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Original Article

Comparison of Neuromuscular Blocking Effects and Reversibility of Cisatracurium versus Atracurium During Thyroid Surgery

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ABSTRACT

Objective: To measure the neuromuscular blocking effects and reversibility of Cisatracurium (0.15mg/kg) with Atracurium (0.5mg/kg) during thyroid surgery.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Anesthesia, Combined Military Hospital, Peshawar, Pakistan from Sep 2022 to Apr 2023.

Methodology: The present study was conducted on sixty patients undergoing thyroid surgery of age ranges from 20-65 years of both gender belonging to American Society of Anesthesiologists (ASA) I and II were included. All the patients were randomly divided into two equal Groups. Patients in Group-A received Atracurium (0.5 mg/kg) while in Group-B, received Cisatracurium (0.15 mg/kg). Patients were intubated three minutes after administration of Neuromuscular Blocking Agents (NMBAs). The outcomes in terms of time for onset of action, intubation conditions and reversibility were recorded.

Results: The mean time for onset of action was 4.67±0.88 minutes in Group-A while 2.37±0.76 minutes in Group-B with *p*-value of 0.001. In Group-A, the mean reversibility time was 41.80±1.69 minutes while 45.33±1.27 minutes in Group-B with *p*-value of 0.001. Intubating conditions assessed clinically were excellent in 10(33.33%), good in 09(30.0%) and poor in 11(36.67%) in Group-A whereas, in Group-B, excellent in 13(43.33%), good in 10(33.33%) and poor in 7(23.33%).

Conclusion: This study concluded that Cisatracurium (0.15mg/kg) is more effective Neuromuscular Blocking Agent (NMBA) than Atracurium (0.5mg/kg) in patients under general anesthesia.

Keywords: Anesthesia, Atracurium, Cisatracurium, Neuromuscular blocking effects, Reversibility.

How to Cite This Article: *Asghar RF, Bhatti AH, Imtiaz N, Ali J, Wasib M, Rehman A. Comparison of Neuromuscular Blocking Effects and Reversibility of Cisatracurium versus Atracurium During Thyroid Surgery. Pak Armed Forces Med J 2025; 75(5): 870-874.*
DOI: https://doi.org/10.51253/pafmj.v75i5.10591

INTRODUCTION

General Anesthesia (GA) is a drug-induced, reversible condition that includes specific behavioral and physiological traits-unconsciousness, amnesia, analgesia, and akinesia-with concomitant stability of the autonomic, cardiovascular, respiratory, and thermoregulatory systems.[1] It is administered to 30-40 million patients daily for various surgical procedures.[2] The purpose of GA is to provide patients with a condition where they can tolerate unpleasant and/or harmful interventions, usually during surgical procedures.[3]

To keep the patient immobile during surgery and GA, muscle relaxants or NBAs are used. In recent years, muscle relaxation has become essential in anaesthesia, intensive and emergency care.[4] and are being routinely used for procedures such as endotracheal intubation and during surgery to facilitate the immobilization of patients.[5,6] Muscle relaxation not only provides relaxation for surgeons, but also enables effective and safe management of the patient's gas exchange, circulation and metabolism. The use of muscle relaxants not only revolutionized anesthesiology, but also ushered in the modern era of surgery.[7,8] The ideal NMBA for intubation should have a rapid onset, brief duration of action, no hemodynamic changes, devoid of residual paralysis and provide excellent intubation conditions such as a fully relaxed jaw, wide open vocal cord and unresponsiveness to intubation.[9] Atracurium and Cisatracurium are intermediate-acting NMBDs used to provide optimal intubation conditions. Cisatracurium lacks histamine-induced cardiovascular and respiratory side effects and is therefore preferred over Atracurium for intubation. Furthermore, due to their non-organ dependent metabolism, Atracurium and Cisatracurium have a significant advantage over other non-depolarizing muscle relaxants.[10] The rationale for

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Received: 06 Jul 2023; revision received: 01 Apr 2024; accepted: 06 May 2024

this study was to compare the neuromuscular blocking effects and reversibility of Atracurium and Cisatracurium in our set up. Minimal local data is available in Pakistan and by comparing these two NMBDs in terms of different parameters can guide anesthetists regarding the superiority of one drug over the other which in term will decrease side effects and improve patient care.

