodynamic changes during induction of patient undergoing CABG with different induction agents.

The secondary aim of our study was to determine whether combination of midazolam and fentanyl as premedication

INTRODUCTION

Haemodynamic stability and attenuation of stress response to laryngoscopy and intubation form the main objective while induction of patients with coronary artery disease (CAD).¹ Various induction agents like Pentothal sodium, propofol, etomidate etc. have been used with supplements like opioids and benzodiazepines. Various authors have expressed concerns with use of full dose of these induction agents as they lack required haemodynamic stability.²⁻⁹ Etomidate is the agent of choice by many for induction in cases with coronary insufficiency but this agent also has drawbacks like suppression of cortisol, reduction in cardiac index, transient coronary insufficiency and poor control of stress response.⁴ Pentothal when used in full dose of induction at 5mg/kg showed rise in heart rate, significant fall in MAP and fall in cardiac index.⁸ Ketamine when used for induction in CAD patients has showed stable haemodynamic

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help in reduction of doses of induction agents with favourable hemodynamics in CABG patients.

The outcome of the study was determined on the basis of requirement of total dose of induction agent, stability of hemodynamics with respect to Heart rate (HR), mean arterial pressure (MAP) and rate pressure product (RPP).

Study objectives were

- 1) To calculate total dose of induction agent used
- 2) To determine effectiveness of combination of midazolam and fentanyl given as premedication.

MATERIAL AND METHODS

Ethics committee approval for the study taken from institutional ethics committee.

After valid informed consent and confirmation of NBM status patients were taken inside operation theatre.

They are attached to Monitors which included ECG, NIBP, SPO₂.

All of them were cannulated with 16 G cannula in peripheral vein after applying topical local anesthetic to reduce pain and infusion of Ringers Lactate/Normal saline started.

Local anaesthetic was injected to facilitate right internal jugular vein cannulation. Similarly right femoral artery was cannulated under local anaesthesia.

Baseline blood pressure as systolic (SBP), diastolic (DBP) and MAP recorded along with heart rate (HR).

All patients were given inj. Ondansetron 4mg, inj. Dexamethasone 8 mg and inj. tranexamic acid 1000 mg as slow bolus from peripheral cannula.

Patients were randomised according to computer generated randomisation chart into 2 groups.

Group 1 inj. Pentothal

Group 2 inj. Propofol

All patients received inj. Midazolam 0.03 mg/kg & Inj. Fentanyl 4 µg/kg over 10 minutes.

According to which group they are randomised to, patients receive Inj. Pentothal or Inj. Propofol till Loss of eyelash reflex or apnoea.

After confirming bag mask ventilation inj. Rocuronium 1mg/kg is used in all patients to facilitate tracheal intubation. Bag mask ventilation was done for one minute before proceeding with intubation to achieve optimal conditions for intubation. Heart rate, systolic blood pressure, Diastolic blood pressure, mean arterial pressure were recorded at baseline (after femoral artery cannulation), after premedication, after induction, At intubation, 1 min after intubation and thereafter at 3mins, 5 mins and 7 mins post intubation.

Anaesthesia was continued with mechanical ventilation and maintenance of anaesthesia was at the discretion of attending anaesthesiologist.

Interventions were done at any stage during induction if Blood pressure rises or drops more than 20 % than baseline pressure in the form of addition of induction agent or inj. Phrenin in boluses of 10 µg respectively.

Inclusion Criteria

1. Age > 18 years
2. Proven Coronary Artery Disease (CAD) on angiography

3. Patients posted for elective Coronary Artery Bypass Graft (CABG) surgery

Exclusion Criteria

1. Patients with known history of allergy to egg lecithine
2. Religious objection towards having animal protein derivatives

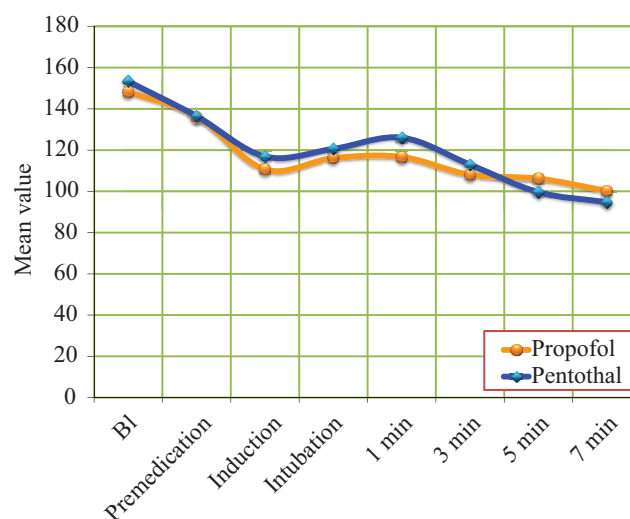
STATISTICAL ANALYSIS

After data entry – data analysis was done with the help of statistical software package (SPSS version 25) Using parametric and non-parametric test.

