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COMPARISON OF ATRACURIUM AND CISATRACURIUM WITH REGARDS TO THEIR POTENCY, ONSET TIME OF NEUROMUSCULAR BLOCKADE AND RECOVERY IN PATIENTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA

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ABSTRACT

Introduction: Neuromuscular blocking drugs were first used in anaesthesia and surgery in 1942, ushering in a new era. Succinylcholine, a depolarizing muscle relaxant, was first introduced in 1952, and it quickly became widely used due to the drug's swift action and ultrashort duration of action. However, it was found to cause several undesirable side effects. Hence, efforts have been concentrated on finding the optimal non-depolarizing muscle relaxant with a quick onset and optimal conditions for intubation.

Aim: To compare Atracurium and Cisatracurium with regards to their potency, onset time of neuromuscular blockade and recovery in patients undergoing surgeries under general anaesthesia. **Material and methods:** We conducted the study in 60 patients of ASA I or ASA II category scheduled for elective surgery under general anaesthesia. Group A (n=30) and Group B (n=30) were given Atracurium (0.5mg/kg) and Cisatracurium (0.15mg/kg) respectively. The onset time of neuromuscular blockade, intubating conditions, duration of neuromuscular blockade, hemodynamic parameters, and presence of any side effects were noted.

Results: The mean onset time of neuromuscular blockade for Group A and Group B were 256.97±8.23 seconds, and 208.70±6.21 seconds, respectively (p value <0.05). In Group A, the conditions of intubation were excellent in 17.24 % of patients and good in 80.65% and while

Group B, excellent conditions were observed in 82.76% of patients and good in 19.35% of patients. The mean duration of neuromuscular blockade was 33.83±1.86 minutes in Group A and 59.20±3.40 minutes in Group B (p value <0.05). No side effects were observed in either group.
Conclusion: Cisatracurium (0.15mg/kg) had a statistically and clinically significant faster onset, excellent intubating conditions, and longer duration of neuromuscular blockade when compared to atracurium (0.5mg/kg). However, atracurium was faster in terms of recovery from the last dose of neuromuscular blockade. Both drugs were stable hemodynamically with no side effects.
Keywords: neuromuscular blockade, atracurium, cisatracurium

INTRODUCTION

Neuromuscular blocking medications were first used in anaesthesia and surgery in 1942, ushering in a new era. The anaesthetist was able to keep the patient's breathing while the surgeon performed a lengthy and complex surgery, allowing him access to body cavities without the need for voluntary or reflex muscle action.[(1)]

Thesleff and Foldes and associates first presented succinylcholine, a depolarizing muscle relaxant, in 1952, and it quickly became widely used due to the drug's swift action and ultrashort duration of action, which enabled quick endotracheal intubation and quick restoration of neuromuscular strength. Even so, in addition to fasciculations, succinylcholine also causes several undesirable effects, including masseter spasm, malignant hyperthermia in patients with pseudocholinesterase deficiency, bradycardia, dysrhythmias, increased potassium release, postoperative myalgia, increased intraocular, intracranial, and intragastric pressure.[(2)]

Since succinylcholine's depolarizing mechanism of action is the cause of these side effects, efforts have been concentrated on finding the optimal non-depolarizing muscle relaxant with a quick onset and optimal conditions for intubation.

Since atracurium and vecuronium were commercially accessible in 1982, a generation of anesthesiologists has been trained who have grown accustomed to their quick onset, shorter and more predictable duration of action, and absence of cardiovascular side effects. The most recent generation of neuromuscular blocking medications seeks to offer even more benefits, including disposition irrespective of organ function, quick onset and offset comparable to succinylcholine, and low side effects.

Atracurium, a muscle relaxant that falls under the non-depolarizing relaxant class and is a member of the benzylisoquinolinium drug family, has been a popular choice for individuals with hepatic and renal impairment because of its independent metabolism from these major body organs. It has been engineered to spontaneously degrade at physiological temperatures and pH levels using a process known as Hoffman elimination, producing the metabolites laudanosine (a tertiary amine) and monoquaternary acrylate. Atracurium can also undergo ester hydrolysis. Hofmann elimination is an entirely chemical process that causes molecular fragmentation to laudanosine and a monoquaternary acrylate, resulting in the elimination of positive charges. Laudanosine is cleared by the liver but rapidly penetrates the blood-brain barrier and has qualities that stimulate the central nervous system. Atracurium administration can cause hemodynamic changes that might be problematic, particularly for cardiovascular patients. These changes are brought on by the release of histamine.

