ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

A comparative study to evaluate the efficacy of cisatracurium and rocuronium for endotracheal intubation in pediatric patients: A prospective randomized study

Deepak R[1], Seema Shende[2], Namrata Jain[3], Sanyukta Paul[4]

[1,4]Postgraduate Resident, Department of Anesthesiology, Gajra Raja Medical College, [2]Associate Professor, [3]Assistant Professor, Department of Anesthesiology, Super Speciality Hospital, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India

Submission: 11-06-2024 Revision: 30-07-2024 Publication: 01-09-2024

ABSTRACT

Background: Cisatracurium and rocuronium are non-depolarizing neuromuscular blockers with an intermediate duration of action and are used safely in short and intermediate-duration surgical procedures in the pediatric population. **Aims and Objectives:** A prospective randomized study is to assess the efficacy of cisatracurium compared to rocuronium in terms of intubating conditions, clinical duration of action, hemodynamic parameters, and side effects in pediatric patients undergoing surgeries under general anesthesia. **Materials and Methods:** In this study, 50 patients aged 2–12 years with the American Society of Anesthesiologists grades I and II were randomly allocated into two groups: Group I received injection cisatracurium 0.15 mg/kg IV and Group II received injection rocuronium 0.6 mg/kg IV for intubation. Intubating conditions by Cooper et al., score, TOF count, hemodynamic parameters, signs of histamine release, and complications if any were noted. **Results:** According to the Cooper et al., score, intubating conditions were excellent in 100% of patients in Group II and 84% of patients in Group I, which was statistically significant. The time required for the first maintenance dose was shorter in Group II (14.04 ± 2.95 min) compared to Group I (20.08 ± 3.68 min). Hemodynamic parameters and demographic profiles were comparable between the two groups. No associated signs of histamine release or any other complications were noted in either group. **Conclusion:** We concluded that rocuronium 0.6 mg/kg provides better intubating conditions and a shorter duration of action compared to cisatracurium 0.15 mg/kg without any signs of histamine release in pediatric patients.

Key words: Rocuronium; Cisatracurium; Intubating conditions; Pediatrics

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i9.67674

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

General anesthesia is the state produced when a patient receives medications to produce amnesia and analgesia with or without reversible muscle paralysis. The ideal neuromuscular blocking agent for intubation should have a rapid onset, a brief duration of action, be free from hemodynamic effects, devoid of residual paralysis, and provide excellent intubating conditions without any side effects.[1] Although the depolarizing neuromuscular blocker (NMB) succinylcholine has an early onset and short duration of action, it must be used cautiously in pediatric patients due to its side effects, such as hyperkalemia, myoglobinuria, rhabdomyolysis, cardiac arrhythmias, masseter spasm, and malignant hyperthermia.[2]

Cisatracurium besylate is a cis-cis isomer (51W89:1R-cis 1"R-cis atracurium), one of the ten stereoisomers of atracurium that constitutes 15% of the atracurium mixture and is about 3–4 times more potent than atracurium and devoid of any cardiovascular side effects in doses up to 8×ED95 in adults and 3×ED95 in childrens.[2] The ED95 of cisatracurium is 0.05 mg/kg. In children, up to 4×ED95

Address for Correspondence:
Dr. Sanyukta Paul, Postgraduate Resident, Department of Anesthesiology, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India.
Mobile: +91-8827430031. **E-mail:** sanyuktasaivikash@gmail.com

has been safely used in previous studies.[3] It undergoes Hofmann's degradation to produce laudanosine and monoquaternary alcohol. It does not lead to histamine release in humans.[4,5]

Rocuronium is a 2-morpholino, 3-desacetyl, 16-n-allyl pyrrolidino derivative of vecuronium with no histamine production, a short onset time, an intermediate duration of action, cardiovascular stability, and rapid recovery properties.[5,6] The ED95 value of rocuronium is 0.3 mg/kg IV, and the dose for intubation is 0.6 mg/kg (2×ED95). Doses up to 1.2 mg/kg have been safely used in adult and pediatric patients.[6] Rocuronium is metabolized to 17-desacetyl rocuronium. Rocuronium is largely excreted unchanged in bile (50–70%) and in urine (10–30%).[4]

Few studies comparing cisatracurium and rocuronium for intubation in pediatric patients have been conducted so far. Thus, the objective of the current study is to compare the effects of 2×ED95 rocuronium and 3×ED95 cisatracurium on pediatric patients undergoing general surgical procedures in terms of intubating conditions, clinical duration, hemodynamic profile, and side effects. We also evaluated the neuromuscular blockage using TOF count at 3 min.

