

## ORIGINAL RESEARCH

# Comparison of Cardiovascular Changes during Induction and Intubation with Thiopentone and Fentanyl in Patients of Mitral Stenosis Undergoing Mitral Valve Replacement Surgery

Vijay R. Shrothey<sup>1</sup>, Shekhar Babu<sup>2</sup>, Amol B. Thakare<sup>3</sup>, Yogesh N. Zanwar<sup>4</sup>

**ABSTRACT**

**Introduction:** Cardiovascular stability is of vital importance in patients undergoing cardiac surgery, who have a limited cardiovascular reserve. The changes in heart rate (HR), rhythm or blood pressure (BP) may not be well tolerated. Therefore, the choice of anaesthetic agents must be based on maintaining optimum haemodynamics and cardiovascular stability. Objective of the study was to find out whether Thiopentone (3mg/kg) offer better cardiovascular stability than Fentanyl (10µg/kg) in patients of mitral stenosis undergoing MVR surgery during induction and intubation.

**Material and Methods:** Patients of mitral stenosis undergoing mitral valve replacement surgery were included in present study. The study design was randomized prospective double blind controlled trial. A group of 50 patients sequentially posted for MVR surgeries in the department of Anesthesiology (CVTS OT), during the period of May 2011 to October 2012, were randomized to two treatment areas (induction group) equally i.e. 25 in F group (Fentanyl) and 25 in T group (Thiopentone). Randomization was done by using computer generated sequence in block size of 2 by software RALLOC.

**Results:** Thiopentone and Fentanyl both caused almost similar fall in blood pressure after induction. Thiopentone caused increase in heart rate more than Fentanyl during laryngoscopy, intubation and cuff inflation. After laryngoscopy, intubation and cuff inflation, blood pressure returns to baseline with Thiopentone, but remains below basal level with Fentanyl. CVP changes are almost similar with Thiopentone and Fentanyl and clinically acceptable.

**Conclusion:** Though Thiopentone (3 mg/kg) is not superior to Fentanyl in all respect for cardiovascular stability in the patients of mitral stenosis undergoing mitral valve replacement surgery, it (Thiopentone 3 mg/kg) seems better choice for induction than Fentanyl (10 µg/kg) when maintenance of Blood pressure is the priority. But if Heart rate control is desirable then Fentanyl (10 µg/kg) seems a better choice.

**Keywords:** Thiopentone, Fentanyl, Mitral Stenosis

**How to cite this article:** Vijay R. Shrothey, Shekhar Babu, Amol B. Thakare, Yogesh N. Zanwar. Comparison of cardiovascular changes during induction and intubation with thiopentone and fentanyl in patients of mitral stenosis undergoing mitral valve replacement surgery. International Journal of Contemporary Medical Research 2015;2(5):1407-1412.

<sup>1</sup>Professor, Department of Anesthesiology, Government Medical College and Super Specialty Hospital, Nagpur, <sup>2</sup>Senior Resident, Post-Doctoral Fellow, NIMHANS, Bangalore, <sup>3,4</sup>Assistant Professor, Government Medical College and Super Specialty Hospital, Nagpur, India

**Corresponding author:** Dr. Vijay R. Shrothey, Professor, Department of Anesthesiology, Government Medical College and Super Specialty Hospital, Nagpur, India

**Source of Support:** Nil

**Conflict of Interest:** None

**INTRODUCTION**

Cardiovascular stability is of vital importance in patients undergoing cardiac surgery, who have a limited cardiovascular reserve. The changes in heart rate (HR), rhythm or blood pressure (BP) may not be well tolerated. Therefore, the choice of anaesthetic agents must be based on maintaining optimum haemodynamics and cardiovascular stability.<sup>1</sup>

Rheumatic mitral stenosis is the most common valvular lesion in India,<sup>2</sup> which requires cardiac surgery and hence the role of specialized cardiac anaesthesia is significant, as various cardiovascular changes occur at the time of induction, intubation, during intraoperative and postoperative period.<sup>3</sup>

Important goals in the anaesthetic management of patients with significant MS –

1. Prevent tachycardia and treat it promptly if it develops in the perioperative period, because this causes decrease in diastolic filling time and causes large increase in left atrial pressure and precipitate pulmonary edema.
2. Prevent bradycardia because of relatively fixed stroke volume.
3. Maintenance of left ventricular preload without exacerbation of pulmonary vascular congestion.
4. Avoid factors that aggravate pulmonary hypertension and impair right ventricular function.
5. Vasodilation leading to hypovolemia.<sup>4</sup>

For that a balance between the premedication, relaxants and

inducing agents, is to be maintained, to minimize the cardiovascular effect caused by drugs and disease itself and maintain the haemodynamic and cardiovascular stability of patients undergoing mitral valve replacement (MVR) surgery.

