

Research Article

Comparative Study of Sevoflurane Versus Desflurane on Hemodynamics in Off Pump Coronary Artery Bypass Grafting

Indu Verma^{1*}, Chandan Verma², Ramnaresh Sharma³, Sandeep Dhaked³

Professor, Department of Anaesthesia, SMS Medical college, Jaipur, India Associate Professor, Department of Pharmacology, SMS Medical college, Jaipur, India Resident, Department of Anesthesiology, SMS Medical college, Jaipur, India

*Corresponding Author: Indu Verma, Professor, Department of Anaesthesia, SMS Medical college, Jaipur, India, E-mail: <u>dr. induverma@gmail.com</u>

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Abstract

Background: Volatile anesthetics like sevoflurane and desflurane have been used in various cardiac surgeries with a purpose of myocardial protection, renal protection, and early extubation. Maintaining hemodynamics during off pump coronary artery bypass grafting (OPCABG) is challenging for cardiac anesthesiologists. We compared desflurane and sevoflurane in patients undergoing OPCABG.

Methods: A sample size of 148 patients were randomly allocated into two groups after permission

from the institutional ethical committee and review board with written and informed consent from each patient. Patients with ASA grade 3 and 4 between the age group 30-60 yrs of either sex, having ejection fraction (EF) >40% undergoing coronary artery bypass grafting under general anesthesia were included in the study. Patients with anticipated difficult intubation, compromised renal and pulmonary function, hypersensitive to drugs used in the study, with altered coagulation profile, diabetes mellitus, obesity, left ventricular ejection fraction <40%, with severe cardiac arrhythmias were excluded from the study.

Results: The primary outcomes included the heart rate, mean arterial pressure, cardiac output, cardiac index, and systemic vascular resistance from baseline 15, 30, 45 and 60 minutes after intubation and 1 hour after surgery. The secondary outcomes included CPK-MB, blood urea, and serum Creatinine and any other side effect 24 hrs postoperatively. There was an increase in the heart rate just after induction and 15 minutes post intubation in the sevoflurane group as compared to the desflurane group with a p value of 0.0001 and 0, 0006 which is statistically significant. There was a statistically significant decrease in the mean arterial blood pressure in the desflurane group with a p value of 0.0001 and 0.001. Cardiac output increased in the desflurane group 30, 45 and 60 minutes after intubation with a p value of 0.04, 0.008 and 0.006 which was statistically significant. Systemic vascular resistance also decreased in the desflurane group with a p value of 0.019 and 0.011. But sevoflurane showed decreased CPK-MB levels 46.61 ± 21.90 S.D as compared to 50.49 ± 26.29 S.D in the desflurane after 24 hrs postoperstively which was not statistically significant . Blood urea and serum Creatinine were also elevated in the desflurane group.

Conclusion: During the crucial period of off pump coronary artery bypass grafting the maintenance of hemodynamic stability was better seen with desflurane as compared to sevoflurane and is suggested to be used for better outcome of patients.

Keywords: Humans Anesthetics; Desflurane; Sevoflurane; Heart Rate; Stroke Volume; Coronary Artery Bypass; Off-Pump; Vascular Resistance

1. Introduction

The administration of volatile inhalational agents during off pump CABG before any event of myocardial ischemia during the coronary graft anastomosis have shown a similar cardio-protection observed after ischemic pre-conditioning [1]. Volatile anaesthetics decrease the effects of ischemia on contractility and decrease the myocardial infarct size that is affected during ischemia [2, 3]. The mechanism of action of volatile anaesthetics is by their effects by opening the mitochondrial K ATP channels [4, 5].

Use of volatile anaesthetic agents in cardiac surgeries are associated with reduced mortality post-operatively as compared to Total intravenous anaesthesia (TIVA)[6]. Volatile anaesthetics cause coronary vasodilatation, by phosphorylation and translocation of cellular proteins, stimulate protective enzymes (early phase of pre-conditioning) and also delayed phase of pre-conditioning [7]. They cause broncho-dilatation which is useful in patients having chronic obstructive lung disease [8]. The anti-inflammatory effects are not only restricted to lungs or heart but affect other organs like brain [9, 10], kidneys [11, 12] and liver [13]. Studies have demonstrated a reduction in acute kidney injury and renal failure after cardiac surgery under general anaesthesia using volatile anaesthetic agents as compared to TIVA[14].

