



## Original Research Article

## Comparison of the effect of cisatracurium with or without magnesium pretreatment on neuromuscular blockade and hemodynamics, in cardiac surgery patients on cardiopulmonary bypass at SMS medical college

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## ABSTRACT

**Background:** An ideal neuromuscular blocking agent should have a high degree of potency, rapid onset of action and short duration of action. It should not cause haemodynamic changes through releasing histamine, ganglion block, anti-muscarinic effects on heart or sympathomimetic action. This study was designed to compare the effect of cisatracurium with or without magnesium pretreatment on neuromuscular blockade and hemodynamics in cardiac surgery patients on cardiopulmonary bypass with objective to assess and compare intubation conditions and timing of intubation in minutes and assess and compare clinical duration of blockade, haemodynamics variable and side effect if any.

**Materials and Methods:** Hospital based, prospective, randomized double blind observational study. Total 60 patients included in the study (30 in each group). Group A Pretreatment with mgso 4(50mg/kg BW in 100ml NS 10 mints before general anesthesia (GA) and muscle relaxant injection Cisatracurium 0.2mg/kg. Group B received 100ml NS 10 mints before general anesthesia (GA) and muscle relaxant injection Cisatracurium 0.2mg/kg.

**Results:** The mean onset of action of injection cis-atracurium after intubating dose in group A was 4.27±1.68 minutes as compared to 5.48±1 minutes in group B(p-value<0.001) which showed that onset of action was significantly less in group A as compared to group B. Duration of action of intubating dose of cisatracurium was prolonged by pre-treatment of Mgso4. Haemodynamic parameters were comparable and there was no statistically significant difference among both the groups. No side effect reported in our study.

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### 1. Introduction

Neuromuscular blockers(NMB) are an essential part of general anaesthesia An ideal neuromuscular blocking agent should have a high degree of potency, rapid onset of action and short duration of action. It should not cause haemodynamic changes through releasing histamine, ganglion block, anti muscarinic effects on heart or sympathomimetic action Cis atarcurium is new non depolarizing benzyloisoqualine neuromuscular blocker it is the 1R cis-1'R cis isomer of atracurium. It is eliminated mainly by the Hofmann degradation one

metabolite laudanosine<sup>1</sup> which has no neuromuscular blocking effect, it does not trigger histamine release and the adult ED95 0.05mg/kg. Magnesium sulphate (Mgso4) has antiarrhythmic, anticonvulsant, and antihypertensive properties, especially in the anesthetic, bstetrical, and cardiac fields. During cardiac surgery, magnesium sulphate is frequently used to control ventricular arrhythhmias or to lower systemic or coronary vascular resistance. Magnesium has been shown the synergistic effects with NMB, Magnesium sulfate is a commonly used for the prophylaxis and treatment of pre-eclampsia.<sup>2</sup> With this background this study was designed to compare the effect of cisatracurium with or without magnesium pretreatment on neuromuscular blockade and hemodynamics in cardiac

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surgery patients on cardiopulmonary bypass with objective to assess and compare intubation conditions and timing of intubation in minutes and assess and compare clinical duration of blockade, haemodynamics variable and side effect if any.

## 2. Materials and Methods

The present study was conducted in the Department of Anesthesiology and cardiothoracic and vascular surgery operation theatre with due permission from the institutional ethics committee after a written informed consent.

### 2.1. Study design

Hospital based, prospective, randomized double blind interventional study

### 2.2. Study period

After approval of the plan by research review board till the desired sample size is completed (2018-2019)

### 2.3. Sample size

Sample size was calculated to be 30 in each group at alpha error 0.05 and study power 80% assuming difference in clinical duration(min) to be 20(+/- 4.28) in both the group. Hence, for study purpose the sample size is increased to 30 in each group Patients were randomly allocated to 2 groups (30 in each group).

**Group "A"**- received injection Mgs04 50mg/kg in 100 ml Normal saline in 10 minutes before induction of general anesthesia (GA) given using and muscle relaxant cisatracurium 0.2mg/kg BW.

**Group "B"** - received 100 ml injection Normal saline in 10 minutes before induction of general anesthesia(GA) using muscle relaxant injection cisatracurium 0.2mg/kgBW

### 2.4. Methodology

Patient was taken into the operation room and monitored by electrocardiography (ECG), pulse oximeter and non-invasive blood pressure), Heart rate(HR), Mean arterial blood pressure(MAP), and Peripheral oxygen saturation(SpO<sub>2</sub>) values are recorded before induction. After an intravenous cannula is placed in the peripheral vein, we started an intravenous infusion of RL 5ml/kg/hr. Neuromuscular function were monitored by assessing the contraction of the adductor pollicis muscle by accelerography (TOF-GUARD) using STIMPOD 450.

