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An Observational Study to Compare the Effects of Cisatracurium Verses Atracurium During General Anaesthesia in Patients Posted for PCNL (Percutaneous Nephrolithotomy)

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Abstract

Background: Cisatracurium is 3 to 4 times more potent than Atracurium and is devoid of histamine release. However $2ED_{95}$ dose of Cistracurium does not provide satisfactory intubation conditions as compared to $2ED_{95}$ dose of Atracurium. *Aims:* To compare the neuromuscular blocking characteristics of $3ED_{95}$ dose of Cisatracurium and $2ED_{95}$ dose of Atracurium. *Material and Methods:* 60 patients were divided into two groups: Group A received 0.5 mg/kg iv of Atracurium ($2ED_{95}$) and Group B received 0.15 mg/kg iv of Cisatracurium ($3ED_{95}$) as intubating dose. Onset time, duration of action, condition of intubation, haemodynamic effects and signs of histamine release were monitored. *Results:* $3ED_{95}$ dose of Cisatracurium had a faster onset time (2.96 ± 0.61 minutes) as compared to $2ED_{95}$ dose of Atracurium (3.55 ± 0.51 minutes ; *p*-value 0.0134). Group B also had longer duration of action than Group A (67.16 ± 9.39 minutes vs 44.87 ± 4.94 minutes respectively; Pvalue 0.0013). Excellent intubating conditions were seen in 53.33% of patients in Group B and 46.67% of patients in Group A. 4 patients had signs of histamine release in Atracurium group and none in Cisatracurium Group. *Conclusion:* $3ED_{95}$ dose of Cisatracurium is a more effective neuromuscular blocking agent than $2ED_{95}$ dose of Atracurium in terms of providing faster onset time, longer duration of action, excellent intubating condition and better hemodynamic stability with no histamine release.

Keywords: Cisatracurium; Atracurium; Neuromuscular blocking agent.

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Introduction

The practice of giving anesthesia was revolutionized with the introduction of neuromuscular blocking agent (NMBA).[1] An ideal NMBA should have fast onset of action, ensures haemodynamic stability with no residual paralysis effect and provides good conditions for intubation.[2]

Succinylcholine, the gold standard of muscle relaxant has some side effects which include muscle fasciculations leading to muscular pain, increase in intraocular and intracranial pressure. This led to the search of newer muscle relaxants.[3] Atracurium and Cisatracurium are non depolarising NMBA with intermediate duration of action. [4] Atracurium is a mixture of 10 optical isomers[2] and Cisatracurium is a purified form of one of the 10 stereoisomers of atracurium and has a potency of approximately 3 to 4 times more than Atracurium. Unlike the parent compound, Cisatracurium is not associated

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with histamine release.[5-7] It may not yield satisfactory intubating conditions such as those seen with equipotent doses of atracurium; so the recommended intubating dose of Cisatracirium is $3ED_{95}$.[8] Both the drugs are eliminated by Hoffmann elimination which is an organ independent process; hence end stage renal or hepatic disease does not affect the pharmacokinetics and pharmacodynamics of these molecules.[4]

The aim of this study was to compare the efficacy of $2ED_{95}$ dose of Atracurium and $3ED_{95}$ dose of Cisatracurium with respect to onset of action, intubating conditions, haemodynamic effects, duration of action and signs of histamine release in patients posted for Percutaneous Nephro Lithotomy (PCNL) under General Anaesthesia.

Material and Methods

This prospective observational study was conducted in a tertiary hospital after approval from the institutional ethics committee and written informed consent

All patients between 18–65 years of age posted for PCNL under general anaesthesia, belonging to American Society of Anaesthesiologists (ASA) Grade I and II were included in this study. Patients having history of Bronchial Asthma, drug allergy or having Mallampatti Grade III or IV on examination were excluded from the study.

Preanaesthetic evaluation was done and 60 patients fulfilling the criteria were included in the study. They were equally divided into two groups. Group A received Injection (Inj) Atracurium 0.5 mg/kg ($2ED_{95}$) intravenous (iv) as intubating dose and 0.1mg/kg iv as maintenance dose. Group B received Inj Cisatracurium 0.15 mg/kg ($3ED_{95}$) as intubating dose and 0.03 mg/kg as maintenance dose.

