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Original Research

Cost Analysis And Safety Comparison Of Atracurium And Cisatracurium In Patient Undergoing General Anesthesia

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ABSTRACT

Introduction: The neuromuscular blocking agent plays an essential role in balanced anaesthesia, and the introduction of skeletal muscle relaxants has revolutionised the field of anaesthesia and critical care. Atracurium and Cisatracurium, intermediate-acting, benzylisoquinoline non depolarising neuromuscular blocking agents. These drugs have fewer side effects, and organ-independent elimination has made it the most commonly used neuromuscular agent. The present study is designed to evaluate the adverse reactions of both drugs, as well as their safety profile and economic benefits.

Methods: A prospective randomized comparative study was done in the Department of Anaesthesiology, Shri. B.M. Patil Medical College, Hospital and Research Centre, Vijayapura After obtaining written informed consent and approval from the institutional ethical clearance committee, 140 patients who were scheduled to undergo elective surgery under general anaesthesia with endotracheal intubation and required intraoperative non depolarising neuromuscular blockers were included in the trial. The patients who were a part of the trial were randomly split into two groups. Group A: 70 patients receiving atracurium 0.5mg/kg. Group B: 70 patients receiving 0.15 mg/kg. After induction, hemodynamic parameters and adverse drug reactions like bradycardia, tachycardia, hypertension, hypotension, flushing, collapse, hyperthermia, wheezing, bronchial secretion, bronchospasm, laryngospasm, dyspnea, apnea, erythema, Itching and urticaria were noted. The groups were compared using Wilcoxon-Mann-Whitney U or Chi-square tests as applicable; a p-value <0.05 was considered significant.

Results: The average mean cost of the atracurium group is 245.98 INR, and cisatracurium is 439.54 INR with a p-value of 0.001, statistically significant that atracurium is cost-effective compared with cisatracurium. In terms of side effects and hemodynamics like wheezing, hypotension, hypertension, tachycardia, and bradycardia are statistically insignificant with p-values> 0.05, and both groups do not have comparable side effects.

Conclusion: Both drugs have a similar safety profile, and cisatracurium is a better choice for patients with hemodynamic instability and those with a risk of histamine related disorders like asthma and anaphylaxis. In terms of economic benefit, atracurium is a better choice.

Key Words: Atracurium, cisatracurium, cost analysis, side safety comparison

INTRODUCTION

The introduction of skeletal muscle relaxants in 1942 into anaesthetic practice was an important development in the field of anaesthesia and critical care. Nondepolarizing NMBA differs in pharmacokinetics in terms of onset of action, duration of action, metabolic route, potency, and adverse effect [1, 2]. Neuromuscular blocking drugs are used in the operation room, and intensive care to provide skeletal muscle relaxation for their muscle relaxation effects are required to improve oxygenation and ventilation, facilitate intubation, produce immobility during

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surgery [3], reduce vocal cord tension and minimize response to laryngoscopy, and position the tube in the trachea with minimal effort. Atracurium and Cisatracurium are two benzylisoquinolinenon depolarizing or competitive NMB agents with an intermediate duration of action [3]. Atracurium was introduced into clinical practice in 1983. It has a rapid onset of action with the intubating condition and can be reached after two x ED95 doses in two to three minutes, with no dependence on any organ for metabolism or elimination, no cumulative effects, it decomposes into inactive metabolites through ester hydrolysis and Hofmann elimination, [4] which has minimal cardiovascular effects and can be easily reversed by neostigmine [5] .Cisatracurium was released in 1995 and is five times more effective than atracurium in other aspects [6, 7]. With a potency of three to four times that of atracurium, it is a stereoisomer of atracurium. Even at doses as high as 0.4 mg/kg (8×ED95), Cisatracurium does not produce histamine and is linked to more stable hemodynamics than atracurium despite its greater potency. [8, 9] .Both drugs have been compared in bolus and injection forms [10]. Both these drugs have been studied and compared for effective cost analysis and to prove which drug has a safety profile .cisatracurium is associated with a lower potency to cause histamine release and has a longer onset time at equal doses when compared with atracurium[11]

