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# A Comparison Between the Hemodynamic Effects of Cisatracurium and Atracurium in Patient with Low Function of Left Ventricle who are Candidate for Open Heart Surgery

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## ABSTRACT

**Background**: The need for muscle relaxants in general anesthesia in different surgeries including cardiac surgeries, and the type of relaxant to be used considering its different hemodynamic effects on patients with heart disease can be of considerable importance. In this study, the hemodynamic effects of two muscle relaxants, Cisatracurium and Atracurium in patients whit low function of left ventricle who are candidate for open heart surgery have been considered. **Method**: This study has been designed as a randomized prospective double-blind clinical trial. The target population included all adult patients with heart disease whose ejection fraction reported by echocardiography or cardiac catheterization was 35% or less before the surgery, and were candidate for open heart surgery in Shahid Rajaei Heart Center. Taking into account the inclusion and exclusion criteria, the patients were randomly placed in two groups of 30 people each. In the induction stage, all the patients received midazolam, etomidate, and one of the considered muscle relaxant, either 0.2 mg/kg of cisatracurium or 0.5mg/kg of Atracurium within one minute. In the maintenance stage of anesthesia, the patients were administered by infusion of midazolam, sufentanil and the same muscle relaxant used in the induction stage. The hemodynamic indexes were recorded and evaluated in different stages of anesthesia and surgery as well as prior to transfer to ICU. **Results**: In regard with descriptive indexes (age and sex distributions, premedication with cardiac drugs, ejection fraction before surgery, basic disease) there was no statistically significant difference between the groups. **Conclusions**: The significant difference of hemodynamic indexes between the two groups of this study, and the need for hemodynamic stability in all stages of surgery for patients with low function of left ventricle who are candidate for open heart surgery, proves that administering Cisatracurium as the muscle relaxant is advantageous and better.

**Key words: muscle relaxant, Atracurium, Cisatracurium, low function of left ventricle, open heart surgery.**

## 1. INTRODUCTION

There is a need for muscle relaxants in general anesthesia in different surgeries including cardiac surgeries, and the type of relaxant to be used considering their different hemodynamic effects on patients with heart disease can be of high

importance (1) in a way that the importance of administering muscle relaxants as a necessary drug in surgeries was suggested in 1942 (2, 3). The muscle relaxants can cause hemodynamic changes through releasing histamine, ganglion block, antimauscarine effects on heart, or sympathomimetic action. Atracurium which is a muscle relaxant in the category of non-depolarizing relaxants belonging to benzy1 isoquinolinum group of drugs, has been attractive option because of independence of its metabolism to main body organs such as liver and kidney, especially in patients with hepatic and renal disease. In the meantime, the hemodynamic changes resulting from release of histamine after administering Atracurium can be a problem especially in cardiovascular patients (4, 5). Cisatracurium, an isomer of Atrucium, will be metabolized like Atracurium through Hoffman mechanism, but contrary to Atracurium, ester hydrolysis has no role in its metabolism (6, 7). When a patient is given a histamine releaser drug, the clinical signs of elevated histamine concentration such as hypotension, tachycardia, head and face erythema will be seen once the plasma concentration is increased by2-3 times its initial level, and the severity of these clinical signs depends on the dose and speed of administration (8, 9). In patients with severe cardiovascular disease, Cisatracurium with a dose of 6Xed95 (the effective dose required to produce 95% of muscle twitch response) or 0.3mg/kg had no effects on mean arterial blood pressure (10, 11). Since Cisatracurium does not increase the plasma histamine level to more than 8x ED95, therefore, side effects resulting from elevated plasma histamine concentration will not be seen in the patients with cardiac disease (12). 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 (13). The purpose of this randomized double-blind clinical trial was to compare the hemodynamic changes of the two muscle relaxants, Atracurium and Cisatracurium, used in patients with low function of left ventricle who were candidate for open heart surgery.

## 2. MATERIALS AND METHODS

The patients were randomly placed in either of two groups using the following inclusion and exclusion criteria. First of all, the dose of the relaxants to be administered, Atracurium or Cisatracurium was identical for both groups. During the induction, the anesthetist gave the patient an IM injection of relaxant within one minute time, without being aware of the type of relaxant. Therefore, both the person filling out the questionnaire and the anesthesiologist were blind to the type of muscle relaxant.

