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Original Article

Sevoflurane versus Isoflurane in Patients Undergoing Valvular Heart Replacements: A Comparative Study

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Abstract

Introduction: Sevoflurane is a volatile anesthetic agent, which is non-irritant with low solubility and lack of arrhythmogenicity, which makes it an ideal agent for ambulatory anesthesia. The aim of our study is to compare the cardiovascular effects at equivalent minimum alveolar concentration (MAC) doses and the recovery profile of sevoflurane and isoflurane, in patients undergoing valvular replacement surgery.

Materials and Methods: This is a hospital-based, randomized, interventional, comparative study with sample size of seventy participants divided into two groups. Group A (35) received sevoflurane (1MAC) and Group B (35) received isoflurane (1MAC). Patients were of the American Society of Anesthesiologists Grade 2–4. The age group was 20–25 years with body weight of 30–65 kg, undergoing valvular heart surgery. The primary outcomes are to compare the changes in heart rate, systolic and diastolic blood pressures, mean arterial pressure, cardiac output (CO), cardiac index, systemic vascular resistance index (SVRI), and stroke volume variable, during maintenance of anesthesia. The secondary outcomes are the time taken for eye opening on verbal commands and extubation.

Results: There was a decrease in blood pressure, CO, and SVRI with both agents (statistically insignificant, $P > 0.05$), but comparatively hemodynamics was more stable along with early recovery with sevoflurane (statistically insignificant).

Conclusions: Sevoflurane and isoflurane can safely be used for fast-track anesthesia in patients undergoing valvular heart surgery. Sevoflurane provided a better hemodynamic profile, early awakening, and extubation as compared with isoflurane, even though the difference was insignificant. Thus, sevoflurane with opioids may be preferred in patients undergoing valvular heart surgery.

Key words: Cardiopulmonary bypass, Hemodynamic profile, Isoflurane, Recovery profile, Sevoflurane, Valvular heart replacement

INTRODUCTION

Volatile inhalational agents provide protection against ischemic–perfusion injury and decrease in myocardial infarct size, thus having a cardioprotective effect.[1] They have myocardial protective effects and faster induction. The endothelial cells exposed to volatile anesthetic agents developed a pronounced resistance against cytokine-induced toxicity, consistent with a pre-conditioning-like effect.[2]

Volatile anesthetic agents are now commonly used for induction and maintenance of anesthesia in cardiac anesthesia, especially with the low solubility and non-irritating volatile agents. These agents facilitate the adequate depth of anesthesia with bispectral index (BIS) monitoring which reduces the requirement of analgesia and early extubation in cardiac intensive care units (ICUs).[3]

Sevoflurane is non-irritating, less soluble, and less arrhythmogenic which makes it an ideal agent for

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anesthesia.[4-6] The use of sevoflurane in valve replacement surgeries has been shown to reduce troponin I release and better preservation of myocardial function.[7]

Isoflurane, synthesized in 1965 by R. C. Terrell, has replaced halothane because of its many advantages.[8] It is neither hepatotoxic nor nephrotoxic and has minimal cardiovascular depressant effect.[9] Isoflurane is rapidly absorbed as well as eliminated from the body since it has low blood/gas partition coefficient.[10]

Very few studies have been published the effects of these two agents in valvular heart surgeries. The aim of our study is to compare the cardiovascular effects at equivalent minimum alveolar concentration (MAC) doses and the recovery profile of sevoflurane and isoflurane in patients undergoing valvular heart replacement surgery.

MATERIALS AND METHODS

This is a hospital-based, randomized, interventional, comparative study. The patients belong to the American Society of Anesthesiologists Grade 2–4, between the age group of 20 and 50 years with body weight of 30–65 kg of either sex undergoing valvular heart surgeries and on the same cardiac medications were included. Patients having compromised renal and pulmonary status, having Hb < 10 g%, fitting in the difficult intubation category, with diabetes mellitus, obesity, coagulation disorder, left ventricular ejection fraction (LVEF) < 40%, and with severe cardiac arrhythmias were excluded from the study. Written and informed consent was obtained from all the patients.