METHODS

This prospective randomized comparative study was done in the Department of Anaesthesiology, Shri. B.M. Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be University), Vijayapura. After obtaining written informed consent and approval from the institutional ethical clearance committee, 140 patients who were between the ages of 17 and 80 years who were scheduled to undergo elective surgery under general anaesthesia (ASA I and II) with endotracheal intubation and required intraoperative non-depolarising neuromuscular blockers were included in the trial whose surgery duration is less than 2 hour. Excluded from the study were patients with Known hypersensitivity to atracurium and cisatracurium .Two study groups of 70 patients in each group were randomly assigned by a computer-generated random sequence number. Group A& B patients were receiving Atracurium 0.5mg/kg IV and cisatracurium 0.15 mg/kg IV, respectively. After obtaining written informed consent and confirming the patient's NPO status, preoperative room vital parameters were recorded, and then Patients were shifted to the operation theatre where ASA standard monitoring devices like EtCO2, sphygmomanometer cuff, pulse oximeter, and ECG leads were used to take baseline readings. After attaching the standard monitoring devices, the baseline vital parameter values were recorded just before the induction of the patient and it is noted as the Time – 0..Patientswere given Glycopyrrolate 0.01 mg/kg, IV. Ondansetron 0.1 mg/kg, IV. Midazolam 0.08 mg/kg IV was given as the premedication. for analgesia, Fentanyl 2 mcg/kg IV and pre-oxygenated with 100% oxygen by facemask for 3 minutes, and induction was done with propofol 2.5 mg/kg IV dose. The neuromuscular blocking agents were given based on the group the patient belonged to. Group A patients were given Atracurium 0.5mg/kg IV body weight, and group B patients were given Cisatracurium 0.15mg/kg IV, and patients were ventilated for 3 minutes, and endotracheal intubation was done, tube position was confirmed with five-point auscultation, and for definitive confirmation, the endotracheal tube is connected to capnography and capnographic waveforms were noted on the monitor. Anaesthesia was maintained with a mixture of 50% N2O and 50% O2, and an inhalational agent for maintenance of anaesthesia was done with Isoflurane (0.2%-1.2% vol%) and assisted then connected to the mechanical ventilator and maintained on low flow anaesthesia throughout the surgery. When the surgery was about to end, the administration of all anaesthetic agents, especially the neuromuscular blocking agents, was stopped, and when the patient started having the spontaneous respiratory effort reversed with IV Neostigmine 0.05mg/kg and IV Glycopyrrolate 0.008mg/kg. Extubation was done after full reversal and when the patient obeys oral comments. Both groups were assessed for the adverse drug reaction and comparison of cost analysis. For the assessment of **adverse reactions** of the NMBA, the vital parameters such as SBP, DBP, PR, SpO2, and temperature were assessed at every 15-minute interval at 15min, 30min, 60min, 90min and 120min. The clinical features and other signs and symptoms noted in both groups of patients are Bradycardia, Tachycardia, Hypertension, Hypotension, Flushing, Collapse, Hyperthermia, Wheezing, Bronchial secretion, Bronchospasm, Laryngospasm, Dyspnea, Apnea, Erythema, Itching Urticaria, Acute quadriplegic myopathy syndrome, Myositis ossificans, Seizure Prolong recovery time, Injection reaction. For the **Cost analysis,** the drug dosing is given according to the weight of the patient. For Group A patients, the dose of the atracurium is 0.5mg/kg IV, and for Group B patients, the dose of cisatracurium is 0.15mg/kg IV. In terms of cost analysis, for the atracurium group, the brand used is InjArtacil 25 mg/ 2.5 ml. That is, each ml 0.5ml contains 5mg/cc, and it costs 162.96 INR. For every 5mg, the cost is 32.55, and for each 1 ml, the cost is 6.51 INR. Similarly, for the cost analysis of the cisatracurium group, the brand used is InjCis article 20mg/ 10 ml. Each ml contains 2mg/cc, and its 10 ml cost is 891 INR rupees, and the cost of each ml that is every 1 mg cost is 44.55 INR. For both groups, the total mg of drug used throughout the surgery is calculated, and the cost of the drug has also been calculated and entered in the proforma sheet. With

