Original Research Article

Comparison of cis-atracurium with atracurium for balanced general anaesthesia: A randomized double blinded controlled study

Shyamlal Thukral[1], Mridul Panditrao[2*], Minnu Panditrao[3], Shalu Punia[4]

[1]Assistant Professor, [2]Professor and HOD, [3]Professor, [4]Jr. Resident, Department of Anaesthesiology and Intensive Care, Adesh Institute of Medical Sciences and Research (AIMSR) Bathinda-151001, Punjab, INDIA.
Email: shamlalthukral@gmail.com

Abstract

Background: Atracurium and Csatracurium are intermediate acting muscle relaxants without any much side effects and recovery due to non-organ dependent elimination. This study was conducted to compare the differences between them. **Aim and Objective:** To compare difference between Atracurium and Cis Atracrium regarding terms of onset, duration of action of first dose, 25% recovery from last supplemental dose and neostigmine reversal **Material and Methods:** Our study conducted was a prospective randomised observational study conducted 60 ASA Grade I, II patients. Patients were divided into two groups of 30 each. Group A (Atracurium), patients were administered atracurium 0.5 mg/kg while Group B (Cisatracurium) patients received cisatracurium 0.2 mg/kg as loading dose. The onset time, duration of block and recovery index were recorded using Train of Four (TOF) response along with the haemodynamic profile. **Results:** Mean duration of action (DOA) of 1ST dose in Cisatracurium group was significantly more (72.5± 2.3 min)as compared to atracurium group (40.23± 8.3mins). The mean 25% recovery in Atracurium group was 32.11±3.2 . The mean 25% recovery in Cisatracurium besylate group was 51.61±2.5. The mean 25% recovery in Atracurium and cis atracurium were statistically significantly different.(P<0.05) .

Key Words: Non Depolarising Neuro Muscular Blockers, Benzylisoquionolium, Cis Atracurium, Atracurium, Cmparative Study, iIntermediate Acting.

***Address for Correspondence:**
Dr. Mridul M. Panditrao, Professor, Head and In-Charge Department of Anaesthesiology and Intensive care Adesh Institute of Medical Sciences and Research (AIMSR), Adesh University, Bathinda-151001, Punjab, INDIA.
Email: shamlalthukral@gmail.com
Received Date: 21/08/2018 Revised Date: 12/09/2018 Accepted Date: 02/10/2018
DOI: https://doi.org/10.26611/10158210

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 26 November 2018

INTRODUCTION

The neuromuscular blocking drugs (NMBDs) have revolutionized management of balanced General Anaesthesia (GA). Since the introduction of d tubocurarine and succinyl choline, there have been significant advances in the field of neuromuscular blockade. The NMBDs offer many advantages during the conduct of General Anaesthesia viz; Long Surgeries can be performed without voluntary and reflex movements, They don't cross blood brain barrier, hence no increase of ICP (except succinyl choline). Reduction of intra operative awareness and recall, allows proper muscle relaxation for prolonged period of time, facilitates complete control of airways, breathing and circulation, maintainance of stable Haeamodynamics, lack cerebral side effects hence can be used in cerebral trauma cases also .These drugs have minimal side effects, rapid metabolism to inactive products, action confined to neuromuscular junctions only can be used in liver and renal diseases also, they don't cross placenta can be used in obstetrtic cases. They are not without dis advantages like cardiovascular effects by benzyl iso quonololinium agents other than doxa curium can cause histamine release, Miva curium cause maximum

How to site this article: Shyamlal Thukral, Mridul Panditrao, Minnu Panditrao, Shalu Punia. Comparison of cis-atracurium with atracurium for balanced general anaesthesia: A randomized double blinded controlled study. *MedPulse International Journal of Anesthesiology.* November 2018; 8(2): 108-112. http://medpulse.in/Anesthsiology/index.php