The 1R cis-1'R cis isomer of atracurium, cisatracurium, will be metabolised through the Hoffman mechanism similarly to atracurium, however unlike atracurium, ester hydrolysis plays no part in its metabolism. Cisatracurium undergoes Hofmann elimination, just like atracurium, and is converted to laudanosine and a monoquaternary alcohol metabolite. 77% of the overall clearance

of 5 to 6 mL/kg/min is due to Hofmann elimination. A total of 23% of the medication is eliminated by organ-dependent processes, with renal clearance making up 16% of this. Since laudanosine is formed in around five times less amounts when cisatracurium is used compared to atracurium, the buildup of this metabolite is not considered to have any clinically significant effects. When administered within the clinical dosage range, cisatracurium does not trigger the release of histamine like atracurium does. This suggests that the histamine release phenomena can be stereospecific.[3]

Cisatracurium has about three times the potency of atracurium besylate when it comes to neuromuscular blockade. Atracurium's ED95 is 0.2 mg/kg, while cisatracurium's is 50 μg/kg. The fundamental advantage of cisatracurium over atracurium and other histamine-releasing neuromuscular blocking drugs is that it does not produce histamine, which enhances cardiovascular stability.[4]

The aim of this study was the comparison of Atracurium and Cisatracurium with regards to their potency, onset time of neuromuscular blockade and recovery in patients undergoing surgeries under general anaesthesia.

MATERIALS AND METHODS

The present comparative study was conducted among 60 patients of ASA I or ASA II category scheduled for elective surgery under general anaesthesia. Group A (n=30) and Group B (n=30) were given Atracurium (0.5mg/kg) and Cisatracurium (0.15mg/kg) respectively.

Inclusion Criteria

1. ASA grade I or II fit patients.
2. Patients aged between 18 and 60 years of age.
3. Patients undergoing surgeries under general anaesthesia.
4. Haemodynamically stable patients with all routine investigations within normal limits and without any comorbidities.
5. Written informed consent from the concerned patient.

Exclusion Criteria

1. Patients who are not willing to participate in the study.
2. Patients with ASA grade III and above physical status.
3. Patients who are aged less than 18 and more than 60 years of age.
4. Patients who are posted for emergency procedures.
5. Patients with known allergy to the study drugs.
6. Patients with difficult intubation.
7. Patients who are obese.
8. Patients who have psychiatric, neurological, neuromuscular, or cardiovascular disease or impairment of hepatic or renal function.

Methodology

Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained. 60 patients of either sex belonging to ASA grade I or II and willing to give informed written and verbal consent posted for surgery under general anaesthesia were allocated. Preanesthetic evaluation and counselling for surgery was done the day before surgery and reviewed on the day of surgery. A detailed medical history

was taken, and systemic examination was carried out and relevant investigations advised. Patients were advised nil per oral from 6 hours prior to surgery. An informed written consent was taken from all the patients, and they were informed about known effects, and side effects of study drug and consent was taken for the study. On the day of surgery in operation theatre, intravenous access was secured with 20G cannula and all the standard monitors such as ECG, non-invasive blood pressure, pulse oximeter, end- tidal carbon dioxide (EtCO2) were connected. Baseline hemodynamic parameters were noted.

Premedication

All patients were given Inj. GLYCOPYRROLATE 0.004 mg/kg IV, Inj. ONDANSETRON 0.1 mg/kg IV, Inj. FENTANYL 1-2 µg/kg IV and Inj MIDAZOLAM 0.02 mg/kg IV. Patients were preoxygenated with 100% oxygen for 3 minutes. Train of four nerve stimulator was attached. Once the current and twitch height were standardized, instrument was switched to TOF mode where supra maximal TOF stimuli (50mA, 2 Hz) was applied to ulnar nerve every 15 s. Calibration and baseline responses were obtained before administering the neuromuscular blocking drug (NMBD). Randomization was done using computer-generated lottery method.

Induction of general anesthesia for all patients was done with Inj. PROPOFOL 2mg/kg with loss of eyelash reflex/loss of verbal response considered to be the endpoint of induction. This was followed by an intubating dose of study drug, i.e., NDMR, over 5 s.

Group A patients were given an intubating dose of ATRACURIUM (0.5mg/kg)

Group B patients were given an intubating dose of CISATRACURIUM (0.15mg/kg)

Cold chain was maintained for both the study drugs.

Time to Maximum Blockade

It is the time interval between administration of the dose of relaxant and disappearance of all four twitches in TOF monitor.