A total of seventy patients were enrolled in the study and were randomly allocated into two groups (35 patients in each group).

Group A: Those who received sevoflurane (1 MAC)

Group B: Those who received isoflurane (1 MAC)

Randomization was done by chit in box method [Flowchart 1].

All patients had arterial and central venous cannulation under local anesthesia and Flow trac Edwards EV 1000 continuous cardiac output (CO) monitor was connected. Intravenous fentanyl 2 μg/kg was administered, and after a period of 5 min, baseline data in the form of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), central venous pressure (CVP), CO, cardiac index (CI), systemic vascular resistance index (SVRI), and stroke volume variation (SVV) were recorded.

After pre-oxygenation with 100% oxygen for 3 min, induction was done with injection midazolam 0.05 mg/kg, injection fentanyl 4 μg/kg, injection etomidate 0.3 mg/kg, and injection rocuronium bromide 1 mg/kg intravenously to facilitate tracheal intubation. Anesthesia was maintained with sevoflurane or isoflurane depending upon the group. Further top up was done with 2 μg/kg/h of fentanyl and vecuronium 2 μg/h until the completion of surgery. BIS was maintained in between 40 and 60.

HR, SBP, DBP, MAP, CVP, CO, CI, SVRI, and SVV were noted at 2 min after induction, at sternotomy, before cardiopulmonary bypass (at aortic cannulation), after bypass (just after coming off cardiopulmonary bypass Cardiopulmonary bypass (CPB), after protamine, and before shifting to ICU.

The primary outcomes were to compare the changes in HR, SBP, DBP, MAP, CO, CI, SVRI, and SVV during maintenance of anesthesia by these two inhalational agents before shifting the patients to cardiac surgery ICU. The secondary outcomes included the recovery characteristics which were time taken for eye opening on verbal commands and extubation [Flowchart 2].

Statistical analysis was done using Student's "*t*"-test and paired "*t*"-test. For significance, *P* value was calculated and $P > 0.05$ was considered as not statistically significant and $P < 0.05$ was considered as statistically significant.