Inclusion criteria:

- Patients with a cardiac disease history for more than 18 years and an ejection fraction of 35% or less who are candidate to undergo an elective cardiac surgery.
- Cardiac surgery using cardiopulmonary bypass.

Exclusion criteria:

- Ejection fraction before surgery more than 35%
- Urgent surgeries;
- Surgery without cardiopulmonary bypass;
- Atrial fibrillation;
- Atrioventricular blocks, degrees 2 and 3.

After obtaining a written consent to inclusion in the study, patients meeting the above criteria were randomly divided in two groups of Atracurium (30 patients) and Cisatrurium (30 patients). They were then admitted in the operating room in supine position and the preliminary steps for a general anesthesia were taken. A peripheral IV was made using an angio-catheter no.16 or 18. After a local anesthesia, the atrial line was secured through the left radial vein for continuous monitoring of systolic and diastolic blood pressure and mean arterial pressure. Monitoring the patients venous $O_2$ saturation and electrocardiogram started immediately upon their reception in the operating room. The anesthesia was include using 5 μg/kg of fentanyl, 0.2 mg/kg of etomidate, and a muscle relaxant, either 0.5 mg/kg of Atracurium or 0.2 mg/kg of Cisatracurium. Before induction, the systolic and diastolic BP as well as mean arterial pressure were recorded in the questionnaire as the basic vital signs. The vital signs were also recorded on minute before tracheal intubation, one minute after intubation, before surgery incision, after surgery incision, after opening the sternum, before starting pumping, after pumping and before transfer to ICU. The anesthesia was administered by infusion of anesthesia agent through perfusion pump or syringe pump ATOM-1235N, sufentanil (0.01 – 0.02 μg/kg/min) as amnestic agent, and the same relaxant used in the induction stage (Cisatracurium 2.5 μg/kg/min or Atracurium 10 μg/kg/min). During the surgery, isoflurane was used to have good level of anesthesia and stable hemodynamic. The patients were under controlled mechanical ventilation (CMV) with volume of 8-10 mm/kg and a respiratory rate 10-12/min with dragger anesthesia machine, and had mechanical ventilation with $O_2$ 100% during the study. In case of heart rate decrease to less than 45/min, 0.5-1 mg of IV atropine was administered, and in case of systolic pressure decrease to less than 80 mmhg, ephedrine was used in alternative doses of 10 mg, and finally if necessary adrenaline or dopamine was infused. If the heart rate increased to more than 100/min, 0.5 mg/kg esmolol (beta blocker) was used for at must two times. In case of increase of systolic blood pressure to more than 140mmhg, the dose of nitroglycerin was increased to 3 μg/kg/min or sodium nitro-proside was used with a dose of 0.5-1 μg/kg/min. Administration of any vasodilator or vasoconstrictor was recorded in the questionnaire. The date were then analyzed with the SPSS 13 software. As it was necessary to consider and evaluate the changes of hemodynamic indexes during the nine phases of monitoring and the influence of time on them in both groups, the variance analysis or repeated measurement analysis of variance was used.

## 3. RESULTS

Comparing the patients of the two groups under study who had received Atracurium or Cisatracurium, there was no statistically meaningful difference between them

| p-value | Atracurium (Standard deviation) | Cisatracurium (Standard deviation) | Indicator |
|---|---|---|---|
| 0.28 | 60(7.5) | 58(10.3) | Age |
| 0.30 | 157.6(12.8) | 159(12.2) | Size |
| 0.4 | 69.69(9) | 67.84(7) | Weight |
| 0.43 | 22 | 26 | Cigarette |
| 0.83 | 1 | 5 | Addiction |
| 0.64 | 10 | 11 | Hypertension |
| 0.66 | 22 | 22 | Beta blocker |
| 0.58 | 21 | 15 | Inhibitors ACE |
| 0.53 | 9 | 12 | Heart- failure |
| 0.55 | 10 | 13 | Diabetes |
| 0.67 | 30 | 28 | Ejection fraction |