Premedication with inj.morphine 0.1mg/kg and inj.phenargan 25mcg/kg given deep intramuscular 45 minutes prior to induction. Before starting injection mgso4 (50mg/kg BW) in 100 ml normal saline in group A or NaCl 100 ml in (group B) 10 minutes. Baseline parameters were noted.

Following pre-oxygenation for 3 minutes, induction was done with inj. Midazolam 0.05mg/kg, inj fentanyl 3mcg/kg and inj.etomidate 0.3mg/kgi.v. After induction and loss of consciousness neuromuscular monitoring was carried out (baseline) by supramaximal stimulus (50mA, 2Hz.). Baseline hemodynamic variables were recorded. Injection cisatracurium 0.2mg/kg was given in the both groups. Patient was ventilated with 100% oxygen. At every 30 seconds TOF stimulation given to assess TOF number tracheal intubation performed by the anaesthetist who was blind to the administered study drugs. When there was no response to nerve stimulation (TOF=0) intubating condition were assessed using Four point scale (4-excellent, 3-good, 2-poor, 1-inadequate). Patients were intubated with appropriate sized endotracheal tube. Anaesthesia was maintained with 100% O<sub>2</sub> and isoflurane (1%). Core body temperature was maintained (28-32oC). At every 5 minutes interval TOF number was assessed till TOF=2 at this time maintenance dose of inj. cisatracurium (0.3mg/kg) was administrated. This time was noted and mentioned as clinical duration of cisatracurium after intubation dose (clinical duration of cisatracurium). Hemodynamics variables were recorded at every 15 minutes interval. During surgery patients were monitored for any side effects (histamine release, bradycardia, hypotension).

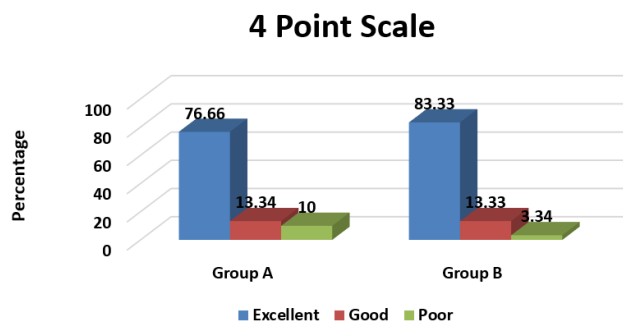
Patients were shifted to ICU on intermittent positive pressure ventilation (IPPV). Extubation was done when patient was hemodynamically stable, regained consciousness and the neuromuscular function recovered adequately.

## 3. Results

In our study both the groups were comparable in terms of age, sex, weight and ASA grade. So as to ensure that there was no confounding bias.

### 3.1. Onset of action of cisatracurium

The Table 1 shows means onset of action (minutes) of injection cisatracurium in the both the groups. Onset of action in group A is shorter than group B. It was observed that this difference is statistically significant.



**Fig. 1:** Comparison of Four point scale among both the groups.

**Table 1:** Showing mean onset of action of injection cisatracurium in the both the groups

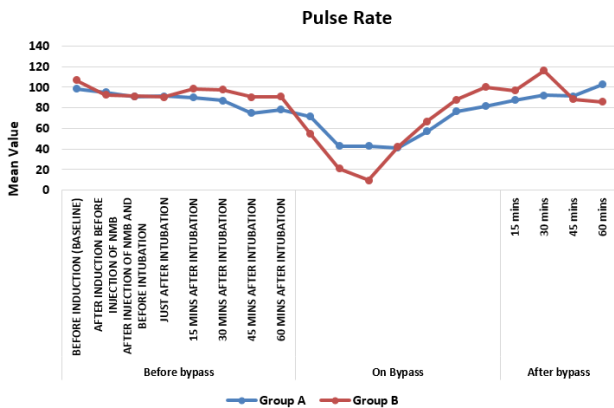
	Group A		Group B		P value
	Mean	SD	Mean	SD	
Onset of action in minutes	4.27	1.68	5.48	1.00	0.001(S)

The Figure 1 shows means four point scale in the both groups. It was observed there is no significant difference in four point scale between both the groups. In group A 23 patients (76.66%) were in excellent FOUR point scale while in group B 25 patients (83.33%) had excellent four point scale. In group A, 4 patients (13.34%) good and 3 patients (10%) had poor four point scale respectively. Whereas in group B 4 patients (13.33%) had good and 1 patients (3.34%) had poor four point scale. These differences in both the groups was not statistically significant

**3.2. Clinical duration-** After intubating bolous dose of cis-atracurium

The Table 2 shows mean clinical duration in the both the groups. In group A clinical duration after intubating dose of cis-atracurium was (60.70+/-7.4 minutes) while in group B it was (43.07+/-4.47 minutes). This difference in clinical duration was statistically significant.

