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AN INTRA-OPERATIVE TRANSESOPHAGEAL ECHOCARDIOGRAPHIC STUDY TO COMPARE THE EFFECT OF SEVOFLURANE AND ISOFLURANE ON LEFT VENTRICULAR DYSFUNCTION IN PATIENTS WITH ISCHEMIC HEART DISEASE UNDERGOING CORONARY ARTERY BYPASS GRAFTING USING CARDIOPULMONARY BYPASS

Anesthesiology

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ABSTRACT

An Intra-operative Transesophageal Echocardiographic Study to Compare The Effect of Sevoflurane and Isoflurane on Left Ventricular Dysfunction In Patients With Ischemic Heart Disease Undergoing Coronary Artery Bypass Grafting Using Cardiopulmonary Bypass

Context : Diastolic dysfunction has been increasingly recognized as an important cause of congestive heart failure (CHF) and resultant morbidity. About 50% patients with CHF have 'diastolic heart failure' in spite of a normal systolic function with preserved ejection fraction. The widely used volatile anesthetic agents, Isoflurane and Sevoflurane, are considered important components of balanced anesthesia technique. However their effects on left ventricular (LV) systolic and diastolic function have not been precisely defined. This study was designed to quantify and compare their effects on left ventricular function by TEE before start of CPB.

Aims : To compare the effects of Isoflurane and Sevoflurane on echocardiographic LV systolic and diastolic parameters.

Settings and design : After obtaining institutional ethics committee clearance and informed consent from 60 patients operated within my study period was included . Data were collected after induction and just before going on bypass.

Materials and Methods : After inducing the patients with institutional protocol one group was given isoflurane(Group I) and another group was given sevoflurane(Group S), both at 1MAC. TEE parameters measuring LV systolic and diastolic functions were done.

Statistical analysis : Data were analysed by Epi Info (TM) 7.2.2.2.

Result and conclusion : Isoflurane was better than sevoflurane in comparism of systolic and diastolic dysfunction.

KEYWORDS

Isoflurane , Sevoflurane , Coronary artery bypass grafting

INTRODUCTION

Diastolic dysfunction has been increasingly recognized as an important cause of congestive heart failure (CHF) and resultant mortality and morbidity. About 50% patients with CHF have 'diastolic heart failure' in spite of a normal systolic function with preserved ejection fraction[1] .The widely used volatile anesthetic agents, Isoflurane and Sevoflurane, are considered indispensable components of balanced anesthesia technique. Their cardiovascular effects on myocardial systolic function, cardiac electrophysiology, coronary vasoregulation, systemic and pulmonary vasculature, baroreceptor reflex and anesthetic preconditioning are well described in the literature[2]. While their effects on left ventricular (LV) systolic function have been described to some extent in animal and few human studies, however their effects on left ventricular (LV) diastolic function have not been precisely defined. This is because the indices of diastolic function could not be measured reliably and non-invasively in the past. This study was designed to quantify and compare the effects of Isoflurane and Sevoflurane on left ventricular function, which was assessed using TEE examination before the establishment of cardiopulmonary bypass (CPB) in patients with ischaemic heart disease (IHD) operated for CABG .

MATERIALS AND METHODS

This prospective, randomized and observational study was conducted at our institute which is a tertiary referral center. A total of 60 patients who were operated for elective CABG using cardiopulmonary bypass aged 50-70 years of either gender, with triple vessel disease having the preoperative left ventricular ejection fraction (LVEF) >50% were included in the study groups. Those with esophageal disease, coexisting valvular heart disease, pre-existing Grade II (pseudonormal filling) and Grade III (restrictive filling) diastolic dysfunction, HOCM/other cardiomyopathies, pericardial disease/ effusion, severe lung disease, age < 50 years or > 70 years, preoperative atrial fibrillation or other haemodynamically significant arrhythmias, pre-CPB inotropic support requirement, LVEF < 50%, pre-existing severe left ventricular hypertrophy, unwilling to give consent for participation in the study , emergency CABG, and with single or double-vessel coronary artery disease were excluded from the study. A computer generated randomization protocol was used to allocate them into two groups with 25 patients in each group(Group – I received Isoflurane, and Group – II received Sevoflurane)

Approval of Institutional Ethics Committee was obtained. After proper informed and written consent patients were enrolled in the study.

