Patients undergoing general anaesthesia: A dosage comparison study of cisatracurium for intubation

Abdul Aneez Cheekylodan CK, Sudeep Mohapatra and Asma Patel

DOI: https://doi.org/10.33545/26649268.2023.v5.1a.17

Abstract
Cisatracurium is a novel, intermediate-lasting neuromuscular blocking medication that belongs to the benzylisoquinolinium class and does not cause depolarization. It serves as a stereoisomer as atracurium having around three to four times the potency of atracurium. At doses up to 0.4mg/kg (8xED95), cisatracurium does not produce histamine release and is linked with greater stability of hemodynamics than atracurium. A 0.15mg/kg (3xED95) intubating dose is advised. High Comparing atracurium to cisatracurium at same doses, most previous clinical investigations have found that atracurium has been more efficacious than cisatracurium at the same dose (2ED95). Raising the daily intake of cisatracurium from ED95 (0.1mg/kg) to ED95 (0.2mg/kg) or ED95 (0.3mg/kg) has been proven in a small number of investigations to result in greater neuromuscular blockage and better cardiovascular stability without a noticeable increase in histamine release. Therefore, the current study was conducted to examine the effects of cisatracurium at 2 ED95 and 4 ED95 on intubating circumstances and hemodynamic stability.

Keywords: Cisatracurium, intubating conditions, general anaesthesia, histamine release

Introduction
One of the greatest leaps forward in the history of anaesthesia was the entry of neuromuscular blocking medications into clinical use, which completely altered the way anaesthesia was administered. Safer and better outcomes have been achieved in both traditional and novel surgical procedures thanks to the use of blocking neuromuscular medications. D.A. Hill and G.L. Turner first synthesised cisatracurium in 1989 as a single isomer molecule, and R. Brandt Maehr and William. B. Wastila conducted additional pharmacological study on cisatracurium. In 1995, the FDA authorized cisatracurium for use in humans. It has an intermediate duration of action and is a non-depolarizing benzylisoquinolinium neuromuscular blocker [2]. It's a stereoisomer of Atracurium that's 3–4 times as powerful as Atracurium [2, 3], causes no histamine release and is linked to more stable hemodynamics when compared with Atracurium at equivalent doses [4, 5]. Doses more than or equal to three times the ED95 (0.15mg/kg) are advised for intubation [5, 6]. Previous clinical investigations have shown that at 2 times the ED95 dose, atracurium is more efficacious than cisatracurium. A higher Cisatracurium dose, specifically 0.2mg/kg (4 times ED95) and 0.3mg/kg (6 times ED95), has been shown in a small number of studies to produce excellent cardiovascular stability and efficient neuromuscular blockade in clinical settings [5, 7]. Therefore, the current study was conducted to examine the effects of Cisatracurium at twice and four times the ED95 dose on intubating ease and hemodynamic stability.

Objectives of the Study
The goals of this study were to assess the effects of two different dosages of cisatracurium (0.1mg/kg and 0.2mg/kg) on:
1. Intubation success rates.
2. Unintended consequences
3. Hemodynamic Reaction

Materials and Methods
Source of Data: "A Clinical Comparative Study of Different Doses of Cisatracurium for intubation"
Intubation in Patients Undergoing General Anaesthesia” is the title of a randomized controlled trial examining this very question.

- A Randomized Controlled Trial Was Conducted To
- Two groups of thirty people were used as the sample size.
- We used a random sampling technique.
- SPSS (the Statistical Package for the Social Sciences) for Windows version 20 was used for the statistical analysis.
- Unpaired T test and chi-square test are used as significance tests. Tables and graphs showing the differences between the 0.1 and 0.2 mg/kg Cisatracurium groups were included.
- At the 5% level of significance, a ‘p’value of 0.05 will be deemed to be significant.

Method of Collection of Data
- After receiving approval from an ethics committee, the study included 60 patients aged 20 to 60 with ASA grade 1 and ASA grade 2 physical status scheduled for elective procedures under general anaesthesia.
- Prior to surgery, doctors visited each patient in person to thoroughly explain the operation and collect their signed consent. All the standard tests needed for preoperative evaluation and the planned surgery have been completed. All patients in the study were given two tablets of pre-medications the night before surgery: alprazolam (0.5mg) and Ranitidine (150mg) tablets. A full fast of no less than 8 hours was permitted.

Inclusion criteria
Men and women between the ages of 20 and 60. As certified by the American Society of Anesthesiologists, Levels 1 and 2. Patients having elective procedures done.

