Section: Anaesthesiology

Research

EFFECT OF PRE-TREATMENT WITH MAGNESIUM SULPHATE ON TWO DIFFERENT INTUBATING DOSES OF CIS-ATRACURIUM DURING GENERAL ANAESTHESIA WITH ENDOTRACHEAL INTUBATION – A RANDOMIZED CONTROLLED STUDY

Logeswari P[1], Sudha Jain[2], Nikhil Yadav[3], Sucheta Tidke[4], Mrinalini Fulzele[5]

[1,3,5]Assistant Professor, Department of Anaesthesiology, MGIMS, Sewagram, Maharashtra, India
[2]Professor, Department of Anaesthesiology, MGIMS, Sewagram, Maharashtra, India
[3]Professor and Head, Department of Anaesthesiology, MGIMS, Sewagram, Maharashtra, India

Received : 14/09/2022
Received in revised form : 19/10/2022
Accepted : 30/10/2022

Keywords:
Muscle Relaxant, Additive, Onset, Duration, Train of Four

Corresponding Author:
Dr. Nikhil Yadav,
Email: nkyrocks@gmail.com
ORCID: 0000-0002-8316-3387

DOI: 10.47009/jamp.2022.4.5.66

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2022; 4 (5); 333-339

Abstract

Background: Cis-atracurium, an intermediate acting non depolarizing neuromuscular blocker is a Cis-Cis isomer of atracurium that is devoid of histamine release. Magnesium sulphate pretreatment on Cis atracurium reduces the onset time of neuromuscular blockade without prolonging the recovery of neuromuscular blocker. To study onset and characteristics of neuromuscular block, duration of action and intubating condition of two different doses of cisatracurium 0.15mg/kg and 0.2mg/kg after pretreatment with magnesium sulphate. **Materials and Methods:** The randomized clinical trial was carried out in a tertiary care hospital in a central India. By using the sealed opaque envelope procedure,210 patients were classified into three randomly allocated groups, Group A (n= 70) was given IV Magnesium Sulphate followed by induction with Cis- atracurium 0.15 mg/kg body weight, Group B (n = 70) received IV Magnesium Sulphate followed by induction with Cis-atracurium 0.20 mg/kg body weight, while Group C (n = 70) received IV regular saline followed by induction with Cis-atracurium 0.20 mg/kg body weight. The neuromuscular blockade was monitored using Train Of Four Ratio (TOF) response to study onset and characteristics of neuromuscular block, duration of action and intubating condition. **Result:** At increasing doses cisatracurium provided rapid onset of action, increase time of first top up, increased duration of action, however intubataing conditions were comparable in all the three groups. In all the three groups intubating conditions were assessed by absence of coughing, bucking and adequate jaw relaxation which was found to be better in group A and group B Time for first top up dose in group A, B and C were 32±2.47, 42±2.48 and 29.21±3.26 minutes, respectively. There was a significant change in heart rate and Mean Arterial Pressure in all three groups over different time points. **Conclusion:** Cis atracurium in doses of 3*ED95 (0.15 mg/kg body wt) and 4*ED95 (0.20mg/kg body wt) following pre-treatment with Magnesium sulphate provided rapid onset of action and increased the duration of action of Cis atracurium.

INTRODUCTION

Cis-atracurium is a Cis-Cis isomer of atracurium that is devoid of histamine release.[1] It is an intermediate acting non depolarizing neuromuscular blocker. The neuromuscular blocking effect of Cis-atracurium is three times that of Atracurium.[2] According to Miller RD et al, potency of neuromuscular blocking drug is best described as effective dose, "The dose of neuromuscular blocking drug required to produce an effect (50%, 90%, 95% depression of twitch height on neuromuscular monitoring, commonly expressed as ED50, ED90 and ED 95 respectively) is its potency".[3] In a study conducted by Kasaby et al, it was found that 2*ED95 dose of Cis-atracurium failed to produce satisfactory intubating conditions. The recommended dose is 3*ED95 that is 0.15 mg/kg body weight and 4*ED95 i.e 0.2 mg/kg for endotracheal intubation during general anesthesia.[4] Magnesium sulphate is widely used during the perioperative period to treat arrhythmia. It is