All patients were thoroughly examined during pre-anaesthetic evaluation. On arrival in operating room ASA standard monitors were attached. Intravenous access was obtained and radial arterial canulation was performed under local anesthesia. General anesthesia was induced with intravenous midazolam 0.05 mg/Kg, fentanyl 5 - 10 micrograms /Kg and etomidate 0.1 to 0.2 mg/kg . Neuromuscular blockade was done with i.v. vecuronium 0.1 mg/kg. Anesthesia was maintained with 1 MAC Sevoflurane or Isoflurane in 50% oxygen and air. BIS was maintained between 40 to 60. A triple lumen central venous catheter was inserted in right internal jugular vein. A multiplanar TEE probe (Vivid™E 95/ Version 202/ model no. GE 000500) was inserted. Anaesthesia was maintained by oxygen and air with isoflurane or sevoflurane at 1 MAC , along with intermittent intravenous top up doses of injection fentanyl (1-2 µg/kg) and injection vecuronium(0.02µg/kg). The heart was examined using TEE and baseline measurements pertaining to the LV diastolic function were obtained as per the ASA/ SCA guidelines. All patients received fluids, inotropes, ionodilators and vasopressors to maintain the central venous pressure (CVP) of 6-10 mm Hg and mean arterial pressure of 70-80 mm Hg. Before giving heparin for going into cardiopulmonary bypass another TEE examination to evaluate LV diastolic functions were obtained.

The study data was obtained in 3 steps:

(1) First, the mid-esophageal 4-chamber view was obtained and pulse wave Doppler examination was performed after placing the sample volume at the tips of the mitral valve leaflets. The peak

flow velocity of early diastolic filling (E), peak flow velocity of late diastolic filling (A), E/A ratio, A wave duration and deceleration time (DT) for early diastolic filling were acquired.

(2) Second, the pulmonary venous flow velocity was measured on PW Doppler keeping the sample volume in left upper pulmonary vein 0.5-1cm distal to its orifice where it joins the left atrium. Values for the peak systolic flow velocity (S), peak diastolic flow velocity (D), peak reverse atrial flow velocity (Ar) and duration of reverse atrial flow (Ar dur) were obtained.

(3) Third, the tissue Doppler imaging was performed after placing the sample volume at the lateral mitral valve ring. The measurements performed were the peak early diastolic tissue velocity (e') , peak late diastolic tissue velocity (a'), e'/a' ratio, E/e' ratio and isovolumic relaxation time (IVRT).

Three readings were obtained and averaged for each parameter.
Anaesthesia and monitoring was continued till the patients were shifted to ITU with stable haemodynamic parameters.

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2. EPI INFO is a trademark of the Centers for Disease Control and Prevention(CDC).

Ethics

A proper institutional ethics committee clearance was obtained prior to undertaking this study.

Statistics

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (2χ) test was performed to find the associations. t-test was used to compare the means of the two groups. Fisher Exact test was used where Chi-square () test was not applicable. p<0.05 was taken to be statistically significant.

RESULTS

Subjects in Group – I received Isoflurane and subjects in Group – II received Sevoflurane as the test agent.

Table 1 : Demographic Characters

Demographic Characters	GROUP 1	GROUP 2	P
AGE	60.23 +/- 6.80	61.67 +/- 6.08	0.42
SEX RATIO(% OF MALE)	80%	83.3%	0.36
BODY WEIGHT	71.20 +/- 10.68	71.37 +/- 9.51	0.61

P<0.05 is considered significant

Thus the patients of the two groups were matched for their age, sex ratio and body weight.