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anticipated proportion hypertension an adverse drug reaction atracurium and cistracurium drugs, 14 % and 0% (ref). Each study group would require a sample size of 70 for the investigation. (i.e., 140 total samples, assuming equal group sizes), in order to obtain an 80% power in identifying a two-sided p-value of 0.05 for a difference in proportions between two groups. Utilizing statulator software, a sample size of 70 per group. (i.e. a total sample size of 140 assuming equal group sizes), to achieve a power of 85%

The data obtained was entered into a Microsoft Excel sheet, and statistical analysis was performed using a statistical package for the social sciences (Version 20). The findings were displayed as Mean±SD, percentages, counts, and graphs. To compare two sets of normally distributed continuous variables, the Independent t test was employed. The mannwhitney U test was utilized for variables that are not regularly distributed. The chi-square test was employed to compare categorical variables between the two groups. A p-value of less than 0.05 indicates statistical significance. Every statistical test was conducted in two-tailed.

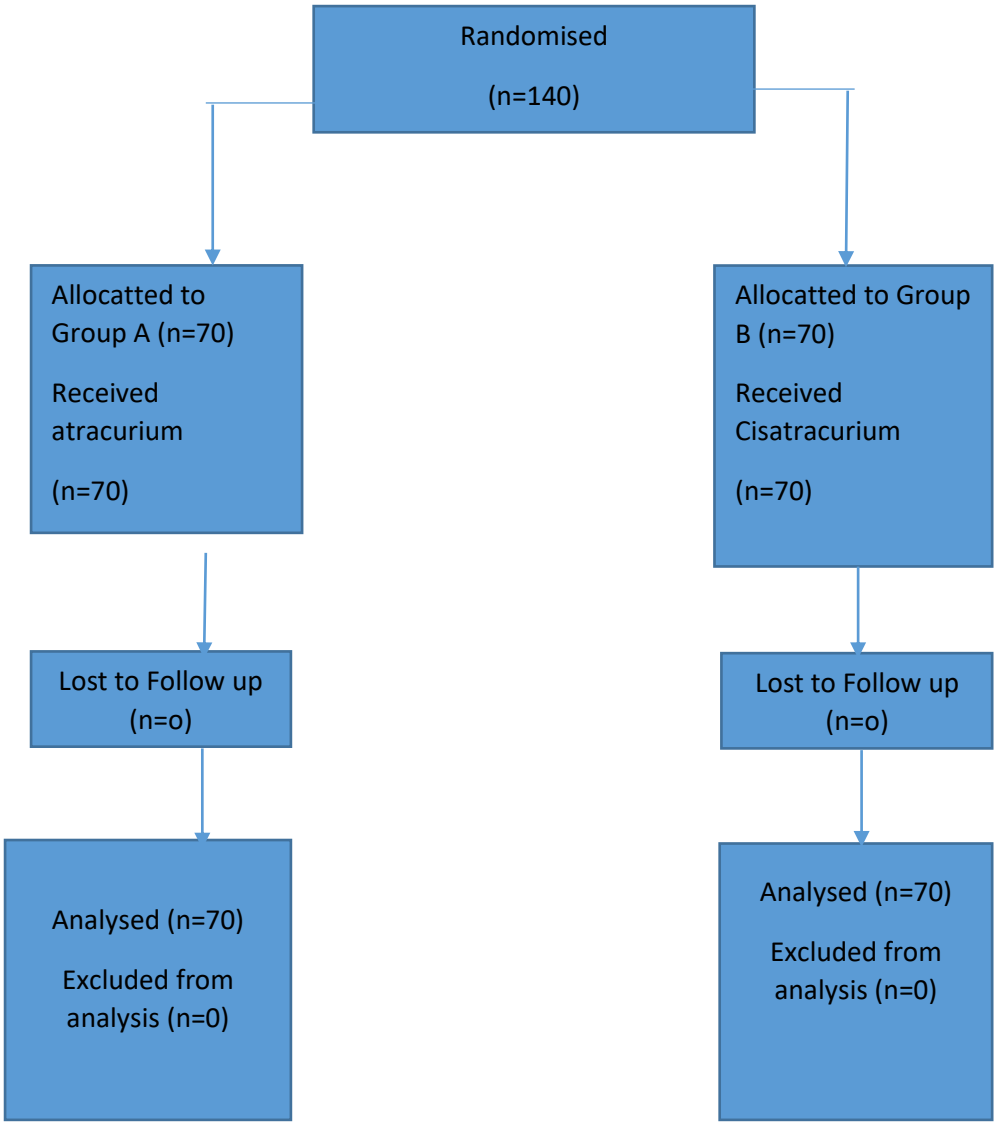

Figure 1: Consort flow diagram.

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RESULT

All the groups were similar with respect to demographic profile (Table 1)

Table 1: Demographic And Baseline Characteristics

