

## COMPARISON BETWEEN HEMODYNAMIC CHANGES OF ATRACURIUM AND CISATRACURIUM IN PATIENTS UNDERGOING CABG SURGERY

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### ABSTRACT

**Objective:** To compare the hemodynamic effects of Atracurium versus Cisatracurium in Cardiac Patients Undergoing coronary artery bypass graft Surgery.

**Study Design:** Randomized controlled trial.

**Place and Duration of Study:** The study was conducted at Armed Forces Institute of Rawalpindi, a tertiary care hospital, after seeking hospital ethics committee permission, from Apr 2019 to Oct 2019.

**Methodology:** A total of 200 consecutive patients were randomized into two equal groups, group-A and group-C (100 in each group). Group-A patients were induced with 0.5mg/kg of Atracurium, followed by infusion @ 10µg/kg/min whereas group C patients received Cisatracurium @ 0.2mg/kg at induction, followed by infusion @ 2µg/kg/min during the maintenance phase. Systolic blood pressure, diastolic blood pressure, Mean arterial pressure and heart rate were noted at different intervals of both groups. Decrease in systolic blood pressure of >20% from baseline or a value <90 mmHg was considered as hypotension.

**Results:** The mean age of patients was 57.5 ± 6.75 years and 56.52 ± 4.46 years in group A and group C respectively. Systolic and diastolic blood pressure was better maintained with cisatracurium than atracurium. Also Mean arterial pressure remained more stable with cisatracurium ( $p < 0.05$ ), but after opening of sternum and before going on cardiopulmonary bypass, the difference was insignificant in both groups ( $p > 0.05$ ). Heart rate remained more steady with cisatracurium ( $p < 0.05$ ) but had insignificant difference before going on cardiopulmonary bypass ( $p > 0.05$ ).

**Conclusion:** Cisatracurium found to be more suitable drug in maintaining the stable hemodynamics and preventing fluctuations in pressure in cardiac patients undergoing on-pump bypass surgery

**Keywords:** Atracurium, Cisatracurium, Diastolic blood pressure, Hemodynamic effects, Heart rate, Mean arterial pressure, Systolic blood pressure.

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### INTRODUCTION

Neuromuscular Blockers act as an adjuvant to General anesthesia for different surgeries including cardiac surgery. Use of muscle relaxants can affect hemodynamics in cardiac patients through release of histamine, sympathomimetic action, ganglionic blockade or via antimuscarinic effects. Thus, choice of muscle relaxant in open heart surgery patients becomes of considerable importance to maintain stable hemodynamics.

Previously long acting neuromuscular blockers such as Pancuronium were routinely used in cardiac surgery patients. Pancuronium was associated with tachycardia and longer paralysis

particularly in patients with disturbed renal function, resulting in prolonged extubation time. With the advent of concept of "Fast-track anaesthesia" in cardiac surgery, it was the need of time that muscle relaxants used for cardiac surgery should have rapid onset, short duration of action, elimination independent of hepatic or renal pathway, and these should not affect hemodynamic stability. Non-depolarizing neuromuscular blocking agents with such characteristics are atracurium and cisatracurium. Both are promising drugs with predictable recovery due to non-organ dependent elimination<sup>1</sup>.

Both agents are benzylisoquinolones with intermediate duration of action and spontaneously degrade at physiological pH via Hofmann elimination to yield laudanosine. Hofmann elimi-

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nation is an organ-independent degradative mechanism so there is little or no risk when using these medications in patients with liver or renal disease. Administration of atracurium, however, is associated with histamine release that can cause cutaneous flushing, hypotension, and tachycardia especially with large bolus doses and rapid infusions<sup>2</sup>. These effects of atracurium are compounded by other anesthesia drugs and patient factors<sup>3</sup>.

Cisatracurium, an R<sup>1</sup>-cis isomer of atracurium, is three to four times more potent for muscle relaxation, but has less influence on autonomic and cardiovascular system. It is not associated with histamine release even in large doses<sup>4,5</sup>. All these characteristics of cisatracurium compared with atracurium make it a favorable choice for patients undergoing coronary artery bypass graft surgery as it causes less effects on hemodynamics<sup>6,7</sup>.

Since Cisatracurium does not increase the plasma histamine level to more than 8x ED<sub>95</sub>, therefore, side effects resulting from elevated plasma histamine concentration will not be seen in the patients with cardiac disease<sup>8</sup>. It seems that Cisatracurium compared to Atracurium is an advantageous muscle relaxant for patients under coronary graft surgery as it causes less effect on hemodynamic indexes<sup>9</sup>.

Cisatracurium, is a relatively newer drug in our setup, so the rationale of the study was to compare it with most commonly used muscle relaxant, Atracurium, in terms of hemodynamic changes in patients undergoing on pump bypass surgery.

