

# Comparative Study on Intubating Conditions and Neuromuscular Blocking Effect of Two Different Doses of CIS - Atracurium

Dr Arun Andappan<sup>1</sup>, Dr Anshika Gier<sup>2</sup>, Dr Khobragade Sneha Dasharath<sup>3</sup>,  
Dr Ramesh Kumar Malaichamy<sup>4</sup>

**Abstract:** *Our study was a comparative study for assessment of intubating conditions with two different doses of cisatracurium, a non-depolarising neuromuscular blockade safer comparable to other drugs of same group. The study was conducted on 50 patients (25 in each group with two doses) posted for elective laparoscopic cholecystectomy under general anaesthesia. The primary outcome of the study was assessing the intubating condition and neuromuscular blocking effect in two different doses of cisatracurium. The result of the study showed that in group A, 18 (72%) patients had excellent intubating conditions and 7 (28%) patients had good intubating conditions. On the other hand in group B, all the patient i. e., 25 (100%) had excellent intubating conditions. No patients were found to have poor or impossible intubation. The principal advantage of cisatracurium is the lack of histamine release which provides better cardiovascular stability compared to atracurium and other histamine releasing neuromuscular blocking agents. Both the doses were associated with stable hemodynamics without statistically significant changes. Allergic reactions or, side-effects were not seen in either of them. Hence, because of faster onset and longer duration of action with larger doses of cisatracurium (0.2mg/kg) and stable hemodynamics, make cisatracurium a more promising alternative muscle relaxant agent for tracheal intubation in clinical practice. Also, higher dose of 0.2mg/kg can be considered in various scenarios including critically ill, to facilitate safe intubating conditions.*

**Keywords:** CIS - Atracurium, Endotracheal Intubation, Neuromuscular blockade, Laryngoscopic view, Intubating Conditions

## 1. Introduction

Neuromuscular blocking drugs transformed the practice of anesthesia, as before their introduction, anesthesia was induced and maintained by intravenous and inhalation agents, and muscle relaxation was secured by deep inhalational anesthesia which had associated risks of respiratory or cardiac depression. After the introduction of muscle relaxants, anesthesia underwent a conceptual change, achieved by the use of neuromuscular blocking agents. Non-depolarizing muscle relaxants offer a better safety profile and are the preferred agents for rapid sequence intubation. Non-depolarizing neuromuscular blocking drugs compete with acetyl choline at the nicotinic receptor without producing conformational changes, unlike depolarizing drugs. Pancuronium is a long acting drug while vecuronium, rocuronium, atracurium and cis-atracurium are intermediate acting. Atracurium has a slow onset and an intermediate duration of activity and undergoes Hoffmann elimination which metabolizes it into laudanosine which has no neuromuscular blocking property and little or no cardiovascular activity. It can cause histamine release which may lead to side-effects like hypotension, tachycardia, bronchospasm and cutaneous flushing.<sup>1, 2, 3</sup>

Cisatracurium is a more potent isomer of atracurium. It does not provoke histamine release and not associated with side-effects like atracurium.<sup>2, 4</sup> It is known that cisatracurium produces good intubating conditions following a dose of 0.1mg/kg to 0.15mg/kg in two minutes. Studies have been done for its use for tracheal intubation and are found that 0.1mg/kg dose of cisatracurium do not create satisfactory intubating conditions. It produces satisfactory intubating conditions when propofol is used as the induction agent. Since propofol itself can provide satisfactory intubating conditions it may affect the quality of the intubating conditions produced by a muscle relaxant<sup>5, 6, 7</sup>. This study

was done to assess two different doses 0.15mg/kg and 0.2mg/kg of cisatracurium, after induction of anaesthesia with propofol for facilitation of intubation.

## 2. Methods

A comparative study for assessment of intubating conditions and neuromuscular blocking effect of two different doses of cisatracurium was undertaken on fifty patients (25 in each group) posted for elective laparoscopic cholecystectomy under general anaesthesia for a period of one year. Patients belonging to ASA I and II classes, age between 18 - 55 years of either sex and Mallampatti Class I and II were included. Patients with airway difficulty, hypersensitivity, pregnancy and neuromuscular disorders were excluded.

