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

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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 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 Glycopyrolate.
- 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.

Table 1: Criteria for determining intubating conditions [8]

Scoring	1	2	3	4
Jaw Relaxation	**Complete**	**Slight tone**	**Stiff**	**Rigid**
Resistance to laryngoscope	Easy	Fair	Difficult	Impossible
Vocal cords movements	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Limb movements	None	Slight	Moderate	Severe

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 2: Demographic variable comparing between two groups

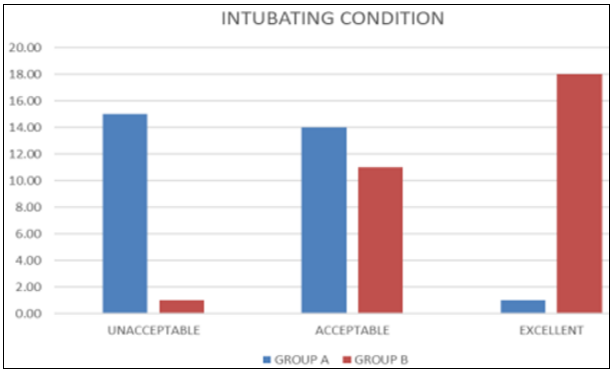
Serial nos	Demographic variables	Group A %	Group b%	P value
1 Gender				
	Male	14 (23.3)	13 (21.7)	0.8
	female	16 (26.7)	17 (28.3)	
2	Age	33.93±6.88	32.23±6.65	0.698
3	Weight	51.63±7.75	57.10±8.39	0.089

Table 3: Intubating conditions among the patients studied

	Group A		Group B		P value
Unacceptable	15	50%	1	3.33%	<0.01
Acceptable	14.00	46.66%	11	36.67%	
Excellent	1.00	3.33%	1s	60%	

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.

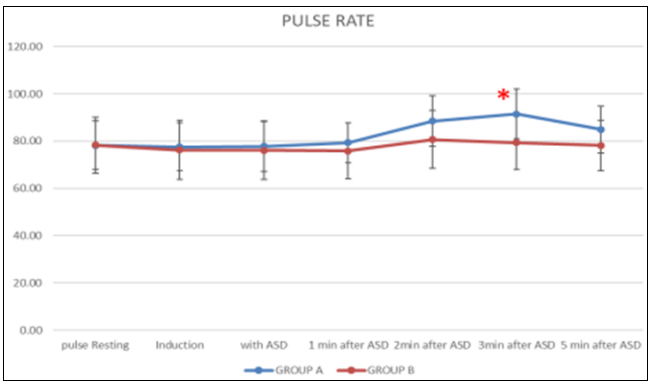
Half of the patients in Group A and 3% of the patients in Group B were found to be in unacceptable conditions. A statistically significant difference (p0.01) in intubating conditions was found between the two groups.



Graph 1: Bar diagram showing intubating conditions among two groups

Table 4: Comparison of mean heart rate of patients studied

	Group A		Group B		P Value
	Mean	Sd	Mean	Sd	
Resting pulse rate	78.23	±10.21	78.27	±11.96	0.45
Induction	77.57	±10.20	76.27	±12.43	0.29
with ASD	77.87	±10.60	76.07	±12.16	0.46
1 min after ASD	79.33	±8.55	75.90	±1135	0.16
2 min after AS!)	88.53	±10.76	80.67	*12.24	0.78
3 min after ASO	91.53	±10.55	79.43	±11.54	0.04
5 min after ASE)	84.93	±9.90	78.17	±10.62	0.97

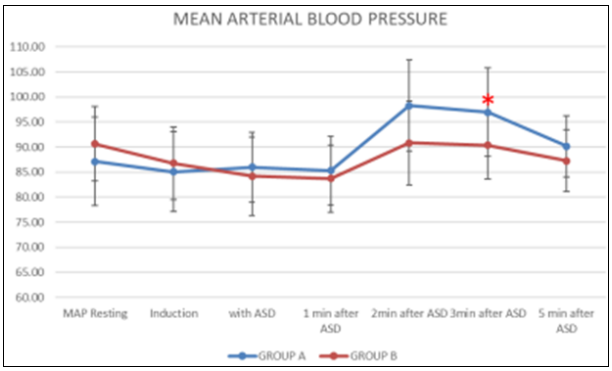


Graph 1: Time specific changes in mean pulse rate among two groups

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 91.5310.55 in group A and 79.4311.54 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

Map	Group A		Group B		P value
	Mean	SD	Mean	SD	
MAP Resting	87.14	8.78	90.63	7.41	0.42
Induction	85.08	8.00	86.76	7.24	0.59
with ASD	85.98	6.97	84.20	7.81	0.88
1 min after ASD	85.36	6.83	83.72	6.69	0.70
2 min after ASD	98.26	9.08	90.80	8.41	0.26
3 min after ASD	96.97	8.86	90.37	6.75	0.01
5 min after ASD	90.17	6.10	87.27	6.22	0.95

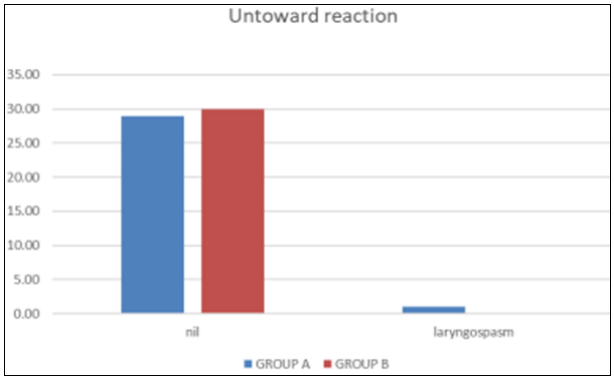


Graph 3: Time specific changes of MAP (mmHg) among two groups

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 96.978.86 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

Untoward reaction	Group A	Group B	p value
Nil	29.00	30.00	0.51
laryngospasm	1.00	0.00	



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 Cistracurium (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.

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Author's Contribution

Not available

Conflict of Interest

Not available

Financial Support

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