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A COMPARATIVE STUDY OF ATRACURIUM AND CIS- ATRACURIUM FOR INTUBATING CONDITIONS UNDER GENERAL ANAESTHESIA

Anaesthesiology

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ABSTRACT

Background: Atracurium and Cisatracurium are intermediate-acting nondepolarizing neuromuscular drugs. They both are promising drugs offering a predictable recovery due to non-organ dependent elimination. However, due to the variability in metabolism and narrow therapeutic window, monitoring of neuromuscular functions has significant importance. Cisatracurium is approximately four times as potent as atracurium. In contrast to Atracurium, Cisatracurium is devoid of chemically mediated histamine release. Routinely atracurium is used for the neuromuscular blockade in most pediatric surgeries. On the other hand, 2 ED95 doses of Cisatracurium do not create satisfactory intubating conditions such as those seen with equipotent doses of atracurium.

Aim:

- To compare the intubating conditions of Atracurium(0.5mg/kg) and Cisatracurium 0.15mg/kg).
- To compare the hemodynamic parameters (MAP, PR, SPO2,) between atracurium and Cisatracurium
- To compare the signs of histamine release potential between atracurium and Cisatracurium.

Materials and Methods :

A Prospective, observational study was conducted at SRI SIDDHARTHA MEDICAL COLLEGE AND RESEARCH INSTITUTE,TUMKUR. from 1st Jan 2021 to 30th June 2022 on 74 patients. **Results:** In Atracurium group, there were 15 patients with ASA grade of 1 and 17 patients with ASA grade of II. In Cis-Atracurium group, there were 15 patients with ASA grade of 1 and 22 patients with ASA grade of II. Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups. Average onset time for Atracurium group was 177 ± 22.4 seconds and same was 184 ± 17.3 seconds in Cis Atracurium group. In Atracurium group, intubation was successful at 1st attempt in 33 subjects, 2nd attempt in 2 subjects, 3rd attempt in 2 subjects. In Cis Atracurium group, intubation was successful at 1st attempt in 35 subjects and 2nd attempt in 2 subjects. In Atracurium group, duration of action of the muscle relaxant was 46 ± 4.9 minutes, Duration of 25% recovery was 33 ± 4.2 minutes, Time of recovery from reversal was 1.7 ± 0.8 minutes. In Cis Atracurium group, duration of action of the muscle relaxant was 68 ± 7.1 minutes, Duration of 25% recovery was 48 ±5.6 minutes, Time of recovery from reversal was 2.2 ± 1.1 minutes. **Conclusion:** Cis atracurium had longer recovery time and duration of action. Atracurium caused significant hemodynamic impact than Cis atracurium. Adverse effects were comparable in both.

KEYWORDS

Atracurium, Cis atracurium, Intubating conditions,

INTRODUCTION

The introduction of muscle relaxants into clinical anesthesia 60 years ago has revolutionized the procedure of intubation in particular and the practice of the specialty. The ideal neuromuscular blocking agent for intubation should have a rapid onset, brief duration of action, free from hemodynamic changes, devoid of residual paralysis and provide excellent intubating conditions like fully relaxed jaw, widely open vocal cord and negligible response to intubation which reduces the time for intubation and thereby reduces the untoward hemodynamic stress response.

Atracurium and Cisatracurium are intermediate-acting nondepolarizing neuromuscular drugs. Atracurium and cisatracurium are promising drugs offering a predictable recovery due to non-organ dependent elimination. However, due to the variability in metabolism and narrow therapeutic window, monitoring of neuromuscular functions has significant importance.

Cisatracurium is approximately four times as potent as atracurium. In contrast to atracurium, Cisatracurium is devoid of chemically mediated histamine release. Routinely atracurium is used for the neuromuscular blockade in most pediatric surgeries. On the other hand, 2 ED95 doses of Cisatracurium do not create satisfactory intubating conditions such as those seen with equipotent doses of atracurium. Hence, the present research intends to compare the intubating conditions between atracurium and cis atracurium under general anaesthesia in a medical college hospital in South India.