Aims and objectives

- To compare the efficacy of Cisatracurium 0.15 mg/kg and Rocuronium 0.6 mg/kg regarding intubating conditions and recovery of the NMB in paediatric patients.
- To observe the haemodynamic changes and side effects of Cisatracurium and Rocuronium, if any.

MATERIALS AND METHODS

After obtaining approval from the hospital ethics committee and written informed consent, the present prospective randomized study was conducted on 50 pediatric patients of either sex scheduled for surgeries under general anesthesia in the Department of Anaesthesiology, Gajra Raja Medical College and J.A. Group of Hospitals, Gwalior (Madhya Pradesh).

Sample size was calculated using the formula from the previous study[7] as

$$n = \frac{\left(Z_{\alpha/2}\sqrt{2PQ} + Z_{1-\beta}\sqrt{P_1Q_1 + P_2Q_2}\right)^2}{\left(P_1 - P_2\right)^2}$$

P_1=51.4, P_2=11.4, P=31.4, Q_1=48.6, Q_2=88.6, Q=68.6, $Z_{\alpha/2}$=1.96, $Z_{1-\beta}$=0.84

$$n = \frac{\left(1.96\sqrt{2 * 31.4 * 68.6} + 0.84\sqrt{51.4 * 48.6 + 11.4 * 88.6}\right)^2}{\left(51.4 - 11.4\right)^2}$$

n=20

So we have taken 25 samples in each group.

Inclusion criteria

Patient's parents giving consent to participate in the study, age between 2 and 12 years, weight between 10 and 0 kg, American Society of Anesthesiologists (ASA) Grade I and II.

Exclusion criteria

ASA grade III and IV, age below 2 years and above 12 years, weight below 10 kg and above 40 kg, patients with known disorders of the cardiovascular, hepatic, renal, or neuromuscular systems, Patients with airway problems and suspected difficult intubation.

Fifty patients of ASA Grades I and II scheduled for surgeries under general anesthesia were divided into two groups by randomization technique using a computer.

Group I (n=25)	Patient received injection cisatracurium−0.15 mg/kg i.v
Group II (n=25)	Patient received injection rocuronium−0.6 mg/kg i.v

All the patients were examined on the day before surgery, and all the required routine investigations, including complete blood count, random blood sugar, blood urea, serum creatinine, and chest X-ray as per hospital protocol, were carried out. The purpose and protocols of the study were explained to the patients' parents/guardians, and informed written consent was obtained.

After confirming nil by mouth according to the standard starvation protocol, patients were taken into the operating theater, and all routine monitors, including a pulse oximeter, blood pressure cuff, electrocardiogram leads, and neuromuscular monitor, were connected, and baseline hemodynamic parameters and TOF count were recorded on CARSCAPE B650 monitor. The neuromuscular monitor was attached to the patient's thumb and index finger. The negative electrode was placed 1 cm proximal to the proximal crease of the wrist, and the positive electrode was placed about 2–5 cm proximal to the negative electrode. The test hand was immobilized in a supine position on an arm board. Pre-oxygenation was done with 100% oxygen for 3 min. All patients were premedicated with injection midazolam 0.01 mg/kg IV, glycopyrrolate 0.001 mg/kg IV,

and injection fentanyl 2 mg/kg IV for analgesia. Anesthesia was induced with injection ketamine 2 mg/kg, and injection cisatracurium 0.15 mg/kg in Group I or rocuronium 0.6 mg/kg in Group II was used for muscle relaxation. After 3 min of ventilation, an experienced anesthetist who was unaware of the type of muscle relaxant used intubated the patient with an appropriate size endotracheal tube, and intubating conditions were noted clinically according to Cooper et al., score[8] criteria as excellent (8–9), good (6–7), fair (3–5), and poor (0–2).