Intubation was done when the TOF ratio turned 0%

Assessment of intubation was done by intubating conditions which were characterised as:

Excellent: Easy passage of Endotracheal tube without coughing. Vocal cords relaxed and abducted

Good: Passage of endotracheal tube with slight coughing and/or bucking. Vocal cords relaxed and abducted.

Poor: Passage of endotracheal tube with moderate coughing and/or bucking. Vocal cords moderately adducted.

Intubating conditions and time required for intubation were graded by a senior anesthesiologist blinded to group allocation. Intubation was confirmed by EtCO2 and bilaterally equal air entry and then connected to a ventilator for intermittent positive pressure ventilation until completion of surgery.

Maintenance of anaesthesia was done with 40% Oxygen + 60% Nitrous Oxide and ISOFLURANE (0.6-1%) and intermittent positive pressure ventilation. Onset time and intubating conditions for ATRACURIUM and CISATRACURIUM were assessed in allocated groups, respectively. Hemodynamic parameters were recorded before induction, after giving study drug, during laryngoscopy and intubation and immediately after 1,5,10, 15, and 30 minutes after tracheal intubation, and throughout the surgery, maintenance dose of neuromuscular blocking drug was given as 0.1 mg/kg ATRACURIUM and 0.03 mg/kg of CISATRACURIUM, at TOF score 2.

At the end of the surgery with 25% recovery of T_1 %, reversal (induced recovery) was achieved by administration of NEOSTIGMINE 0.05 mg/kg + GLYCOPYRROLATE 0.008 mg/kg

through slow IV injection. TOF ratio >0.9 was considered to be sufficient for safe extubation of the endotracheal tube. Patients were then shifted to recovery room for post-operative monitoring. Intraoperatively and postoperatively any side effects like hypotension, bronchospasm, flush, erythema, and wheal were looked for and treated accordingly.

Statistical Analysis

The data was entered in Microsoft **Excel 2019** (Part of Microsoft Office Professional Edition) [computer program]. Microsoft; 2019) and analyzed using,

SPSS v26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp)

MedCalc v18.2.1 (MedCalc Statistical Software version 18.2.1 (MedCalc Software, Ostend, Belgium; http://www.medcalc.org; 2018).

Categorical variables were expressed in terms of frequency and percentages (where applicable), Continuous variables expressed as mean and SD & Median and IQR (where applicable). Normal distribution was verified by Shapiro-Francia test. **Independent t test / Mann-Whitney test** (where applicable) was used to check for significance of observations between two groups. Chi-Square test or Fisher exact test (where applicable) was done to check for the independence of attributes. Repeated measures ANOVA was performed to check the variation between the groups as well within subjects over time. In all the tests performed, **P < 0.05** is considered to be statistically significant.

OBSERVATION AND RESULTS

This study was conducted at Dr. D. Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune. 60 patients of ASA I and II grade, between 18 to 60 years of age and belonging to either gender who had undergone surgeries under general anaesthesia were included.

Both the study groups were comparable with respect to their age, gender, weight, and ASA grading. (Table 1)

TABLE 1: DEMOGRAPHIC PROFILE OF THE STUDY GROUPS

		Group A (n=30)	Group B (n=30)	P value
Age (years)		45.4±11.68	45.6±11.95	0.8644
Gender	Male	16 (53.33%)	13 (43.33%)	0.605
	Female	14 (46.66%)	17 (56.67%)	
Weight (kg)		61.5±8.307	61.36±9.39	0.9233
ASA Grading	I	15	13	0.6078
	II	15	17	

The mean onset time of neuromuscular blockade was 256.97±8.23 seconds in Group A and 208.70±6.21 seconds in Group B. Group B had a faster onset time of neuromuscular blockade in comparison to Group A and this was statistically significant (P value < 0.05). (Table 2)

TABLE 2: DISTRIBUTION OF PATIENTS ACCORDING TO ONSET OF NEUROMUSCULAR BLOCKADE IN STUDY GROUPS

ONSET OF NMB x GROUP	**Mean ± SD (seconds)**	**Median (IQR) (seconds)**	**Minimum**	**Maximum**	**SIGNIFICANCE**
GROUP A	256.97 ±	257	244	270	t =25.631, df=58,

(N = 30)	8.23	(250-264)			P= < 0.0001
GROUP B (N = 30)	208.70 ± 6.21	209.5 (206-213)	196	220	

In group A, 17.24% and 80.65% of patients had excellent and good conditions of intubation respectively, whereas, in group B, 82.76%and 19.35% of patients had excellent and good conditions of intubation. This difference was statistically significant (P value < 0.05) and showed that Group B provided better intubating conditions when compared to Group A. (Table 3)