Inhalational agents have been used in cardiac surgeries for preconditioning, myocardial preservation and early extubation or fast track extubation as shown in previous studies. They often take the advantage of precise control over the depth of anaesthesia with rapid recovery but there are very few studies which show a comparison of hemodynamics of both these agents

during off pump coronary artery bypass grafting which is very crucial during the anastomosis of various grafts in various positions of the heart.

Desflurane is an inhalational general anaesthetic agent which is clear non inflammable with a pungent odor and having a relatively low boiling point (23.5°C) making it extremely volatile. Desflurane has a low blood/ gas solubility of 0.42 as compared to sevofluane 0.67. Because of low blood/gas solubility the anaesthetic alveolar concentration remains near the inspired concentration permitting a rapid anaesthetic depth and early awakening. It can irritate the airway and can cause caughing, breath holding, and laryngospasm which do not occur at 1 MAC. The main objective of this randomised control trial was to compare the effects of sevoflurane and desflurane in terms of their hemodynamic variables, myocardial protection and renal protection on a specific group of patients undergoing off pump coronary artery bypass grafting. Here the control group was of the patients receiving sevoflurane as it was used as a standard inhalational agent in our protocol for patients undergoing CABG whether on pump or off pump. Since desflurane is the latest of the two anaesthetics we hypothesized that desflurane would be better than sevoflurane on the primary and secondary outcomes. The primary outcomes included hemodynamic parameters in terms of heart rate(HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure(MAP), cardiac output(CO), cardiac index(CI), and systemic vascular resistance(SVR). The secondary outcomes included blood urea, serum creatinine, creatine phosphokinase (CPK-MB) levels and any side effects.

2. Patients and Method

2.1 Study location

This study was done in the department of anaesthesia in SMS Medical College and attached group of hospitals with due permission from the institutional ethical committee and after obtaining written and informed consent from each patient.

2. 2 Study date

August 2017 to July 2018.

2.3 Study design

Hospital based, randomised, prospective, comparative, interventional study. A hospital based study includes patient's who are admitted in the hospital and receive services for improving quality of life with intensive care unit services for improving post operative care of the patients. The patient's receiving desflurane were of the test intervention and other group which received the standard inhalational agent (sevoflurane group) was of the standard group.

2.4 Sample size

The sample size was calculated as 74 in each group at 95% confidence and 80% power to verify the expected minimal difference of 5.5 mmHg (\pm 11.78) in the systolic arterial pressure of both groups. The sample size was calculated for each outcome and came to be maximum for the systolic blood pressure with a minimal difference of 5.5mmHg (\pm 11.78)in both the groups. That is why it was taken as a single variable outcome and the size covered all the other variables. This sample size was adequate to cover all other study variables.

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2.5 Groups

Patients were randomly allocated to two groups (74 in each group).

Group A- received sevoflurane (1.0 MAC)

Group B- received desflurane (1.0 MAC).

2.6 Randomization

One hundred and forty eight patients were randomly allocated into two treatment groups using sealed envelope method.

2.7 Inclusion criteria

Patients with ASA grade 2 and 3 between the age group 30-60 yrs of either sex undergoing off pump CABG surgery under general anaesthesia with ejection fraction >0.4.

2.8 Exclusion criteria

Patients having compromised renal and pulmonary function, fitting in a difficult intubation criteria (i.e. Mallampati grade 3 and 4, more than three attempts at intubation and patients in whom duration of laryngoscopy exceeded >30 seconds, hypersensitivity to any of the drugs used in the study, altered coagulation profile, Diabetes mellitus, obesity, left ventricular ejection fraction <40% and having severe cardiac arrhythmias. Laryngoscopy above 30 second would be associated with the rise in heart rate and blood pressure due to stimulation of supraglottic region by tissue tension and associated with rise in catecholamines as shown by previous studies.

Association of diabetes mellitus with coronary artery disease is related to the increased aortic stiffness which promotes adverse hemodynamics resulting in poor or adverse outcomes leading to increased myocardial oxygen consumption. After obtaining permission from institutional ethical committee and review board the patients were taken for surgery. Pre anaesthetic check up was done a day prior to surgery. Informed and written consent was taken from each patient. After arrival of the patient in the O.T, ECG electrodes were attached and intravenous access was obtained. Internal jugular cannulation and arterial cannulation was done under local anaesthesia.