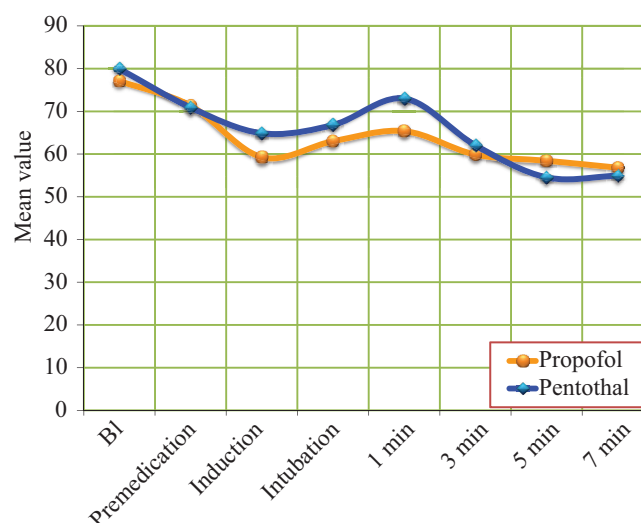
Quantitative data such as heart rate, blood pressure (both systolic & diastolic), Mean arterial pressure and Rate Pressure Product (RPP) was analyzed with help of mean, SD, median. Comparison among study group was done with the help of paired and unpaired t test. 'P' value < 0.05 taken as significant.

RESULTS

Both the groups had comparable baseline systolic blood



Graph-1: Graph showing Systolic Blood Pressure (SBP) at various intervals using Propofol and Pentothal



Graph-2: Diastolic Blood Pressure (DPB) at various intervals using propofol and pentothal

Study Parameter	Propofol		Pentothal		Unpaired T Test	P Value
	Mean	Std.Dev.	Mean	Std.Dev.		
BL SBP	148.30	21.52	153.30	23.86	-0.852	0.398
Premedication	136.37	19.79	136.43	21.91	-0.012	0.990
Induction	110.60	23.29	116.87	24.46	-1.016	0.314
Intubation	116.13	28.62	120.60	23.56	-0.660	0.512
1 Min	116.70	29.82	126.03	25.74	-1.298	0.200
3 Min	108.07	24.16	112.93	26.03	-0.751	0.456
5 Min	106.17	23.99	99.60	22.90	1.085	0.283
7 Min SBP	100.23	21.89	94.73	15.57	1.121	0.267

Table-1: Systolic Blood Pressure

Study Parameter	Propofol		Pentothal		Unpaired T Test	P Value
	Mean	Std.Dev.	Mean	Std.Dev.		
BL DBP	77.10	11.24	79.93	12.28	-0.932	0.355
Premedication	71.30	12.33	70.87	10.92	0.144	0.886
Induction	59.27	14.53	64.87	12.54	-1.598	0.115
Intubation	63.00	19.11	66.80	16.70	-0.820	0.416
1 Min	65.37	17.86	73.00	14.86	-1.799	0.077
3 Min	59.87	14.60	62.03	14.15	-0.584	0.562
5 Min	58.43	14.13	54.53	12.29	1.141	0.259
7 Min DBP	56.80	13.27	54.93	9.18	0.634	0.529

Table-2: Diastolic Blood Pressure

Study Parameter	Propofol		Pentothal		Unpaired T Test	P Value
	Mean	Std.Dev.	Mean	Std.Dev.		
BL MAP	100.83	13.26	104.39	14.68	-0.984	0.329
Premedication	92.99	13.18	92.72	13.46	0.078	0.938
Induction	76.38	16.22	82.20	15.36	-1.428	0.159
Intubation	80.71	21.62	84.73	18.45	-0.775	0.441
1 Min	82.48	21.12	90.68	16.30	-1.683	0.098
3 Min	75.93	17.33	79.00	17.53	-0.681	0.498
5 Min	74.34	16.24	69.56	15.19	1.180	0.243
7 Min MAP	71.28	15.65	68.20	10.80	0.887	0.379