Inclusion Criteria:

- ASA I and II aged 18-60yrs;
- Patients undergoing elective surgeries;
- Weight 45-60kgs
- Mallampatti score 1 and 2
- Patient who has given valid informed consent

Exclusion Criteria:

- ASA Class III or more
- Pregnant women
- Patients with cardiac, hepatic or renal dysfunction,
- Patients with neuromuscular disease
- Patients with anticipated difficult intubation
- Patient posted with respiratory diseases

Materials required:

1) Multiparameter monitor with electrocardiogram, pulse oximetry, End tidal carbon dioxide monitoring and noninvasive blood pressure.
2) Nerve stimulator NS-100 Neuromuscular monitor
3) Inj. Atracurium 0.5mg/kg
4) Inj. Cisatracurium 0.15mg/kg
5) Anaesthesia workstation.

Methodology:

- Following the approval of institutional ethical committee and getting informed consent, 74 patients between the age of 18-60 years who are posted for surgical procedures under general anesthesia was selected for the study. A detailed history, thorough clinical examination and routine surgical investigations was taken.
- Onset time of muscle relaxants, attempts for intubation, duration of action, 25% recovery from reversal and recovery from reversal were noted.
- Signs of histamine release

Parameters Measured:

- Heart rate(beats/min)
- Systolic blood pressure(mmHg)
- Diastolic blood pressure(mmHg)
- Mean arterial blood pressure (mmHg)
- End tidal CO2 (mmHg)

Preparation of Patient:

- Patients were advised overnight fasting – 6hrs for solids, 4hrs for semisolids and 2hrs for liquids. All patients will be given T.Alprazolam 0.5 mg and T.Ranitidine 150 mg on the previous night of surgery.
- IV line inserted, and lactated ringer solution infused 4–6 ml/kg/h.
- All patients were monitored with non-invasive blood pressure (BP), electrocardiograph (ECG), pulse oximeter (SpO2) before induction of general anesthesia (GA), capnography for end-tidal CO2(ETCO2)
- One forearm was immobilized in splint and ulnar nerve at wrist was selected for neuromuscular monitoring using Nerve stimulator NS-100 neuromuscular monitor. The ulnar nerve was stimulated with a supramaximal current (mA). The force of contraction of adductor pollicis muscle was noted by visual and tactile means in the form of index finger flexion and thumb adduction.
- TOF (Train of four) impulses at 2Hz frequency was applied at 0.5 secs interval with a minimum gap of 12 seconds between two stimulation patterns.
- Patients were premedicated with Inj Midazolam 0.02mg/kg and induced with Inj Propofol 2mg/kg followed by Inj Atracurium 0.5mg/kg or Inj Cisatracurium 0.15mg/kg according to group allocation. Muscle relaxant were given over 5 mins.
- Number of attempts of intubation was noted, time taken for intubation was noted from introduction of laryngoscope to visual passing of endotracheal tube beyond vocal cords. The intubating conditions were graded.
- Reversal was achieved at the end of surgery by Inj Neostigmine 0.05mg/kg IV and Inj glycopyrrolate 0.01mg/kg IV and the patient were extubated. TOF ratio >0.9 was taken as sufficient for safe extubation of the trachea.

OBSERVATION AND RESULTS

Tab. 1 Age distribution

Age groups	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
18 – 20 years	4	3	Chi square: 0.97 P – 0.8
20 – 40 years	20	18	
40 – 60 years	13	16	
Total	37	37	

In Atracurium group, there were 4 patients in age group of 18 – 20 years, 20 patients in age group of 20 – 40 years, 13 patients in age group of 40 – 60 years.

Tab.2 ASA distribution

ASA Gradings	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
I	15	17	Chi square: 0.17 P – 0.68
II	22	20	
Total	37	37	

In Atracurium group, there were 15 patients with ASA grade of 1 and 17 patients with ASA grade of II. In Cis-Atracurium group, there were 15 patients with ASA grade of 1 and 22 patients with ASA grade of II.