Table 2 : Echocardiographic diastolic parameters(transmitral diastolic doppler flow profile, pulmonary venous flow profile and tissue doppler imaging) in Group 1 (Isoflurane) (N = 30)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	49.93±11.75	54.02±9.60	0.42
A(cm/sec)	53.55±10.24	53.02±11.05	0.42
E/A	0.96±0.28	1.06±0.27	0.08
DT(ms)	216.40±34.54	200.30±27.48	**0.025**
A duration(ms)	147.73±17.49	143.06±26.41	0.211
Pulmonary venous flow profile			
S (cm/sec)	36.51±7.55	35.65±11.84	0.36
D (cm/sec)	22.56±6.27	26.22±7.48	**0.02**
S/D	1.69±0.40	1.43±0.55	**0.02**
Ar (cm/sec)	12.98±4.60	13.22±5.22	0.42
Ar duration(ms)	95.73±19.98	95.19±23.22	0.46
Tissue Doppler Imaging			
e' (cm/sec)	6.95±1.89	6.97±1.83	0.48
a' (cm/sec)	8.28±2.88	7.71±2.68	0.21
e'/ a'	0.93±0.41	1.03±0.48	0.194
IVRT (ms)	122.93±31.30	117.77±22.93	0.23
E/e'	7.58±2.37	8.32±2.79	0.14

P<0.05 is considered significant.

From table 2 we can see that in Group – I (Isoflurane) patients, there was no statistically significant increase in E velocity but DT decreased significantly ($p < 0.05$) towards normal. A velocity remained unaltered and E/A ratio increased but were not statistically significant.These changes suggest an improvement in LV diastolic relaxation. In the pulmonary venous flow pattern, there was an increase in the diastolic flow velocity D which also suggests better LV relaxation. There was no significant change in the TDI parameters.The E/e'ratio increased suggesting increased LV filling pressures .Thus the results of transmitral blood flow(TMBF) and Pulmonary venous flow suggest better LV relaxation but were not supported by corresponding TDI values.

Table 3 : Echocardiographic diastolic parameters (transmitral diastolic doppler flow profile, pulmonary venous flow profile and tissue doppler imaging) in Group 2 (Sevoflurane) (N = 30).

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	48.42±10.33	41.85±8.22	**0.004**
A(cm/sec)	56.38±14.53	45.09±11.69	**0.0008**
E/A	0.89±0.19	0.97±0.27	0.09
DT(ms)	229.00±25.03	191.30±20.95	**<0.00001**
A duration(ms)	143.30±16.94	140.70±19.36	0.29
Pulmonary venous flow profile			
S (cm/sec)	41.32±12.76	38.13±10.47	0.14
D (cm/sec)	25.03±8.46	22.54±5.78	0.09
S/D	1.75±0.65	1.77±0.60	0.45
Ar (cm/sec)	16.13±3.84	13.79±4.26	**0.014**
Ar duration(ms)	95.73±23.94	97.03±20.05	0.41
Tissue Doppler Imaging			
e' (cm/sec)	7.83±2.92	6.63±2.37	**0.04**
a' (cm/sec)	8.27±2.42	6.31±1.71	**0.0003**
e'/ a'	0.98±0.37	1.10±0.40	0.1
IVRT (ms)	125.37±29.02	122.27±25.57	0.33
E/e'	7.04±2.86	6.90±2.26	0.41

P<0.05 is considered significant.

From table 3 we can see that in Group – II (Sevoflurane) patients, the TMBF Doppler velocities showed a decrease in E and A(statistically significant, $p < 0.05$), while the E/A ratio increased slightly. The DT decreased significantly ($p < 0.05$). The TDI parameters e' and a' decreased significantly ($p < 0.05$). The TMBF velocities suggest improvement in LV relaxation since E/A ratio slightly increased towards normal and DT decreased. But the E velocity decreased which was associated with corresponding decrease in Pulmonary venous D velocity and e' velocity, suggesting a possible deterioration of LV relaxation. Reduction in A and a' suggests decreased LA contractility.