On the day of surgery, patients were kept nil by mouth for 6 hours for solids and 4 hours for clear fluids. On arrival to the operation theatre multichannel monitors were attached and baseline parameters were noted. 18G intravenous (IV) line were secured and infusion of crystalloid solution was started. Neuromuscular monitor was also attached. Inj Glycopyrrolate 0.004 mg/kg iv, Inj Midazolam 0.02 mg/kg iv and Inj Tramadol 1–1.5 mg/kg iv were given as premedication. General anaesthesia was induced with Inj. Propofol 2 mg/kg iv. Patients were given muscle relaxant according to the Group assigned. Time interval between the intubating dose and loss of T_1 (1^{st} response) of Train of Four (TOF) stimuli was noted and was considered as "onset time of intubation". After loss of T_1 of TOF stimuli, laryngoscopy was done in sniffing position and endotracheal intubation done using proper sized tube. Intubation score were assessed by Intubating Conditions Scoring System[9] (Table 1). Intubating conditions[9] were graded based on intubating scores (Table 2).

Haemodynamic parameters namely Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) were noted immediately after intubation and 5, 10, 15 and 20 minutes (min) after intubation. Anaesthesia was maintained with N_2O:O_2 (50:50) mixture and Isoflurane. After intubation, at every 5 min TOF stimulation was recorded and accordingly maintenance dose of muscle relaxant ($1/5^{th}$ of intubating dose) was given with 25% recovery of

Table 1: Intubating Conditions Scoring System

Score	Jaw Relaxation	Vocal Cord Movement	Resonse to Intubation
0	Poor	Closed	Severe coughing or bucking
1	Minimal	Closing	Mild coughing
2	Moderate	Moving	Slight movement of diaphragm
3	Good	Open	None

Table 2: Classification of Intubating Conditions

Intubating Conditions	Score
Excellent	8–9
Good	6–7
Fair	3–5
Poor	0–2

T_1%. The duration of muscle relaxant (time interval from injection of intubating dose of muscle relaxant to 25% recovery of T_1%) was recorded. Patients were monitored for histamine release by monitoring skin changes (flush, erythema or wheals), haemodynamic instability or bronchospasm. At the end of surgery, Inj. Neostigmine 0.05 mg/kg iv and Inj. Glycopyrrolate 0.008 mg/kg iv were given for reversal and extubation was performed when TOF ratio >0.9 was achieved.

Statistical Analysis

Data was processed using SPSS Version 18. Quantitative data was expressed as Means ± SD while qualitative data were expressed as numbers and percentages (%) Paired *t*-test were used to test significance of difference of quantitative variables that follow normal distribution and chi-square test was used to test significance of difference of qualitative variables. A *p*-value <0.05 was considered statistically significant.

Results

Demographic profile were comparable in both the study groups.

Group B patients had faster onset time of intubation as compared to Group A (2.96 ± 0.61 min vs 3.55 ± 0.51 min respectively; *p*-value 0.0134). Also the duration of muscle relaxant action was significantly longer in Group B (67.16 ± 9.39 min) as compared to Group A (44.87 ± 4.94 min; P value 0.0013).

Haemodynamic parameters showed significant increase in HR and MAP from baseline immediately after attempt of intubation in Group A as compared to Group B. (Table 3 and 4)

Table 3: Mean Heart Rate (beats per minute) at different time intervals in both the Groups.

	Group A				Group B			
Time Points	**Mean**	**SD**	***p*-Value**	**Inference**	**Mean**	**SD**	***p*-Value**	**Inference**
Baseline	69.60	6.39	>0.05	NS	70.93	6.11	>0.05	NS
After Injection of Muscle Relaxant	74.17	6.31	>0.05	NS	71.57	5.72	>0.05	NS
After Attempt of Intubation	83.37	6.30	0.0001	55	75.23	5.37	>0.05	NS
5 min	74.57	5.90	>0.05	NS	74.80	5.40	>0.05	NS
10 min	73.57	5.73	>0.05	NS	76.90	5.28	>0.05	NS
15 min	75.13	6.23	>0.05	NS	73.60	4.63	>0.05	NS
20 min	74.27	6.21	>0.05	NS	72.53	4.70	>0.05	NS

MIN – minutes, NS- Not significant, SS- Statistically Significant.