METHODOLOGY

The quasi-experimental study was conducted at the Department of Anesthesia, CMH Peshawar, Pakistan from September 2022 to April 2023, after the permission from Ethical Review Committee (ERC number: ERC/0367/2022/PSC). Sample size was calculated using WHO sample size calculator taking confidence interval 95%, margin of error 5%, mean of onset time in Atracurium Group as 3.24±0.55 and in cisatracuriom Group as 4.37±0.46 minutes.[11]

Inclusion Criteria: Patients of any gender belonging to ASA grade I and II, in the age range of 20-65 years undergoing thyroid surgery with anticipated duration of at least one and half hour were included.

Exclusions Criteria: Patients with ASA classification III and IV, patients with any disorder of the cardiovascular, hepatic, renal, or neuromuscular systems known from history or clinical examination, pregnant or lactating women and on medication known to interact with NMBDs were excluded.

All patients undergoing thyroid surgery and fulfilling inclusion criteria were included in the study. After premedication with Inj metoclopramide 10 mg and Inj dexamethasone 8 mg, anesthesia was induced with Inj propofol 1-2.5 mg/kg and Inj nalbuphine 0.1 mg/kg and maintained with isoflurane and air mixture. The study included a total of 60 patients. They were randomly divided into two Groups, each Group consisting of 30 patients. Patients in Group-A received Atracurium (0.5 mg/kg) while in Group-B, received Cisatracurium (0.15 mg/kg) (Figure).

Patients were intubated after three minutes of administration of NBAs. The standard monitoring of all patients was done by using different monitors such as Electrocardiography (ECG), Pulse oximeter, non-invasive blood pressure device, temperature probe and Capnography. The hand, wrist and half of the forearm were wrapped with a crepe bandage to prevent hypothermia, and the peripheral nerve stimulator electrodes were placed on the ulnar nerve on the volar side of wrist. The ulnar nerve was stimulated at the wrist with a supramaximal stimulus of 0.2ms duration in the Train of four (TOF) modes at 2 Hz every 15 seconds via surface electrodes and the resulting four twitches of adductor pollicis muscles (muscles in the hand that functions to adduct the thumb) were observed. The onset time was determined as the interval from the end of muscle relaxant injection until the maximal suppression of T4 (the fourth twitch of TOF muscle twitch). Similarly, reversibility time was determined clinically as the interval from the end of muscle relaxant injection until the appearance of T4 (the fourth twitch of TOF muscle twitch) equal to T1 (the first twitch of TOF muscle twitch) in strength. Intubating conditions was classified as Excellent, Good and Poor according to the following criteria: Excellent: Easy passage of the tube without coughing. Vocal cords relaxed and abducted, Good: Passage of the tube with slight coughing and/or bucking. Vocal cords relaxed and abducted, Poor: Passage of tubes with moderate coughing and/or bucking vocal cords moderately adducted.

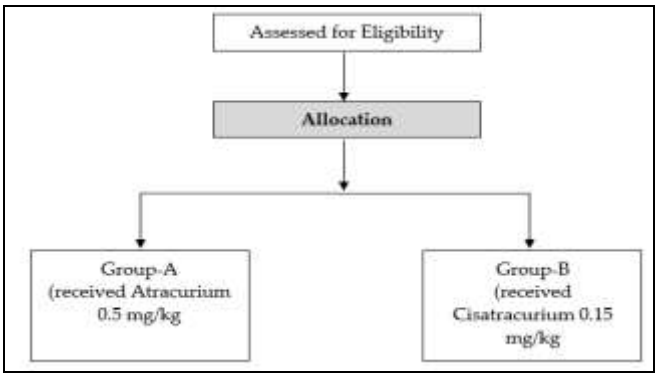

Figure: Patient Flow Diagram (n=60)

A proforma was designed and used to record the outcomes in terms of onset time, intubating conditions and reversibility. Statistical Package for Social Sciences (SPSS) was used for the analysis of data. Descriptive statistics were used for qualitative and quantitative variables. Qualitative variables like gender, ASA class and intubation condition, were measured by frequency or percentage. Quantitative variables like age, onset time, reversibility time and duration of action were presented as Mean±SD. Statistical analysis of the data was done by chi-square and independent sample t test as appropriate. The *p*-value ≤0.05 was taken as significant.