histamine release can result into broncho constriction, flushing . Pancronium and Gallamine can cause tachycardia, Tubo curarine causes vasodilation and hypotension .Now with the introduction of newer Benzyl isoquonolinium derivatives like Atracurium and Cis Atra curium duration of action is maximum as compared to Doxa curium and Miva curium more than 30 to 40 minutes, Their elimination is through ester hydrolysis and holfman elimination a process dependant on pH and temperature whereas steroid derivativtes like Pancuronium and Vecronium, Rocuronium, Piercoronium have elimination through renal or hepatic route. Cisatracurium is a new intermediate duration, non-depolarizing, benzylisoquinolinium neuromuscular blocking drug which is a stereoisomer of atracurium with a potency of approximately 3 to 4 times greater than that of atracurium[1, 2]. Despite the higher potency, cisatracurium is associated with more stable hemodynamics than atracurium and does not cause histamine release even at doses of up to 0.4mg/kg ($8\times ED_{95}$).[3] The same dose ($2\times ED_{95}$) atracurium is more effective neuromuscular blocking agent than cisatracurium. However, higher doses of cisatracurium 0.2mg/kg ($4\times ED_{95}$) and 0.3mg/kg ($6\times ED_{95}$) provide more effective, more rapid neuromuscular blocking with longer duration of action, stable hemodynamic status and no signs of histamine release clinically during abdominal surgery.[4,5] This study was conducted to compare the atracurium and cis atracurium with respect to neuromuscular blockade and recovery characterstics.

AIM AND OBJECTIVE

To compare difference between Atracurium and Cis Atracrium with 2*ED 95 regarding terms of onset, intubating conditions after three minutes of 1_{st} dose, safety and efficacy of both the drugs, Heamodynamic effects, signs any adverse reaction, duration of action of first dose, 25% recovery from last supplemental dose and neostigmine reversal . Because of its intermediate, onset of action, cisatracurium is not recommended for rapid sequence endotracheal intubation in emrgancy cases (i.e., where intubation is uregently and rapidly required to minimize the time the airway is unprotected) Our study was a prospective double blinded randomized controlled study conducted in the Department of Anaesthesia, Adesh institute of medical sciences and research, Bathinda (Punjab). In this prospective study 60 patients undergoing all types of surgeries under balanced general anesthesia were studied.

Inclusion Criteria

1. ASA I and II
2. Age of 18 to 75 years
3. Elective surgery patients

Exclusion Criteria

1. Age above 75and below 18 yrs
2. Emergency surgery patients
3. Patient not willing to participate in study.
4. Patients with any previous history of hypersensitivity or any known side effect of drug
5. Patients at risk for gastric aspiration
6. 6. anticipated difficult airway cases
7. Pregnant and lactating mothers
8. Patients taking drugs that known to interfere with neuromuscular function like amino glycides, antibiotics anti deprresants, anti convulsants, anti arrthymic drugs
9. Patients with electrolyte Imbalance

Study was approved by ethical committee of the institute . a written valid consent was taken from patients after explaining the study to them. All cases of ASA Grade I and II were selected. 30 patients were allocated in each group randomly.

Premedication: Premedication was given half hour before surgery. Each patient were given premedication with analgesic like Inj. Butorphanol 1 mg, Inj. Midzolam 1 mg, and Inj. Glycopyrrolate 0.2 mg half hour before surgery.

MATERIAL AND METHODS

All cases were were given Ringer lactate before induction for all type of surgeries. Standard monitoring were performned with multi para monitor for ECG, HR, Spo2 Temperature, Capnograpgy before anaesthsia and during anaesthesia and neuromuscular monitoring for TOF. Patients age, sex, weight, type of surgery, informed consent and expected duration of surgery were recorded preoperatively .. Group A of 30 patients received injection Cis Atra curium 0.2mg /kg as loading for intubation as well as for conducting surgeries and maintenance dose 0.03 mg /kg. Group B patients were given injection Atracurium 0.5 mg /kg as loading dose and 0.1 mg /kg as maintenance dose. In both groups these muscle relaxants were given after premedication and induction agents like Inj. Propofol 2 mg /kg IV and inhalational agents like Oxygen 100 % 3 litres / N_2O 3 litres and Isoflurane 0.5% to 1% were given to all patients till the intubation and onset time was noted from the time of first dose of muscle relaxant to TOF 0 Zero. After intubation Oxygen and N_2O low flow 1: 1.5 L/ minute were given . Hemodynamic parameters including systolic blood pressure, diastolic blood pressure, MAP and heart rate, side effects in any were monitored one minutes, after three minutes at the time of intubation, after one minutes, three minutes at the time of intubation, after 5 minutes after administration