ISSN (O): 2687-5365; ISSN (P): 2753-6556

effective bronchodilator and is used in severe asthma.[5] It is also used in acute respiratory failure to attenuate blood pressure increases.[6] Pretreatment of Magnesium sulphate on Cis atracurium results in shortening of onset time without prolongation of recovery of neuromuscular blockade. It potentiates the neuromuscular block produced by non-depolarizing neuromuscular blocking agents (NMBAs).[7,8] Magnesium is known to enhance the effects of non-depolarizing neuromuscular blocking drugs.[9,10] Magnesium sulphate 30mg/kg IV is effective for post anesthetic tremor and shivering.[11,12] However limited research has been done on different intubating doses of Cis atracurium along with pre-treatment with Magnesium sulphate.[1] In recent study it was found that 4*ED95 dose of Cisatracurium had shorter duration of action and better intubating conditions as compared to 3*ED95 dose of Cis atracurium.[5]

Therefore this randomized, controlled trial compared 3*ED95 dose of Cis-atracurium (0.15mg/kg body weight) pre-treated with Magnesium sulphate with 4*ED95 dose of Cis-atracurium (0.2 mg/kg body wt.) The study measured the onset ,duration of action and intubating condition with different doses of Cis atracurium. Secondarily, it also measured the hemodynamics and complications, if any.

MATERIALS AND METHODS

The randomized clinical trial was performed at the Department of Anaesthesiology at Kasturba Hospital, which is a rural tertiary care hospital under the Mahatma Gandhi Institute of Medical Sciences. After clearance from the ethical committee of the institute (ref no.5118) he study was conducted from March 2019- December2020.

Study population & design

Inclusion Criteria

A total of 210 patients, aged between 18 and 65 years of age, who belonged to ASA I and ASA II, undergoing surgeries under general anaesthesia at the Medical College were divided into three equal groups of 70 each.

Exclusion Criteria

Neuromuscular diseases, allergic to Magnesium Sulphate and Cis atracurium.

Using the results of apreviously conducted study and considering an α error of 0.001 and β error of 1.282, with power of 90 % and p1 as 98 and p2 as 90, in the below stated formula the sample size of 70 in each group was derived.[4]

$n = 2(Z\alpha+Z\beta)2\ (S12 + S22) / (x1- x2)2$

$Z\alpha=3.29$, $Z\beta=1.282$, power=90% , q=6

S1= standard deviation of group with pretreatment with magnesium sulphate with cisatracurium dose of 0.15mg/kg body weight.

S2= standard deviation of group with pretreatment with magnesium sulphate with cisatracurium dose of 0.20mg/kg body weight.

The participants were explained about the procedure and a written informed consent was taken from them after which they were randomized(sealed envelope technique) into three groups as follows:

Group A (n = 70) received Magnesium sulphate 1.5 gm in 50 ml of normal saline over 5 min, at the rate 10ml/min as IV infusion, before induction, followed by general anaesthesia induced with Inj. Propofol 2mg/kg + Inj. Fentanyl 2 microgram/kg + Inj. Cis-atracurium 0.15mg/kg body weight.

Group B (n= 70) received Magnesium sulphate 1.5 gm in 50 ml of normal saline over 5 minutes, at the rate of 10ml/min as IV infusion, before induction, followed by general anesthesia induced with Inj. Propofol 2mg/kg + Inj. Fentanyl 2 microgram /kg + Inj. Cis- atracurium 0.2 mg/kg body weight.

Group C (n= 70) control patients received same volume of normal saline(50ml placebo) as IV infusion, before induction, followed by general anaesthesia induced with Inj. Propofol 2mg/kg+Inj. Fentanyl 2 microgram/kg + Inj. Cis-atracurium0.2 mg/kg body weight as a control group.

