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A COMPARATIVE STUDY OF HEMODYNAMICS AND CARDIOPROTECTIVE EFFECTS OF SEVOFLURANE & ISOFLURANE IN PATIENTS UNDERGOING OFF PUMP CORONARY ARTERY BYPASS GRAFTING

Anaesthesiology

Dr Sushila Meena Third year P.G. student, Department of Anaesthesia, S.M.S Medical College, Jaipur.
Dr Indu Verma Professor, Department of Anaesthesia, S.M.S Medical College, Jaipur
Dr C.K Vyas Professor, Department of Anaesthesia, S.M.S Medical College, Jaipur
Dr Reema Meena Professor & Head, Department of Anaesthesia, S.M.S Medical College, Jaipur

ABSTRACT

Background: Off pump coronary artery bypass grafting (CABG) avoids the post-operative complications which are related to on pump CABG. But off pump CABG is also associated with hemodynamic instability. Sevoflurane and Isoflurane in addition to Fentanyl & neuromuscular blocking agents are considered safe during off pump CABG. They have been reported to exert myocardial protective effects by decreasing the concentration of cardiac enyzymes & improving the heart functions.

Methods: Fifty patients with Left ventricular EF>40% were given sevoflurane (gp A n=25) or isoflurane (gp B n=25) after induction with etomidate, fenanyl, midazolam & rocuronium in patients undergoing off pump CABG. Hemodynamics were assessed with Edwards Flo Trac continuous cardiac output monitor. Statistical analysis was done by using student t test and paired t test. A p value of less than 0.05 was considered statistically significant and p value > 0.05 was not significant.

Results: Both agents showed favourable intra-operative hemodynamics. There was a tendency to decrease in B.P & H.R with each volatile agent but comparatively hemodynamics were more stable in the sevoflurane group. However these findings were not statistically significant. Time taken for eye opening & verbal command was significantly earlier in sevoflurane group (3.37 ± 0.95 hr) as compared to isoflurane group (3.99 ± 0.98 hr) with a p value =0.027. Extubation was also earlier in the sevoflurane group (7.54 ±1.58 hr) as compared to isoflurane group (8.56±1.99 hr) with a p value =0.049.

Conclusion: Sevoflurane provided a better hemodynamic profile in terms of Heart rate, Blood pressure, cardiac index and enzymes levels even though the difference was not found to be statistically significant. Also sevoflurane provided early awakening & extubation which was statistically significant as compared to isoflurane.

KEYWORDS:

Off pump CABG, hemodynamics, myocardial protection, sevoflurane, isoflurane, cardiac enzymes.

INTRODUCTION

With the increasing incidence of coronary artery disease (CAD) there is increasing rate of coronary artery bypass surgery (CABG) be it off pump or on pump. In the developing countries there is still a trend of off pump CABG because of cost factor which matters a lot here. The anaesthetist always desires to choose an agent which causes rapid induction and emergence and with minimal side effects so as to reduce the peri-operative morbidity & mortality.

Inhalational volatile agents have been proven by many studies to have exert a cardioprotective and hemodynamic stability effect.[1-4] Isoflurane & sevoflurane have been successfully being used for the pre-conditioning effects in cardiac surgery.[4] Protein kinase, Adenosine triphosphate (ATP), sensitive potassium channels & Adenosine A1 receptors play a role in the mechanism of action of volatile agents. Isoflurane produces a coronary steal phenomena, while sevoflurane increases flow in large and small coronary vessels via mechanism which are not dependent on ATP- sensitive potassium (K ATP) channels.[5]

In off-pump CABG the anaesthetist is always making a balance between the anaesthetic technique used for hemodynamic stability and myocardial protection. There are lot of studies which have used Fentanyl and Morphine for their proven myocardial protection effects, so we have also used Fentanyl in both the groups of our study for a balanced anaesthesia sequence.

This study aimed to compare the CPK-MB, Troponin levels and the hemodynamic stability by using sevoflurane and Isoflurane for maintenance of anaesthesia after induction with Fentanyl, midazolam, & etomidate combination in patients undergoing off pump coronary artery bypass surgery. Fentanyl was chosen because of its minimal side effects.

METHODS AND MATERIAL

This study was conducted in the department of anaesthesia, of our medical college with due permission from the institutional ethical committee.