Group	Gender (male/female)	Mean Age ± SD (years)	Weight Mean ± SD (kg)	p-value
Group A (Atracurium)	33/37	39 +/- 16.64	61.5 +/-10.8	0.706230
Group B (Cisatracurium)	30/40	36 +/- 16.91	59.27 +/- 9.7	0.706639
Statistically insignificant p > 0.05				

TABLE NO.2COMPARISON IN TERMS OF COST

Cost analysis (Table 2) differed significantly among the groups. Group A (Atracurium) had a mean cost of 248.98 INR with good economic benefit, compared to 429.54 INR in Group B (Cisatracurium). There was statistical confirmation that these differences were significant by the Mann-whitney u test (173.9, p = 0.001). (figure 2)

	GROUPS				MANN-WHITNEY U TEST	P - VALUE
	ATRACURIUM		CISATRACURIUM			
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
COST IN RUPEES	245.98	55.82	439.54	89.32	173.9	0.001
Statistically significant p < 0.05						

FIGURE No.2 Comparison In Terms Of Cost

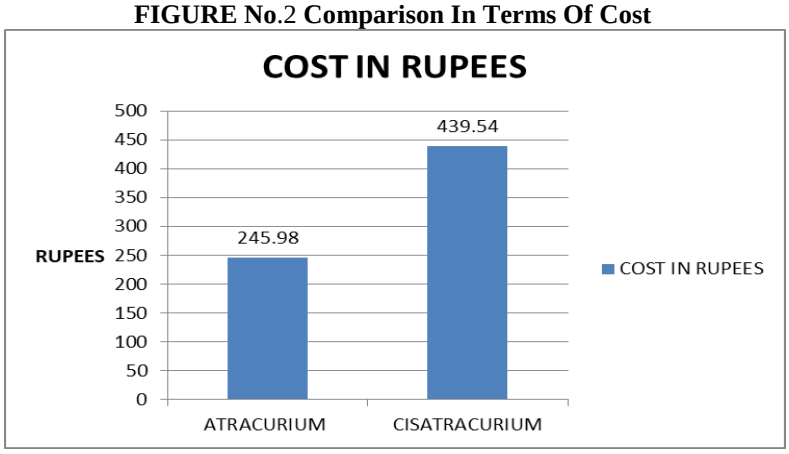

TABLE NO.3COMPARISON IN TERMS OF BRADYCARDIA

In terms of bradycardia (Table 3) as side effect it did not differ significantly among the groups. Group A (Atracurium) had 1.4 % and Group B (Cisatracurium) had 1.4 % . The chi-square test (0.00, p = 1.0) indicated no statistically significant difference (Figure 3)

BRADYCARDIA	GROUPS		CHI SQUARE VALUE	P - VALUE
	ATRACURIUM	CISATRACURIUM		
YES	1 (1.4 %)	1 (1.4 %)	0.00	1.0
NO	69 (98.6 %)	69 (98.6 %))		
Statistically insignificant p > 0.05				

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Figure NO.3comparison In Terms Of Bradycardia