Anaesthesia Technique

Pre-anaesthetic evaluation was done one day prior to surgery. Basic laboratory investigations were done including complete hemogram, urine analysis, blood sugar, serum electrolytes, serum creatinine and ECG .All patients were given tablet Alprazolam 0.5 mg orally on the night before operation and were kept fasting for 8 hours prior to surgery. All patients were premedicated with Inj.Midazolam 1mg IV, Inj. Glycopyrrolate 0.2mg IV. Baseline neuromuscular monitoring in the form of single twitch response was done and recorded. All hemodynamic monitoring parameters were attached and recorded. All patients were preoxygenated for 3- 5 minutes before induction of GA. Single twitch stimulation supramaximal stimulus lasting for 0.2 milliseconds at a frequency of 0.1 Hz was given as a baseline after administering premedication. Standard induction was done in all three groups and then (TOF) response was recorded using neuromuscular monitor by stimulation of ulnar nerve via surface stimulating electrodes placed on wrist using supramaximal stimulus of 2Hz, 2sec (4stimuli at 0.5 interval) applied every 12 seconds. Patient was assessed for mask ventilation and once mask ventilation had been found to be adequate then only the neuromuscular blocking agent as per the selected groups above was administered by another anaesthesiologist. The patients were assist-ventilated and TOF response was checked at 2 mins of Cisatracurium injection and then every minute till 5th minute of cisatracurium. At the end of the 3 minutes direct laryngoscopy was performed and patient was intubated with appropriate size endotracheal tube. The intubating anesthesiologist also graded the ease of intubation based on

ISSN (O): 2687-5365; ISSN (P): 2753-6556

protective reflexes, jaw relaxation and vocal cord relaxation. The observer anaesthesiologist recorded all the data, and also the hemodynamic parameters as per the proforma sheet. After intubation, ETCO2 was also recorded by connecting ETCO2 sensor to the ET tube. Anesthesia was maintained with O2, isoflurane mixture. The time of onset of action of Cis-atracurium was fixed till the point complete loss of TOF response was recorded. The duration of action and characteristics of block was calculated from the time of administration of intubating dose of Cisatracurium to the first top up dose administered. The TOF response was checked every 10 minutes after the intubation dose of Cis-atracurium had been administered, to assess the duration of block till the requirement of first top up dose of Cisatracurium based on TOF and clinical parameters. Top up dose of Cis- atracurium was administered for muscle relaxation when three consecutive twitches of identical amplitude were demonstrated on TOF monitor and this was the end point of duration of intubating dose of Cis-atracurium in all three groups.

Haemodynamic Variability

Heart rate, pulse rate, systolic and diastolic blood pressure, mean arterial pressure, SpO2 were recorded at baseline, after premedication, after infusion of normal saline, after induction, after intubation till 5mins.

Primary Outcome Parameters

Baseline heart rate, systolic and diastolic blood pressure and mean arterial pressure.

Single supramaximal twitch stimuli lasting for 0.2 milliseconds at a frequency of 0.1 Hz (as a baseline after administering premedication).

Secondary Outcome Parameters

TOF stimulation (2 Hz 2 sec) 4 supramaximal stimuli given at a frequency of 2Hz every 0.5 seconds after induction of GA.TOF monitoring 2 minutes after Inj.cisatracurium to decide adequacy for intubation and every minute till 5 minutes. Intubating conditions were checked at the time of laryngoscopy. SpO2 (oxygen saturation) and ETCO2 (end tidal CO2).HR, SBP, DBP, MAP, SPO2 and ETCO 2 throughout the procedure,TOF every 10 mins till 1st TOF response reappears.

Statistical Analysis

All analysis was done with the help of STATA (version 12, stata corporation, Texas USA). The continuous variables between the two groups was compared by applying student's t-test, whereas the binary variables was compared by chi-square test. Data was presented as Mean (SD) wherever applicable. p value of (< 0.05) was presumed to be statistically significant. Student 't' test for nominal data. Chisquare test for categorical data.

RESULTS

Demographic Profile in Three Study Groups

The mean age in Groups A, B and C were 43.46 (13.45), 48.33 (13.40) and 49.26 (10.06) resepectively. The proportion of males and females in each of the groups were equally.