Table-3: Mean Arterial Pressure

Study Parameter	Propofol		Pentothal		Unpaired T Test	P Value
	Mean	Std.Dev.	Mean	Std.Dev.		
BL HR	87.53	16.21	85.67	9.25	0.548	0.586
Premedication	84.10	13.38	83.10	10.78	0.319	0.751
Induction	80.60	12.74	81.40	11.57	-0.255	0.800
Intubation	87.10	16.17	90.07	13.29	-0.776	0.441
1 Min	91.57	12.77	91.27	12.72	0.091	0.928
3 Min	88.07	12.02	88.00	13.90	0.020	0.984
5 Min	85.57	12.79	85.33	12.34	0.072	0.943
7 Min HR	85.07	12.43	84.73	14.09	0.097	0.923

Table-4: Heart Rate

pressure to begin with. At induction the fall in systolic blood pressure was not significant in either of the groups. On comparison between two groups we found no significant difference at induction. From the time of intubation onwards there was no significant rise in SBP in either of the group and it never crossed the baseline value. From the time of intubation till 7 minutes systolic blood pressure remained stable in both the groups. The intergroup comparison also

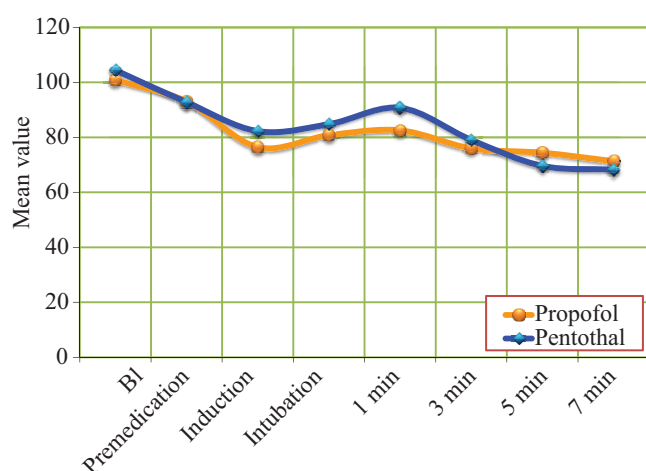
showed that both are comparable at all levels of observation, thus can be said that both drugs are stable and attenuate stress response when used in manner described in our study. Diastolic blood pressure is the pressure at which coronaries get perfused and therefore the most important component in myocardial perfusion. In patients with coronary artery disease due to mechanical obstruction certain part of myocardium gets devoid of this supply. In our study the baseline diastolic

Study Parameter	Propofol		Pentothal		Unpaired T Test	P Value
	Mean	Std.Dev.	Mean	Std.Dev.		
BL RPP	13012.43	3304.34	13128.63	2576.01	-0.152	0.880
Premedication	11896.80	2656.20	11315.00	2471.49	0.878	0.383
Induction	8932.03	2496.75	9513.13	2556.19	-0.891	0.377
Intubation	10267.90	3526.11	10912.50	3084.59	-0.754	0.454
1 Min	10697.53	3056.42	11531.63	2850.43	-1.093	0.279
3 Min	9522.20	2464.97	10009.27	3062.20	-0.679	0.500
5 Min	9046.27	2240.28	8488.50	2218.39	0.969	0.337
7 Min RPP	8533.23	2282.42	8032.77	1936.55	0.916	0.364

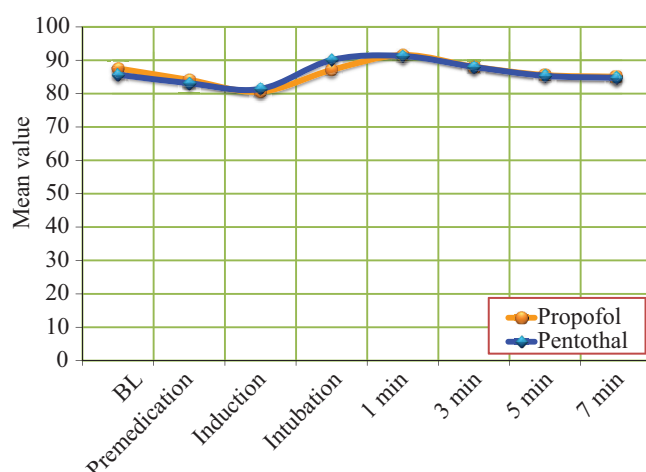
Table-5: Rate Pressure Product (RPP)

Study Parameter	Propofol		Pentothal		Unpaired T Test	P Value
	Mean	Std.Dev.	Mean	Std.Dev.		
DOSE	66.67	22.02	107.90	44.12	-4.580	0.000
Mg/Kg	1.07	0.38	1.71	0.67	-4.509	0.000

Table-6: Dose Requirement



Graph-3: Mean Arterial Pressure (MAP) at various intervals using propofol and pentothal



Graph-4: Heart Rate (HR) at various intervals using propofol and pentothal

pressure was comparable in both groups. The change in DBP occurred in both groups and it lowered till induction. At the time of intubation there was no rise in values in either of the groups. Diastolic blood pressure never went up more than baseline values in either of the groups suggesting that both

propofol and Pentothal are able to attenuate stress response. The values remained stable till last point of observation i.e. 7 minutes post intubation.