The intubating conditions were assessed and classified according to Jonathan H. Weiss et al<sup>9</sup> as Excellent, Good, Poor and Not possible under the factors of ease of laryngoscopy, Position of vocal cords and response to intubation. Heart rate, blood pressure, SpO<sub>2</sub> were recorded every 5 minutes for 30 minutes and then, every 15 minutes until reversal. The anaesthesia was maintained with O<sub>2</sub>: N<sub>2</sub>O mixture in the ratio of 1: 2 and with Isoflurane in the concentration of 0.5 - 1 %. Patients were monitored for any allergic reactions. When the patient made attempts to breathe, sensing the bag and clefts in capnogram, time noted and this was taken as duration of action. Either supplemental dose was given or reversed with Inj Neostigmine 50mcg/kg and Inj Glycopyrolate 10mcg/kg. The above observations were recorded and subjected to statistical analysis. Statistical analysis was carried out using statistical packages for SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous and categorical variables was expressed as mean ± SD and percentages, respectively. Students t - was applied to compare between the two groups. RM -ANOVA was

Volume 12 Issue 2, February 2023

[www.ijsr.net](http://www.ijsr.net)

Licensed Under Creative Commons Attribution CC BY

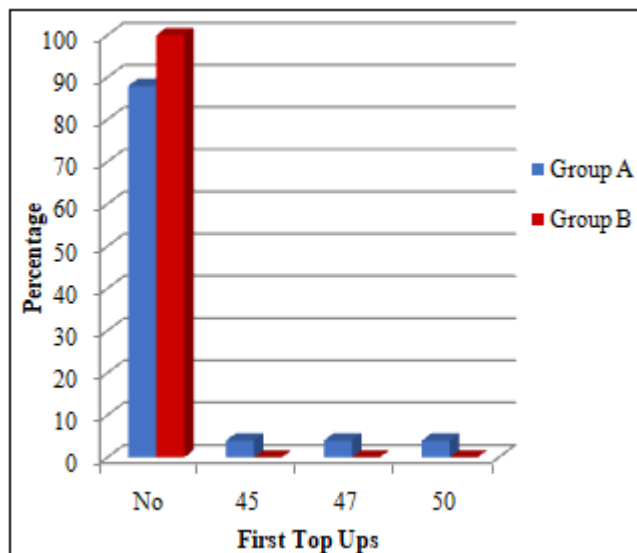
used to compare changes in parameter at each time interval. Two sided p values was considered as statistically significant at  $p < 0.05$ .

### 3. Results

A comparative study for assessment of intubating conditions and neuromuscular blocking effect of two different doses of cisatracurium undertaken on fifty patients (25 in each group) posted for elective laparoscopic cholecystectomy under general anaesthesia, during the period of 1 year and these cases were taken up for the study as outlined in the methodology. The groups were comparable with respect to age, gender and ASA grading. The variations in heart rate, systolic, diastolic blood pressure and Spo2 were not significant. According to above mentioned data, in group A, 18 (72%) patients had excellent intubating conditions and 7 (28%) patients had good intubating conditions. On the other hand, in group B, all the patient i. e., 25 (100%) had excellent intubating conditions. No patients were found to have poor or impossible intubation. The difference was found to be statistically significant ( $p < 0.004$ ).

**Table 1:** Intubating Conditions between the two groups

Intubating Conditions	Group A		Group B	
	No.	%	No.	%
Excellent	18	72	25	100
Good	7	28	0	0
Poor	0	0	0	0
Impossible	0	0	0	0
Total	25	100	25	100
p - Value	0.004			



**Chart 1:** The requirement of first top up was in 5 (20%) patients in group A whereas, no top ups were required for Group B. This was statistically significant ( $p < 0.018$ ).