The cardiovascular effects of the drug is an important criteria used by clinician while selecting a particular induction agent, especially in cardiac surgeries, there is need of selecting an induction agent which causes the least cardiovascular variation in cardiac surgeries like MVR surgery.

Data regarding the effect of induction agents on cardiovascular changes in patients undergoing MVR surgery is inadequate. That's why this study was undertaken to find out whether Thiopentone (3mg/kg) offer better cardiovascular stability than Fentanyl (10µg/kg) in patients of mitral stenosis undergoing MVR surgery during induction and intubation.

## MATERIAL AND METHODS

The present study was carried out in the Department of Anesthesiology (CVTS OT), in our institute, a tertiary care hospital run by State Government. Pilot study was carried out in 5 subjects in each group, to confirm the designs and methods are working as expected; to assess the case proforma and data collection methods and to provide estimated mean values of vital parameters as an input for sample size calculation for the main study.

### Sample Size calculation

Calculation for this RCT was done on the basis of following assumptions –

1. Main outcome measures considered were change in SBP and change in HR.
2. Null hypothesis – There was no difference in vital parameters (SBP, HR) in 2 groups.
3. Alternative hypothesis - The difference in vital parameters (SBP, HR) in 2 groups was significant.
4. Mean change in SBP in Fentanyl group = 40-50 mm Hg.
5. Mean change in SBP in Thiopentone group = 30-40mm Hg.
6. Effect size = 10 mm Hg (minimum significant difference).
7.  $\alpha$  error = 5% (two sided).
8. Power (1-  $\beta$ ) = 90%.

Required n = 46 (minimum), therefore a final of 50 patients were selected for this RCT.

Patients of mitral stenosis undergoing mitral valve replacement surgery were included in present study. The study design was randomized prospective double blind controlled trial. A group of 50 patients sequentially posted for MVR surgeries in the department of Anesthesiology (CVTS OT), during the period of May 2011 to October 2012, were randomized to two treatment areas (induction group) equally i.e. 25 in F group (Fentanyl) and 25 in T group (Thiopentone).

Randomization was done by using computer generated sequence in block size of 2 by a software RALLOC.

### Inclusion Criteria

1. ASA GRADE III and IV.
2. Adults (18 years - 60 years).
3. MITRAL VALVE REPLACEMENT SURGERY for mitral stenosis.

### Exclusion criteria

1. ASA GRADE V.
2. AGE less than 18 and greater than 60 years.
3. Pregnant women.
4. Known allergy to Thiopentone and Fentanyl.
5. Emergency surgery.
6. Patient with severe systemic non cardiac disease. e.g. - End stage renal and liver disease.
7. Patient with other severe valvular disease – severe AS, severe AR, severe MR, severe PS, severe TR.

### Preoperative Requirement

A detailed pre anaesthetic evaluation including history of present illness general examination, systemic examination, airway assessment was carried out in each patient.

All laboratory tests were done as per hospital protocol.

### Intervention

50 patients were randomly assigned in one of the following groups:

GROUP F (Fentanyl): (n=25) Induction was done with Fentanyl 10 µg/Kg IV over 4 - 5 minutes.

GROUP T (Thiopentone) : (n=25) Induction was done with Thiopentone 3 mg/kg IV in small doses over a period of 90 - 120 seconds.

### Methodology

After approval by the institutional ethical committee and pre-operative valid informed consent, patients were included in study. All standard anesthetic guidelines were followed. Patients were interviewed next day after extubation and loss of awareness was confirmed in the form of recall to verbal commands and events of laryngoscopy and intubation.

### STATISTICAL ANALYSIS

Difference in continuous variables between 2 groups were analyzed by unpaired t-test while pre- post changes i.e. changes from baseline within the same group were compared by paired t – test. Categorical variables were analyzed by using Chi-square test. p-value less than 0.05 was considered as statistically significant. Data was analyzed using statistical software STATA Version 10.1, 2009.