The TOF count was noted at 3 min to assess the depth of neuromuscular blockage and was correlated with clinical criteria by the Cooper et al., score. The endotracheal tube was secured after checking for bilateral air entry. The hemodynamic response was noted before induction, just after intubation, and at 5 min, 30 min, and 60 min after intubation.

Further anesthesia was maintained with 66.7% nitrous oxide and 33.3% oxygen, and sevoflurane using a closed-circuit system with controlled ventilation. The patient was closely monitored for any clinical signs indicating the need for muscle relaxation, such as a TOF count of 4, the appearance of spontaneous breathing, or a curare notch in the capnogram. After this, a maintenance dose of 0.1 mg/kg atracurium IV was given to the patient as required. The clinical duration for the requirement of the first maintenance dose was noted. Any adverse reactions to the administered drugs and signs of histamine release, such as bradycardia, tachycardia, hypertension, hypotension, erythema, flushing, itching, urticaria, wheezing, bronchospasm, and injection reactions,[9] were noted until the first maintenance dose was given. At the end of the surgical procedure, all anesthetics were stopped, and 100% oxygen was given. Reversal was done with injection neostigmine 0.08 mg/kg and injection glycopyrrolate 0.05 mg/kg IV.

Data were statistically analyzed using the Statistical Package for the Social Sciences 20 statistical software. Quantitative data were expressed as mean±SD. Qualitative data were expressed in terms of percentages and numbers. For comparison of qualitative data between two groups, the Chi-square or Fisher's exact test was used. Quantitative data were compared using Student's t-test. P>0.05 is considered statistically insignificant, P<0.05 *statistically significant, P<0.001** highly significant.

RESULTS

In our study, as shown in Table 1, it was found that demographic profiles in terms of age, sex, weight, and ASA grade were comparable between the two groups and statistically insignificant (P>0.05).

Tables 2 shows that intubating conditions assessed clinically by Cooper et al., score were better in the rocuronium group compared to the cisatracurium group, which was statistically significant (P<0.05).

Table 3 depicts that the TOF count at the time of intubation was lower in Group II compared to Group I, which was statistically significant (P<0.05).

Graph 1 shows that the time required for the first dose of neuromuscular blocking agent (maintenance dose)

Table 1: Demographic data

Demographic data	Group I (n=25)	Group II (n=25)	P-value
Age (years)	6.79±3.29	7.78±3.29	0.27
Sex (Male/Female)	20/5	19/6	0.73
Weight (Kg)	20.28±8.61	21.1±6.81	0.71
ASA grade (1/2)	10/15	11/14	0.66

P>0.05 statistically insignificant, *P*<0.05 *statistically significant, *P*<0.001** highly significant, ASA: American society of Anesthesiologists

Table 2: Cooper et al., score

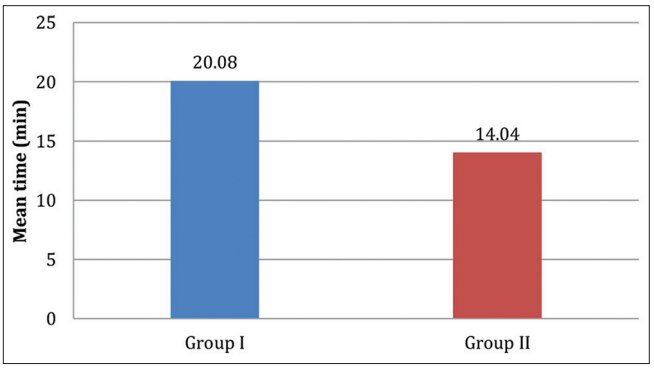
Cooper et al., score	Group I		Group II		P-value
	n	%	n	%	
Excellent	21	84	25	100	0.037*
Good	4	16	0	0	
Fair	0	0	0	0	
Poor	0	0	0	0	