Tab.3 Types of surgeries

Types of surgery	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
Appendicectomy	6	5	Chi square: 1.25 P – 0.87
Cholecystectomy	5	3	
Inguinal hernia	9	8	
Caesareansection	7	12	
Others	10	9	
Total	37	37	

Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab. 4 Onset time of muscle relaxants

Parameters	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
Onset time (Sec)	177 ± 22.4	184 ± 17.3	t :- 10.2 P – .000025

Student t test

- Average onset time for Atracurium group was 177 ± 22.4 seconds and same was 184 ± 17.3 seconds in Cis Atracurium group. Student t test was administered and p value of < 0.05 was derived indicating statistically significant difference between the groups.

Tab.5Attempts for intubation

Variables	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
1st attempt	33	35	Chi square:47.4 P – 0.14
2nd attempt	2	2	
3rd attempt	2	0	

In Atracurium group, intubation was successful at 1st attempt in 33 subjects, 2nd attempt in 2 subjects, 3rd attempt in 2 subjects. In Cis Atracurium group, intubation was successful at 1st attempt in 35 subjects and 2nd attempt in 2 subjects. Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab. 6 Intubating condition of Cis-atracurium and Atracurium according to Copenhagen consensus scoring system

Parameters		Atracurium group (n=37)	Cis Atracurium group (n =37)	Statistic
Laryngoscopy				P : 0.47
	Easy	30	31	
	Fair	7	6	
	Impossible	0	0	
Vocal cords				P : 0.18
	Open	28	30	
	Moving	8	7	
	Closed	1	0	
Cough				P : 0.32
	None	33	34	
	<2	3	3	
	>2	1	0	
Jaw relaxation	Relaxed	33	34	P : 0.16
	Increased tone	2	2	
	Rigid	2	1	
Limb movement	None	33	34	P : 0.25
	Light	3	3	
	Severe	1	0	
CCS	Excellent	31	33	P : 0.81
	Good	2	3	
	Poor	4	1	

In Atracurium group, Laryngoscopy was easy in 29 subjects, fair in 7 subjects. Vocal cords were open in 28 subjects, moving in 8 subjects and closed in 1 subject. There was cough reflex in 4 subjects. Jaw relaxed in 33 subjects, had increased tone in 2 subjects, rigid in 2 subjects. There was no limb movements in 33 subjects, light movements in 3 subjects, severe movement in 1 subject. CCS was excellent in 31 subjects, good in 2 subjects and poor in 4 subjects.

In Cis Atracurium group, Laryngoscopy was easy in 31 subjects, fair in 6 subjects. Vocal cords were open in 30 subjects, moving in 7 subjects and closed in 1 subject. There was cough reflex in 4 subjects. Jaw relaxed in 34 subjects, had increased tone in 2 subjects, rigid in 1 subject. There was no limb movements in 34 subjects, light movements in 3 subjects. CCS was excellent in 33 subjects, good in 3 subjects and poor in 1 subject.

Tab. 7 Hemodynamic parameterspost intubation

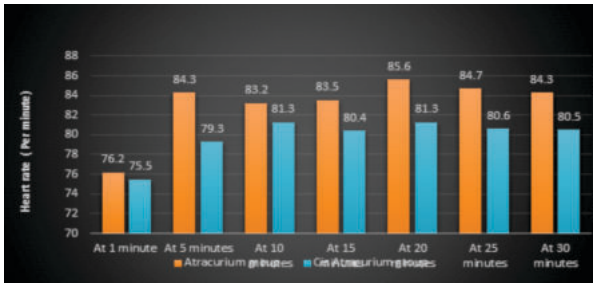
Time	Atracurium group (n =37)			Cis Atracurium group (n =37)			Statistic
	SBP (mmHg)	DBP (mmHg)	Mean BP (mmHg)	SBP (mm Hg)	DBP (mmHg)	Mean BP (mmHg)	P(SBP) – 0.04 P(DBP) –0.01 P(mean BP) –0.02
Baseline	118.4	76.4	90.40	116.1	74.5	88.37	
At Intubation	114.7	72.1	86.30	114.3	74.1	87.50	