### RESULTS

Mean age in years, mean weight (kg), were comparable in both the groups. All baseline parameters like Heart Rate (HR),

Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Blood Pressure (MBP), Rate Pressure Product (RPP) and Central Venous Pressure (CVP) were comparable between both the groups.

Analysis of data in above table shows that, when both the groups are compared, the changes in heart rate is found to be statistically significant during induction, laryngoscopy and

intubation and 2<sup>nd</sup>, 3<sup>rd</sup> and 9<sup>th</sup> minute after cuff inflation.

When the mean change in DBP is compared in both the groups, it is maximum after induction, in F group (-20.24 mm of Hg) and in T group (-19.08 mm of Hg) which is statistically not significant.

When the mean change (fall) in SBP is compared in both the groups, it is maximum after induction, in F group (-37.60) and

Stage	F Group n=25 (Mean ± SD)	T Group n=25 (Mean ± SD)	p Value	Significance
Baseline (After premedication)	0.00 ± 0.00	0.00 ± 0.00		
After Induction	-8.24 ± 18.11	4.28 ± 17.83	0.0174	S
During Laryngoscopy and Intubation	2.28 ± 21.72	15.4 ± 24.10	0.0488	S
Cuff Inflation	10.56 ± 20.90	18.96 ± 21.35	0.1662	NS
1 min	9.76 ± 19.05	17.96 ± 22.00	0.1654	NS
2 min	5.32 ± 18.38	17.88 ± 21.99	0.0333	S
3 min	0.68 ± 15.06	13 ± 22.52	0.0275	S
4 min	0.96 ± 16.88	10.36 ± 22.26	0.099	NS
5 min	-1.6 ± 16.54	7.84 ± 20.40	0.0786	NS
6 min	-2.08 ± 16.22	7.16 ± 21.37	0.0915	NS
7 min	-3.16 ± 15.62	7.72 ± 22.39	0.052	NS
8 min	-3.64 ± 13.74	5.84 ± 22.97	0.0829	NS
9 min	-5.52 ± 12.79	5.16 ± 21.75	0.0395	S
10 min	-6.12 ± 15.78	3.08 ± 20.97	0.0861	NS

(t test. p value is significant if less than 0.05. S-Significant, NS-Not significant)

**Table-1:** Comparison of mean of change of Heart Rate from Baseline Between F group (Fentanyl) and T group (Thiopentone)

Stage	F Group n=25 (Mean ± SD)	T Group n=25 (Mean ± SD)	p Value	Significance
Baseline (After premedication)	0.00	0.00		
After Induction	-20.24 ± 14.85	-19.08 ± 12.91	0.7694	NS
During Laryngoscopy and Intubation	-12.44 ± 16.14	-2.52 ± 18.14	0.0466	S
Cuff Inflation	-6.60 ± 17.86	2.20 ± 15.59	0.0697	NS
1 min	-5.96 ± 14.89	3.44 ± 14.53	0.0284	S
2 min	-7.60 ± 12.94	1.28 ± 13.71	0.0226	S
3 min	-9.52 ± 10.54	-0.44 ± 14.03	0.0127	S
4 min	-11.00 ± 12.46	-1.84 ± 13.08	0.0146	S
5 min	-11.40 ± 13.57	-3.88 ± 13.39	0.0544	NS
6 min	-12.12 ± 12.59	-4.20 ± 12.37	0.0295	S
7 min	-10.40 ± 11.60	-3.72 ± 14.80	0.082	NS
8 min	-11.12 ± 12.06	-3.64 ± 15.46	0.0625	NS
9 min	-11.84 ± 10.72	-4.40 ± 14.30	0.0428	S
10 min	-12.00 ± 11.21	-4.96 ± 12.20	0.0388	S

(t test. p value is significant if less than 0.05. S- Significant, NS-Not significant)

**Table-3:** Comparison of mean of change of Diastolic Blood Pressure (DBP) from Baseline Between F group (Fentanyl) and T group (Thiopentone)