The baseline heart rate, Systolic Blood pressure, Diastolic blood pressure and Mean Arterial Pressure were comparable in all the three groups as shown in [Table 1].

Table 1: Age and gender distribution

Age (Years)	Group			Kruskal Wallis Test	
	A	B	C	$\chi 2$	p value
Mean (SD)	48.46 (13.35)	48.33 (13.40)	49.26 (12.66)	8.487	0.514
Gender					
Male	34 (48.6%)	38 (54.3%)	37 (52.9%)	0.496	0.780
Female	36 (51.4%)	32 (45.7%)	33 (47.1%)		

Table 2: Showing the comparison of mean heart rate (bpm) changes

Heart Rate (BPM)	Group			P value (Kruskal Wallis Test)
	A	B	C	
	Mean (SD)	Mean (SD)	Mean (SD)	
Baseline	78.84 (13.01)	78.56 (13.13)	76.17 (13.73)	0.447
After Pre-Medication	75.33 (13.00)	72.81 (11.31)	68.84 (13.32)	0.001
After Induction	68.99 (13.58)	70.77 (11.81)	76.40 (14.64)	0.019
Before Intubation	74.03 (14.19)	70.10 (13.92)	77.77 (11.47)	0.002
2 Minutes Post-Intubation	70.56 (12.28)	70.54 (12.55)	89.34 (9.72)	<0.001
5 Minutes Post-Intubation	72.04 (14.15)	68.19 (13.42)	82.43 (11.52)	<0.001
P Value for change within each group (Friedman Test)	<0.001	<0.001	<0.001	

There was significant change in heart rate from baseline to 2 minutes and 5 minutes post intubation for all the groups. In group A, the baseline heart rate decreased from 78.84±13.01 to 70.56±12.28, 2 minutes post intubation, in group B it decreased from 78.56±13.54 to 70.54±12.55, 2 minutes post intubation and in group C it increased from 76.17± 13.73 to 89.34± 9.72, 2 minutes post intubation. [Table 2]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 3: Showing the comparison of mean Systolic blood pressure (mm Hg) changes in in three groups

Systolic BP (mmHg)	Group			P value (Kruskal Wallis Test)
	A	B	C	
	Mean (SD)	Mean (SD)	Mean (SD)	
Baseline	121.91 (14.14)	121.43 (12.61)	120.64 (9.52)	0.925
After Pre-Medication	122.80 (14.96)	116.54 (10.64)	118.73 (9.33)	0.027
After Induction	119.04 (12.02)	120.09 (9.52)	117.74 (10.34)	0.198
Before Intubation	120.94 (14.34)	122.64 (16.78)	119.46 (10.35)	0.923
2 Minutes Post-Intubation	119.24 (11.67)	123.70 (13.98)	120.47 (11.34)	0.041
5 Minutes Post-Intubation	119.03 (13.34)	120.39 (8.51)	121.80 (9.15)	0.025
P Value for change over time within each group (Friedman Test)	0.379	0.052	0.212	

After 2 minutes post intubation maximum rise was in group B and at 5 minutes post intubation maximum rise was in group C which was significant among the three groups. The change in SBP within the groups was not significant. [Table 3].

Table 4: Showing the comparison of mean Diastolic blood pressure (mm Hg) changes

Diastolic BP (mmHhrg)	Group			P value*
	A	B	C	
	Mean (SD)	Mean (SD)	Mean (SD)	
Baseline	74.26 (10.21)	74.49 (12.85)	75.64 (13.93)	0.125
After Pre-Medication	70.07 (13.64)	69.33 (12.22)	74.94 (13.80)	0.065
After Induction	71.30 (15.57)	65.50 (9.98)	76.83 (13.74)	<0.001
Before Intubation	70.54 (14.08)	67.76 (12.21)	77.13 (14.20)	<0.001
2 Minutes Post-Intubation	73.11 (14.22)	69.74 (12.17)	76.74 (13.32)	0.016
5 Minutes Post-Intubation	70.99 (12.91)	69.31 (13.48)	74.91 (17.81)	0.197
P Value for change in Diastolic BP (mmHg) over time within each group (Friedman Test)	0.225	0.688	0.286	