## METHODOLOGY

This randomized control trial study was carried out at Department of Anesthesiology and Intensive care, Armed Forces institute of Cardiology from April 2019 to October 2019. Two Hundred patients accomplishing the inclusion/ exclusion standards were chosen for study. They were then distributed into two groups of 100 patients each. Power of the test was kept at 80% and level of significance at 5%. Non probability Consecu-

tive sampling technique was used. Adult patients of both genders, regardless of age, having normal sinus rhythm scheduled for elective CABG were included in the study. While patients undergoing emergency CABG, having Atrial flutter/Atrial Fibrillation, or Atrio-ventricular block degrees 2 and 3 and surgery not requiring Cardiopulmonary bypass were excluded from the study.

After detailed pre-anaesthesia assessment, two hundred patients meeting the selection criteria were included in the study after seeking approval from the hospital ethics committee and an informed written consent obtained. They were then randomly divided into two groups (group A for Atracurium and group C for cisatracurium), with 100 hundred participants in each group, by using computer generated codes. Demographic characteristics like age and sex were taken. Upon arrival in operation theatre, Standard monitoring applied which included baseline measurement of Non invasive Blood pressure (BP) and recording of heart rate (HR), pulse oximetry and electrocardiogram in supine position. Intravenous line maintained peripherally with 16/18-gauge cannula and arterial line secured into left radial artery for continuous measurement of systolic and diastolic blood pressure and mean arterial pressure.

In both groups, Induction of General anaesthesia achieved with IV anaesthetic agent Propofol and opioid morphine. For muscle relaxation, group-A patients received Atracurium @ 0.5mg/kg and group-C received Cisatracurium @ 0.2mg/kg. During the surgery, anaesthesia maintained with volatile anaesthetic isoflurane at 1 MAC and same muscle relaxant used during induction stage by continuous infusion through syringe Pump (Atracurium @10µg/kg/min in group A and Cisatracurium @ 2µg/kg/min in group C). An anaesthesiology resident who was blinded to the study recorded baseline parameters of patients including systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP) and heart rate before induction. The parameters were also noted on 1 minute before intubation, 2 minutes after intubation, after surgical incision, after opening the sternum and before going on

Cardiopulmonary bypass (CPB). MAP were calculated using formula  $(SBP + 2 DBP/3)$ . Change in hemodynamic i.e. blood pressure, MAP and heart rate were calculated.

**Table-I: Demographics of patients.**

|              | Groups      |                |
|--------------|-------------|----------------|
|              | Atracurium  | Cis-atracurium |
| n            | 100         | 100            |
| Age (years)  | 57.5 ± 6.75 | 56.52 ± 4.46   |
| Gender (M:F) | 58 : 42     | 56 : 44        |
| Hypertension | 50          | 54             |
| Diabetes     | 40          | 36             |
| Smoking      | 38          | 42             |

statistical analysis of demographic data, descriptive statistics were done. For comparison of groups, independent student t-test was applied for continuous variables and Chi square test for categorical variables. Statistical significance was determined as  $p$ -value  $\leq 0.05$ .

**RESULTS**

The mean age of patients in atracurium group was  $57.5 \pm 6.75$  years while mean age of patients in cis-atracurium group was  $56.52 \pm 4.46$  years. There were 58 male and 42 females in atracurium group as compared to 56 males and 44 females in cis-atracurium group. Hypertension was present in 50% cases in atracurium group