Stage	F Group n=25 (Mean ± SD)	T Group n=25 (Mean ± SD)	p Value	Significance
Baseline (After premedication)	0.00 ± 0.00	0.00 ± 0.00		
After Induction	-37.60 ± 24.38	-30.56 ± 20.55	0.2752	NS
During Laryngoscopy and Intubation	-28.00 ± 21.44	-12.16 ± 28.44	0.0309	S
Cuff Inflation	-19.96 ± 23.24	-4.48 ± 25.47	0.0294	S
1 min	-15.04 ± 22.39	-0.60 ± 23.15	0.0296	S
2 min	-18.52 ± 21.24	-2.96 ± 22.70	0.0158	S
3 min	-21.4 ± 18.58	-6.04 ± 23.61	0.0138	S
4 min	-24.00 ± 18.76	-7.52 ± 24.72	0.0107	S
5 min	-25.28 ± 19.57	-12.08 ± 25.17	0.0438	S
6 min	-26.8 ± 20.17	-12.20 ± 23.88	0.0237	S
7 min	-25.12 ± 16.28	-12.48 ± 25.08	0.0398	S
8 min	-25.92 ± 17.02	-11.76 ± 25.98	0.0271	S
9 min	-25.80 ± 15.89	-13.44 ± 24.21	0.0379	S
10 min	-27.80 ± 17.41	-13.68 ± 21.86	0.0149	S

(t test. p value is significant if less than 0.05. S- Significant, NS-Not significant)

**Table-2:** Comparison of mean of change of Systolic Blood Pressure (SBP) from Baseline Between F group (Fentanyl) and T group (Thiopentone)

Stage	F Group n=25 (Mean±SD)	T Group n=25 (Mean ± SD)	p Value	Significance
Baseline (After premedication)	0.00	0.00		
After Induction	-24.44 ± 17.31	-22.96 ± 14.45	0.7441	NS
During Laryngoscopy and Intubation	-13.92 ± 17.9	-5.04 ± 21.37	0.1178	NS
Cuff Inflation	-9.44 ± 20.96	0.28 ± 16.83	0.0769	NS
1 min	-7.48 ± 16.99	1.00 ± 15.70	0.073	NS
2 min	-9.68 ± 15.23	-0.04 ± 15.10	0.0292	S
3 min	-11.4 ± 12.37	-1.6 ± 17.54	0.0269	S
4 min	-12.96 ± 13.73	-3.4 ± 16.06	0.0282	S
5 min	-14.56 ± 14.36	-6.08 ± 16.57	0.0590	NS
6 min	-15.32 ± 14.33	-6.4 ± 15.96	0.0429	S
7 min	-14.08 ± 12.69	-6.12 ± 18.04	0.0774	NS
8 min	-14.88 ± 12.98	-5.60 ± 18.78	0.0477	S
9 min	-14.80 ± 12.50	-7.36 ± 16.96	0.0837	NS
10 min	-15.52 ± 12.50	-7.64 ± 15.14	0.0505	NS

(t test. p value is significant if less than 0.05. S- Significant, NS-Not significant)

**Table-4:** Comparison of mean of change of Mean Blood Pressure (MBP) from Baseline Between F group (Fentanyl) and T group (Thiopentone)

Stage	F Group n=25 (Mean ± SD)	T Group n=25 (Mean ± SD)	p Value	Significance
Baseline (After premedication)	0.00	0.00		
After Induction	-4439.24 ± 4058.42	-2759.76 ± 2327.34	0.079	NS
During Laryngoscopy and Intubation	-2537.32 ± 4028.95	433.24 ± 5014.85	0.0253	S
Cuff Inflation	-747.28 ± 4233.16	1613.64 ± 4173.77	0.0528	NS
1 min	-359.2 ± 3908.86	1928.96 ± 3783.86	0.0407	S
2 min	-1364.96 ± 3716.61	1778.6 ± 3729.65	0.0044	S
3 min	-2127.4 ± 2900.86	826.8 ± 3849.2	0.0036	S
4 min	-2199.88 ± 3402.56	374.72 ± 3921.94	0.0167	S
5 min	-2560 ± 3407.95	-351.88 ± 3688.58	0.0328	S
6 min	-2787.28 ± 3237.7	-412.88 ± 3646.74	0.0187	S
7 min	-2803.24 ± 2926.35	-389.68 ± 3915.35	0.0172	S
8 min	-2947.72 ± 2790.27	-442.72 ± 4240.54	0.0172	S
9 min	-3129.24 ± 2581.19	-676 ± 3898.03	0.0116	S
10 min	-3433.04 ± 2841.36	-945.04 ± 3528.23	0.0085	S

(t test . p value is significant if less than 0.05. S- Significant, NS- Not significant)

**Table-5:** Comparison of mean of change of Rate pressure Product (RPP) from Baseline Between F group (Fentanyl) and T group (Thiopentone)

in T group (-30.56) which is statistically not significant. However later on changes remain significant till the end of study. Table 4 shows that, when the mean change in MBP is compared in both the groups, it is maximum after induction, in F group (-24.44 mm of Hg) and in T group (-22.96 mm of Hg) which is statistically not significant.