TABLE 3: DISTRIBUTION OF PATIENTS ACCORDING TO INTUBATING CONDITIONS IN STUDY GROUPS

	GROUP		**TOTAL**	**SIGNIFICANCE**
	A (%) (N = 30)	**B (%) (N=30)**		
EXCELLENT	5 (17.24%)	24 (82.76%)	29 (100%)	Chi-squared=21.62 df=1 P = <0.001
GOOD	25 (80.65%)	6 (19.35%)	31 (100%)	
Total	30 (50%)	30 (50%)	60 (100%)	

The mean duration of neuromuscular blockade was 33.83±1.86 minutes in Group A and 59.20±3.40 minutes in Group B. Group B had a longer duration of neuromuscular blockade in comparison to Group A and this was statistically significant (P value < 0.05). (Table 4)

TABLE 4: DISTRIBUTION OF PATIENTS ACCORDING TO DURATION OF NEUROMUSCULAR BLOCKADE IN STUDY GROUPS

DURATION OF NMB x GROUP	**Mean ± SD (minutes)**	**Median (IQR) (minutes)**	**Minimum**	**Maximum**	**SIGNIFICANCE**
GROUP A (N = 30)	33.8333 ± 1.86	34 (33-35)	29.0000	37.0000	*Mann-Whitney U=0.00 Z =6.667 =P < 0.0001
GROUP B (N = 30)	59.20 ± 3.40	60 (58-61)	50.0000	63.0000	

The mean time of recovery from last dose of neuromuscular blockade prior to extubation was 26.80±2.50 minutes in Group A and 43.13±1.83 minutes in Group B. This difference was statistically significant (P value < 0.05) and showed that the recovery from the last dose of neuromuscular blockade prior to extubation was faster with Group A when compared to Group B. (Table 5)

TABLE 5: DISTRIBUTION OF PATIENTS ACCORDING TO TIME OF RECOVERY FROM LAST DOSE OF NEUROMUSCULAR BLOCKADE IN STUDY GROUPS

TIME OF RECOVERY x GROUP	**Mean ± SD (minutes)**	**Median (IQR) (minutes)**	**Minimum**	**Maximum**	**SIGNIFICANCE**
GROUP A (N = 30)	26.80 ± 2.50	27.5000 (25-28)	22.0000	31.0000	t= -28.880, df = 58, P < 0.0001
GROUP B	43.13 ± 1.83	43.0000	40.0000	46.0000	

(N = 30)		(42-44)			

The mean heart rate and mean arterial pressure were comparable between the study groups at all time points and the difference was statistically insignificant (P>0.05). (Figure 1 and Figure 2)

