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A Comparative Study of Neuromuscular Blocking Effects and Reversibility of Cisatracurium and Vecuronium

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Abstract

Context: Cisatracurium is a cis isomer of parent compound atracurium, devoid of histamine release, thus possessing hemodynamic & cardiovascular stability. *Aims:* We compared the intubating conditions, hemodynamic stability & recovery of atracurium & vecuronium. *Settings and Design:* We carried out prospective, double blind randomized study after approval of ethical committee. 100 adult patients of ASA 1 & 2 with comparable demographic data were selected. Divided in Two Groups C (Cisatracurium) & V (Vecuronium). Standard monitoring was done & following routine premedication & induction agents, patients were intubated at 2 mins after administration of cisatracurium 0.15 mg/kg & vecuronium 0.1 mg/kg respectively, maintained on intermittent dose of cisatracurium: 0.03 mg/kg & vecuronium: 0.02 mg/kg. Intubation conditions were assessed according to Time to 25% recovery of t1/tc following initial doses, Time to 25% recovery of t1/tc following repeated boluses, Time to 25% recovery of t1/tc following last dose, Return of t4/t1 ratio 0.8 spontaneous recovery at end of operation. *Statistical analysis used:* The results were evaluated by applying paired *t*-test and *p* - value using SPSS Statistical Software. *Results:* Intubating conditions at 2 mins following administration appeared satisfactory & laryngoscopy condition was good in 98% in Group C & 97% in Group V, Time taken for 25% recovery following First Dose & Subsequent Doses was longer for Group C than Group V. Time taken to 25% recovery of t1/tc following Last Dose was shorter in Group C patients as compared to Group V, duration of action of Group C was longer than Group V, both demonstrated equal hemodynamic & cardiovascular effect. *Conclusions:* Cisatracurium is intermediate onset nondepolarizing muscle relaxant devoid of histamine release with longer duration of action & faster recovery.

Keywords: Cisatracurium; Vecuronium; Intubating conditions; Recovery; Hemodynamic profile.

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Introduction

Rapid and safe endotracheal intubation is of prime importance in general anesthesia. The role of muscle relaxant serves to facilitate endotracheal intubation and provides surgical relaxation.[1-3] The ease of performing endotracheal intubation depends on the degree of muscle relaxation, depth of anesthesia and skill of anesthesiologist.[2] The onset time, duration of muscle relaxation, type of patient and surgery are factors in choosing the appropriate muscle relaxant to achieve rapid, successful

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tracheal intubation.[4] Cisatracurium is a cis isomer of parent compound atracurium. However, it is more appealing as it is devoid of histamine release and thus possessing hemodynamic and cardiovascular stability. It possesses organ independent Hoffman elimination and intermediate duration of action. Vecuronium is nondepolarizing muscle relaxant with intermediate duration of action, metabolizes in liver and hepatorenal organ dependent clearance. Hence, forth considering the above properties of cisatracurium in this study we compared the intubating conditions, hemodynamic stability and recovery of these two agents.

Materials and Methods

We carried out prospective, double blind randomized study after approval of ethical committee. Written and informed consent was obtained from all the participating patients. We studied 100 adult patients of physical status ASA 1 and 2, of either sex, age ranging from 18 to 65 years, weighing 40 to 70 kg, posted for elective surgeries under General anesthesia lasting for maximum of 2 to 3 hours. A detailed and formal airway evaluation was done preoperatively and patients with mpg 1 and mpg 2 were included.

Patients excluded were with grading score 3 and 4 according to Sampson and young modification of mallampati grading, anticipated difficult mask ventilation and airway, Patient refusal, patients of ASA 3 and 4, on therapy with drugs known to interfere with neuromuscular transmission, suspected pregnancy, liver or renal disease, prolonged preoperative bed rest, Uncontrolled hypertension, History of reactive airway disease, history of allergy or sensitivity to any medication, latex or egg, emergency surgical intervention or obesity (BMI ≥ 25). All patients were given T Alprazolam 0.5 mg on night prior to the surgery and were kept nil by mouth for 8 hrs.