The values of both systolic and diastolic blood pressure were higher in Pentothal group at all points of observation. Here incidentally the values in pentothal group were higher even at baseline levels and thus carry little significance at the time of comparison.

Mean arterial Pressure (MAP) is the perfusion pressure for tissues. In patients with coronary artery disease, rise in MAP leads to more systemic vascular resistance and thus can cause more strain on left ventricle. During induction and intubation every attempt is made to control MAP as this is one of the surrogate marker for left ventricular strain.

In our study mean value of MAP was comparable amongst two groups. MAP decreased gradually from baseline till induction. Values of MAP never increased more than baseline in any of the group at intubation and there was no stress response. Amongst the two groups propofol attenuated stress response to intubation more as compared to pentothal. MAP remained below baseline till 7 minutes post intubation but never became too low to warrant any intervention.

Heart rate is one of the important factor next to systolic blood pressure which helps us to determine myocardial work, myocardial oxygen consumption. Every effort is made to keep HR as low as possible which in turn helps to keep myocardial work and myocardial oxygen consumption low. In our study HR in both the groups was comparable at baseline. It remained stable till induction in both groups. Rise in heart rate was seen at the time of intubation, but was not statistically significant. Heart rate reached the baseline at 5 minutes post intubation in both the groups. In individual groups also HR was seen to be stable and never raised to a level of statistical significance from baseline.

In the context to find out stress on myocardium we take heart rate and systolic blood pressure into consideration. The product of these two is RPP. Every effort is made to keep RPP less than 14000 to minimise load on left ventricle.

In both the groups the baseline RPP was comparable and

was on higher side to begin with. This can be attributed to anxiety causing higher HR and underlying hypertension as a component of disease process. On premedication and RPP lowered well from baseline in both the groups. There was a small rise in RPP during induction and intubation seen but never went more than baseline in either of the groups. BY 7 minutes post intubation RPP settled well in comfortable range in both the groups.

The rise of RPP during induction was seen more in Pentothal group may be due to inherent property of Pentothal to cause tachycardia. This was seen in observation of HR as there was rise in HR in pentothal group during induction.

However by 7 minutes post intubation RPP settled well in both groups suggesting cardiostability and hemodynamic stability.

The mean dose required for propofol was 1.07 mg/kg which is lower than conventional dose of 2 mg/kg to 2.5 mg/kg.

The mean dose of Pentothal was also lower at 1.71 mg/kg than conventional dose of 5 mg/kg.

The premedication used in both the groups was same and fentanyl was used at 4 µg/kg which was also lower dose than many of the studies used to attenuate response to laryngoscopy and intubation.

DISCUSSION

During induction of anaesthesia in patients with compromised left ventricular function it is commonly observed that if we use conventional full doses of induction agents viz. thiopentone 5 mg/kg, propofol 2 mg/kg, we have significant hemodynamic instability most commonly seen as hypotension. Reiz et al did a study where they used thiopentone sodium in a dose of 6 mg/kg in patients with coronary artery disease and found significant fall in MAP and Cardiac Index hampering myocardial perfusion.⁸ The use of these doses in patients posted to undergo coronary artery bypass surgery can be catastrophic. Masoud Lahsae, et al. suggested use of low dose of thiopentone or propofol for induction of anesthesia. They further suggested combination of these induction agents will cause significant reduction in dose of each drug and will be very useful in patients with heart disease. When combination of induction agent was used the dose of Pentothal was reduced to 2.5 mg/kg and that for propofol 1.5 mg/kg. They observed that fall of blood pressure was highest with use of propofol (2.5 mg/kg) as compared to Pentothal (5 mg/Kg) and combination of these two drugs.¹²

In our study we used inj. pentothal Sodium and inj. Propofol in doses just sufficient to achieve our end point of induction i.e. Loss of eye-lash reflex or apnoea whichever is achieved early. When we analysed the requirement of doses we found that mean dose of 1.07 mg/kg of propofol was sufficient to achieve end point of induction. There was 1.71 mg/kg of mean dose of Pentothal required to achieve end point of induction. Thus with very low doses of induction agents can be used in induction of patients with coronary artery disease. In our study we used 1.07 mg/kg of propofol as a mean dose and pentothal as 1.17mg/kg. These doses were much lower than what was used by the authors as separate agents and as

combination (1.5 and 2.5 mg/kg respectively).¹²

These doses of propofol and Pentothal were very less than the conventional doses used otherwise. Also stable haemodynamic can be achieved after induction with these doses when used along with fixed dose combination of midazolam and fentanyl.