Table 4 : Echocardiographic diastolic parameters(transmitral diastolic doppler flow profile, pulmonary venous flow profile and tissue doppler imaging) in patients with normal diastolic function in Group 1 (Isoflurane) (N = 10)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	61.93 +/- 6.47	56.43 +/- 8.46	0.06
A(cm/sec)	50.57± 7.99	49.68± 7.70	0.40
E/A	1.25±0.25	1.16±0.28	0.23
DT(ms)	195.3±19.47	193.70±18.87	0.43
A duration(ms)	148.60±20.75	140.50±32.64	0.26
Pulmonary venous flow profile			
S (cm/sec)	36.18±3.65	35.97±12.38	0.48
D (cm/sec)	23.71±8.25	24.68±7.97	0.39
S/D	1.69±0.62	1.63±0.84	0.42

Ar (cm/sec)	11.62±3.95	12.11±5.01	0.40
Ar duration(ms)	103.8±20.99	98.5±17.94	0.27
Tissue Doppler Imaging			
e' (cm/sec)	8.34±2.04	6.71±1.71	**0.03**
a' (cm/sec)	7.001±2.68	6.57±2.45	0.35
e'/ a'	1.29±0.44	1.17±0.56	0.3
IVRT (ms)	124.6±24.28	112.1±23	0.13
E/e'	8.04±3.003	8.94±2.82	0.25

P<0.05 is considered significant.

From table 4 we can see that in patients with normal diastolic function there was decrease in E, decrease in A and DT; but none were statistically significant.

e' was decreased to a statistically significant level and a' decreased but was not statistically significant. Thus in this patient group , there was an apparent improvement in LV relaxation in TMBF velocities but the TDI parameters showed some impaired LV relaxation as e' decreased to a value < 8cm/sec. But the same was not reflected in e'/a' ratio or E/e' ratio. So in patients with normal diastolic function isoflurane didn't cause any impaired relaxation.

Table 5 : Echocardiographic diastolic parameters(transmitral diastolic doppler flow profile, pulmonary venous flow profile and tissue doppler imaging) in patients with impaired relaxation in Group 1 (Isoflurane) (N = 20)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	43.93 +/- 8.79	52.81 +/- 10.11	**0.003**
A(cm/sec)	55.03± 11.07	54.68± 12.22	0.46
E/A	0.81±0.12	1±0.25	**0.002**
DT(ms)	226.95±35.91	203.6±30.81	**0.02**
A duration(ms)	147.3±16.19	144.34±23.55	0.32
Pulmonary venous flow profile			
S (cm/sec)	36.67±8.98	35.49±11.89	0.36
D (cm/sec)	21.98±5.68	26.98±7.30	**0.01**
S/D	1.68±0.24	1.33±0.31	**0.0002**
Ar (cm/sec)	13.66±4.84	13.78±8.35	0.48
Ar duration(ms)	91.7±18.68	93.54±25.73	0.39
Tissue Doppler Imaging			
e' (cm/sec)	6.25±1.39	7.10±1.92	0.06
a' (cm/sec)	8.92±2.81	8.27±2.66	0.22
e'/ a'	0.75±0.23	0.96±0.43	**0.03**
IVRT (ms)	122.1±33.78	120.6±20.94	0.43
E/e'	7.35±2.03	8.01±2.79	0.19

P<0.05 is considered significant.

From table 5 we can see that in patients with pre-existing impaired LV relaxation, there was a greater increase in E than patients with normal diastolic function, which was, statistically significant. The corresponding increase in diastolic flow in pulmonary veins D was also statistically significant. The DT also decreased significantly.