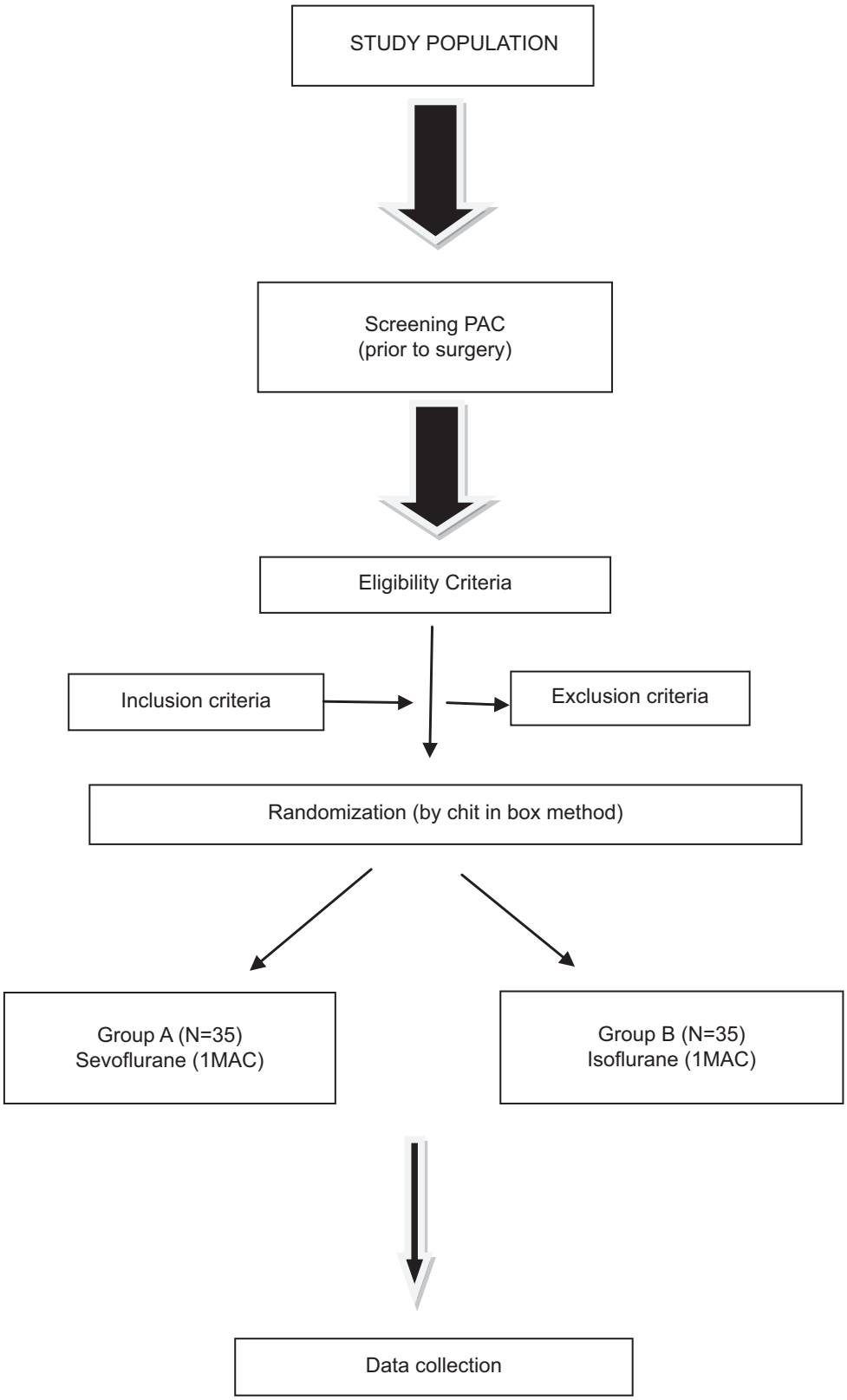
This study received ethical approval (Ethics Committee No. 2265/MC/EC/2016) from the Ethics Committee of SMS Medical College and attached hospital, Jaipur, Rajasthan on March 29, 2016.

RESULTS

A total of seventy participants were enrolled in the study, who were divided into two groups. Group A received sevoflurane and Group B received isoflurane. In Group A, the mean age of participants was 37.9 ± 8.6 years, and in Group B, it was 39.1 ± 9.1 years. In Group A, the mean weight of participants was 46.5 ± 7.0 kg, and in Group B, it was 47.7 ± 7.8 kg. In Group A, the mean height of participants was 163.5 ± 4.5 cm, and in Group B, it was 164.5 ± 5.4 cm. The mean LVEF in participants of Group A was 57.1 ± 4.6% and in participants of Group B, it was 55.8 ± 6.2% [Table 1]. HR, SBP, DBP, mean arterial blood pressure (MABP), CO, CI, and SVRI were compared in both groups at different intervals [Table 2].