Table 4: Mean Arterial Pressure (MAP) in mmHg at different time intervals in both the Groups

Time Points	Group A				Group B			
	MAP	**SD**	***p*-Value**	**Inference**	**Mean**	**SD**	***p*-Value**	**Inference**
Baseline	81.42	4.37	>0.05	NS	82.72	5.09	>0.05	NS
After Injection of Muscle Relaxant	79.38	4.35	>0.05	NS	82.07	5.26	>0.05	NS
After Attempt of Intubation	91.18	4.98	0.0018	SS	84.27	4.84	>0.05	NS
5 min	86.45	4.30	>0.05	NS	83.47	3.89	>0.05	NS
10 min	82.45	4.27	>0.05	NS	85.53	3.86	>0.05	NS
15 min	81.02	4.24	>0.05	NS	84.52	7.12	>0.05	NS
20 min	80.13	4.18	>0.05	NS	86.13	6.85	>0.05	NS

MIN – minutes, NS- Not significant, SS- Statistically Significant

On evaluating the Intubation Scores and Intubating Conditions it was seen that higher proportion of patients in Group B had greater score (score 3) for jaw relaxation, vocal cord movement and response to intubation and had higher percentage of excellent intubating conditions (53.33%) as compared to Group A (46.67%) (Figs. 1, 2).

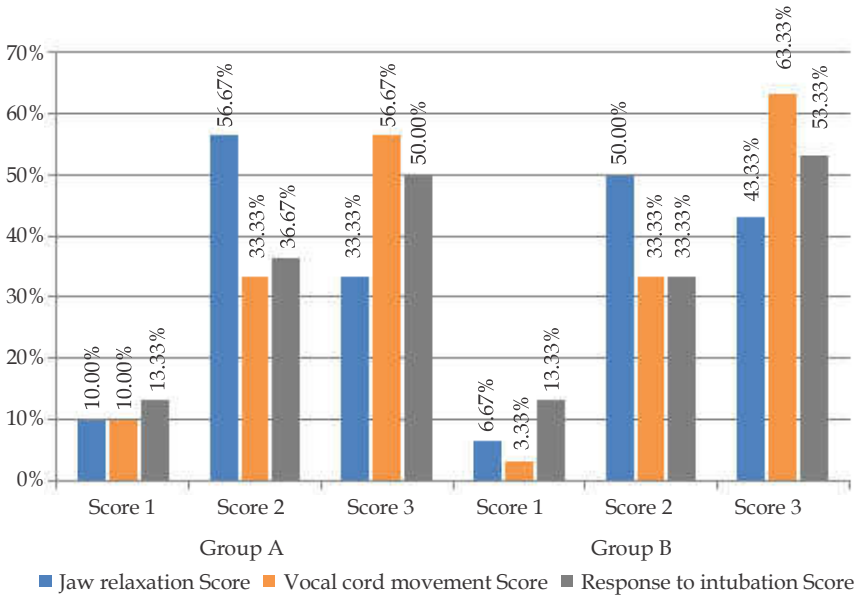

Fig. 1: Graph comparing Intubation Scores between the Groups.

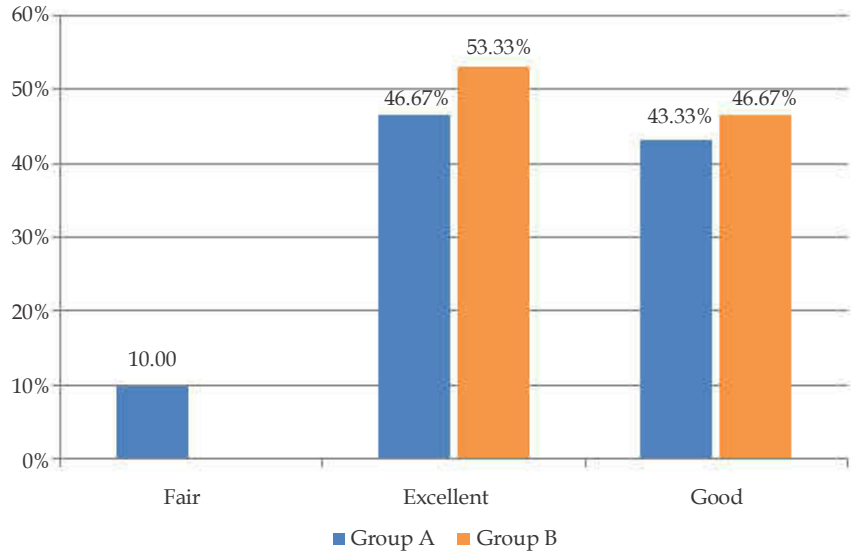

Fig. 2: Graph comparing Intubation Conditions between the Groups.

It was observed that 4 out of 30 patients in Atracurium Group had signs of histamine release while none of the patients in Cisatracurium had similar findings (Table 5).

Table 5: Signs of Histamine release between the Groups.