Table 6 :Echocardiographic diastolic parameters (Transmitral diastolic doppler flow profile, Pulmonary venous flow profile and Tissue doppler imaging)in patients with normal diastolic function in Group 2 (Sevoflurane) (N = 7)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	49.26 +/- 7.17	45.14 +/- 6.11	0.13
A(cm/sec)	44.16± 10.05	35.97± 5.35	**0.04**
E/A	1.14±0.16	1.27±0.18	0.08
DT(ms)	223.57±11.54	206.57±25.01	0.06
A duration(ms)	142.43±20.63	151.71±12.53	0.16
Pulmonary venous flow profile			
S (cm/sec)	41.74±14.49	32.83±11.11	0.11
D (cm/sec)	29.83±9.79	23.66±7.43	0.10
S/D	1.40±0.27	1.42±0.46	0.46
Ar (cm/sec)	16.03±3.85	13.49±4.32	0.13
Ar duration(ms)	108.14±36.68	108.71±21.23	0.48
Tissue Doppler Imaging			
e' (cm/sec)	10.54±3.22	8.94±2.42	0.15
a' (cm/sec)	7.62±2.40	6.15±1.50	0.09
e'/ a'	1.40±0.27	1.49±0.36	0.30
IVRT (ms)	127.71±15.05	112.28±15.41	**0.04**
E/e'	5.13±1.90	5.36±1.53	0.40

P<0.05 is considered significant.

From table 6 we can see that in patients with normal diastolic function in sevoflurane group ,there was decrease in TMBF velocities E and Awith A being statistically significant, but E/Aratio were increased. The TDI velocities e'and a' both decreased . Thus TMBF and TDI parameters suggested that LV relaxation may have improved slightly.

Table 7: Echocardiographic diastolic parameters (transmitral diastolic doppler flow profile, pulmonary venous flow profile and tissue doppler imaging)in patients with impaired relaxation in Group 2 (Sevoflurane) (N = 23)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	49.13+/- 7.92	40.85+/- 5.05	**0.00006**
A(cm/sec)	59.63± 10.98	42.41± 13.37	**0.00001**
E/A	0.83±0.06	1.03±0.24	**0.0002**
DT(ms)	209.78±21.97	194±20.64	**0.008**
A duration(ms)	141.74±16.13	141.73±17.51	0.49
Pulmonary venous flow profile			
S (cm/sec)	38.38±12.51	42.73±8.19	0.08
D (cm/sec)	20.32±7.43	23.46±3.83	**0.04**
S/D	1.99±0.65	1.86±0.47	0.22
Ar (cm/sec)	14.07±3.54	13.28±2.63	0.19
Ar duration(ms)	86.78±13.83	100.22±19.72	**0.005**
Tissue Doppler Imaging			
e' (cm/sec)	7.88±1.27	6.23±1.55	**0.0001**
a' (cm/sec)	9.20±2.37	5.69±1.65	**<0.00001**
e'/ a'	0.90±0.24	1.13±0.24	**0.001**
IVRT (ms)	119.91±17.49	113.69±19.03	0.12
E/e'	6.43±1.71	6.94±2.15	0.19

P<0.05 is considered significant.

From table 7 we can see that in this group, the decrease in DT as significant. E and A also decreased significantly. The E/A ratio was increased significantly suggesting improvement in LV relaxation. The corresponding increase in diastolic flow in pulmonary veins D was also statistically significant In the TDI parameters, e' and a'decreased significantly and the e'/a'increased significantly. Thus unlike TMBF and pulmonary flow velocities, TDI values show significant deteoration in early and late ventricular filling.

Table 8 : Comparison Of Echocardiographic Diastolic Parameters Between Group 1(isoflurane) And Group 2 (Sevoflurane) In The Baseline Period (n = 30)

TEE PARAMETERS	Isoflurane	Sevoflurane	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	49.93± 11.75	48.42±10.33	0.29
A(cm/sec)	53.35±10.24	56.38±14.53	0.19
E/A	0.96±0.28	0.89±0.19	0.45
DT(ms)	216.40±34.54	229.00±25.03	0.06
A duration(ms)	147.73±17.49	143.30±16.94	0.16
Pulmonary venous flow profile			
S (cm/sec)	36.51±7.55	41.32±12.76	0.05
D (cm/sec)	22.56±6.27	25.03±8.46	0.10
S/D	1.69±0.40	1.75±0.65	0.33
Ar (cm/sec)	12.98±4.60	16.13±3.84	**0.003**
Ar duration(ms)	95.73±19.98	95.73±23.94	0.50
Tissue Doppler Imaging			
e' (cm/sec)	6.95±1.89	7.83±2.92	0.08
a' (cm/sec)	8.28±2.88	8.27±2.42	0.46
e'/ a'	0.93±0.41	0.98±0.37	0.31