Table 1. Patients in both groups compared to baseline indicators

| p-value | Atracurium | Cisatracurium | The basic hemodynamic parameters |
|---|---|---|---|
| 0.28 | 141 | 125 | Systolic blood pressure |
| 0.46 | 71 | 68 | Diastolic blood pressure |
| 0.13 | 93 | 86 | Mean arterial pressure |
| 0.52 | 80 | 77 | Heart rate |

Table 2. Comparison of baseline hemodynamic parameters in patients

in regard with age, sex, height, smoking, addiction to narcotics, using drugs such as beta blockers, calcium blockers, ACE inhibitors, and ejection fraction (Table 1).

The groups didn't show any statistically meaningful difference in basic hemodynamic indexes including systolic pressure, diastolic pressure, mean arterial pressure, and heart rate either (Table 2).

After recording the basic hemodynamic indexes and induction of general anesthesia, the hemodynamic indexes were recorded again in the following stage: 1 minute before tracheal intubation, 1 minute after intubation, before surgical incision, after surgical incision, after sternotomy, before connection the pump, after disconnecting the pump, and before transferring the patients to ICU.

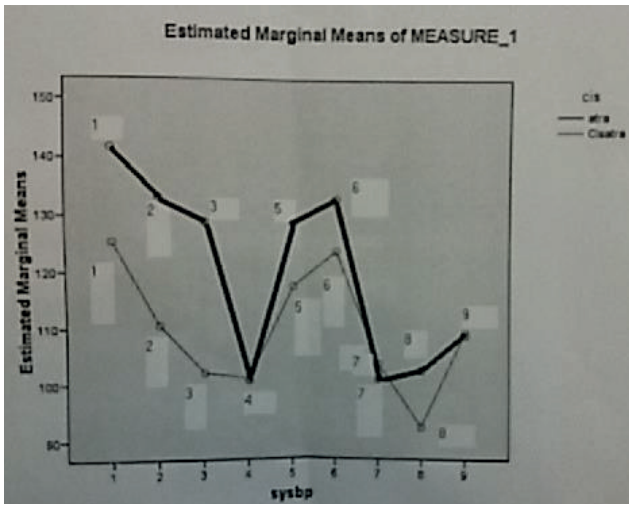


Figure 1. Comparison of changes in systolic blood pressure between the two groups in nine steps. 1. Before induction, 2. One minute before intubation, 3. One minute after intubation, 4. Before surgical, 5. After surgical, 6. After Sternotomy, 7. Before the pump, 8. After removing the pump, 9. Before being transferred to the intensive care unit,

Considering Figure 1, the flow of changes in systolic pressure in patients receiving Cisatracurium is smoother, and there is statistically meaningful difference between the two groups in this regard.(P-value =0.00)

According to Figure 2, the changes in diastolic pressure in Cisatracurium group compared to Atracurium group had meaningful difference (P-value=0.00), in a way that the decrease in diastolic pressure before surgical incision and after disconnecting the pump was more in Atracurium group.

The changes in mean arterial pressure had no statistically significant difference in the groups (P-value = 0.05).

As seen in Figure 3, there was a significant difference between the groups in regard with the range of changes in heart rate (P-value = 0.01)

Using vasoconstrictive and inotropic drugs made no significant difference in the groups (P-value = 0.3).

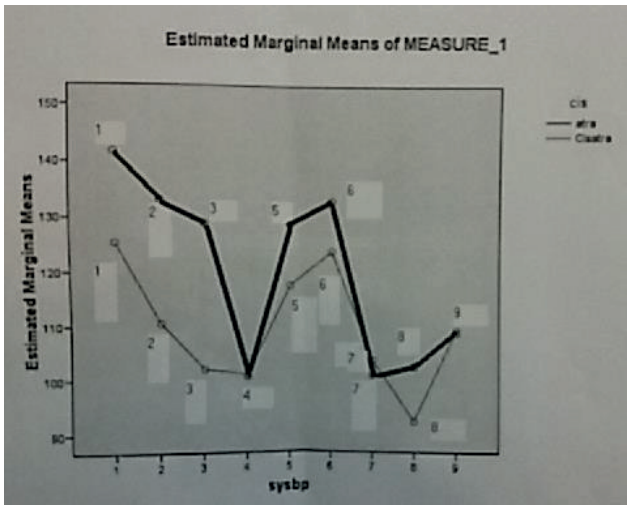


Figure 2. Comparison of changes in diastolic blood pressure between the two groups in nine steps. 1. Before induction, 2. One minute before intubation, 3. One minute after intubation, 4. Before surgical, 5. After surgical, 6. After Sternotomy, 7. Before the pump, 8. After removing the pump, 9. Before being transferred to the intensive care unit,