FIGURE 1: LINE DIAGRAM SHOWING DISTRIBUTION OF MEAN HEART RATE IN STUDY GROUPS

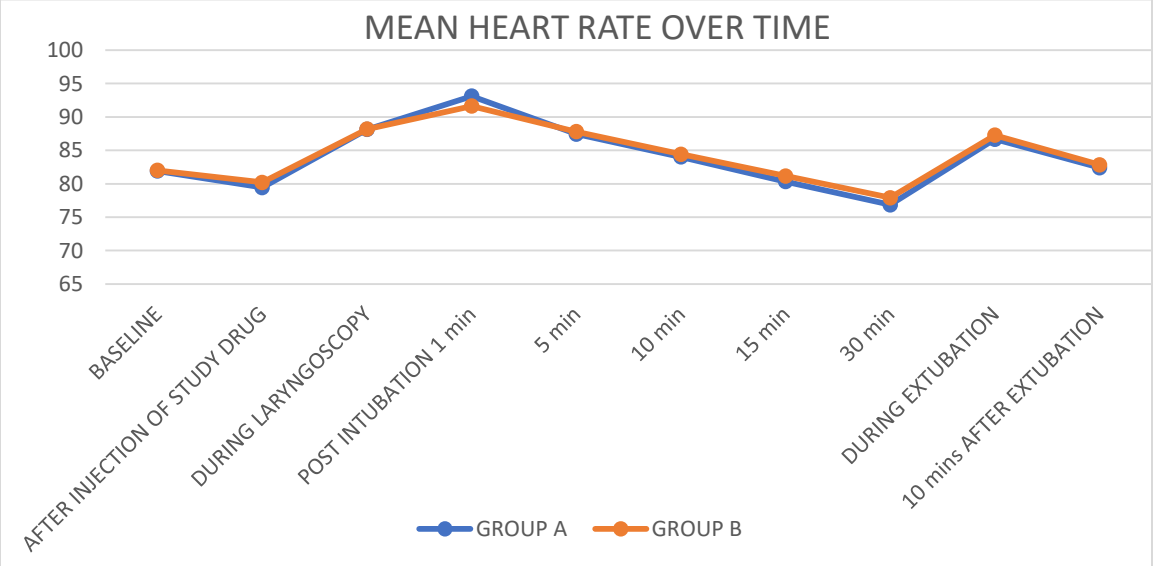
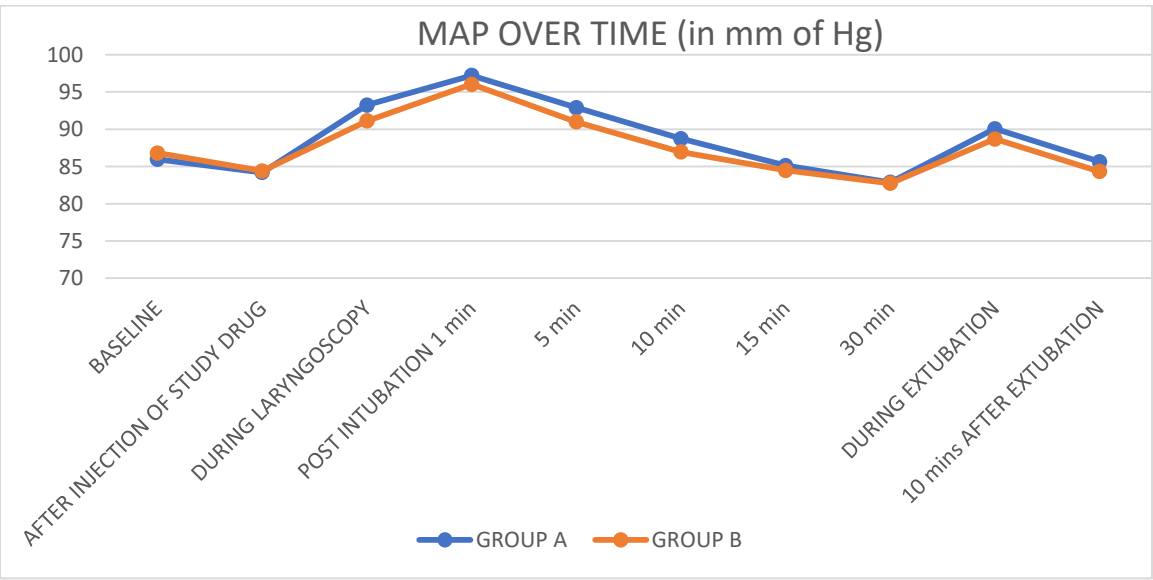


FIGURE 2: LINE DIAGRAM SHOWING DISTRIBUTION OF MEAN ARTERIAL PRESSURE IN STUDY GROUPS



No side effects due to histamine release like flushing, erythema, wheal, bronchospasm, or hypotension were observed in either group at any point of time.

DISCUSSION

Anaesthesia was formerly produced and sustained by intravenous or inhalation medications before the development of muscle relaxants. Tracheal intubation was rare, and when it was necessary, deep inhalation anaesthesia was used to achieve muscle relaxation at the risk of respiratory or cardiac depression. Anaesthesia experienced a conceptual shift after the advent of muscle relaxants. The three effects of narcosis, analgesia and muscular relaxation were combined to form the new definition of anaesthesia.[5]

Since then, neuromuscular blocking medications have totally transformed how balanced anaesthesia is delivered. The development and launch of succinylcholine, a depolarizing muscle relaxant in 1952 enabled adequate relaxation for quick endotracheal intubation and quick restoration of neuromuscular strength. However, the undesirable cardiovascular side effects of succinylcholine pushed the search for better and safer neuromuscular blocking agents.

Numerous non-depolarizing neuromuscular blocking agents were introduced into clinical practice, but they were not appropriate for use in certain clinical situations, such as liver and kidney disorders because of their side effects, which included cardiovascular instability, the possibility of recurarisation, and residual paralysis. A combination of 10 optical isomers known as atracurium is an intermediate-acting NDMR that is frequently utilised in liver and renal failure. Its metabolism is through Hoffman's elimination and nonspecific ester hydrolysis but its association with histamine release can lead to hypotension and anaphylaxis.[6]

Cisatracurium is one of the ten stereoisomers of atracurium that has been isolated, and it has a potency that is around three to four times more than that of atracurium. Unlike the parent chemical, however, it is not linked to dose-dependent histamine release in people and 5 times less laudanosine is produced during metabolism. Cisatracurium might not produce the same favourable intubating circumstances as atracurium at equivalent dosages and the recommended dosage of cisatracurium for intubation is 0.15mg/kg (3xED95).[6]

Our study compared Atracurium and Cisatracurium with regards to their potency, onset time of neuromuscular blockade and recovery in patients undergoing surgeries under general anaesthesia.