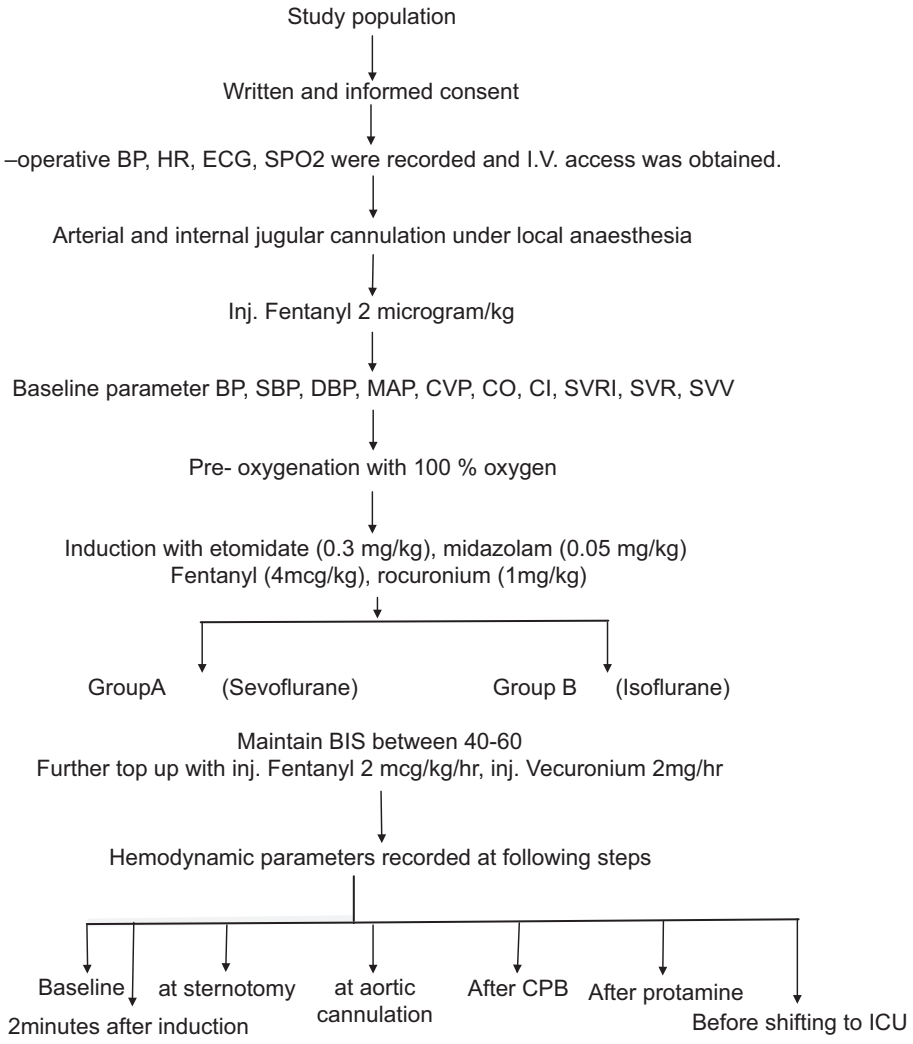
HR

Basal HR in Group A was 87.6 ± 19.5 beats/min and 95.7 ± 16.0 beats/min in Group B with $P > 0.05$. Before



Flowchart 1: Summarized chart of materials and methods

sifting to cardiac surgery ICU, the HR was 92.4 ± 11.2 in Group A and 98.5 ± 11.8 beats/min in Group B. The HR tended to be higher in isoflurane group as compared to the sevoflurane group at all time intervals, even though



Flow Chart 2: Methodology

Table 1: Demographic profile

Factors	Group A		Group B		*P-value*
	Mean	SD	Mean	SD	
Age (y)	37.9	8.6	39.1	9.1	0.5723
Weight (kg)	46.5	7.0	47.7	7.8	0.5221
Height (cm)	163.5	4.5	164.5	5.4	0.4151
LVEF (%)	57.1	4.6	55.8	6.2	0.3164

LVEF: Left ventricular ejection fraction, SD: Standard deviation

the difference was found to be statistically insignificant ($P > 0.05$).

SBP

Baseline SBP in Group A sevoflurane was 120 ± 13.7 mm Hg and in the isoflurane group, it was 117.3 ± 14.3 mm Hg. Two minutes after induction, it came down to 101.8 ± 16.2 in Group A and 104.5 ± 15.5 in Group B. In both the groups, there was a significant fall in SBP from baseline at 2 min after induction, at aortic cannulation, just after CPB, after protamine, and just before shifting to ICU. The mean SBP did not fall below 90 mmHg at any time interval.

DBP

The baseline DBP was 65.5 ± 9.1 mmHg in Group A and 63.0 ± 12.2 mmHg in Group B. Just before shifting to ICU, it was 58.3 ± 13.6 mmHg in Group A and 55.7 ± 12.2 mmHg in Group B with $P > 0.05$ which was statistically insignificant.