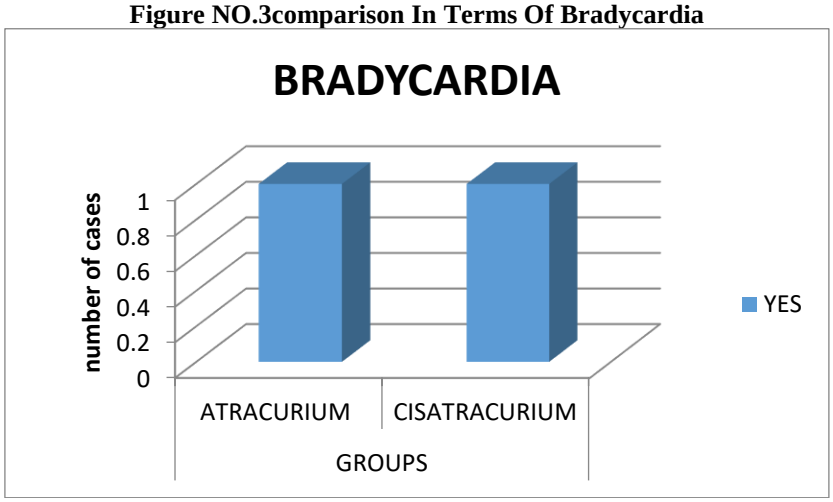

TABLE NO. 4COMPARISON IN TERMS OF TACHYCARDIA

In terms of Tachycardia (Table 4) as side effect it did not differ significantly among the groups. Group A (Atracurium) had 32.9 % and Group B (Cisatracurium) had 22.9 % . The chi-square test (1.742, p = 0.187) indicated no statistically significant difference (figure 4)

TACHYCARDIA	GROUPS		CHI SQUARE VALUE	P - VALUE
	ATRACURIUM	CISATRACURIUM		
YES	23 (32.9 %)	16 (22.9 %)	1.742	0.187
NO	47 (67.1 %)	54 (77.1 %))		
Statistically insignificant p > 0.05				

FIGURE NO. 4 Comparison In Terms Of Tachycardia

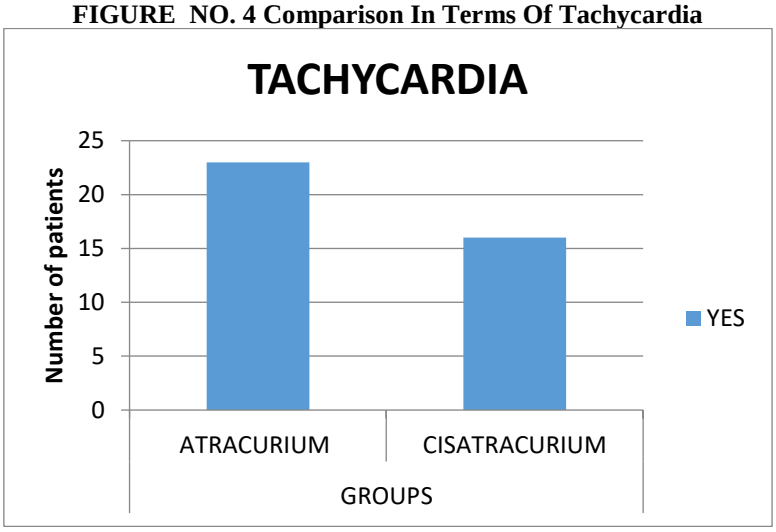

TABLE NO. 5COMPARISON IN TERMS OF HYPERTENSION

In terms of hypertension (Table 5) as side effect it did not differ significantly among the groups. Group A (Atracurium) had 32.9 % and Group B (Cisatracurium) had 22.9 % . The chi-square test (2.745, p = 0.098) indicated no statistically significant difference (figure 5)

HYPERTENSION	GROUPS		CHI SQUARE VALUE	P - VALUE
	ATRACURIUM	CISATRACURIUM		
YES	23 (32.9 %)	16 (22.9 %)	2.745	0.098
NO	47 (67.1 %)	54 (77.1 %))		
Statistically insignificant p > 0.05				

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GRAPH NO. 5Comparison In Terms Of Hypertension