Study design:

Hospital based randomized, comparative, interventional study.

Sample size:

The sample size was calculated to be 7 subjects for each of the two groups at an alpha error of 0.05 and power of 80% assuming difference in mean to be detected 53 with standard deviation 0f 36, so for study purposes, sample size 25 was taken for each group.

Sampling Technique:

Patients between the age group 40-70 yrs with body weight of 30-65 kg of either sex with an ejection fraction of >40% of either sex willing to give written informed consent undergoing off pump CABG under general anaesthesia were included.

The exclusion criteria included patients having compromised renal status, pulmonary status (e.g. COPD, bronchial asthma).Patients having anemia (Hb<10 gm%), patients having difficult intubation (Mallampati grade 3&4), & more than three attempts at intubation. Patients hypersensitive to any of the drugs used in the study, having blood coagulation disorder, Diabetes Mellitus, obesity, LVEF< 40% were also excluded.

After screening the proforma and pre-anaesthetic check-up,written informed consent was taken from all the patients. Randomization was done by chit and box method and they were divided into two groups. Group A n=25 Sevoflurane (1MAC) and Group B n=25 Isoflurane (1 MAC).

Patients were kept nil by mouth from mid night pre-operatively. Peripheral cannula of 18 gauge was inserted into right antecubital vein. All patients were started with ringer lactate in the peripheral line.

Five lead ECG, BIS electrode and pulse oximeter were attached and central venous catheter was inserted into right internal jugular vein. Arterial cannulation was done in either of the femoral artery. Femoral artery was chosen so as to avoid the dampning effects usually seen in the radial artery after a certain period of time. All cannulations were done under local anaesthesia.

Baseline data in the form of heart rate, mean arterial pressure, central

venous pressure, cardiac index were recorded.

Patients were pre- oxygenated with 100% oxygen. Induction was done with midazolam 0.05 mg/kg, fentanyl 4 microgram /kg, etomidate 0.3 mg/kg and rocuronium 0.9 mg/kg was given to facilitate tracheal intubation.

After confirming the position of endotracheal tube and fixing it anaesthesia was maintained either by sevoflurane or isoflurane depending on the group in which patient was allocated. Further top up with bolus 2 microgram fentanyl with vecuronium 2mg/hr until the completion of surgery was done. BIS was maintained in between 40-60.

The primary outcome was to see the haemodynamic variation between both the groups in off pump CABG so as to see the myocardium protection throughout the surgery so as to see which inhalational agent was superior. Secondary outcome was to see the Troponin and CPK –MB enzyme levels post operatively after 9 hrs.

Haemodynamic parameter like heart rate(H.R), mean arterial pressure (MAP), central venous pressure (CVP), cardiac index (C.I.) were noted at baseline, post induction, post coronary anastomosis, and before shifting patient to ICU. After completing surgery patient were shifted to ICU. Then the time of awakening and extubation of patient was noted. The levels of CPK –MB & Troponin were measured.

STATISTICALANALYSIS

Statistical analysis was done by using student t test and paired t test. A p value of less than 0.05 was considered statistically significant and p value > 0.05 was not significant.

RESULTS

Demographic parameters are presented in table 1. There was no significant difference between the two groups in terms of age, sex, weight, height and LVEF.

Effect on **Heart rate:** There was slight increase in heart rate in the isoflurane group as compared to sevoflurane group after anastomosis 96.72±11.44 beats/min and 91.92±7.79 beats/min and before shifting to ICU 92±11.85 beats/min and 90.57±11.16 beats/min. These were statistically not significant.

There was a more fall in the **mean arterial pressure** in the isoflurane group (group B) as compared to sevoflurane group (group A) before shifting the patient to ICU and this effect was statistically not significant.

Cardiac index was increased more in the sevoflurane group as compared to isoflurane group, but this was also statistically insignificant.4.04±1.00 l/min/m2 and 3.78±0.65 l/min/m2 respectively from the baseline.

There was a decrease in **CVP** in group B (isoflurane) as compared with group A (sevoflurane).Group B required an additional dose of fentanyl as compared to group A.

Group A (sevoflurane) showed a lesser increase in **CPK-MB** as compared to group B at 9 hrs post operatively 63.40±35.77 & 74.40±23.13 which was statistically insignificant. The Troponin levels were also decreased in group A than group B at 9hrs post operatively.
Lastly **eye opening** was earlier in group A then group B 3.37±0.95 hrs and 3.99±0.98 hrs post operatively which was statistically significant and showing **earlier extubation** in group A than group B.