At 1 minute	112.3	73.6	86.50	114.6	75.1	88.27	
At 5 minutes	113.8	73.8	87.13	115.3	74.8	88.30	
At 10 minutes	113.6	74.2	87.33	115.2	74.9	88.33	
At 15 minutes	113.9	74.5	87.63	115.7	74.7	88.37	
At 20 minutes	114.6	75.2	88.33	116.3	75.2	88.90	
At 25 minutes	114.9	74.8	88.17	116.6	75.5	89.20	
At 30 minutes	114.8	74.1	87.67	116.5	75.4	89.10	

Hemodynamic parameters were compared. There was statistical difference between systolic BP of Atracurium group and Cis Atracurium group with p value of 0.04. There was statistical difference between diastolic BP of Atracurium group and Cis Atracurium group with p value of 0.01.There was statistical difference between mean BP of Atracurium group and Cis Atracurium group with p value of 0.02.

Tab.8 Heart rate

Time	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
At 1 minute	76.2	75.5	Chi square: 7.06 P – 0.029
At 5 minutes	84.3	79.3	
At 10 minutes	83.2	81.3	
At 15 minutes	83.5	80.4	
At 20 minutes	85.6	81.3	
At 25 minutes	84.7	80.6	
At 30 minutes	84.3	80.5	



Heart ratewas compared. There was statistical difference between systolic BP of Atracurium group and Cis Atracurium group with p value of 0.029.

Tab. 9 Duration of action, 25% recovery, and recovery from reversal

Adverse effects	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
Duration of action (min)	46 ± 4.9	68± 7.1	t: - 23 P - < .00001
Duration of 25% recovery (min)	33± 4.2	48±5.6	t: - 18.35 P: < .00001
Time of recovery from reversal (min)	1.7± 0.8	2.2± 1.1	t: - 5.47 P: .000774

In Atracurium group, duration of action of the muscle relaxant was 46 ± 4.9 minutes, Duration of 25% recovery was 33± 4.2 minutes, Time of recovery from reversal was 1.7± 0.8 minutes.

In Cis Atracurium group, duration of action of the muscle relaxant was 68± 7.1 minutes, Duration of 25% recovery was 48±5.6 minutes, Time of recovery from reversal was 2.2± 1.1 minutes.

Chi square test was performed between the 2 groups and p value was observed to be < 0.05 indicating no statistically significant difference between the groups.

Tab. 10Adverse reactions

Adverse effects	Atracurium group (n =37)	Cis Atracurium group (n =37)	Statistic
Flush	2	1	Chi square: 2.2 P – 0.53
Erythema	0	1	
Wheals	1	0	
Total	3	2	

In Atracurium group, 2 subjects had flush, 1 had wheal. In Cis Atracurium group, 1 subject had flush, 1 had wheal. Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

DISCUSSION

The present study titled "COMPARATIVE STUDY OF ATRACURIUM AND CIS ATRACURIUM FOR INTUBATING CONDITIONS UNDER GENERAL ANAESTHESIA." was conducted at Sri Siddhartha Medical College and research institute Tumkur, Karnataka for 18 months. The study was a prospective clinical study conducted on 74 patients of ASA physical status 1 and 2 in the age group of 18 years to 60 years, posted for various surgeries under general anaesthesia.

Cisatracurium is a nondepolarising neuromuscular blocking agent with an intermediate duration of action. It is the cis isomer of atracurium besilate, and is approximately 3 to 4-fold more potent than the mixture of isomers that constitute the parent drug. However, Cisatracurium produces laudanosine about five times less than atracurium, and accumulation of this metabolite is not thought to be of any consequence in clinical practice. Relative to atracurium, Cisatracurium has a lower propensity to cause histamine release, which is more potent but has a slightly longer onset time at equipotent doses.