of the first dose and then every 10 minutes throughout the surgery. Recovery profile were concluded. Using Train of Four (TOF) response with nerve stimulator using 50 Ma 2HZ power through electrodes to stimulate ulnar nerve every 15 seconds. Subsequent dose of Muscle relaxant were given when TOF was 2 . when at the end of surgery when TOF recovery was 25% from the last dose, reversal was achieved by administration of neostigmine and glycopyrrolate mixture (0.05 mg/kg neostigmine and 8µk/kg glycopyrrolate) through slow IV injection.

RESULTS

The onset of action time was fixed as 3 minutes for intubation for both the groups . During intubation after first dose of muscle relaxant, we observed condition of larnygoscopy, vocal cords, reaction 1to intubation as under

Table 1:

	Laryngoscopy	Vocal cords	Reaction/Response to intubation
Excellent	Jaw relaxed, No resistence to laryngeal blade,	Abducted but no Movements	Easy paasage of ET tube, No Movements of limbs, no Coughing
Good	Jaw relaxed, slight resistance	Intermediate but abducted	Slight reistance and slight Coughing
Poor	very poor relaxation of jaw and active resistance	Closed	Vigorous movements of limbs, Bucking, Coughing
Not possible	Not relaxed	Closed	Coughing, active limbs movements present

Table 1: Results of in tubating condition within 3 minutes

	Cistracurium	Atracurium	Percentage of cases
Excellent	18 (60%)	20 (66.66%)	63.33%
Good	9 (30%)	8 (26.66%)	28.33%
Poor	3 (10%)	2 (6.66)	8.33%
\p value	0.05	0.05	

Table 2: Comparison of Atracurium and Cis atracurium group according to variables

Sr no	Variables	Atracurium GP(30)	Cisatracurium GP(30)	P Value
1	Age (years)	32.57± 5.64	34.82± 5.31	>0.05
2	Systolic blood pressure(mm/hg)	131± 21.69	134± 23.41	>0.05
3	Diastolic blood pressure(mm/hg)	84± 19.35	86± 12.32	>0.05
4.	Pulse rate /min	78± 7.3	75±4.2	>0.05

Table 3: Comparison of atracurium and cis atracurium group according to variables

Sr no	Variables	Atracurium GP(30)	Cisatracurium GP(30)	P Value
1	Mean duration of action (min)	40.23± 8.3	72.5± 2.3	**<0.05**
2	Mean 25% recovery(min)	32.11±3.2	51.61±2.5	**<0.05**
3	Mean time of recovery from reversal (min)	2.1±0.3	2.5±0.2	**<0.05**

Table 4: Heart rate changes before and after administration of Atracurium or Cisatracurium

Pulse rate Mean ±SD	Grroup A Cis atracurium n=30	GroupB Atracurium n=30	P value
Base line	86.4 ±5.32	76.8±6.61	<0.05
Prior intubation	82.6 ±6.12	78.6 ±6.65	<0.05
Post intubation	87.7±5.32	85.6±7.12	<0.05
1 min	97.4±6.52	94.8±7.22	<0.05
5 min	91.5±5.81	86.7±7.21	<0.05
10 min	86.5±5.76	80.4±6.82	<0.05
20 min	88.6±5.64	82.6±6.51	<0.05
30 min	90.02±4.36	88.4±5.22	<0.05
40 min	91.87±5.87	86.6±6.11	<0.05
50 min	89.56±6.31	78.55±6.73	<0.05
60 min	92.95±6.44	76.54±6.34	<0.05

Baseline recording were not significantly different (*P*-value < 0.05) There was a statistically significant increase in Pulse Rate, Mean Arterial Pressure post intubation when compared to baseline and post injection of 2×ED_{95} dose of atracurium in group 2 and the same dose of cisatracurium in group 1. Pulse Rate, Mean arterial blood pressure changes 5-30 minutes later were not statistically significant