DISCUSSION

The present study aimed to compare sevoflurane and isoflurane on haemodynamic parameters & cardioprotective effects in patients undergoing coronary artery bypass graft surgery.

The baseline demographic variables were comparable in both the groups.

Haemodynamic parameters

Haemodynamic stability is very important for patients undergoing off pump CABG. Measuring vitals like heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), cardiac index (CI) at various intervals revealed that they were comparable (statistically insignificant, p value > 0.05) in both the groups. There was a tendency to decrease the B.P &C.O with each volatile agent. But comparatively hemodynamics were more stable in the sevoflurane group. However these findings were statistically not significant.

We used Fentanyl during the induction period as Fentanyl has been used in many studies showing its cardioprotective effect by alleviating post ischemic effects in rat models and limited the infarct area as shown by Kato et al.[6-8]

Sevoflurane has been shown to provide stable cardiovascular conditions and a better heart rate profile in volunteers & in patients undergoing elective surgery compared to other volatile anaesthetics (Ebert TJ et al)[9]. In our study, both agents showed a similar favourable intra-operative hemodynamics. But sevoflurane provided a better myocardial protection and a stable hemodynamic status to the patients. This is supported by a study by Haroun-Bizri S and et al showing that volatile anaesthetic agents are more effective than opioids in protecting the myocardium[10].

In another study by Bennet SR et al[5] both sevoflurane & isoflurane showed similar hemodynamic effects at 0.5 & 1.0 MAC, but sevoflurane showed a tendency to have lower HR & CI compared to isoflurane. This effect i.e. mild myocardial depression maybe desirable during OPCABG, as myocardial oxygen consumption will be decreased in a beating ischaemic heart. In our study sevoflurane group showed a tendency for better preservation of cardiac index as compared to isoflurane group. However values were not statistically significant.

CI increased in sevoflurane group after anastomosis and before shifting to the ICU was not statistically significant. Other studies also showed an increase in CO &CI which also showed an anaesthetic preconditioning & ischemic preconditioning.[10-12]

Conzen et al[13] have shown that patients receiving sevoflurane for OPCABG had less myocardial injury during the first 24 hrs post op period than patients receiving propofol. Isoflurane & sevoflurane inhibit the increase the of LPO (lipid peroxides) levels to attenuate myocardial ischemia /reperfusion injuries mediated by oxygen free radicals during open heart surgeries, The use of sevoflurane in AVR surgery was associated with better preservation of myocardial function and reduced post op release of Troponin I release.[5]

In a study sevoflurane preconditioning significantly decreased postoperative release of NT-pro BNP, a highly sensitive biochemical marker of the myocardial injury in patients undergoing CABG on CPB. This study also showed the concept of PKC translocation as an important step for preconditioning elicited by sevoflurane in the human myocardium[14].

In our study, time for awakening & extubation was significantly shorter in sevoflurane group than isoflurane group, possibly because of low solubility of sevoflurane which facilitates rapid elimination via the lungs. Rate of elimination is faster as compared with isoflurane. Bennet SR et al found that sevoflurane allowed early eye opening & extubation as compared to isoflurane.[5]

The objective of early extubation was achieved using a propofol based technique in a study by Cheng et al[15] and later a combination of isoflurane & fentanyl was successfully used to achieve the same goal by Engoren MC et al[16]. However use of isoflurane maybe associated with tachycardia, which can increase the myocardial oxygen demand & can be detrimental to ischemia patients undergoing cardiac surgery. This was not observed in our study. On the other hand sevoflurane does not have these characteristics, it appears to be less potent coronary vasodilator than isoflurane & is not associated with coronary steal, Eber et al[9]. Probably because we maintained adequate analgesia in both groups & used both inhalational agents only at 1 MAC which was well within the therapeutic range.

CONCLUSION

In conclusion sevoflurane and isoflurane can safely be used for off pump CABG without compromising safety. Sevoflurane provided a better hemodynamic profile in terms of heart rate, BP, CI, and enzyme levels even though the difference was not found to be significant. However sevoflurane provides significantly early awakening and extubation as compared with Isoflurane. Thus sevoflurane though

costly along with opioids may be preferred in patients undergoing off pump coronary artery bypass graft heart surgery.