Patients will be randomly divided into 2 Groups of 50 each:

- Group C (50 patients) for Cisatracurium;
- Group V (50 patients) for Vecuronium.

A written and informed consent was taken from the patient. On the day of surgery, In the preoperative room base line vital parameters (pulse, blood pressure, respiratory rate, SpO_2 and temperature) were recorded. A large bore 18 gauge IV peripheral line was secured, a slow infusion of lactated Ringer's solution was started. All resuscitation equipments were kept ready. Standard monitors were connected and the preinduction Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Heart Rate (HR), Oxygen Saturation (SpO_2), ECG were recorded. In the operation theatre the patients were premedicated with Inj ondansetron 4 mg IV Inj Glycopyrollate 0.2 mg IV, Inj midazolam 0.1 mg/kg IV, Inj fentanyl 10 microgram/kg IV, just before induction. Patient were preoxygenated with 100% oxygen at 10 litre/min fresh gas flow for 3 minutes using closed circuit, induced with IV propofol 2 mg/kg followed by cisatracurium or vecuronium and IPPV wih 100% oxygen on bag and mask after they were randomly allocated to Group C (Cisatracurium) or Group V (Vecuronium). After adequate relaxation for 2 minutes patient were intubated with appropriate sized endotracheal tube and was fixed after checking equal air entry bilaterally.

Grroup C: Cisatracurium intubating dose 0.15 mg/kg;

Group V: Vecuronium intubating dose 0.1mg/kg.

Intubation conditions were assessed according to the criteria: Laryngoscopy condition, vocal cord position, vocal cord movement all being excellent or scarce and if there was reaction to Endotracheal tube insertion of cuff inflation by limb movement or cough shown in (Table 2). Patient were maintained on controlled mechanical ventilation with 50% oxygen, 50% nitrous oxide (N_2O) Inhalational agent (sevoflurane 3%) and maintainance dose of nondepolarizing muscle relaxant (Cisatracurium: 0.03 mg/kg and Vecuronium: 0.02 mg/kg). The Adductor Policies muscle evoked response (AP), Train of Four (TOF) stimulation after supramaximal ulnar nerve stimulation were measured. With TOF the time for recording baseline response was standard 5 mins prior to administration of muscle relaxant. Repeated consequent doses were administered when AP response recovered to 25% of control twitch height, at the end of surgery monitoring was continued until 95% of T1 and T4/T1 (80% at the end of surgery).

At the end of the operation, anesthetic agents were discontinued and adequate oral suctioning was done. Pt were then reversed with inj Glycopyrollate (0.008 mg/kg) and inj neostigmine (0.05 mg/kg) and extubated after regains consciousness and responded to verbal command. All patients were monitored for HR (Heart Rate), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), S_PO_2, $ETCO_2$ and fluid requirement was calculated and replaced accordingly. The following variables were recorded in minutes: (1) Time to 25% recovery of t1/tc following initial doses (2) Time to 25%

recovery of t1/tc following repeated boluses (3) Time to 25% recovery of t1/tc following last dose (4) Return of t4/t1 ratio 0.8 spontaneous recovery at end of operation (Spontaneous Complete Recovery, (SCRT).

Results

After studying 100 cases, observation and results are summarized in tabulated form and described below. Both groups comprised of 50 patients, (Table 1). No significant difference was seen in male-female ratio,weight and age of patients between both the groups. Intubating conditions at 2 mins following administration appeared satisfactory & laryngoscopy condition wasgood in 98% in group C & 97% in Group V, shown as in Figs. 1–2, both demonstrated equal hemodynamic & cardiovascular effect, Figs. 3–4, Time taken for 25% recovery following first dose & subsequent doses was longer for Group C than Group V, Time taken to 25% recovery of t1/tc following Last Dose was shorter in Group C patients as compared to Group V, duration of action of Group C was longer than Group V, (Table 2).