**Table-II: Comparison of hemodynamics in both groups.**

| Parameter                              | Group        |                | p-value |
|--|--------------|----------------|---------|
|  | Atracurium   | Cis-atracurium |         |
| <b>Systolic Blood Pressure</b>         |              |                |         |
| At baseline                            | 152.00±11.50 | 150.00±13.78   | 0.267   |
| 1 minute before intubation             | 105.80±6.31  | 110.80±4.86    | 0.000   |
| 2 minutes after intubation             | 102.00±4.61  | 107.70±7.99    | 0.000   |
| After surgical incision                | 119.40±4.34  | 121.80±8.45    | 0.012   |
| After opening the sternum              | 130.10±4.87  | 127.90±4.28    | 0.001   |
| Before going on cardiopulmonary bypass | 99.90±3.26   | 98.00±3.18     | 0.000   |
| <b>Diastolic Blood Pressure</b>        |              |                |         |
| At baseline                            | 89.00±6.59   | 89.00±8.17     | >0.999  |
| 1 minute before intubation             | 62.54±4.40   | 64.0±4.97      | 0.001   |
| 2 minutes after intubation             | 61.90±3.88   | 64.90±3.96     | 0.000   |
| After surgical incision                | 71.90±3.16   | 73.30±3.27     | 0.002   |
| After opening the sternum              | 79.76±4.50   | 77.30±3.05     | 0.000   |
| Before going on cardiopulmonary bypass | 57.68±3.94   | 57.20±3.91     | 0.388   |
| <b>MAP</b>                             |              |                |         |
| At baseline                            | 99.82±8.17   | 103.90±9.50    | 0.001   |
| 1 minute before intubation             | 70.30±4.43   | 74.90±4.87     | 0.000   |
| 2 minutes after intubation             | 69.22±2.87   | 72.90±4.62     | 0.000   |
| After surgical incision                | 78.34±3.26   | 81.10±2.89     | 0.000   |
| After opening the sternum              | 84.90±3.69   | 85.20±3.01     | 0.529   |
| Before going on cardiopulmonary bypass | 66.40±3.34   | 66.00±3.76     | 0.427   |
| <b>Heart Rate</b>                      |              |                |         |
| At baseline                            | 64.32±5.34   | 66.32±6.08     | 0.014   |
| 1 minute before intubation             | 71.72±4.43   | 73.30±5.56     | 0.027   |
| 2 minutes after intubation             | 72.68±3.86   | 73.56±3.36     | 0.184   |
| After surgical incision                | 80.16±3.51   | 81.40±4.72     | 0.036   |
| After opening the sternum              | 83.92±3.71   | 82.30±4.29     | 0.005   |
| Before going on cardiopulmonary bypass | 74.20±3.49   | 74.60±3.31     | 0.406   |

Statistical package for social sciences (SPSS) version 23.0 was used to analyze the data. For

while in 54% cases in cis-atracurium group. Diabetes was present in 40% cases in atracurium

group while in 36% cases in cis-atracurium group (table-I).

Systolic and diastolic blood pressure was significantly better maintained with cis-atracurium than atracurium. Mean arterial pressure (MAP) remained more stable with cis-atracurium ( $p < 0.05$ ), but after opening of sternum and before

### DISCUSSION

Modern day surgeries are done with ease of using neuro-muscular blocking agents<sup>10</sup>. Among such blockers, Atracurium, rocuronium, cis-atracurium and vecuronium are good options in cardiac patients because of their favorable cardiovascular profile.

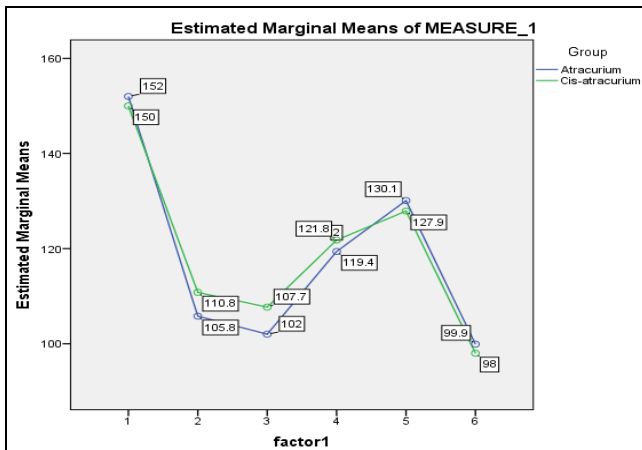


Figure-1: Showing change in systolic blood pressure in both group on follow-up ( $p > 0.05$ ).

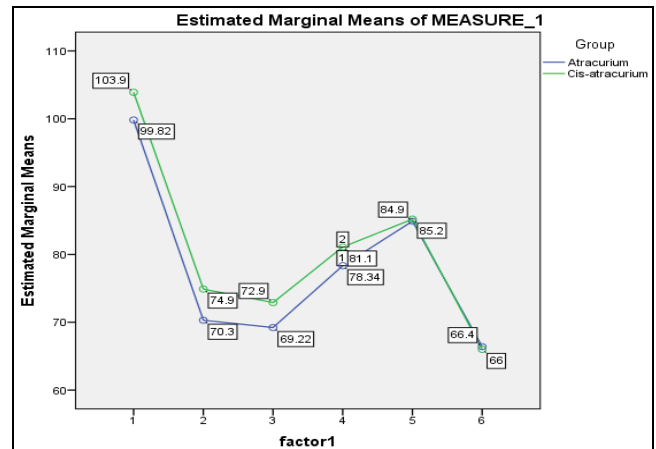


Figure-3: Showing change in mean arterial pressure in both group on follow-up ( $p < 0.05$ ).