Demography and ASA gradings

In the present study we found that data was comparable between atracurium group and cis-atracurium group regarding age distribution, sex distribution, ASA type and type of surgery as the p value was >0.05 in these aspects. Similar findings were observed in the study conducted by El-Kasaby, et al, Harpreet Kaur et al. and M.T. Carroll et al. (66,77,43)This rule out the possibility of differences in the dosages based on confounding factors.

Speed of onset

The speed of onset is inversely proportional to the potency of non-depolarizing neuromuscular blocking agents. It has been reported earlier that 2×ED95 dose of atracurium has a faster onset of action as compared to 4×ED95 dose of Cisatracurium. Presumably Cisatracurium has greater potency than atracurium resulting in fewer molecules being administered even with the higher doses. So Cisatracurium with higher doses has faster onset of action as compared to atracurium.

In our study in terms of onset of action between two groups we found that the mean onset of action in atracurium group was 177 ± 22.4 seconds as compared to 184 ± 17.3 seconds in Cis Atracurium group but with no statistically significant difference as the p value was 0.082.

Similar results were obtained by El –kasaby et al. In thier study while comparing 3 groups of cisatracurium in different doses (2×ED95, 4×ED95, 6×ED95 dose) with 1 group of atracurium (2×ED95 dose). They observed that with the higher doses of Cisatracurium (4×ED95 and 6×ED95) onset of action was significantly faster than with atracurium. M.T. Carroll et al., also had similar observations in their study. Bluestein and colleagues also compared 3different doses of Cisatracurium (2×ED95, 3×ED95, 4×ED95 dose) with 1 group of atracurium (2×ED95) and had similar results regarding mean time of onset of action.

Intubating condition

In our study, intubating conditions in both Cisatracurium group and Atracurium groups were comparable. Laryngoscopy was easy and jaw relaxation was adequate in most cases in both the groups.

In concurrence with our study, Harpreet Kaur et al and M.T. Carroll et al observed that intubating conditions were comparable in both Cisatracurium group and Atracurium groups.

However, El Kasaby et al observed that excellent to good intubating conditions could be achieved only with 0.20 mg/kg at 90 seconds with Cisatracurium. Similar observation was noted in a study in Alturi et al,where 83% of patients treated with cis atracurium had excellent intubating conditions as compared to 47% with atracurium which was significant.

Duration of 25% recovery

In our study, Cis atracurium had significantly longer time for 25 %

recovery than Atracurium group with 33 ± 4.2 minutes 48 ±5.6 minutes respectively. In cooccurrence with our study, and Ranjan et al and Thukral et al also observed the same.

Recovery comes to rely more on drug elimination than distribution (i.e. 25% to 75% or greater). Study by Ranjan et al observed that the mean duration of 25% recovery from reversal in atracurium group was 32.4 ±1.90 minutes which was significantly less as compared to 49.46 ±1.86 minutes of cis-atracurium group as the p value we found was s <0.001. Shyamlal Thukral et al. also in their study found 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.

Time of recovery from reversal

Among the array of muscle relaxants available, the most important concern of an anaesthesiologist after their administration, is the complete recovery of the muscle function post-surgery. This implies that postoperative recovery of muscle power should be more predictable and ensures patient safety especially in the elderly as well as in patients with compromised organ functions.

In our study, in Cis atracurium group, the time of recovery from reversal of the muscle relaxant was 2.2 ± 1.1 minutes1 which was significantly longer than 1.7 ± 0.8 minutes in atracurium group.

Duration of action

In our study, in Cis Atracurium group, the duration of action of the muscle relaxant was 68 ± 7.1 minutes which was significantly longer than 46 ± 4.9 minutes.