The mean DBP started to rise in group A and group C after induction and started to decrease in group B after induction. It further started to rise in groups A and C after intubation and 2 minutes post intubation and remained the same in group B. [Table 4]

Table 5: Showing the comparison of Mean Arterial Pressure (MAP) (mm Hg) changes

MAP (mmHg)	Group			P value for (Kruskal Wallis Test)*
	A	B	C	
	Mean (SD)	Mean (SD)	Mean (SD)	
Baseline	90.14 (8.99)	89.92(10.02)	90.69 (9.55)	0.523
After Pre-Medication	87.59 (10.99)	85.03 (8.77)	89.54 (9.03)	0.019
After Induction	83.37 (7.14)	87.49 (11.04)	90.49 (9.95)	<0.001
Before Intubation	85.47 (9.07)	87.96 (10.67)	91.21 (9.95)	0.004
2 Minutes Post-Intubation	86.21 (8.30)	89.94 (11.09)	91.29 (10.32)	0.021
5 Minutes Post-Intubation	85.94 (10.10)	87.46 (9.12)	90.49 (11.64)	0.043
P Value for change over time within each group (Friedman Test)	<0.001	0.027	0.190	

In terms of Mean Arterial Pressure too, there was a significant change in MAP in all three groups. The MAP at baseline in groups A,B and C are 90.14±7.99, 85.56±10.38 and 90.69±9.55 respectively. There was a significant change in MAP from baseline to all time points in groups A, B and C. The maximum change in MAP in group A was after induction and after premedication in groups B and C. [Table 5]

Table 6: Showing the comparison in Terms of change in TOF over time

TOF	Group			P value for (Kruskal Wallis Test)
	A	B	C	
	Mean (SD)	Mean (SD)	Mean (SD)	
After NS	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	-
After GA	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	-
2 Minutes After Cis-Atracurium	0.74 (0.10)	0.56 (0.06)	0.82 (0.06)	<0.001
3 Minutes After Cis-Atracurium	0.55 (0.06)	0.39 (0.07)	0.67 (0.06)	<0.001
4 Minutes After Cis-Atracurium	0	0	0.55 (0.06)	<0.001
5 Minutes After Cis-Atracurium	0	0	0	-
10 Minutes After Cis-Atracurium	0	0	0	-
20 Minutes After Cis-Atracurium	0	0	0.09 (0.16)	<0.001
30 Minutes After Cis-Atracurium	0.37 (0.00)	0	0.28 (0.16)	<0.001
40 Minutes After Cis-Atracurium	0	0.37 (0.00)	0	<0.001
50 Minutes After Cis-Atracurium	0	0	0	-
P Value for change in TOF (Friedman Test)	<0.001	<0.001	<0.001	

ISSN (O): 2687-5365; ISSN (P): 2753-6556

[Table 6] shows that TOF significantly decreased from baseline to 4 minutes post intubation in groups A and B and 5 minutes post intubation in group C. TOF in all groups disappeared at 5 minutes post intubation. In group C, TOF reappeared early that is at 20 minutes post intubation and the first top-up was given at 20 minutes. In group A, the TOF reappeared at 30 minutes post intubation and in group B at 40 minutes post intubation during which the first top-up was given.

Table 7: showing time of onset of action of Cis atracurium

	Group A	Group B	Group C
Time of onset	4 minutes	4 minutes	5 minutes
Time to first top up	32 ± 2.47	42 ± 2.48	29.21 ± 3.26

The time of onset of action of Cis atracurium in groups A and B was 4 minutes and in group C was 5 minutes which was highly significant, p<0.001. The time to first top was increased in group B which was significant.