In the current study, the mean ± SD time for the onset of neuromuscular blockade for the Atracurium group (0.5mg/kg) and the Cisatracurium group (0.15mg/kg), were 256.97±8.23 seconds, and 208.70±6.21 seconds, respectively. Table 2 shows this difference was statistically significant (P value < 0.05) and cisatracurium (0.15mg/kg) had a faster onset time in comparison to atracurium (0.5mg/kg). In 1996, Bluestein, et al.[7] compared the onset time to maximal neuromuscular blockade of atracurium (0.5 mg/kg), and cisatracurium at 0.1 mg/kg, 0.15 mg/kg & 0.2 mg/kg doses. The study was conducted in 80 patients divided randomly into 4 groups: Group A (cisatracurium at 0.1mg/kg), Group B (atracurium at 0.5mg/kg), Group C (cisatracurium at0.2mg/kg) and Group D (cisatracurium at 0.15mg/kg). The mean onset times were 4.6 minutes, 4.0 minutes, 2.8 minutes, and 3.4 minutes respectively in the study groups A, B, C & D respectively. This difference was statistically significant with p value < 0.05. The onset time was observed to be faster with cisatracurium (0.15mg/kg and 0.2mg/kg) when compared to atracurium at a dose of 0.5mg/kg. In 2018, Arun Kumar Mohanty, et al.[8] compared atracurium and 2 doses of cisatracurium in 60 patients divided into three groups, Group A (atracurium 0.5mg/kg), Group C1 (cisatracurium 0.1mg/kg) and Group C2 (cisatracurium 0.15mg/kg). The mean onset time of neuromuscular blockade was 168.10±10.60 seconds, 242.45±11.64 seconds & 159.15±10.49 seconds in groups A, C1 & C2 respectively. Thus, the onset time was found to be faster with cisatracurium at 0.15mg/kg when compared to atracurium at 0.5mg/kg and this

difference was statistically significant with p = 0.000. In 2019, Athaluri, et al.[9] in their study compared atracurium at 0.5mg/kg (Group A), cisatracurium at 0.1 mg/kg (Group B) and 0.15mg/kg (Group C) in 150 patients undergoing surgeries under general anaesthesia. The mean onset time of neuromuscular blockade was 142.2±14.504 seconds, 127.8±14.2914 seconds & 97.2±14.9292 seconds, in groups A, B & C respectively. They concluded that cisatracurium at a dose of 0.15 mg/kg (group C) when compared to atracurium at 0.5mg/kg (Group A) offers superior intubating circumstances with a quick onset, a longer neuromuscular blockade, and no discernible hemodynamic changes and this difference was statistically significant with p = 0.001. The findings from these three studies regarding onset time of neuromuscular blockade were in accordance with the findings from our study.

In the present study, the conditions of intubation were excellent in 17.24 % of patients and good in 80.65% of the patients in the atracurium group while in the cisatracurium group, excellent conditions were observed in 82.76% of patients and good in 19.35% of patients. The conditions were never poor in either group. Table 3 shows that this difference was statistically significant (p < 0.05). In 2010, El-Kasaby, et al.[10] compared atracurium (0.5 mg/kg), and cisatracurium at 0.1 mg/kg, 0.2 mg/kg & 0.3 mg/kg doses. The study was conducted in 64 patients divided randomly into 4 groups: Group 1 (atracurium at 0.5mg/kg), Group 2 (cisatracurium at 0.1mg/kg), Group 3 (cisatracurium at 0.2mg/kg) and Group D (cisatracurium at 0.3mg/kg). They found that after the administration of cisatracurium (0.2 mg/kg), 62.5% and 31.25% of patients had excellent and good intubating conditions, respectively, compared to 37.5% and 50% after the administration of atracurium (0.5 mg/kg). In 2020, Dr. S. Niranjana, et al.[11] compared the efficacy of atracurium at 0.5mg/kg (Group A) and cisatracurium at 0.3mg/kg (Group B) in 60 patients undergoing abdominal surgeries under general anaesthesia. They concluded that 83.3% of patients in cisatracurium group had excellent intubating conditions in comparison 46.7% of patients in atracurium group and this difference was statistically significant with p = 0.006. The findings from these two studies regarding intubating conditions are in accordance with the findings from the present study.