P>0.05 statistically insignificant, *P*<0.05 *statistically significant, *P*<0.001** highly significant

Table 3: TOF count at the time of intubation

Groups	n	Mean±SD	P-value
Group I	25	1.36±0.74	0.005*
Group II	25	0.76±0.72	

P>0.05 statistically insignificant, P<0.05 *statistically significant, P<0.001** highly significant, TOF: Total organic fluorine, SD: Standard deviation



Graph 1: Intergroup analysis of the time requirement for the first dose of neuromuscular blocking agent

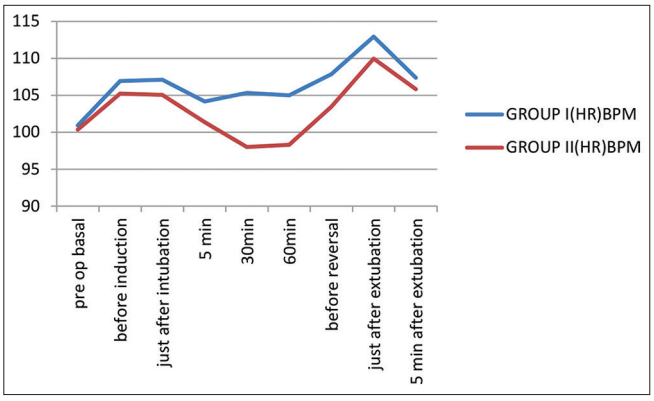
was shorter in Group II (14.04±2.95 minutes) compared to Group I (20.08±3.68 minutes), which was statistically highly significant (p<0.001).

Graphs 2 and 3 show heart rate and mean arterial pressure which were noted down at baseline, before induction, just after intubation, 5 min, 30 min, 60 min, before reversal, just after extubation, and 5 min after extubation and compared between the two groups and the results were statistically insignificant (P>0.05).

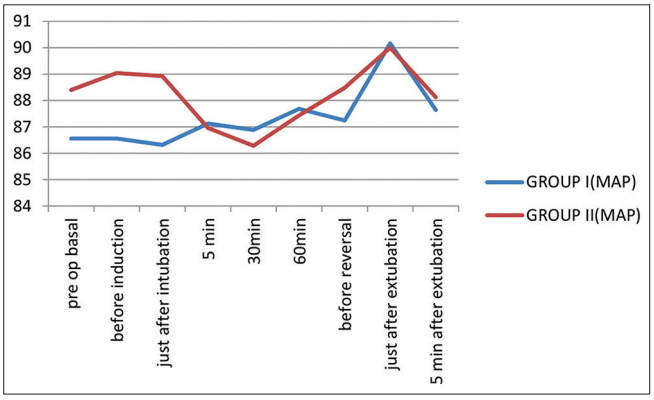
None of the patients in both groups had any significant signs of histamine release, except for one patient in cisatracurium group who had tachycardia which was insignificant.

DISCUSSION

In our study, we compared two non-depolarizing muscle relaxants injection rocuronium 0.6 mg/kg (2ED95) and injection cisatracurium 0.15 mg/kg (3ED95) with respect to intubating conditions, duration of action, hemodynamic parameters, and side effects in pediatric patients. Demographic profiles were statistically insignificant between the groups (P>0.05), and similar results were observed by Bansal et al.,[10] Scheiber et al.,[11] and Kumar et al.,[7] in their studies.



Graph 2: Intergroup analysis of pulse rate



Graph 3: Intergroup analysis of mean arterial pressure

The adequacy of conditions for tracheal intubation is a function of several factors, including the depth of anesthesia and the level of neuromuscular blockade at the time of the intubation attempt.[12] In our study, intubating conditions were assessed clinically by the Cooper et al., score and correlated with the TOF count at the time of intubation. Intubation was attempted after a fixed interval of 3 min following the administration of the muscle relaxant.