DISCUSSION

Intermediate acting neuromuscular blocking agent, Cisatracurium is a cis-cis isomer of Atracurium. Laudanosine is a metabolite of the neuromuscular-blocking drugs Atracurium and Cisatracurium with potentially toxic systemic effects. However, Cis atracurium is devoid of histamine release and has no or very minimal side effects on the organ systems of the body.[13] Effective Dose(ED) has been defined as the dose of the neuromuscular blocker required to produce an effect. It is commonly expressed as ED95, ED90, ED50 etc that is 95%, 90%, 50% depression of twitch height following administration of neuromuscular blocker.

Studies have found that when equipotent doses (2*ED95) of Cis atracurium and Atracurium were used, Atracurium produced potent neuromuscular blockade with rapid onset of action and prolonged duration of action.[5] When the effects of 3*ED 95 dose of Cis atracurium was compared with 2*ED95 dose of Atracurium and Cis Atracurium, it was concluded that at higher doses Cis atracurium produced rapid onset of action and also prolonged the duration of the block.[3] Magnesium sulphate has been used in many conditions asthma, COPD, Severe preeclampsia and it is the drug of choice for many arrhythmias. In clinical anaesthesia it has been found to be effective in prolonging the action of neuromuscular blocking agents.[5] However limited research has been done on different intubating doses of Cis atracurium along with pre-treatment with Magnesium sulphate. The primary aim of the study was to study onset and characteristics of neuromuscular block,duration of action of the two different doses of cisatracurium after pretreatment with magnesium sulphate as compared to the group receiving only cisatracurium without pretreatment with magnesium sulpahte for general anesthesia with endotracheal intubation It was found that using cis atracurium in higher doses produces faster onset of action and delays the top up dose of cis atracurium.

Dosage of cis Atracurium

It was evident that 2*ED95 dose of Cis atracurium had the same onset time and duration of action as opposed to the equipotent dose of Atracurium used.

Kasaby et al, Jammar et al. and Mohanty et al proved that 3*ED95 and 4*ED95 doses of Cis atracurium produced rapid onset of action and also prolonged the duration of neuromuscular blockade. From the above studies it was evident that 2*ED95 dose of Cis atracurium had the same onset time and duration of action as opposed to the equipotent dose of Atracurium used.[14,15,16,17,18,19]

Doenicke et al, Cao et al studied the effect of different doses of Cis atracurium in cancer surgery and concluded that at higher doses cis atracurium produced effective and prolonged neuromuscular blockade. Hence in accordance with previous literature, 3*ED95 and 4*ED 95 dose of Cis atracurium i.e, 0.15mg/kg body weight and 0.20mg/kg body weight has been used for induction following intravenous Magnesium sulphate infusion.[17,18]

Changes in Heart Rate

The difference in change in heart rate within the three groups over time has been found to be significant.ue to stressor response the heart rate at 5 minutes post intubation increased Ghodarty et al, Kasaby et al, Kim et al too concluded that hemodynamic changes were significant in patients belonging to the study group who were administered different intubating doses of Cis atracurium.[5,8,9] The changes in heart rate immediately after intubation due to sympathetic stimulation was maximum in group C (control group) and minimum in group B (pretreated with magnesium sulphate). So it can be interpreted that pretreatment with magnesium sulpahte results in attentation of pressor response due to intubation.

Changes in systolic and diastolic blood pressure and mean arterial pressure

There was a significant change in systolic blood pressure from the baseline to the different time points the change in systolic blood pressure within the groups was also significant. With regards to diastolic blood pressure, the change in mean baseline pressure was not significant, p=0.428. The change in Diastolic Blood Pressure within the groups too was not significant. In groups A and B, there was a significant change in the Mean Arterial Pressure (MAP). It decreased from the baseline to

ISSN (O): 2687-5365; ISSN (P): 2753-6556

the time point after induction and then significantly increased 5 minutes post intubation in group A and increased from baseline to the time point after premedication and then significantly increased at 5 minutes post intubation in group B. The hemodynamic changes particularly during the post intubation period is probably due to the stress caused during intubation. Ten minutes post intubation, the hemodynamic parameters normalized due to the complete relaxation caused by the neuromuscular blockade. These changes are in accordance with the findings of Kasaby et al and Jammar et al, wherein the HR and MABP changes were significant in patients receiving Cis Atracurium but they were minimal in comparison to the group of patients receiving Atracurium. In the randomized control trial conducted by Kasaby et al 2*ED95 dose of Atracurium was compared with various doses of cisatracurium such as, 2*ED95, 3*ED95, 4*ED95. Similarly in Jammar et al, 0.15 mg/kg of cisatracurium was compared with 0.2mg/kg of cisatracurium and it was proved that the latter provided longer duration of action as compared to the former.[5,19,20]