Edwards Flotrac continuous cardiac output monitor was attached and the baseline parameters like heart rate(H.R), cardiac output(C.O), cardiac index (C.I), systolic blood pressure (SBP), diastolic blood pressure(DBP), mean arterial pressure (MAP) and systemic vascular resistance (SVR) were noted. (NMT) Neuromuscular monitoring with а hemodynamic software module for NMT inbuilt in the GE anesthesia workstation was also used. After preoxygenation with 100% oxygen for 3-5 minutes anaesthesia was induced with injection midazolam 0.15 mg/kg, fentanyl 5microgram/kg, etomidate 0.3 mg/kg, and rocuronium bromide 0. 9mg/kg intravenously, to maintain a BIS value between 40-50. Intubation was done with the appropriate cuffed disposable endotracheal tube and the MAP was maintained above 70 mmHg and cardiac index above 2.0 dynes-sec-m²cm⁻⁵ with the support of inotropes if needed.

Data of H. R, SBP, DBP, MAP, CO, CI, SVR were recorded at baseline, after induction 15, 30, 45 and 60 minutes after intubation and 1 hour after surgery. Blood urea, serum creatinine and CPK-MB were recorded before and 24 hours after surgery. Anaesthesia was maintained with oxygen, midazolam, fentanyl, vecuronium and inhalational agents like

desflurane/sevoflurane. At the end of surgery the patients were shifted to cardiac surgery ICU and were allowed to recover undisturbed and non-sedated.

2.9 Statistical analysis

Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test.

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The quantitative data was presented as mean and standard deviation and were compared by students t-test. Probability was considered to be significant if less than 0.05. For

significance cut off values are as follows \rightarrow

- p > 0.05 = not significant
- p < 0.05 = significant





Anesthesia and Critical Care

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3. Results

The demographic data and clinical profile were comparable in both the groups without any statistical significance as shown in Table 1.

3.1 Heart rate

Heart rate increased from baseline, after induction till 60 min after surgery in both the groups. But there was

comparatively more increase in heart rate in the sevoflurane group as compared to desflurane group with a p value of 0.0001, 0.0006, 0.0053 and 0.0213 after induction, at 15 min, 30 min and 45 min after induction which is statistically significant (P value <0.05) as shown in Table 2.

No. of Patients (74)		Group-A (Sevoflurane)		Group-A (desflurane)		P value
		Mean	S.D.	Mean	S.D.	
	Female	9	-	10	-	-
Sex	Male	65	-	64	-	-
Age		56.69	10.3	58.36	10.28	0.323
Height		167.81	8.33	168.09	9.54	0.847
Weight		62.14	9.85	61.34	10.99	0.642

 Table 1: Demographic Profile.

	Sevoflurane		Desflurane		P value	95% CI
	Mean	SD	Mean	SD		
Baseline	91.78	19.81	85.66	17.89	0.0504	-0.012 to 12.26
After induction	99.88	18.14	88.20	16.19	0.0001	6.089 to 17.26
15 min	99.69	19.34	89.78	15.13	0.0006	4.265 to 15.55
30 min	97.46	18.98	89.47	15.15	0.0053	2.406 to 13.57
45 min	94.01	18.18	87.78	14.15	0.0213	0.936 to 11.52
60 min	92.88	18.41	87.47	14.90	0.051	-0.036 to 10.85
1 hr after sx	99.45	19.41	97.14	12.37	0.389	2.97 to 7.59

Table 2: Mean Heart Rate in both the Group (Beats per minute).

3. 2 Mean arterial pressure

Mean arterial pressure decreased from baseline, after induction till 60 min after surgery in both the groups. But in desflurane group mean arterial pressuer decreased more as compared to sevoflurane group with a p value of 0.0001 and 0.001 just after induction and 15 min after starting the inhalational agent. This was statistically significant as shown in Table 3.

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	Sevoflurane (N=74)		Desflurane (N=74)		P value	95% CI	
	Mean	SD	Mean	SD			
Baseline	109.59	11.10	103.82	13.35	0.004	1.78 to 9.75	
After induction	94.78	9.22	88.12	11.59	0.0001	3.26 to 10.06	
15 minutes	97.62	7.45	92.80	10.43	0.001	1.88 to 7.76	
30 minutes	93.43	8.96	90.62	9.34	0.063	-0.162 to 5.78	
45 minutes	89.64	8.13	88.89	9.68	0.613	-2.16 to 3.64	
60 minutes	87.93	9.45	86.41	8.93	0.314	-1.46 to 4.51	
1 hour after sex	98.81	9.66	96.34	13.15	0.194	-1.27 to 6.22	

 Table 3: Trend of mean arterial pressure (mmHg).