### 4. Discussion

In the present study, we have compared between two higher doses, 0.15mg/kg and 0.2mg/kg of cisatracurium for intubating conditions in two minutes. These doses were selected on the basis of previous studies which had found that 0.1mg/kg dose of cisatracurium do not create satisfactory intubating conditions.<sup>7</sup> In the present study

intubation was done at 120 seconds after injection of loading dose. The intubating conditions were assessed and classified. So, it was found that in group A (0.15mg/kg), 18 (72%) had excellent and 7 (28%) out of 25 patients had good intubating conditions. And, in group B (0.2mg/kg), all the patients (100%) were observed to have excellent intubating conditions. No group were found to have poor or, not possible conditions for intubation. These findings are in consonance with Prakash Jamar et al (2017) who observed that tracheal intubation can be accomplished with good to excellent intubating conditions at 2 minutes following 0.15 mg/kg and 0.2 mg/kg of cisatracurium.<sup>5</sup> J. M. Rimaniol et al observed that good to excellent conditions were present at 2 minutes in 97% of patients after 0.2mg/kg of cisatracurium but in only 80% after 0.15mg/kg.<sup>8</sup> A. M. El - Kasaby, H. M. Atef, et al (2010) have observed that after cisatracurium (0.2mg/kg), 62.5% and 31.25% of patients had excellent and good intubating conditions respectively as compared to 37.5% and 50% after atracurium (0.5mg/kg), 2 minutes after administering the drug, which correlate with our study results.<sup>7</sup> Bluestein LS, Stinson LW, et al (1996) compared the intubating conditions of cisatracurium 0.1mg/kg, 0.15mg/kg and 0.2mg/kg and atracurium 0.5mg/kg during propofol / fentanyl anaesthesia. Good or, excellent intubation conditions were produced in 89% of patients two min following an initial dose of 0.1 mg/kg cisatracurium and in 100% of patients 1.5 min following an initial dose of 0.15 or 0.2 mg/kg cisatracurium, which correlate with our study results.<sup>10</sup> Schmautz E, Deriaz H, et al (1994) concluded that doses of 0.15 mg/ kg ( $3 \times ED_{95}$ ) and 0.2 mg/kg ( $4 \times ED_{95}$ ) of cisatracurium, as components of a propofol / nitrous oxide / oxygen induction intubation technique, may produce generally good or excellent conditions of intubation in 2.0 and 1.5 min, respectively. These findings correlate with our study.<sup>4</sup> In our present study, duration of action of muscle relaxant was noted as requirement of first top - up after bolus dose of cisatracurium. Laparoscopic cholecystectomy usually finishes in 45min in our institute, therefore, generally there would not be requirement of any top ups. In our study, we observed that in Group A, 5 (20%) out of 25 patients required top up and in Group B, no patient required a top up. So, the difference is statistically significant ( $p$  - value is 0.018). This result correlates well with other studies.<sup>5,7</sup>

Bisbenzylquinolinium compounds, in general tend to cause histamine release, which can result in facial flushing and hemodynamic aberrations. The cardiovascular effects normally noted secondary to histamine release are a decrease in mean arterial pressure and a compensatory increase in heart rate. These responses normally are transient and are related to both the size of the dose of the relaxant administered and the time course over which the relaxant is given.<sup>11</sup> The circulatory changes are transient, occurring 60 - 90 seconds after administration of atracurium and disappearing within 5 minutes. Cisatracurium is devoid of histamine - releasing effects, so that cardiovascular changes do not accompany the rapid IV administration of even large doses of cisatracurium.<sup>2, 12</sup> In our study, baseline preoperative heart rate was  $77.16 \pm 5.26$  bpm in Group A and  $75.92 \pm 4.12$  bpm in Group B. Baseline preoperative mean systolic blood pressure was  $125.16 \pm 8.57$  mmHg in Group A and  $125.92 \pm 7.09$  mmHg in Group B and the mean