Exclusion criteria
1. Patients with ASA scores of 0 and 2.
2. Those who are expected to have trouble breathing because of their airway.
3. Patient with Allergic Reactions
4. Mothers-to-be and nursing mothers.
5. Patients using medications that are known to interact negatively with neuromuscular blocking agents.
6. Patients with a disease of the heart, muscles, liver, or kidneys.

Methodology
Patients were split into two groups upon entering the operating room, and the anesthesiologist who was not involved in the study randomly selected which group each patient would be assigned to and which drug would be delivered based on the sealed envelope technique.

- Group A: Cisatracurium of 0.1mg/kg 30 patients
- Group B: Cisatracurium of 0.2mg/kg 30 patients
- Standard monitoring involving NIBP, SPO2, and ECG was performed after intravenous cannulas (18G / 20G) were inserted.
- Hemodynamic parameters were measured at baseline. (SBP, DBP, MAP, HR).
- All patients were given a premedication of 0.005mg/kg intravenous Glycopyrrolate.
- Following preoxygenation, all groups received identical doses of intravenous (IV) propofol (2 mg/kg) and fentanyl (2 mcg/kg).
- Patients in each group received the prescribed starting dose of a muscle relaxant, and then two minutes of oxygen ventilation.
- When the two minutes were up, an appropriate sized Macintosh laryngoscope blade and endotracheal tube were used to perform an endotracheal intubation.
- Jaw unwinding, refusal to perform laryngoscopy, voice box position, limb movement, and coughing were used to evaluate intubation status.

A grading system was used to evaluate the state of the intubation, with a perfect score indicating that all criteria had been met. Having all criteria at or below 2 indicates an acceptable condition. If one or more of the five criteria have a value greater than 2, the condition is unacceptable.

- Oxygen, nitrous oxide, a liquid anaesthetic (Sevoflurane or Isoflurane), and occasional positive pressure breathing were used to sustain anaesthesia. Cisatracurium was administered on an as-needed basis in intermittent dosages.
- Intravenous doses of neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg) were administered to bring about reversal. After obtaining written consent from all patients in both groups, doctors conducted the standard pre-operative tests listed below.

Observations and Results
Objectives: To evaluate the intubating circumstances, hemodynamic responses, and any adverse effects of 0.1mg/kg and 0.2mg/kg Cisatracurium in a double-blind, randomized clinical study.

Table 1: Criteria for determining intubating conditions [8]

<table>
<thead>
<tr>
<th>Jaw Relaxation</th>
<th>Complete</th>
<th>Slight tone</th>
<th>Stiff</th>
<th>Rigid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance to laryngoscope</td>
<td>Easy</td>
<td>Fair</td>
<td>Difficult</td>
<td>Impossible</td>
</tr>
<tr>
<td>Vocal cords movements</td>
<td>Open</td>
<td>Moving</td>
<td>Closing</td>
<td>Closed</td>
</tr>
<tr>
<td>Coughing</td>
<td>None</td>
<td>Slight</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Limb movements</td>
<td>None</td>
<td>Slight</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Table 2: Demographic variable comparing between two groups

<table>
<thead>
<tr>
<th>Serial nos</th>
<th>Demographic variables</th>
<th>Group A %</th>
<th>Group b %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 (23.3)</td>
<td>13 (21.7)</td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>female</td>
<td>16 (26.7)</td>
<td>17 (28.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Age</td>
<td>33.93±6.88</td>
<td>32.23±6.65</td>
<td></td>
<td>0.698</td>
</tr>
<tr>
<td>3 Weight</td>
<td>51.63±7.75</td>
<td>57.10±8.39</td>
<td></td>
<td>0.089</td>
</tr>
</tbody>
</table>
Table 3: Intubating conditions among the patients studied

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unacceptable</td>
<td>15</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Acceptable</td>
<td>14.00</td>
<td>46.66%</td>
<td>11</td>
</tr>
<tr>
<td>Excellent</td>
<td>1.00</td>
<td>3.33%</td>
<td>1s</td>
</tr>
</tbody>
</table>

Only 3% of group A patients had excellent intubating conditions, while 60% of group B patients did. Patients in group A had a 46% acceptance rate, whereas individuals in group B had a 36% acceptance rate.

Half of the patients in Group A and 3% of the patients in Group B were found to be in unacceptable conditions. A statistically significant difference (p<0.01) in intubating conditions was found between the two groups.