3.3 Cardiac index

The baseline C.I., after induction, 15 min, 30 min, 60 after induction and 1 hour after surgery between two inhalation groups did not show any statistical significance (P >0.05). After 45 min of induction C. I.

significantly increased in the Desflurane group 2.97 ± 0.68 S.D. (L/Min/M²) with respect to 2.73 ± 0.67 S. D. in Sevoflurane group and P value 0.032 and C.I. -0.460 to -0.020 as show in Figure 1.



Figure 1: Cardiac Index (L/min/m²).

3. 4 Systemic vascular resistance

The SVR showed a decrease in the Desflurane group as compared to the sevoflurane group with a p value <0.05 which was statistically significant as shown in Figure 2.



Figure 2: Systemic Vascular Resistance (dynes/sec/cm⁻⁵).

3.5 Cardiac output

The baseline C. O., after induction, 15 min after induction and 1 hour after surgery showed no difference between two inhalational groups which was not significant (P >0. 05). After 30 min of induction

C.O. significantly increased in Desflurane group 4. 97 \pm 1. 26 S. D. L/min with respect to 4. 61 \pm 0. 89 S. D. in Sevoflurane group and P value 0. 049 and C. I. -0. 709 to -0. 001 as shown in Figure 3.



Figure 3: Cardiac Output (L/Min).

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3.6 Blood urea

Preoperative urea level in sevoflurane group was 25.20 \pm 7.36 SD mg/dL and 27.13 \pm 7.27mg/dL. Postoperative after 24 hours in sevoflurane group was 33.27 \pm 13.16 SD mg/dL and 40.10 \pm 10.64 mg/dL. After 24 hours of surgery blood urea level significantly increased in the desflurane group as compare to sevoflurane group with a p value of 0.001 which was statistically significant as shown in Table 4.

Blood Urea (mg/dL)							
	Sevoflurane (N=	30)	Desflurane (N=3	P value			
	Mean	SD	Mean	SD	1 value		
Preoperative	25.20	7.36	27.13	7.27	0.310		
Postoperative	33.27	13.16	40.10	10.64	0.030		

Table 4: Blood Urea.

3.7 Serum creatinine

Pre-operative creatinine level in Sevoflurane group was 1.13 ± 0.20 S.D. mg/dL and 1.15 ± 0.30 S.D. mg/dL in Desflurane group with a P value 0.553. Post operative creatinine levels after 24 hour in Sevoflurane group

was 1.35 ± 0.25 S.D. mg/dL and 1.56 ± 0.47 S.D. mg/dL in Desflurane group with a P value 0.0006 as shown in Table 5 creatinine level significantly increased in the desflurane group.

Serum Creatinine (mg/dL)							
	Sevoflurane (N	=74)	Desflurane (N=7	P value			
	Mean	SD	Mean	SD	1 value		
Preoperative	1.13	0.20	1.13	0.28	0.937		
Postoperative	1.34	0.26	1.54	0.46	0.049		

 Table 5: Serum Creatinine.

3.8 CPK-MB enzyme level (IU/L)

Pre-operative CPK-MB level in Sevoflurane group was 30.09 ± 10.05 S.D. IU/L and 31.61 ± 9.32 S.D. (IU/L) in Desflurane group with a P value 0.101. Post-operative after 24 hours in Sevoflurane group it was 46.61 ± 21.90 S.D. (IU/L) and 50.49 ± 26.29 S.D.

(IU/L) in Desflurane group with a P value 0.331 as shown in Table 6. After 24 hours of surgery CPK-MB level increased in desflurane group as compared to sevoflurane group with a p value of 0.331 which is not statistically significant.

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	Sevoflurane (N=74)		Desflurane (N=74)		P value
	Mean	SD	Mean	SD	
Pre Op.	30.09	10.05	31.61	9.32	0.101
Post Op.	46.61	21.90	50.49	26.29	0.331

 Table 6: CPK MB enzyme level (IU/L).

4. Discussion

There was no change in the mean age, height, weight, ejection fraction, and sex in both the groups. Both groups were comparable without any statistical significance. Increase in heart rate was more in sevoflurane group as compared to desflurane group with a p value of 0.006, 0.0053 and 0.0213, after 15, 30 and 45 minutes respectively. Our study was similar to Nihal G. Ozarslan et al. [15] in which there was increased in heart rate from base line till the end of surgery in the sevoflurane group. But the desflurane group showed that heart rate was more or less stable. Umesh Sivanna et al. [16] showed a decrease in heart rate in sevoflurane group which was not seen in our study. Since there was a gradual increase in the concentration to attain 1 MAC the heart rate did not rise as that compared to sevoflurane group. Fentanyl did not attenuate the effect because it was used in low doses indicating that the increase was due to circulating catecholamines[17]. Rapid rise in concentration of desflurane greater than 1.25 MAC leads to more sympathetic stimulation as shown by Moore MA et al. [18]. Desflurane doesn't appear to have a specific direct effect on the sympathetic nervous system as suggested by Boban N et al. [19] Muzi M et al. [20] showed an increase in heart rate by desflurane from stimulation to rapidly adapting upper airway receptors, or by central activation of the sympathetic nervous system rather than via a carotid sinus reflex.