IVRT (ms)	122.93±31.30	125.37±29.02	0.38
E/e'	7.58±2.37	7.04±2.86	0.21

Table 9 : Comparison of echocardiographic diastolic parameters between Group 1(Isoflurane) and Group 2 (Sevoflurane) in the study period (N = 30)

TEE PARAMETERS	Isoflurane	Sevoflurane	p-value
Transmitral diastolic doppler flow profile			
E (cm/sec)	54.02±9.60	41.85±8.22	**<0.00001**
A(cm/sec)	53.02±11.05	45.09±11.69	**0.004**
E/A	1.06±0.27	0.97±0.27	0.10
DT(ms)	200.30±27.48	191.30±20.95	0.08
A duration(ms)	143.06±26.41	140.70±19.36	0.35
Pulmonary venous flow profile			
S (cm/sec)	35.65±11.84	38.13±10.47	0.19
D (cm/sec)	26.22±7.48	22.54±5.78	**0.02**
S/D	1.43±0.55	1.77±0.60	**0.012**
Ar (cm/sec)	13.22±5.22	13.79±4.26	0.32
Ar duration(ms)	95.19±23.22	97.03±20.05	0.37
Tissue Doppler Imaging			
e' (cm/sec)	6.97±1.83	6.63±2.37	0.27
a' (cm/sec)	7.71±2.68	6.31±1.71	**0.009**
e'/ a'	1.03±0.48	1.10±0.40	0.27
IVRT (ms)	117.77±22.93	122.27±25.57	0.24
E/e'	8.32±2.79	6.90±2.26	**0.017**

P<0.05 is considered significant.

From tables 8 and 9 we can see that in the baseline period there wasn't any statistically significant difference between isoflurane and sevoflurane. But in the study period there was statistically significant difference in E and A velocity in transmitral blood flow profile. There was a significant decrease in D velocity and corresponding increase in S/D ratio. All these suggest an impaired early diastolic filling when isoflurane and sevoflurane are compared. Also there was a significant decrease in a' velocity and E/e' ratio.

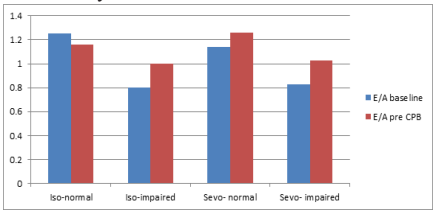

Figure 1 : Comparison between E/A of patients within the study groups

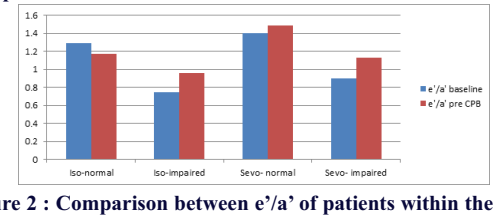

Figure 2 : Comparison between e'/a' of patients within the study groups

Table 10 : Echocardiographic systolic parameters in Group 1 (Isoflurane) (N = 30)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Ejection Fraction	53.07±4.57	52.57±4.10	0.32
FAC	44.00±5.66	43.53±5.42	0.37

P<0.05 is considered significant

Table 11 : Echocardiographic systolic parameters in Group 2 (Sevoflurane) (N = 30)

TEE PARAMETERS	BASELINE PERIOD	STUDY PERIOD	p-value
Ejection Fraction	52.77±4.56	50.80±4.09	**0.04**
FAC	44.00±5.66	42.23±5.16	0.105

P<0.05 is considered significant

From Table 10 and 11 we can see that only ejection fraction in sevoflurane group decreased to a significantly lower level in the pre-CPB period (study period).