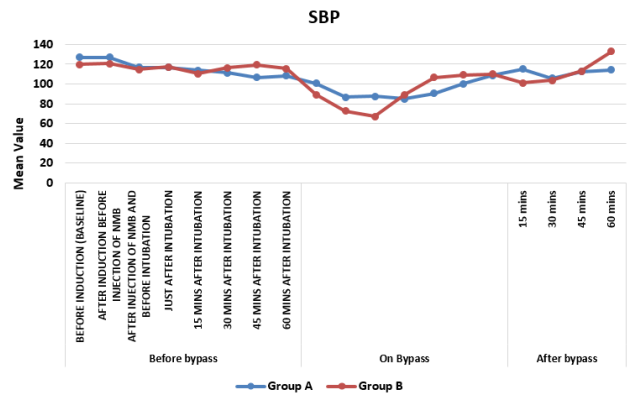
**3.3. Hemodynamic variables**



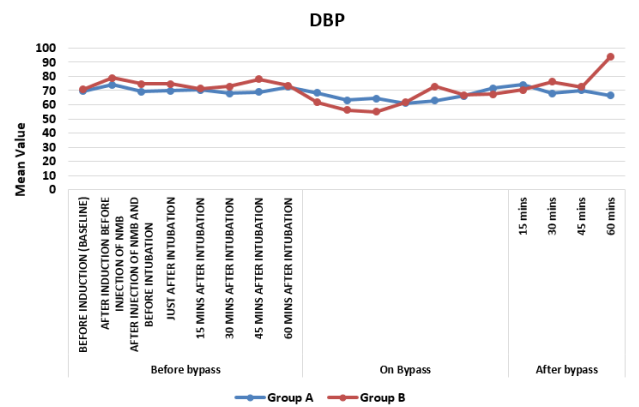
**Fig. 2:** Comparison of heart rates among both the groups

**4. Discussion**

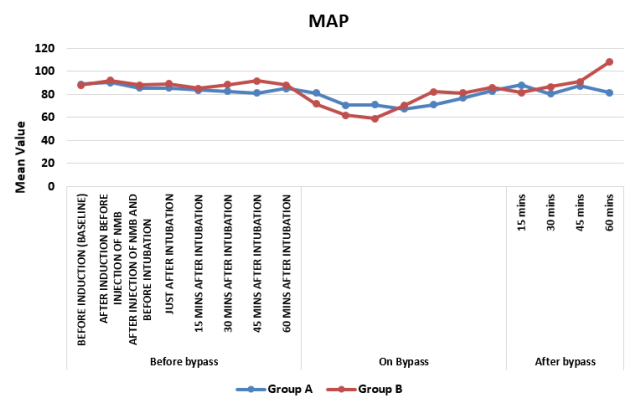
In our study both groups were comparable in terms of age, sex, weight and ASA grade so as to ensure that there was no confounding bias. The mean age in group-A was 45.17 ± 13.59 years and in group-B was 39.23 ± 11.82 years. Magdy Omera et al<sup>3</sup> in 2005 studied Inj. cis-atracurium 0.1mg/kg and inj.rocuronium 0.6mg/kg and their both groups were comparable as regards age, weight, mallampati class.



**Fig. 3:** Comparison of systolic blood pressure among both the groups



**Fig. 4:** Comparison of diastolic blood pressure among both the groups



**Fig. 5:** Comparison of mean arterial blood pressure among both the groups

**Table 2:** Showing mean clinical duration(minutes) in the both groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Clinical Duration in minutes	60.70	7.40	43.07	4.47	p<0.001

The mean onset of action of injection cis-atracurium after intubating dose, in group A was 4.27±1.68 minutes as compared to 5.48±1 minutes in comparison of group B (p-value<0.001) which showed that onset of action was significantly less in group A as compared to group B.