Table 1 : Demographic Data

	GROUP A SEVOFLURANE N=25	GROUP B ISOFLURANE N=25	P VALUE
Age (years)	61.40±6.46	58.84±8.18	0.225
Sex	21/4	20/5	0.719
Weight (Kg)	64.36±8.30	61.60±13.58	0.390
Height (cms)	170.92±7.88	169.80±8.07	0.621
LVEF%	50.68±6.43	50±6.66	0.714

Table 2 : Haemodynamic data in the two groups

	GROUP A SEVOFLURANE N=25	GROUP B ISOFLURANE N=25	P VALUE
HR (Beat/min)			
Basal	85.88±15.57	87.92±13.50	0.622
Post induction	86.08±9.87	84.20±14.26	0.590
Post anastomosis	91.92±7.79	96.72±11.44	0.089
Before transfer to icu	90.52±11.16	92±11.85	0.651
MAP (mm Hg)			
Basal	89.68±16.59	91.24±17.43	0.747
Post induction	85.20±14.57	86.12±11.52	0.805
Post anastomosis	75.08±7.12	73.04±8.29	0.355
Before transfer to icu	77.52±9.32	73.16±7.73	0.078
CVP (mmHg)			
Basal	10.36±4.06	8.48±4.42	0.123
Post induction	10.68±4.31	8.48±3.82	0.062
Post anastomosis	9.12±3.35	8.84±3.08	0.759
Before transfer to icu	8.56±2.86	8.88±3.14	0.708
CI (L/min/m2)			
Basal	3.00±0.95	3.40±0.76	0.109
Post induction	3.06±1.07	3.16±0.87	0.717
Post anastomosis	3.70±1.06	3.65±0.79	0.833
Before transfer to icu	4.04±1.00	3.78±0.65	0.279

Table No 3 : Comparison of requirement of additional dose of Fentanyl between the two groups

	GROUP A SEVOFLURANE	GROUP B ISOFLURANE	P value
Mean ± SD	0.03±0.01	0.04±0.01	0.019

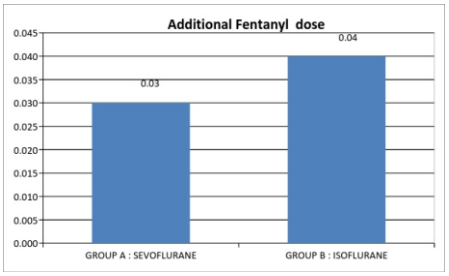
Table No 4 : Comparison of myocardial protection Level of CPKMB

	GROUP A SEVOFLURANE	GROUP B ISOFLURANE	P value
Baseline	36.04±18.37	39.79±16.51	0.451
9hr post op	63.40±35.77	74.40±23.13	0.202

Table No. 5 : Level of Troponin-T

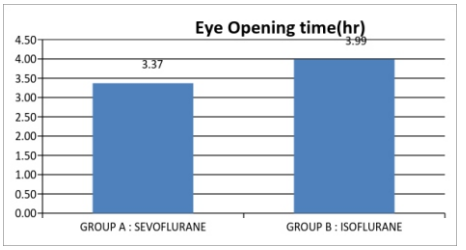
	GROUP A SEVOFLURANE	GROUP B ISOFLURANE	P value
Baseline(-/+)	23/2	22/3	0.645
9hr post op (-/+)	19/6	20/5	0.739

Chart No 1. : Requirement of Additional dose of Fentanyl



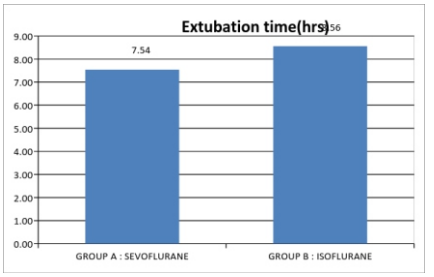
The graph shows additional fentanyl dose requirement in the isoflurane group as compared the sevoflurane group.

Chart No 2. : Comparison of recovery characteristics



The graph shows Sevoflurane shows early eye opening as compared to isoflurane.

Chart No 3. : Extubation time (Hrs.)