When compared the mean change of RPP in both the groups, it is maximum after induction, in F group (-4439.24) and in T group (-2759.76) which is statistically not significant. However later on changes remain significant in both groups till the end of study except at cuff inflation as shown in Table 5.

Analysis of data in Table 6 shows that when both the groups are compared the changes in CVP are statistically not significant at all time points during the study period.

## DISCUSSION

### Heart Rate changes with Thiopentone

J. N. Broadly<sup>5</sup> found that with induction the heart rate was unchanged. Laryngoscopy and endotracheal intubation caused an increase in heart rate. Grounds RM et al<sup>6</sup> observed an initial, but statistically insignificant increase in heart rate was found with Thiopentone. Kling D et al<sup>7</sup> noted an increase in heart rate during induction. Joerg Tarnow et al<sup>8</sup> observed a small increase in heart rate with Thiopentone. Minati Choudhury et al<sup>9</sup> shown that there was a significant decrease in the heart rate in comparison to the baseline (-7 to -15%, P = 0.001) after induction. They attributed it to the loss of sympathetic stimulation on induction.

Present study had shown results similar to all previous studies except Minati Choudhury et al<sup>9</sup> in which they have found decrease in heart rate during induction.

### Heart Rate changes with Fentanyl

Thwdore H. Stanley et al<sup>10</sup> noted that with Fentanyl (20 µg / kg) there was decrease in heart rate. Waller JL et al<sup>11</sup> observed

Stage	F Group n=25 (Mean ± SD)	T Group n=25 (Mean ± SD)	p Value	Significance
Baseline (After premedication)	0.00	0.00		
After Induction	-0.4 ± 2.27	-0.84 ± 2.19	0.4894	NS
During Laryngoscopy and Intubation	0.64 ± 2.71	0.64 ± 2.77	1.0000	NS
Cuff Inflation	1.12 ± 2.88	0.88 ± 2.17	0.7404	NS
1 min	1.12 ± 2.6	0.8 ± 2.38	0.6522	NS
2 min	1.08 ± 2.64	0.88 ± 2.65	0.7906	NS
3 min	0.84 ± 2.41	1.36 ± 2.43	0.4512	NS
4 min	1.16 ± 2.82	1.2 ± 2.61	0.9588	NS
5 min	1.28 ± 3.08	0.68 ± 2.41	0.4464	NS
6 min	1.2 ± 2.71	0.8 ± 2.58	0.5954	NS
7 min	0.88 ± 2.55	1.04 ± 2.64	0.8285	NS
8 min	1.04 ± 2.39	0.96 ± 2.42	0.9069	NS
9 min	1.12 ± 2.47	0.96 ± 2.65	0.8263	NS
10 min	1.08 ± 2.53	0.92 ± 2.58	0.8258	NS

(t test . p value is significant if less than 0.05. S- Significant, NS- Not significant)

**Table-6:** Comparison of mean of change of Central Venous Pressure (CVP) from Baseline between F group (Fentanyl) and T group (Thiopentone)

that heart rate decreased after induction with 10 µg/kg Fentanyl and increased after tracheal intubation from control value, though the HR increased after administration of full dose of Fentanyl (50 µg/kg) along with Pancuronium. Barash PG et al<sup>12</sup> concluded that heart rate was unchanged during induction and intubation. C. K. Spiss et al<sup>13</sup> found that both groups (Alfentanil 5 mg vs. Fentanyl 0.5 mg) manifested significant decreases in heart rate (17-22%). James G. Bovill et al<sup>14</sup> reported that the heart rate increased after induction and intubation. Bazaral MG et al<sup>15</sup> concluded that the use of a Pancuronium bromide and Metocurine iodide mixture at a dose twice the ED<sub>95</sub>, does have an effect on HR similar to the changes observed in this study. In present study we used Vecuronium

as muscle relaxant.