Our result were similar to the study by the Dr Barun Ram et al.<sup>4</sup> They studied the effect of Mgso4 on the speed of onset of action and duration of neuromuscular block produced by the Rocuronium bromide, they observed that onset time in group A (Mgso4 pre-treatment group) was 85.84±17.83 seconds as compare to group B(control group) which was 89.2±20.70 seconds this difference was statistically not significant

In our study in contrast to other studies like Doenicke et al.<sup>5</sup> And Magdyomera et al acceptable intubating condition was obtained after 4.27 minutes while in above studies acceptable intubating condition was obtained with in 2.6 minutes.

A study by Kim et al,<sup>6</sup> was in accordance to present study where in both the study groups onset of action of cis-atracurium with acceptable intubating conditions were obtained after 3 minutes.

Jean-Yves Lepage et al<sup>7</sup> reported onset of action with Inj. cis -atracurium 0.1mg/kg as 4.8 min in their study which is slightly more as compared to our study with magnesium pre-treatment 4.27±1.68.

Alfred W. Doenicke et al<sup>8</sup> observed median onset time of 5.2 min with 0.1mg/kg cis-atracurium which was with accordance with in our study 4.27 group A and 5.48 in group B.

The excellent intubating conditions in our study were seen in 23 patients in group A and in 25 patients in the Group B. Good intubating conditions were seen in 4 patient with group A and in 4 patients in group B. Poor intubating conditions were found in 1 patient in both the groups B.

The intubating conditions were found appropriate in our study after 4.27±1.68 minutes and 5.48±1.00 in group A and group B respectively. This is similar to the result of Kim et al. who recorded acceptable conditions after 3 minutes.

The clinical duration as reported in our study is in agreement with that reported by M. T. Carroll et al who observed dose of injection cisatracurium 0.1mg/kg and 0.6mg/kg the clinical duration was 33 min and 47 minutes respectively Lepage et al<sup>6</sup> in 1996 showed that median duration of action with Inj. cisatracurium at 0.1mg/kg with magnesium pretreatment as 60.70 min and with Inj.cisatracurium without magnesium pretreatment had clinical duration of 43.07 min, which is similar to our study.

They quoted that cis-atracurium was potent NMB with an intermediate duration of action characterized

In a study by Magdy Omera et al who compared rocuronium with cis-atracurium and found evidences of significant clinical cardiovascular changes in both the groups. The heart rate were significantly elevated in the both the groups (p<0.05) after intubation, but in our study heart rate was significant higher in group B than group A (15,30,45 minutes) after intubation.

This rise of heart rate in group B was suggested due to no pretreatment of mgs04 leading to sympathetic stimulation demonstrated by rise of norepinephrine level which was seeded by Derbyshire et al<sup>9</sup> in 1983.

In our study except 45 minutes after intubation there was no statistically significant difference in SBP, DBP and MAP in both the study groups.

Mgso4 may enhance the action of non depolarizing neuromuscular blocker by the reducing endplate sensitivity and decrease muscular fiber excitability. Secondly magnesium may interact with calcium and vascular membrane and decrease peripheral vascular resistance.

Laryngoscopy and tracheal intubation elicited potentially harmful cardiovascular response. This was explained by symphatic stimulation demonstrated by the rise of nor-epinephrine level observed by Derbyshire et al, in 1983. Changes in SBP DBP and HR after intubation. Prior administration of Mgso4 resulted in prevention of hemodynamically stimulation observed in group A.

## 5. Conclusion

In conclusion, Inj.cis-atracurium 0.2mg/kg with magnesium pretreatment exhibited a fast onset of action than Inj.cis-atracurium 0.2mg/kg without magnesium pretreatment but provides excellent intubating conditions in the majority of patients after 180 seconds. The clinical duration was significantly more with Injectioncis-atracurium with magnesium pretreatment as compared to injection cisatracurium with saline. These data suggest that Inj. cis-atracurium with magnesium sulphate pretreatment is useful addition to the armamentarium of currently available non-depolarizing neuromuscular blocking drugs for patients undergoing long duration on cardiopulmonary by pass cardiacsurgery procedures as well as magnesium is cardio vascular satbale.

## 6. By our Study we Conclude that

1. Pre treatment of mgso4 decreases the onset of action of inj cisatracurium.

2. Duration of action of intubating dose of inj cisatracurium was prolonged by pre-treatment of Mgso4.
3. Haemodynamic parameters were comparable and there was no statistically significant difference among both the groups.

### 7. Source of Funding

None.

### 8. Conflict of Interest

None.

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