Table 5: Comparison of Mean Arterial Pressure changes before and after intubation

Pulse rate Mean ±SD	Grroup A Cis atracurium	Group B Atracurium	P value
Base line	77 ± 10.7	72.5±6.5	<0.05
Prior intubation	78.8 ± 10.5	71.3±7.2	<0.05
Post intubation	91.6 ± 7.49	78.6±7.66	<0.05
1min	87.4 ± 8.61	79.2±6.52	<0.05
5min	83.5± 9.43	68.6±5.32	<0.05
10 min	83.7 ± 7.23	72.3±7.42	<0.05
20min	85.6 ± 6.33	70.4±7.19	<0.05
30min	83.5 ± 8.93	74.4±8.12	<0.05
40min	78.6±7.43	76.6±8.14	<0.05
50min	74.5±8.34	75.3±8.56	<0.05
60min	72.6±8.12	74.4±8.43	<0.05

*Statistically significant difference versus Baseline reading (*P*-value < 0.05

Table 6: Adverse reaction profile

		Cisatracurium group (n=30) 2×ED_{95}	Atracurium group (n=30) 2×ED_{95}	*P*-value
Flush	N (%)	0 (0)	1 (3.33)	0.5
Erythema	N (%)	0 (0)	1 (3.33)	Not significant
Wheals	N (%)	0 (0)	0 (0)	

Mean age in atracurium group was 32.57± 5.64 years while Mean age in cis atracurium was 34.82± 5.31years.(p value >0.05). Mean Systolic and diastolic blood pressures and pulse rate in atracurium group were 131± 21.69, mm of hg, 84± 19.35mm of hg and 78± 7.3 per minute respectively while in cis atracurium group were 134± 23.41 mm of Hg, 86± 12.32 mm of Hg and 75±4.2 respectively. Difference between them was statistically not significant.(p >0.05) Table 3 showed comparison between both groups for neuromuscular blockade and recovery profile. Mean onset of action in Atracurium and cis atracurium group it was kept 3 minutes to see intubating conditions as per Table no. 1 while relaxation was excellent in 66.66% with atracuriumm and 60% in cisatracurium .Relaxation was good in 26.66% with atracurium and 30% with cis atracurium cases while relaxation was poor at the time of intubation in 6.66% cases withnatracurium and 10% with cis atracurium there were no significant difference for intubating conditions Mean duration of action (DOA) of 1ST dose in Cisatracurium group was more (72.5± 2.3 min)as compared to atracurium group (40.23± 8.3mins).this difference was statistically significant.(<0.05) The mean 25% recovery in Atracurium group was 32.11±3.2 . The mean 25% recovery in Cisatracurium besylate group was 51.61±2.5 . This difference was statistically significant. (p<0.05) The mean time of recovery from reversal in atracurium and cis atracurium was 2.1±0.3 and 2.5±0.2 respectively. This difference was statistically significant. (p<0.05)

DISCUSSION

Mean age, systolic blood pressure, diastolic blood pressure and pulse rate were comparable and difference between them is statistically not significant. simlar findings were observed in M.T. Carroll *et al*[6],El – kasaby *et al*[7]. They studied different doses of cis atracurium with atracurium and they observed that with the higher doses of cisatracurium (4×ED95 and 6×ED95) onset of action was significantly faster than with atracurium. Mean duration of action (DOA) of 1ST dose in Cisatracurium group was significantly more (72.5± 2.3 min)as compared to atracurium group (40.23± 8.3mins). Similar results were observed by El – kasaby *et al*. where they found statistically significant difference in both the drugs.[7] Bluestein and colleagues in their study observed that increasing the dose of cisatracurium (from 0.1 to 0.15 and 0.2 mg/kg) increases the mean time of clinically effective duration (45 to 55 and 61 min, respectively).[8] Also C.E. Smith, observed that duration of action of cisatracurium and atracurium were comparable but statistically not significant.[9] The mean 25% recovery in Atracurium group was 32.11±3.2 . The mean 25% recovery in Cisatracurium besylate group was 51.61±2.5. This difference was statistically significant. (p<0.05). M. T. Carroll in his study observed the time from drug