Similar results were observed by El – kasaby et al.. where they found statistically significant difference in both the drugs. 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). (66) In contrast to our observation, C.E. Smith et al also observed that duration of action of cisatracurium and atracurium were comparable and statistically not significant. (46)

Haemodynamic profile

In terms of mean heart rate between two groups we found that there was a statistically significant increase in heart rate of post intubation when compared to baseline reading of atracurium group and cis-atracurium group. The comparison of mean arterial blood pressure between two groups showed that there was a statistically significant increase in MABP of post intubation compared to baseline reading.

According to a clinical comparative study of two intubating doses of cis atracurium during general anaesthesia for gynecological surgery in Silchar Medical College. After induction, mean arterial pressure and heart rate shows decrease in both groups but neither statistically nor clinically significant. Better hemodynamic stability and longer duration of action was found in group B compared to group A. No adverse effects noted in both groups.

Adverse effects

In our study, in Atracurium group, 2 subjects had flush, 1 had wheal. In Cis Atracurium group, 1 subject had flush, 1 had wheal. However, difference in occurrence of adverse events was not significant. None of the patients in any group had episodes of hypotension, bronchospasm, tachycardia or urticaria.

Hughes R and Chapple DJ that despite 10-20 times increase in the plasma histamine levels atracurium is not vagolytic and does not block the innervation by autonomic ganglia. In a study conducted by Kumar A et al, the frequency of urticaria after administration of atracurium was assessed. They concluded that in conventional doses atracurium is not associated with formation of urticarias although significant changes in haemodynamics may occur. (44)

CONCLUSION

Atracurium was significantly faster than Cisatracurium in terms onset of action. Cisatracurium and Atracurium, both provided excellent intubating conditions.

Cisatracurium had significantly longer time for 25 % recovery than atracurium. Time of recovery from reversal was significantly higher in Cis atracurium than atracurium group. Duration of action of Cisatracurium was longer than that of Atracurium.

There was a significant increase in heart rate of post intubation with Atracurium than with Cis atracurium. Atracurium resulted in significant decrease in systolic BP, Diastolic BP and mean BP post intubation with Atracurium when compared with Cisatracurium.

Adverse events due to histamine release were not significantly greater in Atracurium than Cisatracurium. No life-threatening adverse events were observed in Atracurium and Cisatracurium.

Hence, Cisatracurium can replace atracurium in the routine clinical practice where hemodynamic stability is of most important. However, in cases of day care surgeries where longer recovery from muscle relaxant is undesirable, Atracurium will be a better choice than Cisatracurium.

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No

Conflict of Interest:

No conflict of interest

REFERENCES

1. Wani TM, Bissonnette B, Engelhardt T, Buchh B, Arnous H, AlGhamdi F, Tobias JD. The airway: Historical concepts, new findings, and what matters. Int J Pediatr Otorhinolaryngol. 2019 Jun;121:29-33.
2. Patwa A, Shah A. Anatomy and physiology of respiratory system relevant to anaesthesia. Indian J Anaesth. 2015 Sep;59(9):533-41.
3. Benner A, Sharma P, Sharma S. Treasure Island (FL). Anatomy, Head and Neck, Cervical, Respiratory, Larynx, and Cricoarytenoid. 2021: 14 – 36
4. Saran M, Georgakopoulos B, Bordoni B. StatPearls . Pearls Publishing; Treasure Island (FL): Aug 11, 2021. Anatomy, Head and Neck, Larynx Vocal Cords.2020: 10 – 55
5. Clark CM, Kugler K, Carr MM. Common causes of congenital stridor in infants. JAAPA. 2018 Nov;31(11):36-40.
6. De Rose V, Molloy K, Gohy S, Pilette C, Greene CM. Airway Epithelium Dysfunction in Cystic Fibrosis and COPD. Mediators Inflamm. 2018;2018:1309746.
7. Olszewska E, Woodson BT. Palatal anatomy for sleep apnea surgery. Laryngoscope Investig Otolaryngol. 2019 Feb;4(1):181-187.
8. Estime SR, Kuza CM. Trauma Airway Management: Induction Agents, Rapid Versus Slower Sequence Intubations, and Special Considerations. Anesthesiol Clin. 2019 Mar;37(1):33-50.