This graph shows early extubation in the Sevoflurane group as compared to Isoflurane group.

REFERENCES:

1) De Hert SG, Turani F, Mathur S, et al : Cardioprotection with volatile anaesthetics : Mechanism & clinical implications. Anesth Analg 100: 1584- 1593, 2005
2) Chiari P, Bouvet F, : Anaesthetic – induced myocardial pre-conditioning: Fundamental basis and clinical implications. Ann Fr Anaesth Reanim 241:383 – 396.2005
3) De Hert SG: Volatile anaesthetics and cardiac function. Semin. cardiothoracic vasc. Anaesth 10:33 -42, 2006.
4) De Hert SG : The concept of anaesthetic induced cardioprotection :Clinical relevance. Best Pract Res clin Anaesthesiol 19:445-459, 2005.
5) Bennet SR, GoiffinsC. Sevoflurane versus Isoflurane in patients undergoing valvular cardiac surgery. J Cardiothoracic vasc Anesth 2001;15:175-178.
6) Kato R, Ross R, Foex P. Fentanyl protects the heart against ishemic injury via op Ioid receptors, adenosine A1 receptors and K ATP channel linked mechanism in rats. BJA 2000:84; 204-14
7) Kato R, Foex P. Myocardial protection by anaesthetics agents against ischemic reperfusion injury : an update for anaesthesiologist Cann J Anaesth 2002:49 777-91
8) Kato R, Foex P. Fentanyl reduces infarction but not stunning vi Delta-opiod receptors and protein kinase c in rats. BJA 2000:84:608-14
9) Ebert TJ. Harkin CP, Muzi M. Cardiovascular response to sevoflurane; A review. Anesth Analg 1995; 81: 5 11-22
10) Haroun-Bizer S, Khoury SS, Chehab JR, Kassas CM, Baraka A. Does Isoflurane optimize myocardial protection during cardiopulmonary bypass. J Cardiothoracic vasc Anesth 2001;15:418-21
11) De Hert SG, Cromheecke S, Ten Broecke PW, Mertens E, De Blier IG, Stockman BA, et al. Effects of propofol, desflurane, & sevoflurane on recovery of myocardial function after coronary surgery in elderly high risk patients. Anesthesiology 2003;99:314-23
12) De Hert SG, Ten Broecke PW, Mertens E, Van Sommeren EW, De Blier IG, Stockman BA, et al. Sevoflurane but not propofol preserves myocardial function in coronary surgery patient. Anesthesiology 2002;97:42-9
13) Conzen PF, Fischer S, Delter C, Peter K . Sevoflurane provides greater protection of the myocardium than propofol in patients undergoing off pump coronary artery bypass surgery. Anesthesiology 2003;99:826-33
14) Julier K, da Silva R, Garcia C, Bestman, Frascarolo P, Zollinger A, et al. dysfunction in CAB Gdouble blinded, placebo, controlled, multicenter study. Anesthesiology 2003, 98: 1315-27.
15) Cheng DC, Kaiski J, Peniston C et al. Early tracheal extubation after coronary artery bypass graft surgery reduces costs & improves resource use. A prospective randomized controllrd trial. Anesthesiology 1996;85:1300-1310
16) Engoren MH, Hofmeister J, Behl R. Sevoflurane supplementation of three induction doses of fentanyl for anaesthesia of adult patients undergoing cardiac surgery. J Anesth 2003;19:109-114.
17) Symons J A, Myles PS: Myocardial protection with volatile anaesthetic agents during coronary bypass surgery: A meta analysis. BJA 97: 127-136, 2006.
18) Myles PS, Symons JA: Myocardial preconditioning with volatile anaesthetic agents during coronary artery bypass surgery: A metaanalysis. Anaesthesiology 103:A328, 2005 (abstr).
19) Aysegul Ozgok, Senem Kornuk, Dilek nazanci, Gulsevin saydam,: A comparison of total intravenous anaesthesia, sevoflurane and isoflurane anaesthesia for preconditioning in cardiac surgery. T uek Goguskalp Dama 2012: 20 (2) :200-208.
20) Kerston JR, Schmeling T, Tessmer J, Hettrick DA, Pagel PS, Warltier DC, sevoflurane selectively increases coronary collateral blood flow independent of K ATP channels in vivo. Anaesthesiology 1999;90:246-56.