We found that rocuronium 0.6 mg/kg (2ED95) provided excellent intubating conditions and was better when compared to cisatracurium 0.15 mg/kg (3ED95), which was statistically significant (P<0.05). In a similar study, Scheiber et al.,[10] also found that rocuronium 0.6 mg/kg provides excellent intubating conditions in the pediatric population. Bansal et al.,[11] also found that rocuronium provides excellent intubating conditions with faster induction time and a high recovery index than atracurium in pediatric patients. Similarly, in a study by Kumar et al.,[7] they found that rocuronium has a rapid onset and produces excellent to good intubating conditions in 50–90 s with a dose of 0.6 mg/kg in adults with minimal hemodynamic changes and no adverse effects compared to cisatracurium.

In our study, the TOF count was correlated with clinical intubation conditions at 3 min after the dose of muscle relaxants, and the results indicate that the TOF count was lower in Group II (0.76±0.72) compared to Group I (1.92±0.95), which was statistically highly significant (P<0.001).

In our study, the mean duration for the requirement of the 1st maintenance dose of NMB was found to be shorter in the rocuronium group (14.04±2.95 min) when compared to the cisatracurium group (20.08±3.68 min), which was statistically highly significant (P<0.001).

Similar results were found by Kumar et al.,[7] in which rocuronium (0.6 mg/kg) had a duration of 53±10.23 min, which was shorter when compared to cisatracurium 0.15 mg/kg, which had a duration of 59.33±15.56 min.

Bansal et al.,[11] found that recovery time after the intubation dose of rocuronium (0.6 mg/kg) was shorter (35.86±4.2 min) when compared to atracurium (0.5 mg/kg), which had a duration of 47.28±7.26 min, which was comparable with our study.

In a study by Guo et al.,[13] the clinical duration of muscle relaxation for cisatracurium was 26.50±4.51 min in the

adult group, 20.03±3.31 min in the child group, and 34.63±5.13 min in the infant group, which was comparable with our study.

In our study, hemodynamic parameters measured at different intervals were found comparable and statistically insignificant (P>0.05) in both groups, which was similar to the findings of the studies done by Kumar et al.,[7] Bansal et al.,[11] and Narasimha Gnani and Uma.[14]

None of the patients in either group had any significant signs of histamine release, except for one patient in the cisatracurium group who had tachycardia, which was insignificant. Shrey and Singam,[15] found that cisatracurium at a dose of 0.2 mg/kg had no signs of histamine release in pediatric patients. Similarly, in a study by El-Kasaby et al.,[16] no signs of histamine release were found in any of the doses (2ED95, 4ED95, 6ED95) of cisatracurium.

Limitations of the study

A notable limitation of this study is the small sample size; the limited number of participants restricts the generalizability of our results.

CONCLUSION

In the present study, we conclude that rocuronium produced excellent intubating conditions and a shorter duration of action than cisatracurium. Both drugs produced minimal hemodynamic changes and side effects. Hence, they can be used as alternatives to succinylcholine in pediatric patients for endotracheal intubation.

ACKNOWLEDGMENT

We are grateful to the patients and their families for their cooperation in the study. Besides this, the entire team of Department of Anesthesiology, Gajra Raja Medical College, helped a lot in this research work.