Anesthesia and Critical Care

In humans, sevoflurane has little or no effect on peripheral sympathetic nerve activity. But sevoflurane may have some effects on sympathetic nerve tone. It has little or no effect on heart rate variability because of its mild cardiovascular depression. In humans sevoflurane attenuates baroreflex control of heart rate [21]. In our study there was a slight increase in heart rate after intubation can be attributed to the slower rise end tidal concentration. The slight slower rise in the end-tidal concentration of sevoflurane might be due to the slightly greater blood gas partition co-efficient of sevoflurane compared to desflurane (0.60 vs 0.42) and perhaps due to a small extent to the greater degree of metabolism of sevoflurane (3% vs 0.02%). The more gradual increase in the alveolar concentration of sevoflurane resulted in achievement of a lower MAC equivalent of sevoflurane. This is the most likely explanation of increase in the heart rate in the sevoflurane group [22].

The mean arterial pressure (MAP) showed a decrease in the desflurane group as compared to the sevoflurane group which was statistically significant. Our study was supported by Nihal G. Ozarslan et al. [15] who showed a more decrease in the mean arterial pressure in the desflurane group even 24 hours after surgery. De Baerdemaeker LE et al. [23] also showed similar results. But Gabriele Rodig et al. [24] showed a decrease in mean arterial pressure in the sevoflurane

group as compared to desflurane group. The decrease in MAP was attributed to either due to direct effect on vascular smooth muscle or due to a combination effect of fentanyl and etomidate just after induction. The decrease in MAP was more in the desflurane group suggesting that desflurane has more potent direct effect on vascular smooth muscle.

Cardiac output(C.O) was less in sevoflurane group as compared to desflurane group which was also seen by Nihal Gokbulut Ozarslan et al. [15] who showed that C.O remained elevated after induction, at the end of surgery and 24 hours in desflurane groups. The cardiac index (C.I) increased in the desflurane group as compared to sevoflurane group except just after induction. It was more elevated at 45 and 60 minutes after induction with a p value of 0.03 and 0.05 which was statistically significant which is in contrast to G, De Hert SG et al. [25].

The systemic vascular resistance (SVR) was decreased more in the desflurane group at all time intervals after induction and remained so even 1 hr after surgery with a p value <0.05. Peter F. Conzen et al. [26] showed that SVR decreased in the Propofol group as compared to the sevoflurane group similar to our study. Gabriele Rodig et al. [24] compared the hemodynamic effects of desflurane and sevoflurane showed the reverse effects as compared to our study and attributed higher concentration of catecholamines (adrenaline) as the cause of rise in the desflurane group. Nihal G. Ozarslan et al. [15] showed that desflurane caused a decrease in pulmonary capillary wedge pressure even 24 hrs after surgery, with a least extubation time with sevoflurane.

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The CPK-MB showed a rise in the desflurane group which was not seen by Umesh et al. [16] who showed that desflurane has a better myocardial protection than sevoflurane in patient undergoing off pump CABG surgeries as the myocardial performance index (MPI) was increased in the sevoflurane group. Desflurane administration resulted in a significant decrease in MAP, SVR, LVESI, stroke work (PRSW), end-systolic elastase(EES) and ejection fraction. All diastolic variables also had a dose dependent decrease and returned to baseline values after discontinuation of desflurane concluding that desflurane was cardiodepressive at small doses also [27]. Blood Urea and serum creatinine levels were not elevated in the sevoflurane group but on the second post-op day both were within normal limits. The main limitations of our study was that it could not be blinded because of the vaporizers.

5. Conclusion

Our study suggests that the use of desflurane inhalational agent is a better choice than sevoflurane in terms of hemodynamic stability which is desirable in off pump coronary artery bypass grafting.

6. Declarations

Ethics approval and consent to participate

Consent and approval for the study was obtained from the institutional ethics committee (EC) No:3294/MC/EC/2017. Dated 27/7/17.

Availability of supporting data

The datasets used and analysed during the current study are available from the corresponding author on reasonable request and also copies are available in the institute and the department of anesthesia.

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Anesthesia and Critical Care

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