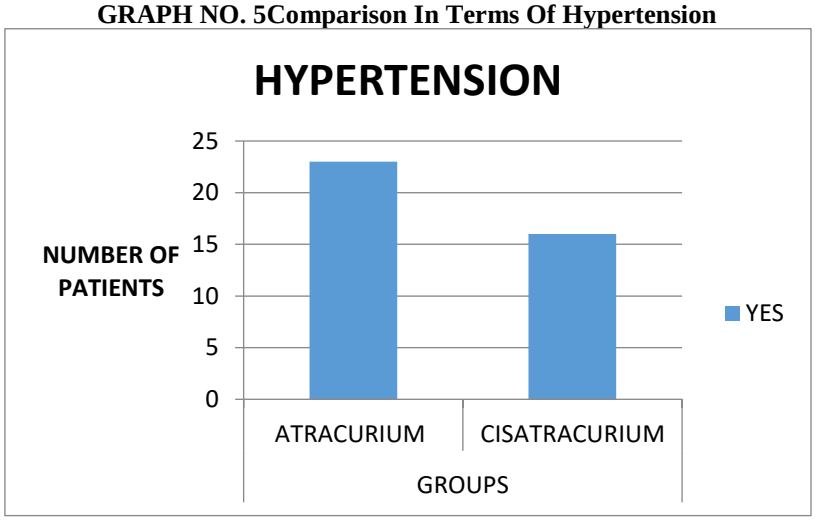

TABLE NO.6 .COMPARISON IN TERMS OF HYPOTENSION

In terms of Hypotension (Table 6) as side effect it did not differ significantly among the groups. Group A (Atracurium) had 2.9 % and Group B (Cisatracurium) had 4.3 % . The chi-square test (0.207, p = 0.649) indicated no statistically significant difference (Figure 6)

HYPOTENSION	GROUPS		CHI SQUARE VALUE	P - VALUE
	ATRACURIUM	CISATRACURIUM		
YES	2 (2.9 %)	3 (4.3 %)	0.207	0.649
NO	68 (97.1 %)	67(95.7 %))		
Statistically insignificant p > 0.05				

FIGURE NO.6 .Comparison In Terms Of Hypotension

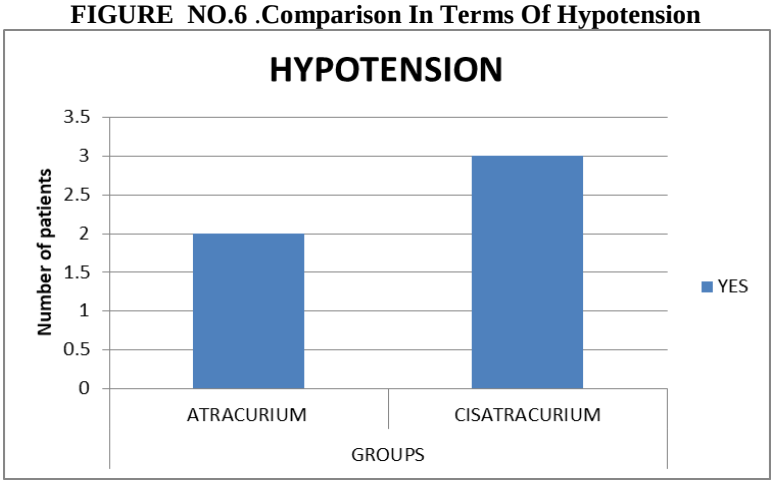

Table No.7 .Comparison In Terms Of Wheezing

In terms of wheezing (Table 7) as side effect it did not differ significantly among the groups. Group A (Atracurium) had 1.4 % and Group B (Cisatracurium) had 00 % . The chi-square test (1.007, p = 0.316) indicated no statistically significant differenceb(Figure 7)

	GROUPS		CHI SQUARE VALUE	P - VALUE
	ATRACURIUM	CISATRACURIUM		
YES	01(1.4 %)	00 (00%)	1.007	0.316
NO	69 (69.6 %)	70 (100%)		
Statistically insignificant p > 0.05				