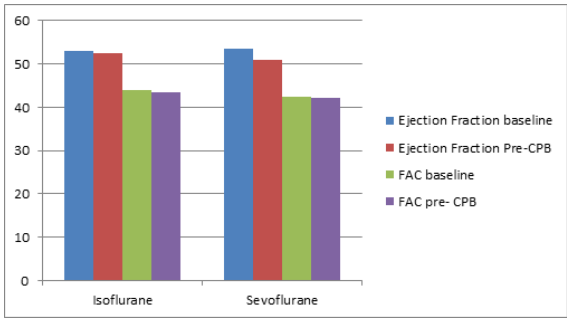

Figure 3 : Comparison between Ejection fraction and FAC of patients within the study groups

DISCUSSION AND CONCLUSION

Volatile agents are integral part of balanced anaesthesia technique. Inadequate general anaesthesia may lead to intraoperative awareness with recall and an increased risk of postoperative complications for the patient.[3] Cardiac surgical patients might be at higher risk of intraoperative awareness. It is generally believed that awareness will not occur if general anaesthesia is maintained with a volatile agent delivered to the patient's blood at a concentration of at least 0.5 to 1 minimum alveolar concentration (MAC).[4,5] But injudicious use of inhalational agents at higher MAC can cause both systolic and diastolic dysfunction. So we decided to use 1MAC of inhalational agent(i.e. isoflurane and sevoflurane) in our study.

The utility of the traditional Trans Mitral Blood Flow(TMBF) echocardiographic parameters throughout the perioperative period is limited by the unavoidable effects of changes in preload, afterload, heart rate, and rhythm on peak velocities and proportions of early and late filling [6] resulting in erroneous evaluation of LV diastolic function. Thus it is necessary to correlate the TMBF parameters with another modality, which will be least influenced by these factors. Sohn et al [7] showed that TDI parameters E' and E'/A' ratio did not change significantly after preload alterations. Tissue Doppler imaging parameters, being independent of loading condition, can help to differentiate between normal patients and those with pseudonormal LV filling.

In the present study, we have included those with Normal diastolic function and Grade I diastolic dysfunction. Grade II & III diastolic dysfunction were excluded from the study.

In our study, from table 4 we observed that in patients with normal diastolic function, 1 MAC isoflurane caused a small decrease in E(from 61.93+/- 6.47 m/s to 56.43 +/- 8.46 m/s) , decrease in A(from 50.57+/- 7.99 m/s to 49.68+/-7.70 m/s), decreased E/A ratio (1.25 +/- 0.25 to 1.16+/- 0.28)and decreased DT (195.3±19.47 ms to 193.70±18.87 ms). But none reached statistical significant value. There were no significant corresponding changes in pulmonary venous flow profile and TDI parameters except a significant decrease in e' velocity(8.34±2.04 cm/s to 6.71±1.71cm/s; p =0.03)). Our findings are consistent with other previously published studies . Oxorn et al [8], reported in their study in healthy patients undergoing peripheral orthopedic surgery, isoflurane anesthesia at MAC 1 and MAC 1.5 resulted in no statistically significant changes in TMBF parameters with preservation of pulmonary venous velocity. Bolliger et al [9] also noted that isoflurane did not cause impairment of LV diastolic function in normal subjects during spontaneous ventilation and IPPV.

From table 5 we can see that in patients with Grade I diastolic dysfunction, the TMBF and pulmonary venous flow profiles suggested an statistically significant improvement in the indices of diastolic function(E improved from43.93 +/- 8.79m/sec to 52.81 +/- 10.11m/s; p=0.003), although, these changes are not reflected in TDI measurements. Thus , these changes may be attributed to changes in preload and afterload due to isoflurane rather than due to improvement in LV relaxation, since TDI measurements are less affected by changes in loading condition.

Similarly Neuhauser et al [10] , in their study in patients with diastolic

dysfunction due to concentric hypertrophy and ischemic heart disease , concluded that changes in loading conditions as well as the inotropic state are more likely to cause the LV to operate on a steeper region of the pressure-volume curve, rather than direct alterations of the intrinsic viscoelastic properties of the myocardium.