MABP

The baseline MAP in Group A was 83.8 ± 8.2 and 81.1 ± 10.6 mmHg in Group B. It decreased to 77.0 ± 11.1 in Group A and 74.1 ± 10.4 in Group B just before shifting to ICU which was statistically insignificant with $P > 0.05$. Although there was a significant fall in MAP from baseline in both groups at aortic cannulation, just after CPB, after

Table 2: Comparison of study parameters

Parameters	Baseline		2 min. After induction		At sternotomy		At aortic cannulation		Just after CPB		After protamine		Just before shifting to ICU	
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
Heart rate (beats/min)	87.6±19.5	95.7±16.0	90.7±19.0	96.5±18.1	90.0±15.9	98.9±18.9	91.8±19.9	94.1±17.9	94.9±14.8	98.8±14.1	93.8±13.6	96.9±11.8	92.4±11.2	98.5±11.8
MAP (mmHg)	83.8±8.2	81.1±10.6	74.0±13.2	75.2±11.2	83.5±12.7	83.7±12.6	68.8±12.0	71.2±13.0	66.0±11.5	68.9±10.0	71.0±10.8	69.5±7.4	77.0±11.1	74.1±10.4
CO	5.3±1.2	5.0±0.6	4.5±0.8	4.1±0.7	4.9±0.9	4.6±0.5	4.9±1.0	4.6±0.5	6.5±1.8	6.0±0.9	6.7±2.3	6.0±1.6	5.8±1.6	5.5±0.7
CI (L/min/m^2)	3.5±1.0	3.2±0.6	3.0±0.6	2.7±0.5	3.3±0.8	3.1±0.4	3.3±1.0	3.0±0.4	4.5±1.3	4.1±0.6	4.6±1.7	4.0±1.1	4.0±1.3	3.6±0.6
SVRI	2119.1± 353.9	2130± 248.6	1963.8± 483.1	1870.0± 188.0	2019.8± 438.2	1998.3± 260.5	1739.6± 308.9	1704.9± 279.9	1500.2± 260.4	1392.7± 22.4	1545.1± 306.4	1479.1± 257.4	1791.3± 280.9	1681.5± 209.4
SVV	12.1±5.1	12.5±3.1	12.7±5.9	11.9±3.6	12.2±5.4	11.0±3.2	12.4±5.0	11.2±3.5	9.7±4.4	8.3±4.2	8.9±4.0	8.0±2.4	10.3±4.2	9.7±2.4

MAP: Mean arterial pressure, CO: Cardiac output, CI: Cardiac index, SVRI: Systemic vascular resistance index, SVV: Stroke volume variable

protamine administration, and just before shifting to ICU, the MAP did not fall below 65 mm Hg at any time interval.

CO

The baseline CO was 5.3 ± 1.2 SD in Group A and 5.0 ± 0.6 in Group B. Although there was significant fall in CO from baseline in both the groups at 2 min after induction (4.5 ± 0.8 in Group A and 4.1 ± 0.7 in Group B), there was a significant increase in CO in both groups after CPB, after protamine administration, and just before shifting the patients to ICU. However, the difference was not statistically significant.

CI

The baseline CI was 3.5 ± 1.0 L/min/m^2 in Group A and 3.2 ± 0.6 in Group B. There was a significant fall in CI from baseline in both groups 2 min after introduction (3.0 ± 0.6 in Group A and 2.7 ± 0.5 in Group B) but was statistically not significant, $P > 0.05$. An increase in CI in both groups was observed after CPB, protamine administration, and just before shifting to ICU (4.0 ± 1.3 in Group A and 3.6 ± 0.6 in Group B). However, the difference was not significant between the two groups, $P > 0.05$.

SVRI

The baseline SVRI was 2119.1 ± 353.9 in Group A and 2130 ± 248.6 in Group B. There was a decrease in SVRI from baseline in both groups after aortic cannulation to shifting to ICU. Fall in SVRI was less in sevoflurane group as compared to isoflurane group. However, difference was not statistically significant between the two groups, $P > 0.05$.