REFERENCES

1. Belmont MR, Lien CA, Quessy S, Abou-Donia MM, Abalos A, Eppich L, et al. The clinical neuromuscular pharmacology of 51W89 in patients receiving nitrous oxide/opioid/barbiturate anesthesia. Anesthesiology. 1995;82(5):1139-1145.
https://doi.org/10.1097/00000542-199505000-00008
2. Meakin GH. Neuromuscular blocking drugs in infants and children. Contin Educ Anaesth Crit Care Pain. 2007;7(5):143-147.
https://doi.org/10.1093/bjaceaccp/mkn009
3. Kenaan CA, Estacio RL and Bikhazi GB. Pharmacodynamics and intubating conditions of Cisatracurium in children during halothane and opioid anaesthesia. J Clin Anaesth. 2000;12(3):173-176.
https://doi.org/10.1016/S0952-8180(00)00132-X
4. Stoelting RK and Hiller SC. Pharmacology and Physiology in Anaesthetic Practice. 5th ed., Ch. 2. Philadelphia, PA: Lippincott Williams and Wilkins; 2006. p. 323-344.
5. Welch RM, Brown A, Ravitch J and Dahl R. The *in vitro* degradation of cisatracurium, the R, cis-R'-isomer of atracurium, in human and rat plasma. Clin Pharmacol Ther. 1995;58(2): 1321-1342.
https://doi.org/10.1016/0009-9236(95)90190-6
6. Kumar A, Kumar A, Bharti AK, Choudhary A, Hussain M and Dhiraj S. A Randomized double-blind comparative study of the intubating conditions and hemodynamic effects of rocuronium and succinylcholine in pediatric patients. Cureus. 2023;15(9):e44631.
https://doi.org/10.7759%2Fcureus.44631
7. Kumar UG, Rao BK, Suggala KK. Endotracheal intubation with cisatracurium vs rocuronium: A comparative study. J Med Sci Clin Res. 2019;7:1131-1137.
https://dx.doi.org/10.18535/jmscr/v7i3.193
8. Cooper RA, Mirakhur RK, Clarke RS and Boules Z. Comparison of intubating conditions after administration of org 9426 (rocuronium) and suxamethonium. Br J Anaesth. 1992;69(3): 269-273.
https://doi.org/10.1093/bja/69.3.269
9. Simons FE, Ardusso LR, Bilò MB, El-Gamal YM, Ledford DK, Ring J, et al. World allergy organization guidelines for the assessment and management of anaphylaxis. World Allergy Organ J. 2011;4(2):13-37.
https://doi.org/10.1097/WOX.0b013e318211496c
10. Scheiber G, Ribeiro FC, Marichal A, Bredendiek M and Renzing K. Intubating conditions and onset of action after rocuronium, vecuronium, and atracurium in young children. Anaesth Analg. 1996;83(2):320-324.
https://doi.org/10.1097/00000539-199608000-00020
11. Bansal S, Rao MM and Rao MM. Intubating conditions and efficacy of rocuronium versus atracurium in paediatric patients undergoing elective surgeries under general anaesthesia: A randomised clinical trial. J Clin Diagn Res. 2023;17(1):UC36-UC40.
https://doi.org/10.7860/JCDR/2023/61085.17427
12. Mandal P. Intubating conditions after Cisatracurium administration-a dose response study in adults. J Anaesth Clin Pharmacol. 2002;18(2):147-151.
13. Guo J, Zhou X, Yuan X, Shen H and Zhang Y. Age and the neuromuscular blockading effects of Cisatracurium. Int J Clin Exp Med. 2015;8(9):16664-16669.
14. Narasimha Gnani BC and Uma BR. A clinical comparative study of succinylcholine versus Rocuronium in various doses for paediatric intubation. Indian J Clin Anaesth. 2017; 4(2):214-218.
https://doi.org/10.18231/2394-4994.2017.0045
15. Shrey S and Singam A. A comparative study of atracurium and cisatracurium in paediatric cleft lip and cleft palate surgeries. Res J Pharm Technol. 2020;13(2):867-870.
https://doi.org/10.5958/0974-360X.2020.00164.X
16. El-Kasaby AM, Atef HM, Helmy AM and Abo El-Nasr M. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery. Saudi J Anaesth. 2010;4(3):152-157.
https://doi.org/10.4103%2F1658-354X.71571

Authors Contribution:
SP- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **SS**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **NJ**- Design of study, statistical analysis and interpretation, review manuscript; **DR-** Literature survey and preparation of figures, coordination, and manuscript revision.

Work attributed to:
Gajra Raja Medical College, Department of Anaesthesiology, Gwalior, Madhya Pradesh, India.

Orcid ID:
Deepak R - https://orcid.org/0009-0005-4221-6269
Seema Shende - https://orcid.org/0000-0003-2542-3053
Namrata Jain - https://orcid.org/0000-0002-2212-4296
Sanyukta Paul - https://orcid.org/0009-0007-4984-1459

Source of Support: Nil, **Conflicts of Interest:** None declared.