In the present study, the mean and median duration of neuromuscular blockade was 33.83±1.86 minutes and 34 minutes (IQR =33-35) in Group A and 59.20±3.40 minutes and 60 mins (IQR=58-61) in Group B respectively. Table 4 shows that this difference was statistically significant (P value < 0.05) and atracurium at a dose of 0.5mg/kg had a shorter duration of action in comparison to cisatracurium at a dose of 0.15mg/kg. In 2010, El-Kasaby, et al.[10] compared atracurium (0.5 mg/kg), and cisatracurium at 0.1 mg/kg, 0.2 mg/kg & 0.3 mg/kg doses. The study was conducted in 64 patients divided randomly into 4 groups: Group 1 (atracurium at 0.5mg/kg), Group 2 (cisatracurium at 0.1mg/kg), Group 3 (cisatracurium at 0.2mg/kg) and Group D (cisatracurium at 0.3mg/kg). the mean duration of neuromuscular blockade was 44.4±4.13 minutes, 43.6±4.15 minutes, 65.5±10.5 minutes & 78.4±8.6 minutes in groups 1, 2, 3 & 4 respectively. They concluded that atracurium at 0.5mg/kg is more effective neuromuscular blocking agent than cisatracurium at 0.1mg/kg. Higher doses of cisatracurium at 0.2mg/kg and 0.3mg/kg provide more effective, more rapid neuromuscular blocking with longer duration of action and these differences were statistically significant with p <0.05. In 2018, Arun Kumar Mohanty, et al.[8] compared atracurium and 2 doses of cisatracurium in 60 patients divided into three groups, Group A (atracurium 0.5mg/kg), Group C1 (cisatracurium 0.1mg/kg) and Group C2 (cisatracurium 0.15mg/kg). The mean duration of neuromuscular blockade was 43±2.27 minutes, 43.2±2.72 minutes & 64.6±4.83 minutess, in groups A, C1 & C2 respectively. They concluded that compared to 0.5 mg/kg atracurium and 0.1 mg/kg cisatracurium, 0.15 mg/kg

cisatracurium had a longer duration of neuromuscular blockade and this difference was statistically significant with p = 0.000). In 2019, Athaluri, et al.[9] in their study compared atracurium at 0.5mg/kg (Group A), cisatracurium at 0.1 mg/kg (Group B) and 0.15mg/kg (Group C) in 150 patients undergoing surgeries under general anaesthesia. The mean duration of neuromuscular blockade was 43.34±3.4736 minutes, 43.06±4.3632 minutes & 42.06±3.8778 minutes, in groups A, B & C respectively. They concluded that when compared to cisatracurium 0.1 mg/kg and atracurium 0.5 mg/kg, cisatracurium at a dose of 0.15 mg/kg offers superior intubating circumstances with a quick onset of action, a longer duration of action, and no discernible hemodynamic changes and this difference was statistically significant with p = 0.001. The findings from these three studies regarding duration of neuromuscular blockade were in accordance with the findings from the present study.