diastolic blood pressure was  $72.32 \pm 6.2$  mmHg and  $72.88 \pm 6.52$  mmHg in Group A and in Group B, respectively. In our present study, heart rate and mean systolic and diastolic pressures were noted every 5 minutes for 30 minutes and then, every 30 minutes until reversal, after administering the muscle relaxant cisatracurium, 0.15mg/kg in Group A and 0.2mg/kg in Group B. Clinically significant changes were defined as deviations of more than 20% from the basal preoperative value.<sup>11</sup> In our study, no significant differences in mean heart rates and mean blood pressures were noted between Group A and B after administration of cisatracurium. El - Kasaby AM, H. M. Atef, et al (2010) stated that hemodynamic stability for both mean arterial pressure (MAP) and heart rate (HR) were more evident among higher doses of cisatracurium ( $4 \times ED_{95}$  and  $6 \times ED_{95}$ ), which correlates with our study.<sup>7</sup> Agavelian EG and Arkharova TB (1999) reported that cisatracurium in a dose of 0.15mg did not produce fluctuation in hemodynamic parameters.<sup>13</sup> Jean - Yves Lepage, et al (1996) reported in their study that bolus administration of cisatracurium at higher doses caused no dose - related clinically significant effects on HR or, MAP, which correlates with our study.<sup>14</sup>

In our study, none of the patients have showed allergic reactions. Allergic reactions (due to histamine release) like skin rashes, bronchospasm and hemodynamic changes were not noted in any of the patients. Atracurium releases histamine after  $3 \times ED_{95}$  dose. It contains tertiary ammonium ions which are divalent, thus they cross link cell surface IgE and precipitate mediator release from mast cells and basophils. Cisatracurium is devoid of histamine releasing effects even after a large dose. El - Kasaby AM, H. M. Atef, et al (2010) reported that no signs of histamine release were noted after different doses of cisatracurium while it was noted with atracurium. These findings correlate with our study.<sup>7</sup> Bluestein LS, Stinson LW, et al (1996) reported that flushing occurred in 2/20 patients treated with atracurium (0.5mg/kg) and in 0/60 patients treated with cisatracurium (0.1, 0.15 and 0.15mg/kg), which correlates with our study.<sup>10</sup> Jean - Yves Lepage, Jean - Marc Malinovsky, et al (1996) reported that there were no changes in plasma histamine concentration during the first 5 min after administration of cisatracurium at higher doses injected over 5 - 10 seconds. No cutaneous flushing or, bronchospasm was noted.<sup>14</sup> Cynthia A. Lien, Matthew R. Belmont, et al (1995) stated that no cutaneous flushing was noted after rapid injection of higher doses of cisatracurium.<sup>15</sup> Littlejohn IH, Abhay K, et al (1995) concluded that there was no clinical evidence of histamine release in the groups receiving different doses of cisatracurium, which correlates with our study.<sup>16</sup>

## 5. Conclusion

Cisatracurium is a potent intermediate acting non - depolarizing neuromuscular blocking agent and tracheal intubation can be accomplished with good to excellent intubating conditions at 2 minutes following 0.15 mg/kg and 0.2 mg/kg of cisatracurium. At higher dose of 0.2mg/kg provides favorable intubating conditions in two minutes and also, lasts longer when compare to a lower dose of 0.15mg/kg. The principal advantage of cisatracurium is lack of histamine release which provides better cardiovascular

stability compared to atracurium and other histamine releasing neuromuscular blocking agents. Both the doses were associated with stable hemodynamics without statistically significant changes. Allergic reactions or, side - effects were not seen in either of them. Faster onset and longer duration of action with larger doses of cisatracurium (0.2mg/kg) and stable hemodynamics, make cisatracurium a more promising alternative muscle relaxant agent for tracheal intubation in clinical practice in various scenarios including critically ill, to facilitate safe intubating conditions.