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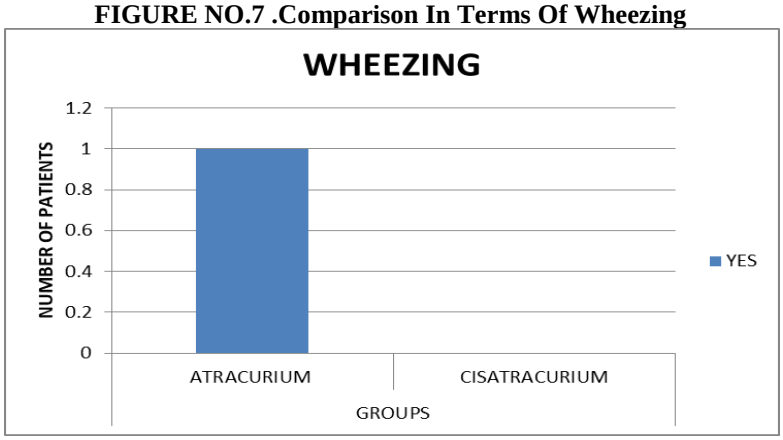
FIGURE NO.7 .Comparison In Terms Of Wheezing



DISCUSSION

This study was done to compare the duration of action, first dose, and recovery of two non-depolarizing muscle relaxants with intermediate duration of action: atracurium and cisatracurium. Throughout the duration of the surgical procedure under general anaesthesia, hemodynamic parameters such as heart rate, systolic and diastolic blood pressure, mean arterial pressure and 60 minutes were recorded every 0 minutes, 15 minutes, 30 minutes, 60 minutes, 90 minutes, and 120 minutes..Neuromuscular blockers (NMB) have been an essential component in the armament of anaesthetists. They lessen the need for anaesthesia, help with mechanical breathing and endotracheal intubation, make lengthy procedures easier, and use less oxygen. The optimal neuromuscular blocking agent should not cause any adverse effects, act quickly to generate good intubating conditions, act for an intermediate to brief period of time, regulate the airway quickly, and allow for sufficient recovery and cardiovascular stability. When contrasting two neuromuscular blocking medications, it's crucial to consider certain factors such as adverse reaction, drug safety profile, and costs. In the present study, for both drugs, adverse drug reactions and drug safety profiles were compared. Differences between adverse reactions of these drugs (atracurium and cisatracurium) were statistically insignificant. In Atracurium group, the incidence of side effects like tachycardia, bradycardia and wheezing was more when compared to cisatracurium which was statistically insignificant. .

MOVAFEGH et al. [12] conducted a study in 2013, comparing the two study drugs, it was determined that there were statistically insignificant differences in the adverse reactions of these drugs (atracurium and cisatracurium) and that their safety profiles and adverse drug reactions were similar. MANISHA BAGHAT et al conducted a study in 2018, to evaluate the adverse drug reactions (ADRs) within the atracurium group which was higher than that of the cisatracurium group, but this difference was not statistically significant. To assess the safety profile and differences between cisatracurium and atracurium, which are commonly used in adult patients for general anesthesia. USHA BADOLE et al. conducted a study in 2021. It was concluded that patients who received six times the recommended dosage of cisatracurium (ED95) had better results than those who received two times the recommended dosage of atracurium (ED95). These patients had faster onset of action, better intubating conditions, better hemodynamic stability, longer duration of action, and no side effects. Drug costs vary between countries as well as between hospitals within a same country. In addition, the cost of medications is a dynamic and active process; therefore, pharmacoeconomic analyses should be carried out to determine the most suitable medication regimen in light of changing drug prices and clinical practices. Drug costs in hospitals are influenced by various factors.