administration to 25% recovery with cisatracurium 0.15 mg.kg−1 (51–59 min) was longer compared with both cisatracurium 0.1 mg.kg−1 (45–48 min) and atracurium 0.5mg/kg (47–48 min) but the difference was not statisticaly significant.[6] Antagonism of neuromuscular blockade should be initiated preferably when two to four TOF responses are observed. The mean time of recovery from reversal in atracurium and cis atracurium was 2.1±0.3 and 2.5±0.2 respectively.this difference was statistically significant. ($p<0.05$) In our study in cisatracurium group reversal was given at a mean TOF of 44.90% along with assessment of clinical parameters. This TOF was 2.5minutes from TOF 25%. In atracurium group reversal was initiated at mean TOF of 42.07% after assessing clinical parameters which was 2.1 minutes TOF ratio 25%. Bergeron *et al* in his study while comparing 3 different doses of cisatracurium 0.05mg/kg, 0.15mg/kg and 0.3 mg/kg; observed that onset time was not significantly different between the doses in adults, but recovery time increased, 23 and 24 minutes respectively.[10]

CONCLUSION

Cisatracurium has a faster onset, good intraoperative hemodynamic parameters and better recovery profile

REFERENCES

1. Matthew R. Belmont, Cynthia A. Lien, Steve Quessy, Martha M. Abou-Donia, Amy Abalos, John J. Savarese, et al. “The clinical neuromuscular pharmacology of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anesthesia”. Anesthesiology. 1995; 82: 1139-1145.
2. Jean-Yves Lepage, Jean-Marc Malinovsky, Myriam Malinge, Thierry Lechevalier, Christine Dupuch, Antonie Cozian, et al. “Pharmacodynamic dose-response and safety of cisatracurium (51W89) in adult surgical patients during N_2O-O_2-Opioid anesthesia”. Anesth Analg. 1996; 83: 823-9.
3. Cynthia A. Lien, Matthew R. Belmont, Amy Abalos, Larissa Eppich, Steve Quessy, Martha M. Abou-Donia, et al. “The cardiovascular effects and histamine-releasing properties of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anesthesia”. Anesthesiology. 1995; 82:1131-1138.
4. A. M. El-Kasaby, H. M. Atef, A. M. Helmy, and M. Abo El-Nasr. “Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery”. Saudi J Anaesth. 2010; Sep-Dec; 4(3):152-157.
5. Jirasiritham S, and Tantivitayatan. “A comparision of efficacy of cisatracurium and atracurium in kidney transplantation operation”. J Med Assoc Thai. 2004 Jan; 87(1): 73-9.
6. M. T. Carroll,1 R. K. Mirakhur,1 D. W. Lowry,1 K. C. McCourt1 and C. Kerr2, A comparision of the neuromuscular blocking effects and reversibility 0f cisatracurium and atracurium, Anesthesia 1998,53,page 744
7. M. El-Kasaby, H. M. Atef, A. M. Helmy, and M. Abo El-Nas, Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgerySaudi J Anaesth. 2010 Sep-Dec; 4(3): 152–157. 11.
8. Bluestein LS, Stinson LW, Lennon RL, Wilson RM. Evaluation of cisatracurium, anew neuromuscular blocking agent for tracheal intubation. CAN J ANAESTH. 1996;43:925–31.
9. Smith CE, van Miert MM, Parker CJ, Hunter JMA comparison of the infusion pharmacokinetics and pharmacodynamics of cisatracurium, the 1R-cis 1'R-cis isomer of atracurium, with atracurium besylate in healthy patients. Anaesthesia. 1997 Sep;52(9):833-41.)
10. Bergeron L, Bevan DR, Berrill A, Kahwaji R, Varin F: Concentration-effect relationship of cisatracurium at three different dose levels in the anesthetized patient . Anesthesiology 95 314-23, 2001

Source of Support: None Conflict of conflict of Interest: None