## References

- [1] Jonas Appaiah - Ankam, Jennifer M Hunter. Pharmacology of neuromuscular blocking drugs. British Journal Anaesthesia 2004 February; 4: 2 - 7.
- [2] Naguib M, Lien CA. Pharmacology of Neuromuscular Blocking Drugs, Chapter 34 In: Miller's Anaesthesia, 8<sup>th</sup> Ed. Philadelphia: Elsevier - Churchill Livingstone, 2014; 959 - 980.
- [3] Stoelting RK & Hillier SC. Neuromuscular blocking drugs and reversal agents, Chapter 8 In: Pharmacology and Physiology in Anesthetic Practice, 5<sup>th</sup> Ed. Philadelphia: 323 - 334
- [4] Schmautz E, Deriaz H, Vrillon M. Evaluation of 51W89 for endotracheal intubation in surgical patients during N<sub>2</sub>O / O<sub>2</sub> / propofol anesthesia. Anesthesia. 1994; 81: A1081.
- [5] Jamar P, Pathak DG, Begum I, Chauhan RC. A clinical comparative study of two intubating doses of cis - atracurium during general anaesthesia for gynaecological surgery. Int J Basic Clin Pharmacol 2017; 6: 1206 - 1210.
- [6] Amini S, Akramifard AA, Roudbari M, Comparison of the effects of different doses of cisatracurium on appropriate time for endotracheal intubation and hemodynamic changes during anesthesia. Zahedan J Res Med Sci (ZJRMS) 2011; 13 (7): 13 - 17.
- [7] M. El - Kasaby, H. M. Atef, A. M. Helmy, and M. Abo El - Nasr, Cisatracurium in different dose versus atracurium during general anaesthesia for abdominal surgery. Saudi Journal of Anaesthesia, 2010; 4 (3): 152 - 157.
- [8] Rimaniol JM, Kersuzan Y, Duvaldestin P. Intubating conditions using cisatracurium after induction of anaesthesia with thiopentone. Anaesthesia 1997; 52: 998 - 1014.
- [9] Jonathan H Weiss et al, Double - blind comparison of two different doses of rocuronium and succinylcholine for rapid sequence intubation. Journal of Clinical Anaesthesia 1997; 9: 379 - 382.
- [10] Linda S. Bluestein, Lawrence W. Stinson Jr., Robert L. Lennon DO, Stephen N. Quessy, Rebecca M. Wilson. Evaluation of cisatracurium, a new neuromuscular blocking agent, for tracheal intubation. Can J Anaesth 1996; 43 (8): 925 - 931.
- [11] Cynthia A. Lien, Mathew R. Belmont, Amy Abalos, Larissa Eppich, Steve Quessy, Martha M. Abou - Donia, John J. Savarese. The cardiovascular effects and histamine releasing properties of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anaesthesia. Anesthesiology 1995; 82: 1131 - 1138.

- [12] Stoelting RK & Hillier SC. Neuromuscular blocking drugs and reversal agents, Chapter 8 In: Pharmacology and Physiology in Anesthetic Practice, 5<sup>th</sup> Ed. Philadelphia: 323 - 334
- [13] Agavelian EG, Arkharova TB. Evaluation of the effectiveness of a new myorelaxant nimbex (cisatracurium besylate) in children. *Anesteziol Reanimatol.* 1999 Jul - Aug; (4): 16 - 18.
- [14] Jean - Yves Lepage, Jean - Marc Malinovsky, Myriam Malinge, Thierry Lechevalier, Christine Dupuch, Antoine Cozian, Michel Pinaud, Remy Souron. Pharmacodynamic dose - response and safety study of Cisatracurium (51W89) in adult surgical patients during N<sub>2</sub>O - O<sub>2</sub> - opioid anaesthesia. *Anesth Analg* 1996; 83: 823 - 829.
- [15] Mathew R. Belmont, Cynthia A. Lien, Steve Quessy, Martha M. Donia, Amy Abalos, Larissa Eppich, John J. Savarese. The clinical neuromuscular pharmacology of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anaesthesia. *Anesthesiology* 1995; 82: 1139 - 1145.
- [16] Littlejohn IH, Abhay K, EL Sayed A, Broomhead CJ, Duvaldestin P, Flynn PJ. Intubating conditions following 1R CIS, 1'R CIS atracurium (51W89). *Anaesthesia* 1995 June; 50 (6): 499 - 502.