RESULTS

A total 60 patients were selected in the study. The data presented in Table-1 shows that the mean age

of study participants was 49.21±7.63 years with age range of 30-65. Majority of the patients 37(61.67%) were between 46 to 65 years of age. In Group-A, the mean age of patients was 49.37±8.24 years, while in Group-B was 49.07±7.07 years. Out of all, 15(25.0%) were males and 45(75.0%) were females with male to female ratio of 1:3. In addition, 25(41.67%) and 35(58.33%) of patients were from ASA Grade I, and II respectively.

Table-I: Distribution of Patients According to their Age, Gender and American Society of Anesthesiologists (ASA) Status (n=60)

Parameters	Study Groups	
	Group-A n=30	Group-B n=30
Age (Years)		
30-45	11(36.67%)	12(40.0%)
46-65	19(63.33%)	18(60.0%)
Gender		
Male	8(26.67%)	7(23.33%)
Female	22(73.33%)	23(76.67%)
American Society of Anesthesiologists (ASA) Status		
I	13(43.33%)	12(40.0%)
II	17(56.67%)	18(60.0%)

Table-II showed the mean time of onset and reversibility. It was revealed that the mean time of onset was 4.67±0.88 minutes in Group-A while 2.37±0.76 minutes in Group-B. Onset of action in Group-B was rapid compared to Group-A with *p*-value of 0.001. Whereas, the mean reversibility time was 41.80±1.69 minutes in Group A while 45.33±1.27 minutes in Group B. The result was statistically significant with *p*-value of 0.001.

Table-II: Comparison of the Neuromuscular Blocking Effects and Reversibility of Cisatracurium (0.15mg/kg) versus Atracurium (0.5mg/kg) for Thyroid surgery (n=60)

Outcomes	Group-A n=30	Group-B n=30	*p*-value
Time of onset (min)	4.67±0.88	2.37±0.76	0.001
Reversibility (min)	41.80±1.69	45.33±1.27	0.001

Intubating conditions of Cisatracurium (0.15mg/kg) vs. Atracurium (0.5mg/kg) for Thyroid surgery are enumerated in Table-III, showing that more patients of Group-B had excellent and good condition of intubation than the patients of Group-A. This difference was not statistically significant but showed that Group-B provided better intubating conditions when compared to Group-A.

Table-III: Comparison of the Intubating Conditions of Cisatracurium (0.15mg/kg) Versus Atracurium (0.5mg/kg) for Thyroid surgery (n=60)

Intubating Conditions	Group-A n=30	Group-B n=30	*p*-value
Excellent	10 (33.33%)	13 (43.33%)	0.514
Good	9 (30.0%)	10 (33.33%)	
Poor	11 (36.67%)	7 (23.33%)	

DISCUSSION

Neuromuscular blocking drugs are used extensively by anesthesiologists in operating rooms and Intensive Care Units (ICU). Among the range of muscle relaxants available, the main concern of the anesthesiologist after their administration is the complete recovery of muscle function after surgery.[13] Various non-depolarizing NMBDs have been introduced into clinical practice but have many side effects such as cardiovascular instability, recurrence and residual paralysis and are not suitable for use in certain clinical conditions such as liver and kidney disorders. Atracurium is an intermediate-acting NDMR, a mixture of 10 optical isomers, commonly used in renal and hepatic failure. It is metabolized by Hoffmann elimination and non-specific ester hydrolysis, but is associated with histamine release, causing hypotension.[14,15,16] Cisatracurium, the purified form of one of the ten stereoisomers of Atracurium and has approximately three to four times more potency than that of Atracurium, which unlike parent compound, is not associated with the dose-dependent histamine release in the humans. In the process of metabolism, 5 times less lidanosine is produced.[17,18] We compared the neuromuscular blocking effects and reversibility of Cisatracurium (0.15mg/kg) with Atracurium (0.5mg/kg) during thyroid surgery and found that the mean time of onset was 4.67±0.88 minutes in Group A while 2.37±0.76 minutes in Group B with *p*-value of 0.001 and showing lesser onset time taken in patients who have received the Cisatracurium. We also recorded the mean reversibility time in our study which was 41.80±1.69 minutes in Group A while 45.33±1.27 minutes in Group B. The result was statistically significant with *p*-value of 0.0001. In terms of intubation condition, the intubating conditions in Group A was found to be excellent in 10(33.33%), good in 09(30.0%) and poor in 11(36.67%) patients. Whereas, in Group B, excellent in 13(43.33%), good in 10(33.33%) and poor in 7(23.33%) patients which showing that more patients of Group-B had excellent and good condition of intubation than the patients of Group-A. However, the difference between two Groups was statistically not significant.