The current study, the mean recovery time from last dose of neuromuscular blockade prior to extubation was 26.80±2.50 minutes in Group A and 43.13±1.83 minutes in Group B. Table 5 shows that this difference was statistically significant (P value < 0.05) and the recovery from the last dose of neuromuscular blockade prior to extubation was faster with atracurium at a dose of 0.5mg/kg shorter duration of action when compared to cisatracurium at a dose of 0.15mg/kg. In 1997, MT Carroll, et al.[12] compared atracurium at 0.5 mg/kg with cisatracurium at doses 0.1 mg/kg & 0.15mg/kg in 90 patients. After cisatracurium 0.1 mg.kg¹1 had been given, the median time to recovery of the train-of-four ratio to 0.8 ('adequate recovery') was 74min during spontaneous recovery, 48 min after reversal with neostigmine when the first twitch of the train-of-four had returned to 10% of control and 50 min after reversal when the first twitch of the train-of-four had returned to 25% of control. These times for cisatracurium 0.15 mg.kg¹1 and atracurium 0.5 mg.kg¹1 were 90, 66 and 57 min and 75, 56 and 54 min, respectively. They concluded that the period from drug administration to recovery of T1 to 25% was prolonged with cisatracurium (0.15mg/kg) and this was statistically significant with p <0.05. In 2016, Dr.Rochana G Bakhshi et al.[13] compared atracurium at a dose of 0.5mg/kg (Group A) with cisatracurium at a dose of 0.2mg/kg (Group B) in 60 patients. The mean 25% recovery in Cisatracurium besylate group was 48.73 minutes which was more as compared to 33.63 minutes in Atracurium besylate group and this difference was statistically significant with p = 0.001. In 2018, Harpreet Kaur, et al.[14] in their study involving 60 patients compared the recovery profile of atracurium at 0.5mg/kg (Group A) and cisatracurium at 0.1mg/kg (Group C). The recovery index was 14.63±1.84 minutes in group A and 15.30±1.96 minutes in Group C. They concluded that the recovery profile of both drugs in equipotent doses were comparable and statistically insignificant with p = 0.181. In 2020, Pritish Ranjan, et al.[15] in their study involving 100 patients compared atracuroum at a dose of 0.5mg/kg (Group A) and cisatracurium at a dose of 0.15mg/kg (Group B). The mean duration of recovery from reversal in cis-atracurium group was 2.18 ±0.82 minutes which was significantly more as compared to 1.8 ±0.75 minutes of atracurium group as the p value was 0.02. They concluded that cisatracurium at a dose of 0.15mg/kg took longer time for 25% TOF ratio recovery from the last dose of neuromuscular blockade when compared to atracurium at a dose of 0.5mg/kg and this difference was statistically significant with p <0.001. The findings from the present study were in accordance with the findings from these four studies with regards to the recovery profile of the study drugs.

In the present study, hemodynamic parameters like heart rate and mean arterial pressure were recorded during baseline, after injection of study, during laryngoscopy, 1min, 5min, 10min, 15min, and 30 min after intubation, during extubation and 10 min after extubation. Our study shows that the mean heart rates and mean arterial pressures were comparable at all time points

between the two study groups and were statistically insignificant (p >0.05). (Figure 1 and Figure 2). In 2018, Arun Kumar Mohanty, et al.[8] found that compared to 0.5 mg/kg atracurium and 0.1 mg/kg cisatracurium, 0.15 mg/kg cisatracurium and concluded that cisatracurium and atracurium were comparable with respect to their hemodynamic changes with no statistical significance (p >0.05). In 2018, Harpreet Kaur, et al.[14] in their study involving 60 patients compared the recovery profile of atracurium and cisatracurium in equipotent dose and concluded that both the study drugs were comparable with respect to their hemodynamic changes with no statistical significance (p >0.05). In 2020, Dr. S. Niranjana, et al.[11] compared atracurium (0.5mg/kg) and cisatracurium (0.3mg/kg) in 60 patients undergoing abdominal surgeries under general anaesthesia and concluded that both the study drugs were comparable with respect to their hemodynamic stability and the changes in heart rate and mean arterial pressure were not significant (p >0.05). The findings from the current study regarding hemodynamic changes were consistent with the findings from these three studies.

No side effects due to histamine release like flushing, erythema, wheal, bronchospasm, or hypotension were observed in either group at any point of time. In 2019, Athaluri, et al.[9] in their study compared atracurium 0.5mg/kg, and cisatracurium at the doses of 0.1mgkg ad 0.15mg/kg. No side effects were seen in any of their study groups. In 2020, Pritish Ranjan, et al.[15] in their study compared atracurium (0.5mg/kg) and cisatracurium (0.15mg/kg) in 100 patients and reported side effects in 2 out of 50 cases in the atracurium group. The side effects were 1 incidence of erythema and 1 incidence of flushing. The cisatracurium group however did not produce any side effects. However, this was not statistically significant as p value = 1.00. In 2021, Ranjan, et al.[16] in their study comparing atracurium 0.5mg/kg and cisatracurium 0.15mg/kg found no side effects in either of their study groups. The present study did not observe any side effects in either of the study groups and these findings were more in accordance with the findings from these three studies.

Limitations

The sample size of our study was small as the number of participants willing to participate were limited. Our study's non-invasive blood pressure measurement method was another limitation. However, the ASA I and ASA II patients in our research were generally healthy, thus it was not necessary to invasively monitor their blood pressure.

CONCLUSION

Cisatracurium at the dose of 0.15mg/kg has a faster onset of neuromuscular blockade, excellent intubating conditions, and a longer duration of action in comparison to atracurium at the dose of 0.5mg/kg. The time of recovery from the last dose of neuromuscular blockade prior to extubation was found to be shorter with atracurium. Both drugs have good hemodynamic stability and did not produce any side effects.

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