Table 1: Demographic Data

Parameters	Group C (n = 50)	Group V (n = 50)	p - value	Inference
Sex (M/F)	38:12	40:10	> 0.05	NS
Age (Years)	30.96 ± 7.68	32.4 ±10.01	> 0.05	NS
Weight (kg)	56.72 ± 8.5	60.04 ± 6.943	> 0.05	NS
Height (cm)	165.6 ± 4	168 ± 7.1	> 0.05	NS
ASA Grade 1				
ASA Grade 2	44:6	40:10	–	–
Duration of surgery (min)	100 ± 10	110 ± 15	–	–

Table 2: Recovery characteristics of both groups (n -100)

Parameters	Group C	Group V	p - value
Time (mins) to 25% recovery of t1/tc following initial doses	57.3 ± 11.2	41.2 ± 7.0	< 0.0001
Time (mins)to 25% recovery of t1/tc following repeated boluses	35.5 ± 8.49	30.02 ± 3.9	< 0.0002
Time (mins) to 25% recovery of t1/tc following last dose	36.75 ± 4.8	31.6 ± 4.71	< 0.0001
Return of t4/t1 ratio 0.8 spontaneous recovery at end of operation (mins)	43.5 ± 4.6	46.5 ± 7.25	< 0.015

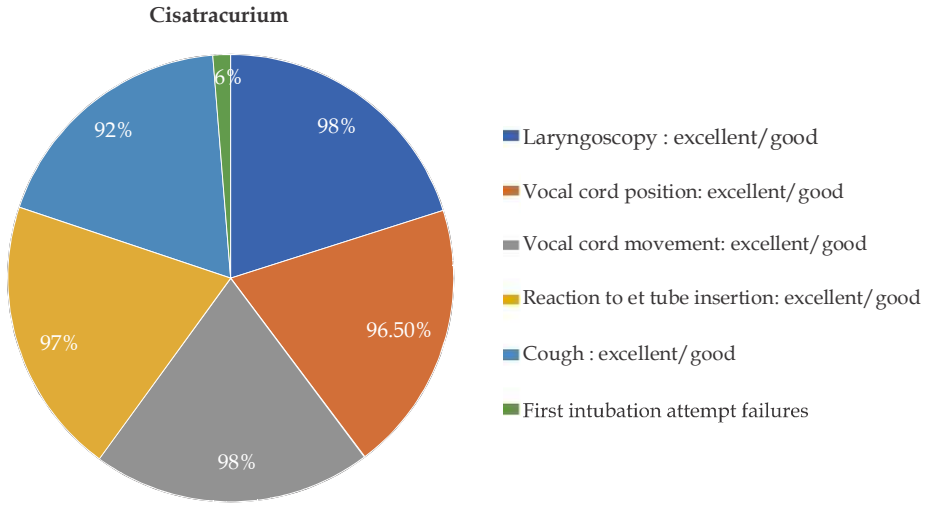

Fig. 1: Cisatracurium-intubating conditions.

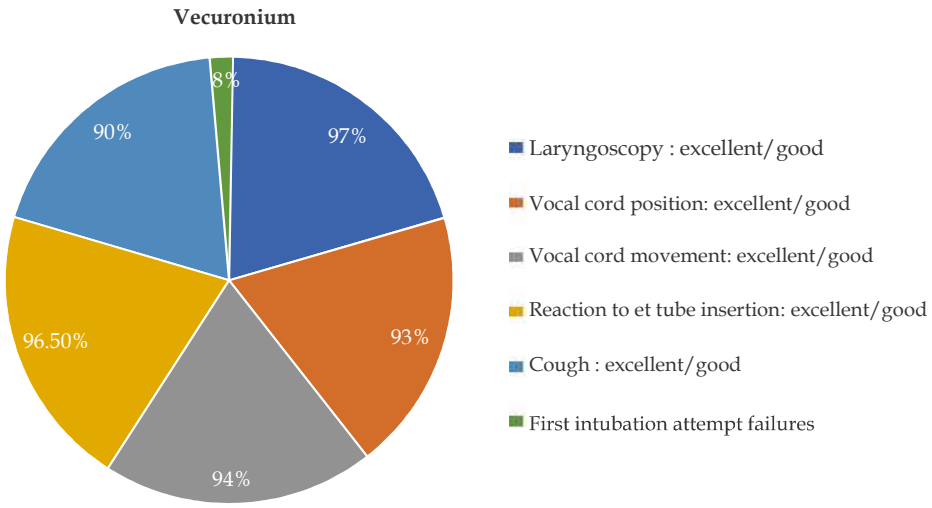

Fig. 2: Vecuronium-intubating conditions.