Present study had shown results similar to all previous studies, except James G. Bovill et al<sup>14</sup>, John M. Murkin et al<sup>16</sup>, Bazara MG et al.<sup>15</sup> In all these three studies there was increase in heart rate after induction with Fentanyl, in which they have used Pancuronium as muscle relaxant and attributed it for these changes.

#### **Blood Pressure changes with Thiopentone**

J. N. Broadly<sup>5</sup> noted a reduction of arterial pressure. Laryngoscopy and endotracheal intubation caused an increase in arterial pressure. Grounds RM et al<sup>6</sup> found the fall in arterial blood pressure with Thiopentone. Joerg Tarnow et al<sup>8</sup> reported that Thiopentone caused little changes in systolic, diastolic and in mean arterial pressure. Reiz S et al<sup>17</sup> noted a decrease in arterial blood pressure (-27%).

Present study had shown results similar to all previous studies in which they have found decrease in blood pressure after induction with Thiopentone, with slight increase from baseline during laryngoscopy and intubation.

#### **Blood Pressure changes with Fentanyl**

Thwodore H. Stanley et al<sup>10</sup> found that with Fentanyl (20 µg / kg) there was decrease in arterial blood pressure. Barash PG et al<sup>12</sup> concluded that SBP was unchanged during induction and intubation. Bazara MG et al<sup>15</sup> found that there was a decrease in the MAP after induction then it increased after intubation. Present study had shown results similar to all previous studies in which they have found decrease in blood pressure during induction with Fentanyl.

#### **RPP Changes**

Soon Hong Moon et al<sup>18</sup> found that RPP revealed no significant change. During intubation RPP slightly increased but was not statistically significant ( $p > 0.05$ ). Waller JL et al<sup>11</sup> observed that there was decrease in RPP after induction with Fentanyl 10 µg/kg. These findings are similar to the present study.

#### **CVP changes with Thiopentone-**

Al-Khudhatri D et al<sup>19</sup> observed no significant changes in either group in central venous pressure. Minati Choudhury et al<sup>9</sup> in their study has given all patients Morphine 0.2 mg/kg and Fentanyl 4µg/kg. There was no significant change in central venous pressure during induction and intubation.

#### **CVP changes with Fentanyl**

Barash PG et al<sup>12</sup> concluded that heart rate was unchanged during induction and intubation. Bovill JG et al<sup>14</sup> concluded that the changes were insignificant. Bazara MG et al<sup>15</sup> found that there was increase in CVP after intubation.

Present study had shown results similar to all previous studies in which they have found no significant change in CVP.

#### **Awareness**

No patients in the present study had awareness after induction, during laryngoscopy and intubation. Stanley TH et al<sup>10</sup> found that unresponsiveness was achieved with an average of  $11 \pm 3$  µg/kg of Fentanyl. Waller JL et al<sup>11</sup> observed that patients failed to respond to commands after they had received  $10 \pm 3$  µg/kg Fentanyl. Bazara MG et al<sup>15</sup> stated that no patients recalled events in the operating room subsequent to breathing through an anesthesia mask.

#### **Limitations of the present study –**

Patients receiving Atropine and Vasopressors / Inotropes for bradycardia and hypotension should have been dropped for further data collection in the study.

Sample size is limited. Larger sample size may be studied.

The other cardiovascular parameters like Cardiac Output, Pulmonary Artery Pressure, ST- changes etc. are not studied.

#### **CONCLUSION**

Though Thiopentone (3 mg/kg) is not superior to Fentanyl in all respect for cardiovascular stability in the patients of mitral stenosis undergoing mitral valve replacement surgery, it (Thiopentone 3 mg/kg) seems better choice for induction than Fentanyl (10 µg/kg) when maintenance of Blood pressure is the priority. But if Heart rate control is desirable then Fentanyl (10 µg/kg) seems a better choice.