Raveen singh et al studied hemodynamic changes using etomidate (0.2 mg/kg), propofol (1.5 mg/kg), midazolam (0.15 mg/kg) and thiopental (5 mg/kg) in patients with coronary artery disease and reduced left ventricular function. Fentanyl 4 µg/kg was used in all groups as premedication. They found most stable hemodynamics with midazolam and least stable with etomidate. The most important observation made by them is reduction in cardiac index upto 40% with all agents.¹⁴ Schullte-sasse et al studied hemodynamic stability and attenuation of stress response in patients with coronary artery disease when they used midazolam in dose of 0.2 mg/kg and fentanyl 7.5 µg/kg. They found this regimen useful and capable of giving stable hemodynamics. They have not used any induction agent. The use of fentanyl is also at higher doses as compared to the dose used by us.¹⁰

In our study we used fixed dose combination of midazolam 0.03 mg/kg with fentanyl 4 µg/kg in all the patients. With above observations in mind we can say that even when low dose of opioid like fentanyl (4 µg/kg) is used along with easily available induction agents effective haemodynamic and cardiostability can be achieved while induction of patients with coronary artery disease.

When we compared systolic blood pressure, both the groups had comparable baseline systolic blood pressure to begin with. At induction the fall in systolic blood pressure was not significant in either of the groups. On comparison between two groups we found no significant difference at induction. From the time of intubation onwards there was no significant rise in SBP in either of the group and it never crossed the baseline value. From the time of intubation till 7 minutes systolic blood pressure remained stable in both the groups. The intergroup comparison also showed that both are comparable at all levels of observation. It is further observed that individual drug also did not show any rise or fall of more than 20% from baseline at any point of observation. Thus can be said that both drugs are stable and attenuate stress response when used in manner described in our study.

We compared Diastolic blood pressure at various levels of observations, we did not find statistically significant difference amongst Pentothal and propofol groups both as individual drug and in intergroup comparison.

As evident from above systolic and diastolic blood pressure at various levels of observation compared between two groups were comparable and statistically not significant, the mean arterial pressure also was comparable. This shows that both Pentothal and propofol are equally cardiostable. They are thus can be said to be haemodynamically stable as well. Rate Pressure Product (RPP) is considered as surrogate marker of myocardial stress and oxygen consumption. The optimum range is said to be between 10000 to 14000, which gives minimal myocardial stress and myocardial oxygen

consumption.³ Gobel et al confirmed in a study that Rate Pressure Product(RPP) is an index which correlates best in determining MVO₂ in patients with coronary artery disease.¹³ We compared RPP and found that it was comparable between two groups. Thus it can be said that both drugs are equally comparable in providing cardiostability while patients of Coronary artery disease undergo the process of induction and intubation. Both propofol and pentothal were equally able to provide required stability even when standard doses of benzodiazepines and opioids were used.

We performed this study without any of the modern monitoring facilities eg. Cardiac Output, Stroke volume (SV), Stroke volume Variation (SVV), Stroke Volume Index (SVI), SVRI etc. Therefore, the data obtained may be very primitive and not upto the international standards. But we believe that there are many institutions not only in India but around the world which are working with conditions similar to ours. Such institutions are doing surgeries on patients with cardiac diseases and CABG would be one of them. With such working scenarios in mind if we analyse our study it will be understood that we need to move away from fixed conventional ideas to induce patients with designated doses. If advanced monitoring facilities are not available one can still perform safe induction with freely available induction agents like pentothal sodium and propofol with just invasive blood pressure monitoring. The data available from invasive monitoring of blood pressure and derivation of rate pressure product may help us to be within safe margins so as not to have adverse haemodynamic responses while induction. This is of importance in those patients who are having very poor left ventricular function.

CONCLUSION

Lower doses of commonly available induction agents when combined with premedication of benzodiazepines and opioids, with slow and watchful induction can give safe induction in patients with coronary artery disease even without advanced monitoring equipments.

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