In a study conducted by El-kasaby *et al*.[12] they compared the Atracurium (2×ED95) with different doses of Cisatracurium (2×ED95, 4×ED95, and 6×ED95) concerning onset time, intubation condition, duration of action, hemodynamic effects, and signs of histamine release, and they found that the time of

onset to be significantly shorter with the 2×ED95 dose of Atracurium (3.24±0.55) compared to the same dose of Cisatracurium (4.37±0.46). However, at the same time, the higher dose (4×ED95 and 6×ED95) of Cisatracurium showed an time of onset that was significantly shorter than that of Atracurium and with the lower dose (2×ED95) of Cisatracurium. Similarly, the duration of action with 2xED95 doses of Atracurium and Cisatracurium was 44.4±4.13 and 43.6±4.15 minutes respectively and found to be statistically non significant. However, the higher dose of Cisatracurium (4×ED95 and 6×ED95) showed a statistically significant longer duration of action than the lower dose of Cisatracurium and Atracurium (2×ED95). In case of intubating condition, they observed that intubation condition of the patients was better who have received the same dose of Atracurium (2×ED95) when compared to Cisatracurium (2×ED95). They concluded that at the same dose (2×ED95) Atracurium is more effective NBA in comparison of Cisatracurium. However, higher doses of the Cisatracurium provide more effective, more rapid neuromuscular blocking with longer duration of action, stable hemodynamic state, and no clinically significant histamine release-related signs.[12]

Bluestein *et al*., who conducted a study on 80 patients and the patients, were randomly assigned into four Groups i.e. A-D. A Group received Cisatracurium 0.1 mg/kg (2×ED95), B Group received Atracurium 0.5 mg/kg (2×ED95) while Group C and D were treated with Cisatracurium 0.2 mg/kg (4×ED95) and 0.15 mg/kg (3×ED95) respectively. They also reported a shorter onset time for Cisatracurium 0.15mg/kg (3.4 minutes) when compared to Atracurium 0.5mg/kg (4.0 minutes). With regard to the mean time of clinically effective duration, they reported that the mean time of clinically effective duration with Cisatracurium 0.15mg/kg was 54.5 minutes as compared to Atracurium 0.5mg/kg (45.6 minutes) and found to be statistically significant.[19]

The results of our study were also accordance to those of Anjali *et al*., who compared the onset time, intubating conditions, and average duration of action of three and four times ED95 doses (3xED95 and 4xED95) of Cisatracurium with 2xED95 dose of Atracurium, They assessed that the onset time for Cisatracurium 0.15mg/kg was faster (204.71±39.407 seconds) as compared to Atracurium 0.5mg/kg (292.06±61.486 seconds). Similarly, the average duration of action was longer in the patients who have received the dose of Cisatracurium 0.15mg/kg (48.24±5.888 minutes) as compared to Atracurium 0.5mg/kg (40.44±5.275 minutes). Likewise, intubating conditions as judged by mean intubation score which was best in patients who have received the dose of Cisatracurium 0.15mg/kg (16.06±1.127) as compared to Atracurium 0.5mg/kg (15.24±1.458).[20]

CONCLUSION

This study concluded that Cisatracurium (0.15mg/kg) is more effective neuromuscular blocking agent s compared to Atracurium (0.5mg/kg) in providing faster onset and longer duration of action along with better intubationg conditions in patients during general anesthesia.

Conflict of Interest: None.

Funding Source: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

RFA & AHB: Data acquisition, critical review, approval of the final version to be published.

NI & JA: Conception, study design, drafting the manuscript, approval of the final version to be published.

MW & AR: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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