For instance, the cost of pharmaceutical units, insurance policies, and certain indirect elements like the price of treating adverse effects or reversing the effects of a treatment. Furthermore, the availability of pharmacological dosage forms significantly impacted the treatment's overall cost. In our practice, cisatracurium and atracurium were available as 20 mg/10 ml and 25 mg/2.5 ml vials, respectively. The mean cost of atracurium was 245.98 INR, and cisatracurium was 439.54 INR. There was a significant difference in cost between the two NMBs (p-value of 0.001). Based on our study, we recommend the use of cisatracurium when a haemodynamic instability is suspected and atracurium in the remaining cases as it has a lesser cost. If just one neuromuscular blocking drug can be included in the drug formulary we would select cisatracurium due to its pharmacological advantages over atracurium with a small increment in cost. MOVAFEGH **et al.** concluded in their study that atracurium and cisatracurium had comparable safety profiles and, at first loading dosages, atracurium was more cost-effective than cisatracurium. When patients' hemodynamic values were unstable, cisatracurium was the better choice.

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CONCLUSION

In conclusion, in terms of safety comparison, both the drugs provide a similar safety profile, and cisatracurium is slightly a safer drug as it does not cause much hemodynamic changes and nil histamine release and can be safely used in asthma and other histamine-related disorders. In terms of cost analysis, Atracurium has more economic benefits than cisatracurium.

REFERENCES

1. MOORE EW, HUNTER JM. The new neuromuscular blocking agents: do they offer any advantages. Br J Anaesth 2001; 87: 912-925.
2. MERTES PM, LAXENAIRE MC. Adverse reactions to neuromuscular blocking agents. Curr Allergy Asthma Rep 2004; 4: 7-16.
3. Matthew R, Belmont Cynthia A, Lien Steve Quessy, Martha M, Abou-Donia, Amy Abalos et al. The clinical neuromuscular pharmacology of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anesthesia. Anesthesiology. 1995; 82:1139-1145.
4. Kitts JB, Fisher DM, Canfell PC, Spellman MJ, Caldwell JE, Heier T, et al.Pharmacokinetics and pharmacodynamics of atracurium in the elderly. Anesthesiology 1990;72:272-5
5. Basta SJ, Ali HH, Savarese JJ, Sunder N, Gionfriddo M, Cloutier G, Lineberry C, Cato AE (1982). "Clinical pharmacology of atracuriumbesylate (BW 33A): a new non-depolarizing muscle relaxant". Anesthesia and Analgesia. 61 (9): 723–729.
6. William B. Wastila, PhD; Robert B. Maehr, BS; Geoffrey L. Turner, PhD.; Derek A. Hill; M. Phil.; et al Comparative Pharmacology of Cisatracurium (51W89), Atracurium, and Five Isomers in Cats Anesthesiology 7 1996, Vol.85, 169-177
7. Bryson HM, Faulds D. Cisatracuriumbesilate. Drugs. 1997 May 1;53(5):848-66
8. Jean-Yves Lepage, Jean-Marc Malinovsky, MyriamMalinge, Thierry Lechevalier, Christine Dupuch, AntonieCozian et al. Pharmacodynamicdoseresponse and safety of cisatracurium (51W89) in adult surgical patients during N2O-O2-Opioid anesthesia. AnesthAnalg. 1996; 83:823-
9. Carroll MT, Mirakhur RK, Lowry DW, McCourt KC, Kerr C. A comparison of the neuromuscular blocking effects and reversibility 0f cisatracurium and atracurium, Anesthesia. 1998; 53:744.
10. Smith CE1 van Miert MM, Parker CJ, Hunter JM. A comparison of the infusion pharmacokinetics and pharmacodynamics of cisatracurium, the 1R-cis 1'R-cis isomer of atracurium, with atracuriumbesylate in healthy patients. Anaesthesia. 1997 Sep;52(9):833-41.
11. SPARR HJ, BEAUFORT TM, FUCHS-BUDER T. Newer neuromuscular blocking agents how do they compare with established agents.Drugs 2001; 61: 919-942
12. 12.Movafegh A, Amini S, Sharifnia H, Torkamandi H, Hayatshahi A, Javadi M. Cost analysis and safety comparison of Cisatracurium and Atracurium in patients undergoing general anesthesia. Eur Rev Med Pharmacol Sci. 2013 Feb;17(4):447-50. PMID: 23467941.
13. Badole U, Gupta S, Sankar U, Patel KA. Comparison between cisatracurium and atracurium during general anaesthesia for abdominal surgery. IJMA. 2021;4(3):172-7.