Changes in Train of Four Stimulation

Train of Four stimulation pattern was used to assess the effect of neuromuscular blockade. In groups A and B, TOF ratio decreased from baseline to 4 minutes post intubation and TOF decreased from baseline to 5 minutes post intubation in group C. In groups A and B TOF ratio was zero at 4 minutes post intubation and in group C TOF ratio was zero at 5 minutes post intubation. This change in TOF was significant in all the three groups. There was no significant change between the study groups A and B in terms of change in trend of TOF. As the TOF ratio in groups A and B disappeared at 4 minutes it is evident pre-treatment with Magnesium sulphate has resulted in early neuromuscular blockade as compared with patients in group C where the twitch responses disappeared at 5 minutes post intubation. There was a significant difference in the time of onset of action of Cis atracurium in 4.00 minutes each in group A and group B and 5.00 minutes in group C. The onset time was shorter in groups A and B where Magnesium sulphate was used as pre-treatment. Kim et al, Mellinghof et al, who conducted randomized controlled trial too concluded that pre-treatment with Magnesium sulphate significantly shortened the time of onset of action. In the trial conducted by Kim et al Cisatracurium 0.15mg/kg was used and Magnesium sulphate in the dosage of 30mg/kg was used. In the study conducted by Mellinghoff et al the dose of cisatracurium used was 0.1mg/kg.[8,20] The time of first top up was significantly increased in group B as compared to group A and C. This concludes that use of Magnesium sulphate has prolonged the action of neuromuscular blockade thereby increasing the time of first top-up dose of neuromuscular blocker.

Ease of Intubation

Pre-treatment with Magnesium sulphate produced good intubating conditions in groups A and B. Ease of intubation was assessed at 3 minutes after giving Cisatracurium clinically by experienced anesthesiologists based on patient's reaction to intubation like coughing, bucking, vocal cord relaxation and jaw relaxation. There was also significant difference in the intubating conditions when two different intubating doses of Cis atracurium were used.[20] In group B, where Cis atracurium,0.20 mg/kg body weight was used more than 90% of the patients had good intubating conditions as compared to group A and group C, p=<0.007.

CONCLUSION

From the present study it can be concluded that, Pretreatment with magnesium sulphate provided statistically significant rapid onset and prolonged duration of action of Cis atracurium and also provided good Intubating conditions in all the three groups but statistically significant at 4*ED95 dose without affecting hemodynamics.

Limitation

This was a single-center study, Since this study was carried out among ASA I-II further studies are required in other population. we used TOF for the onset and duration of action. Advanced monitors are available in the market which can give more precise readings

REFERENCES

1. Wastila WB, Maehr RB, Turner GL, Hill DA, Savarese JJ. Comparative pharmacology of cisatracurium (51W89), atracurium, and five isomers in cats. Anesthesiology. 1996;85(1):169-77. doi: 10.1097/00000542-199607000-00023.
2. Lien CA, Belmont MR, Abalos A, Eppich L, Quessy S, Abou-Donia MM, Savarese JJ. The cardiovascular effects and histamine-releasing properties of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anesthesia. Anesthesiology. 1995;82(5):1131-8. doi: 10.1097/00000542-199505000-00007.
3. El-Kasaby AM, Atef HM, Helmy AM, El-Nasr MA. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery. Saudi J Anaesth. 2010;4(3):152-7. doi: 10.4103/1658-354X.71571.
4. Sparr HJ, Beaufort TM, Fuchs-Buder T. Newer neuromuscular blocking agents: how do they compare with established agents? Drugs. 2001;61(7):919-42. doi: 10.2165/00003495-200161070-00003.
5. El-Kasaby AM, Atef HM, Helmy AM, El-Nasr MA. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery. Saudi J Anaesth. 2010;4(3):152-7. doi: 10.4103/1658-354X.71571.
6. Noppen M, Vanmaele L, Impens N, Schandevyl W. Bronchodilating effect of intravenous magnesium sulfate in acute severe bronchial asthma. Chest. 1990;97(2):373-6. doi: 10.1378/chest.97.2.373.
7. Okayama H, Aikawa T, Okayama M, Sasaki H, Mue S, Takishima T. Bronchodilating effect of intravenous magnesium sulfate in bronchial asthma. JAMA. 1987;257(8):1076-8.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