Histamine Release	Group A		Group B	
	N	%	*N*	%
Flush	2	6.67	0	0.00
Erythema	1	3.33	0	0.00
Wheal	1	3.33	0	0.00
Total	4	13.33	0	0.00

N- number

Discussion

Muscle relaxant is used to facilitate endotracheal intubation and to provide surgical relaxation.[10] In selecting a neuromuscular blocking agent the three goals that need to be achieved are rapid adequate muscle relaxation, haemodynamic stability and predictable complete return of skeletal muscle function.[11] Hence through this study we wanted to compare the potency and neuromuscular blocking properties of 3 × ED_{95} dose of Cisatracurium and 2 × ED_{95} dose of Atracurium.

Mohanty et al.[12] did a prospective randomised study of 60 patients who were allocated to 3 groups. Group A received 0.5 mg/kg of Atracurium (2 × ED_{95}), Group C_1 received 0.1 mg/kg of Cisatracurium (2 × ED_{95}) and Group C_2 received 0.15 mg/kg of Cisatracurium (3 × ED_{95}). Onset time of intubation was significantly faster with Group C_2 (2.65 ± 0.17 min) as compared to Group C_1 and Group A (4.04 ± 0.19 min and 2.80 ± 0.19 min respectively; *P*-value 0.001). Group C_2 also had a longer duration of action (64.6 ± 4.83 min) than Group C_1 and Group A (43.2 ± 2.72 min and 43 ± 2.27 min respectively). Higher proportion of patients in Group C_2 had excellent intubating conditions as compared to Group C_1 and Atracurium Group.(70% vs 65% and 60%).[12]

Likewise another study done by Kasaby et al.,[13] evaluated the neuromuscular blocking characteristics of Atracurium (2 × ED_{95}) and different doses of Cisatracurium (2 × ED_{95}, 4 × ED_{95} and 6 × ED_{95}). They concluded that higher doses of Cisatracurium (6 × ED_{95} and 4 × ED_{95}) showed significant faster onset time of intubation (2 ± 1.2 min and 2.9 ± 1.4 min respectively) as compared to 2 × ED_{95} dose of Atracurium and Cisatracurium (3.24 ± 0.55 and 4.37 ± 0.46 min respectively; P value < 0.05). 6 × ED_{95} and 4 × ED_{95} dose of Cisatracurium had a longer duration of action (78.4 ± 8.6 min and 65.5±10.5 min respectively) than 2 × ED_{95} dose of Atracurium and Cisatracurium (44.4 ± 4.13 and 43.6 ± 4.15 min respectively; *P*-value <0.05). On evaluating the conditions of intubation, regarding the assessment of vocal cords, 2 × ED_{95} dose of Atracurium and Cisatracurium were similar while 4 × ED_{95} and 6 × ED_{95} doses of Cisatracurium were significantly better than 2 × ED_{95} dose of Atracurium and Cisatracurium.[13]

The observations of our study were in concordance with these results. In our study, Cisatracurium group (3 × ED_{95}) had faster onset time of intubation and longer duration of action than Atracurium group (2 × ED_{95}). Intubating conditions in Cisatracurium group were Excellent in 53.33% and Good in 46.67% of patients which was better than the intubating conditions seen in Atracurium group, in which, only 46.67% were Excellent and 43.33% were Good.

Regarding haemodynamics, Kasaby et al.[13] observed an increased stress response to intubation in patients who received 2 × ED_{95} dose of Atracurium and Cisatracurium but not in patients who received 4 × ED_{95} and 6 × ED_{95} dose of Cisatracurium. The analysis done in our study was consistent with this conclusion. Our results also showed a statistically significant increase in HR and MAP from baseline post intubation in Atracurium Group (Group A). This may be because that the patients were not fully relaxed which lead to an increased stress response to intubation.

Lien CA et al.[14] concluded from their study that in patients who received 2 × ED_{95} dose of Atracurium, there was a greater increase in median plasma Histamine concenteration as compared to patients who received 2 × ED_{95}, 4 × ED_{95} and 8 × ED_{95} dose of Cisatracurium. The findings in our study were similar to this observation. In our study we found that 4 patients in Atracurium group had signs of histamine release and none of the patients in Cisatracurium had similar findings.

Conclusion

We conclude that 3 × ED_{95} dose of Cisatracurium is a more potent neuromuscular blocking agent than 2 × ED_{95} dose of Atracurium in terms of faster onset of action and longer duration of action. It also ensures better haemodynamic stability with no stress response during intubation. 3 × ED_{95} dose of Cisatracurium provides excellent conditions for intubation and is not associated with any signs of histamine release as compared to 2 × ED_{95} dose of Atracurium.

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