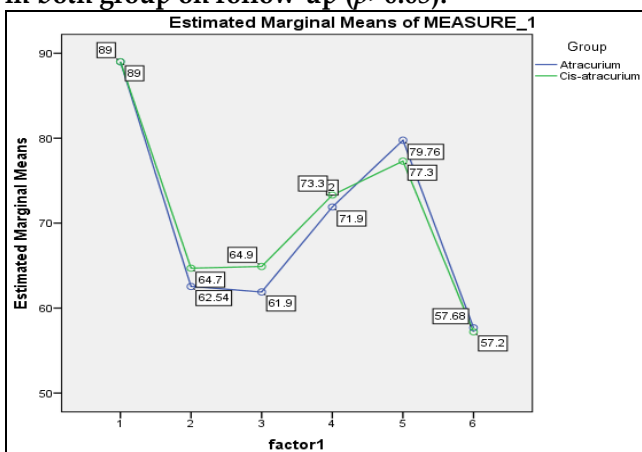


Figure-2: Showing change in diastolic blood pressure in both group on follow-up ( $p > 0.05$ ).

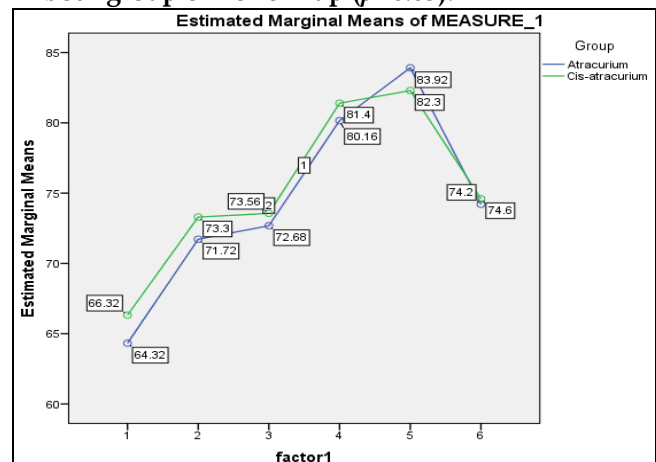


Figure-4: Showing change in heart rate in both group on follow-up ( $p > 0.05$ ).

going on cardiopulmonary bypass, the difference was insignificant in both groups ( $p > 0.05$ ). Heart rate was also more steady with cis-atracurium as compared to atracurium ( $p < 0.05$ ) but had insignificant difference before going on cardiopulmonary bypass ( $p > 0.05$ ) (table-II).

Overall, there was insignificant difference observed between both groups for systolic, diastolic blood pressure and heart rate while significant for MAP (fig-1 to 4).

Perioperative management of patients with cardiac disease may become quite challenging, especially if there is any underlying pre-excitation syndrome or even worse, if it is undiagnosed. It is possible that the poorly controlled or unknown underlying electro-physiological abnormality will become unmasked during anaesthesia and surgery, giving rise to potentially life-threatening arrhythmias<sup>11</sup>.



Atracurium is the most commonly used drug for Skeletal muscle relaxation and endotracheal intubation but its use in cardiac patients is complicated by release of histamine. The most common side effects associated with histamine release are flushing and erythema. Less commonly, more severe adverse effects can occur and include tachycardia, bradycardia, hypotension, dyspnea, bronchospasm, urticaria, laryngospasm or wheezing<sup>12</sup>. Studies have previously demonstrated that a MAP fall of 30mmHg can be seen within 2 minutes of administration. In the meantime, care should be used when using muscle relaxants<sup>13</sup>.

Cisatracurium, on the other hand, has lower tendency for histamine release, is more potent but with slightly longer onset time and more predictable recovery profile<sup>14</sup>. Its use in cardiac surgery is increasing because of its favorable cardiovascular profile<sup>14</sup>, suitability as adjuvant for fast tracking cardiac surgery<sup>15</sup> and facilitating early extubation after surgery, thus reducing postoperative ICU stay<sup>16</sup>.

In our trial, the maintenance of systolic and diastolic blood pressure was significantly better with cis-atracurium than atracurium. Also Mean arterial pressure and heart rate remained more steady with cisatracurium but had insignificant difference before going on cardiopulmonary bypass ( $p>0.05$ ). Ghorbanlo *et al*, also observed significant difference between both groups regarding the hemodynamics of patients, in all stages of open heart surgery and found that administering Cisatracurium as the muscle relaxant is advantageous and better<sup>17</sup>.

In another randomized trial in cardiac patients undergoing for coronary graft surgery, Cis-atracurium was given 0.1–0.4mg/kg and there was no high plasma histamine level. Significant changes in hemodynamic indexes including heart rate and MAP was not observed, either between cis-atracurium and other muscle relaxant<sup>17</sup>. Cis-atracurium 0.1mg/kg showed slow onset of action and provided excellent intubating conditions. Clinical duration and recovery

scores were significantly better with cisatracurium. It is persuasive and safe drug with exceptional cardiovascular steadiness<sup>18</sup>.

## CONCLUSION

Our study concluded that administration of cisatracurium in patients undergoing coronary bypass surgery was associated with more stable hemodynamic indices as compared to atracurium.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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