#### **REFERENCES**

1. Howie MB, Gravlee GP. Induction of Anesthesia. In: Hensley FA, Martin DE, Gravlee GP, editors. Practical approach to cardiac anaesthesia, 4<sup>th</sup> ed. Philadelphia: Lippincott Williams and Wilkins; 2008. p. 164.
2. Padmavathi S. Rheumatic fever and rheumatic heart disease in developing countries. Bull World Health Organ. 1978;56:543-50.
3. Deepak Tempe. Clinical practice of Cardiac anaesthesia, 3<sup>rd</sup> ed. New Delhi: CBS Publishers; 2013. p.96.
4. Kalpan JA, Reich DL, Savino JS, editors. Kaplan's Cardiac Anaesthesia, 5<sup>th</sup> ed. Page no- 679.
5. Broadly JN, Taylor PA. An assessment of Althesin for the induction of anaesthesia in cardiac surgical patients: a comparison with Thiopentone. British J Anaesth. 1974;46:687-91.
6. Grounds RM, Twigley AJ, Carli F, Whitwam JG, Morgan M The haemodynamic effects of intravenous induction. Comparison of the effects of Thiopentone and Propofol. Anaesthesia. 1985;40:735-40.
7. Kling D, Laubenthal H, Börner U, Boldt J, Hempelmann G. Comparative hemodynamic study of anesthesia induction with Propofol (Diprivan), Thiopental, Methohexital, Etomidate and Midazolam in patients with coronary disease. Anaesthesist. 1987;36:541-7.
8. Joerg T, Wolfgang H, Walter KE. Alfathesin and Thiopentone as induction agents for coronary artery surgery.

- Canadian Anaesthetists' Society Journal 1980;27:338-44.
9. Choudhury M, Singh R, Kapoor PM, Kiran U. A randomized trial of anesthetic induction agents in patients with coronary artery disease and left ventricular dysfunction. *Ann Card Anaesth* 2010;13:217-223.
  10. Thwdore H. Stanley, MD Lynn R. Webster, MD. Anesthetic Requirements and Cardiovascular effects of Fentanyl- Oxygen and Fentanyl- Diazepam- Oxygen anesthesia in Man. Salt Lake City, Utah. *Anesth Anal* 57:411-416, 1978.
  11. Waller JL, Hug CC Jr, Nagle DM, Craver JM. Hemodynamic changes during Fentanyl-Oxygen anesthesia for aortocoronary bypass operation. *Anesthesiology*. 1981 Sep;55:212-7.
  12. Barash PG, Giles R, Marx P, Berger H, and Zaret B. Yale. Intubation: Is Low Dose Fentanyl Really Effective? University School of Medicine, New Haven, Connecticut. *Anesthesia and Analgesia* Vol 61. No 2, February 1982 Page 168-69.
  13. Spiss CK, Coraim F, Haider W, White PF. Haemodynamic effects of Fentanyl or Alfentanil as Adjuvants to Etomidate for Induction of Anaesthesia in Cardiac Patients *Acta Anaesthesiologica Scandinavica* 1984;28:554-6.
  14. James G. Bovill, MD, FFARCSI, Patrick J. Warren, MD, Jaap L. Schuller, MD, Harry B. van Wezel, MD and Martine H. Hoeneveld. Comparison of Fentanyl, Sufentanil, and Alfentanil Anesthesia in Patients Undergoing Valvular Heart Surgery. Department of Anaesthesia, Academic Hospital, University of Amsterdam, Wilhelmina Gasthuis, Amsterdam, The Netherlands. *A and A* December 1984;63:1081-6.
  15. Bazaral MG, Wagner R, Abi-Nader E, Estafanous FG. Comparison of the effects of 15 and 60 micrograms/kg Fentanyl used for induction of anesthesia in patients with coronary artery disease. *Anesth Analg*. 1985 Mar; 64:312-8.
  16. Murkin JM, Moldenhauer CC, Hug Jr. CC. High-dose Fentanyl for rapid induction of anaesthesia in patients with coronary artery disease. *Can Anaesth Soc J* 1985;32:320-5.
  17. Reiz S, Balfors E, Friedman A, et al. Effects of Thiopentone on cardiac performance, coronary hemodynamics and myocardial oxygen consumption in chronic ischemic heart disease. *Acta Anaesthesiol Scand* 1981 Apr; 25:103-10.
  18. Moon SH, Kwon ML. Cardiovascular Responses during Fentanyl - O<sub>2</sub> Anesthesia for Cardiac Valvular Replacement Operation. *Journal of Korean Society of Anaesthesiologists* 1989;22:49-55.
  19. Al-Khudhatri D, Whitwam JG, Chakrabarti MK, Askitopoulou H, Grundy EM, Powrie S. Haemodynamic effects of Midazolam and Thiopentone during induction of anaesthesia for coronary artery surgery. *British J Anaesth* 1982;54:831-833.