Thus, we observed that 1 MAC isoflurane does not cause any significant change in diastolic function in patients with normal diastolic function and impaired relaxation. An apparent improvement in early diastolic filling may be seen, which is more evident in patients with impaired relaxation, and may be attributed to changes in loading conditions rather than due to any direct effect on myocardial relaxation properties.

From table 6 we can see that in patients with normal diastolic function, sevoflurane resulted in significant deterioration in both early and late diastolic filling. Sevoflurane decreased E (from 49.26 +/- 7.17m/s to 45.14 +/- 6.11m/s)and A(44.16± 10.05m/s to 35.97± 5.35m/s) velocities in TMBF profile. There was a statistically significant decrease in A velocity ($p < 0.05$), and a decrease in DT. There was also a significant decrease in e' and a'. The PV diastolic velocity D also decreased. The observation is similar to study of Bolliger D and co-workers who observed in their study on the effects of sevoflurane, desflurane, and isoflurane on early and late left ventricular diastolic function in young healthy adults, that there was decreased E, A, e' and a'. In contrast to isoflurane group, the changes in TMBF are also accompanied by corresponding changes in TDI measurements. So sevoflurane probably impairs both early and late diastolic function at 1 MAC .Bolliger D and co-workers suggested that the sympathoa drenergic effects of desflurane and isoflurane could have resulted in better diastolic performance compared with sevoflurane. However since e' was within the normal range in the sevoflurane group in their study, they suggested that sevoflurane might not have a clinically relevant direct effect on early diastolic function in healthy individuals. Late diastolic filling due to atrial contraction was significantly depressed by all 3 agents. From table 7 it can be seen that in patients with Grade I diastolic dysfunction, the early diastolic filling is not much affected by sevoflurane but late diastolic filling is significantly depressed. In this group, the decrease in DT **(** from 209.78±21.97 ms to194±20.64; p= 0.08) was significant. E and A also decreased significantly(E decreased from 49.13+/- 7.92 to 40.85+/- 5.05 m/s ; p=0.00006; A decreased from(59.63± 10.98 m/s to 42.41± 13.37 m/s; p= 0.0001) . The E/A ratio was increased significantly. In the TDI parameters, e' and a'decreased significantly. Therefore the e'/a'increased significantly. Thus in patients with pre-existing impaired relaxation, there was minimal change in early ventricular filling parameters , but late diastolic filling is significantly impaired probably due to impaired LA contractility.

The observations are similar to study of Filipovic M and co-workers[10]who worked on finding the effects of sevoflurane and propofol on left ventricular diastolic function in patients with pre-existing diastolic dysfunction. They observed that during anesthesia and IPPV, there was no difference in e' between the study groups. However, during spontaneous breathing and consecutive elevation of end tidal carbon dioxide, sevoflurane slightly improved early diastolic function whereas propofol had negligible effect. In contrast, during IPPV and normal end-tidal carbon dioxide the early diastolic function in both the groups were impaired in similar manner . They further noted that sevoflurane impaired systolic atrial and ventricular functions, as indicated by decrease of s' and a'.

Thus we observed that in patients with impaired relaxation, the early diastolic filling is not much affected by sevoflurane. But late diastolic filling is significantly depressed. Isoflurane does not significantly alter LV diastolic function in patients with normal diastolic function and impaired relaxation. An apparent improvement in early diastolic filling may be seen, which is more evident in patients with impaired relaxation, which may be attributed to changes in loading conditions.

Sevoflurane causes significant impairment in late diastolic filling in both patients with normal diastolic function as well as impaired relaxation. Sevoflurane also impairs early diastolic filling, more significantly in patients with normal diastolic function.

From table 10 and 11 we can see that only Sevoflurane caused significant decrease in ejection fraction in these patients.

Limitations of the study

It is a non-blinded study. Blinding was not feasible in our operating room set-up since the vaporizers and anesthetic gas monitors could not be masked from the echocardiographer.

Also the study is single-centred and multicentric studies with more number of patients is required to validate my results.

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