Comparison of Recovery Characteristics

Eye opening on verbal commands was significantly earlier in sevoflurane group ($P = 0.01$) with a mean value of 39.5 min in Group A as compared to 44.9 min Group B. Extubation was also significantly earlier in the sevoflurane group with mean of 247.4 min as compared to isoflurane group where the mean time taken for extubation was 278.4 min ($P = 0.0009$) [Table 3 and Figure 1].

In both the groups, cardiac morbidity in the form of M.I. was monitored by electrocardiogram (ECG) until extubation of patient (ST depression >1 mm, appearance of new q waves). Electrocardiographically did not detect any ischemic changes in both groups.

Table 3: Comparison of recovery characteristics

Parameters	Group A		Group B		*P*-value
	Mean	SD	Mean	SD	
Eye opening on verbal command (minutes)	39.5	8.2	44.9	10.0	0.0167
Extubation (minutes)	247.4	31.4	278.4	26.3	0.0009

SD: Standard deviation

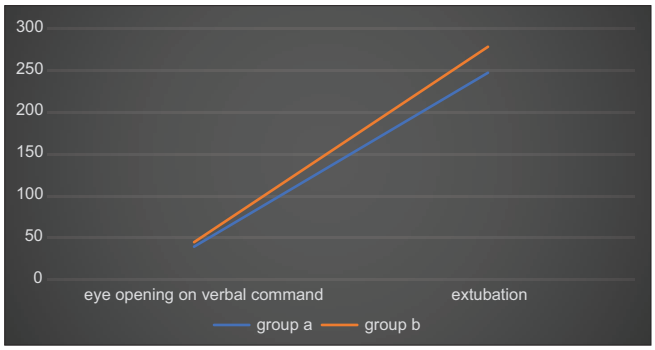


Figure 1: Comparison of recovery characteristics

DISCUSSION

The present study was aimed to compare sevoflurane and isoflurane on hemodynamic parameters and secondary outcomes in patients undergoing valvular heart replacement. Measuring the vital parameters, such as HR, SBP, DBP, MAP, CVP, CO, CI, SVRI, SVR, and SVV, at various surgical steps revealed that they were comparable (statistically insignificant, $P > 0.05$) in both groups. There was a tendency to decrease blood pressure, CO, and vascular resistance with each volatile agent, but comparatively hemodynamic parameters were more stable in sevoflurane group. However, these findings were statistically insignificant. We continuously monitored ECG which did not detect any evidence of myocardial ischemia in any of the patient.

Our study is similar to a study done by Ebert *et al.*[11] They concluded that sevoflurane provided better and stable hemodynamic profile as compared to isoflurane and desflurane. This study showed that sevoflurane did not increase the HR in adult patients. However, isoflurane and desflurane when used with higher MACs, they caused tachycardia. Sevoflurane is not associated with coronary steal phenomena and arrhythmias.

Our study data were also similar to results of Rolf *et al.*[12] as they also found that sevoflurane did not increase the HR, but isoflurane and desflurane did it at higher concentration. Sevoflurane produces less coronary dilatation than isoflurane. Sevoflurane has not been associated with a reduction of blood flow to collateral-dependent myocardium in dogs with steal-prone anatomy. Sevoflurane preserves cerebral blood flow and reduces cerebral metabolic rate much like isoflurane. However, the use of isoflurane may be associated with tachycardia which can increase the myocardial oxygen demand and can be detrimental to ischemic patients undergoing cardiac surgery. This was not observed in our study.

Similar findings were observed in a study done by Bennett *et al.*,[13] who compared sevoflurane and isoflurane, and both agents showed similar hemodynamic effects at 0.5 and 1.0 MAC. Sevoflurane decreased HR and CI as compared to isoflurane. This effect may be desirable during valvular heart replacement surgeries and also off-pump coronary artery bypass grafting (OPCABG) as myocardial oxygen consumption will be decreased with a decrease in HR. They observed that times to eye opening and extubation were similar with both agents, with sevoflurane tending to be earlier than isoflurane. These findings were not statistically significant, however.