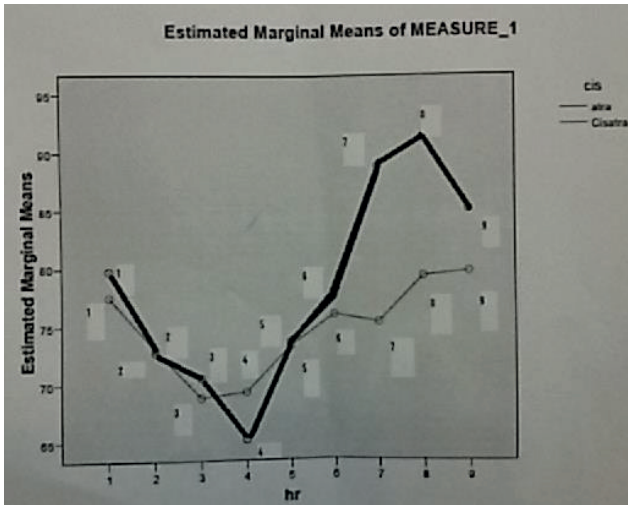


Figure 3. Compared changes in heart rate in both groups in nine steps, 1. Before induction, 2. One minute before intubation, 3. One minute after intubation, 4. Before surgical, 5. After surgical, 6. After Sternotomy, 7. Before the pump, 8. After removing the pump, 9. Before being transferred to the intensive care unit,

## 4. CONCLUSIONS

Using muscle relaxant in anesthesia for tracheal intubation and muscle paralysis during surgery has been proved, and in many surgery centers the most commonly used muscle relaxant in cardiac surgeries is "pancronium" (14). The desirability of pancuronium and using large doses of narcotics in cardiac surgeries goes back to years ago. In this method, pancuronium is administered to avoid the decrease in heart rate which results from use of narcotics. Nowadays, with increase of tendency to methods which require early and on time removal of tracheal tube as well as the tachycardia resulting from pancuronium in the induction stage, there is less tendency for its use. (15) Furthermore, contrary to intermediate-acting non depolarizing muscle relaxants, infusion of pancronium will cause longer paralysis after long surgeries.

Administering maximum 6Xed95 of IV Cisatracurium (equivalent to 0.3mg/kg) in patients with severe cardiovascular disease did not reveal undesired and significant clinical effects on heart rate and mean arterial blood pressure (16). In a clinical trial carried out on 141 patients volunteer for coronary graft surgery, Cisatracurium was administered 2-8xED95 (equivalent to 0.1 – 0.4 mg/kg)and there was no elevated plasma histamine concentration. In the same trial, significant changes in hemodynamic indexes including heart rate and mean arterial blood pressure was not seen, either (17). Another clinical trial made on 100 coronary graft surgery patients to compare the hemodynamic effects of Atracurium and Cisatracurium, reported similar stable hemodynamic. In the aforesaid trial, the range of mean without considering the standard deviation of patients ejection fraction was 42/6-45/9%. The premedication with beta and calcium channel blocker are also effective on hemodynamic indexes (18), but in our study, the two groups didn't show any difference in the frequency distribution of premedication with these drugs.

As it can be seen in the result of this study, the absence of a significant statistical difference between the two groups in regard with the changes in the mean arterial blood pressure ($p = 0.5$) was due to similarity of systolic and diastolic pressure ratio.

In this study, the maximum ejection fraction of all the patients was 35% and according to recorded result it seems that the hemodynamic indexes were more stable in Cisatracurium group.

• Conflict of interest: none declared.

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