Table 4: Comparison of mean heart rate of patients studied

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting pulse</td>
<td>78.23</td>
<td>±10.21</td>
<td>78.27</td>
</tr>
<tr>
<td>Induction</td>
<td>77.57</td>
<td>±10.20</td>
<td>76.27</td>
</tr>
<tr>
<td>with ASD</td>
<td>77.87</td>
<td>±10.60</td>
<td>76.07</td>
</tr>
<tr>
<td>1 min after ASD</td>
<td>79.33</td>
<td>±8.55</td>
<td>75.90</td>
</tr>
<tr>
<td>2 min after AS</td>
<td>88.53</td>
<td>±10.76</td>
<td>80.67</td>
</tr>
<tr>
<td>3 min after AS</td>
<td>91.53</td>
<td>±10.55</td>
<td>79.43</td>
</tr>
<tr>
<td>5 min after AS</td>
<td>84.93</td>
<td>±9.90</td>
<td>78.17</td>
</tr>
</tbody>
</table>

Graph 1: Bar diagram showing intubating conditions among two groups

Resting heart rates were similar between the two groups, and the effects of the study drugs were neither statistically or clinically significant. The mean rate of pulse was 91.53 ± 10.55 in group A and 79.43 ± 11.54 in group B 3 minutes after receiving the research medication. The p value for this was 0.04, making it statistically significant.

Table 5: Comparison of MAP (mmHg) of patients studied

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP Resting</td>
<td>87.14</td>
<td>8.78</td>
<td>90.63</td>
</tr>
<tr>
<td>Induction</td>
<td>85.08</td>
<td>8.00</td>
<td>86.76</td>
</tr>
<tr>
<td>with ASD</td>
<td>85.98</td>
<td>6.97</td>
<td>84.20</td>
</tr>
<tr>
<td>1 min after ASD</td>
<td>85.36</td>
<td>6.83</td>
<td>83.72</td>
</tr>
<tr>
<td>2 min after ASD</td>
<td>98.26</td>
<td>9.08</td>
<td>90.80</td>
</tr>
<tr>
<td>3 min after ASD</td>
<td>96.97</td>
<td>8.86</td>
<td>90.37</td>
</tr>
<tr>
<td>5 min after ASD</td>
<td>90.17</td>
<td>6.10</td>
<td>87.27</td>
</tr>
</tbody>
</table>

Graph 2: Time specific changes of MAP (mmHg) among two groups

Both groups showed similar and clinically insignificant changes in average arterial pressure during rest to study medication administration. Three minutes after receiving the study medicine, the average blood pressure in Group A was 96.978.88 mm Hg, while in Group B it was 90.376.75 mm Hg. With a ‘p’ value of 0.001, this is statistically significant.

Table 6: Untoward effects among patients studied

<table>
<thead>
<tr>
<th>Untoward reaction</th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>29.00</td>
<td>30.00</td>
<td>0.51</td>
</tr>
<tr>
<td>laryngospasm</td>
<td>1.00</td>
<td>0.00</td>
<td></td>
</tr>
</tbody>
</table>

Graph 4: Bar diagram showing untoward effects

There are no adverse effects in groups A and B, as stated in the table, with the exception of a single instance in group B. The ‘p’ value for this was 0.51; so, it was not statistically significant.
Discussion
When choosing a neuromuscular blockade drug for insertion or skeletal muscle relaxation, anesthesiologists prioritise speed of onset, ease of intubation, hemodynamic stability, and the capacity to reverse the effect spontaneously. One such muscle relaxant that doesn't cause histamine release is cisatracurium, a novel isomer of atracurium with increased efficacy and stable hemodynamics. The literature describes an extensive spectrum of intubating doses for cisatracurium, from 2 ED95 to 8 ED95, making it a relatively new and rarely used medicine. To demonstrate the improved potency of the drug with the desired clinical benefits and to prevent any undesirable effects related with increased/decreased dosage, we used two dosages [2ED95 and 4ED95] in the present investigation. In this study, we compared the intubating circumstances, hemodynamic response, and adverse effects of two dosages of the non-depolarizing benzylisoquinolinium muscle relaxant Cisatracurium (0.1mg/kg [2ED95] and 0.2mg/kg [4ED95]). Due to a lack of trials and a need to learn about the drug's effectiveness at the lowest possible dose, the aforementioned nonequivalent doses were chosen.

Conclusion
A wide variety of intubating dosages are available for cisatracurium, a novel medication with limited clinical application in India. Lower dosages of Cisatracurium were employed in the trial with varying doses for assessing the potent doses with the desired clinical effect. Excellent intubating circumstances, hemodynamic stability, and the absence of histamine-related alterations in HR and MAP were all achieved with a dosage of cisatracurium four times the ED95. As a result, Cisatracurium is the superior isomer of Atracurium and has a higher price tag. To learn more about the pharmacodynamics of Cisatracurium, trials with varying dosages for intubation should be planned in the future.

Acknowledgement
Not available

Author’s Contribution
Not available

Conflict of Interest
Not available

Financial Support
Not available

References


How to Cite This Article

Creative Commons (CC) License
This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0) License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.