Jones *et al.*[14] compared similar agents sevoflurane and isoflurane which we compared in our study, in cardiac surgery and concluded that sevoflurane was not inferior to isoflurane in their primary outcome, i.e., the length of ICU stay or 30 day mortality. The secondary outcomes such as cardiac troponin T sample after 6 h of surgery and serum creatinine levels were decreased in the isoflurane group as compared to the sevoflurane group. They found that there was no clinical difference between the two groups. In fact, sevoflurane was costlier (eight times) than isoflurane.

Bernald *et al.*[15] compared the effects of sevoflurane and isoflurane on cardiac and coronary dynamics in chronically instrumented dogs and concluded that sevoflurane at MAC values of 1.2 and 2 produced increase in HR. Except for HR, sevoflurane and isoflurane showed identical hemodynamic effects. They also mentioned that humans' sevoflurane would appear to be a superior anesthetic agent to isoflurane because of the faster induction emergence coupled with similar hemodynamic profile.

In a study by Xiang – Lin Yang *et al.*[16] sevoflurane had better myocardial protective effects as compared to propofol in patients undergoing valvular heart replacement. Sevoflurane did not depress the cardiac functions and showed lighter inflammatory response which provided minimal need of mechanical ventilation, period of ICU stay, and time to hospital discharge as compared to propofol.

Hemmerling *et al.*[17] studied forty patients undergoing OPCABG with high thoracic epidural analgesia and immediate extubation at the end of surgery. Sevoflurane and isoflurane gave the same cardioprotective effects as troponin T concentration was not significantly different between the two groups. There was no difference in the hemodynamic values during and after OPCABG. Sevoflurane allowed a more rapid recovery. They concluded that both agents were similar in ultra-fast-track extubation in OPCABG surgery.

Conzen *et al.*[18] conducted a prospective study to compare sevoflurane and propofol regarding their cardioprotective

property. They concluded that patients received sevoflurane for off-pump coronary vascular surgery had less myocardial injury than patients received propofol for the same intervention due to significantly lower release of troponin I during the first 24 post-operative hours. Recovery of cardiac function was also better with sevoflurane, as CO increased after revascularization with sevoflurane.

Rabie Soliman *et al*.[19] compared the myocardial effects of sevoflurane and isoflurane in high-risk patients undergoing CABG surgery and found that isoflurane increased the HR, MAP, CI, SVR, and PVR, but sevoflurane decreased the HR, MAP, CI, MAP, SVR, and PVR. Sevoflurane diminished the work performed by the heart. Thus, its use leads to low oxygen demand and improves the oxygen supply/demand ratio, therefore protecting the myocardium from ischemia. They concluded that sevoflurane is superior to isoflurane in terms of cardioprotection.

Xu J Chang *et al*.[20] suggested that isoflurane and sevoflurane can inhibit increasing of lipid peroxides levels to attenuate myocardial ischemia–reperfusion injuries mediated by oxygen-free radicals during open-heart surgery in patients undergoing cardiac valve replacement. Cromheecke S Pepermans *et al*.[7] found that the use of sevoflurane in aortic valve surgery led to better preservation of myocardium functioning and a decrease release of Troponin I. Kortekaas *et al*.[21] observed in patients undergoing mitral valve repair that intramyocardial delivery as compared to the systemic delivery of sevoflurane more strongly attenuated the systemic inflammatory response after CPB without reducing post-operative markers of myocardial cell damage. All these four studies suggest myocardial protection by inhalational agents (sevoflurane/isoflurane) by different mechanism.

The limitations of our study were that it was not blinded, and size of study population was small. Previous literatures favor that sevoflurane and isoflurane have cardioprotective property, but still there is need of more studies to prove their role in valvular heart surgeries. The study makes it possible to recognize the cardioprotective effects of sevoflurane over isoflurane.

CONCLUSION

We conclude that sevoflurane and isoflurane can safely be used for fast-track anesthesia protocol in patients undergoing valvular cardiac surgery without compromising safety. Sevoflurane provided a better hemodynamic profile in terms of BP, SVR, and CO even though the difference was not found to be significant. However, sevoflurane provides significantly early awakening and extubation as compared with isoflurane. Thus, sevoflurane along with opioids may be preferred in patients undergoing valvular heart surgery.

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