8. Kim SH, So KY, Jung KT. Effect of magnesium sulfate pretreatment on onset and recovery characteristics of cisatracurium. Korean J Anesthesiol. 2012;62(6):518-23. doi: 10.4097/kjae.2012.62.6.518.
9. Ghodraty MR, Saif AA, Kholdebarin AR, Rokhtabnak F, Pournajafian AR, Nikzad-Jamnani AR, et al. The effects of magnesium sulfate on neuromuscular blockade by cisatracurium during induction of anesthesia. J Anesth. 2012;26(6):858-63. doi: 10.1007/s00540-012-1439-x.
10. Sinatra RS, Philip BK, Naulty JS, Ostheimer GW. Prolonged neuromuscular blockade with vecuronium in a patient treated with magnesium sulfate. Anesth Analg. 1985;64(12):1220–2.
11. Ghoneim MM, Long JP. The interaction between magnesium and other neuromuscular blocking agents. Anesthesiology. 1970;32(1):23–7.
12. Kizilirmak S, Karakaş SE, Akça O, Ozkan T, Yavru A, Pembeci K, et al. Magnesium sulfate stops postanesthetic shivering. Ann N Y Acad Sci. 1997;813:799-806. doi: 10.1111/j.1749-6632.1997.tb51784.x.
13. Wadhwa A, Sengupta P, Durrani J, Akça O, Lenhardt R, Sessler DI, et al. Magnesium sulphate only slightly reduces the shivering threshold in humans. Br J Anaesth. 2005;94(6):756–62.
14. Pinard AM, Donati F, Martineau R, Denault AY, Taillefer J, Carrier M. Magnesium potentiates neuromuscular blockade with cisatracurium during cardiac surgery. Can J Anaesth. 2003;50(2):172-8. doi: 10.1007/BF03017852.
15. Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet. 2002;359(9321):1877-90. doi: 10.1016/s0140-6736(02)08778-0.
16. El-Kasaby AM, Atef HM, Helmy AM, El-Nasr MA. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery. Saudi J Anaesth. 2010;4(3):152-7. doi: 10.4103/1658-354X.71571.
17. Cao Q, Tian X, Dong C, Bu H, Cheng Y. Effects of different doses of cisatracurium besilate on hemodynamics and postoperative cognitive function in patients undergoing radical resection of lung cancer. Oncol Lett. 2019;18(2):1761-1766. doi: 10.3892/ol.2019.10503.
18. Doenicke AW, Czeslick E, Moss J, Hoernecke R. Onset time, endotracheal intubating conditions, and plasma histamine after cisatracurium and vecuronium administration. Anesth Analg. 1998;87(2):434-8. doi: 10.1097/00000539-199808000-00038.
19. Jammar P, Pathak DG, Begum I, Chauhan RC. A clinical comparative study of two intubating doses of cis-atracurium during general anaesthesia for gynaecological surgery. Int J Basic Clin Pharmacol. 2017;6(5):1206–10.
20. Mellinghoff H, Radbruch L, Diefenbach C, Buzello W. A comparison of cisatracurium and atracurium: onset of neuromuscular block after bolus injection and recovery after subsequent infusion. Anesth Analg. 1996;83(5):1072-5. doi: 10.1097/00000539-199611000-00030.

ISSN (O): 2687-5365; ISSN (P): 2753-6556