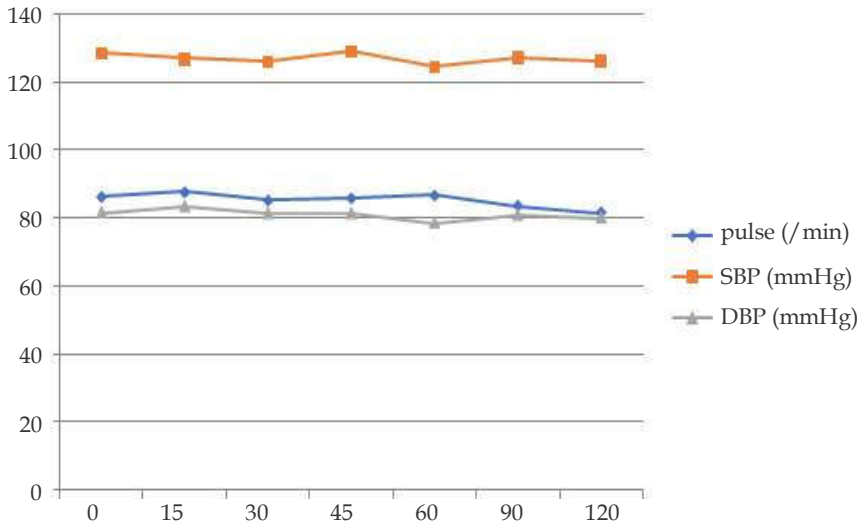

Fig. 3: Cisatracurium vitals (pulse, systolic blood pressure, diastolic blood pressure).

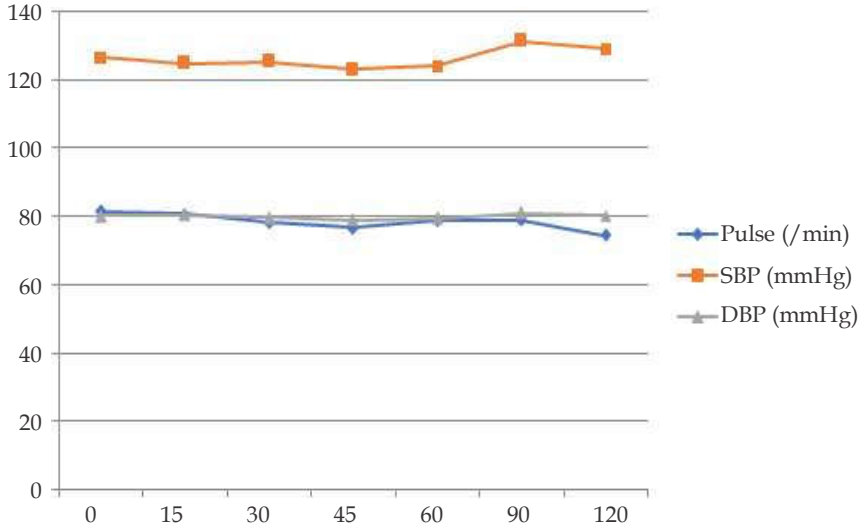

Fig. 4: Vecuronium vitals (pulse, systolic blood pressure, diastolic blood pressure).

Discussion

In our study, Intubating conditions at 2 mins following both drugs administration appeared satisfactory and laryngoscopy conditions - excellent/good in 98% cases in Group C and 97% in Group V respectively.

C Melloni's study "Cisatracurium *versus* vecuronium: A comparative, double blind study, randomized in adult patient under propofol/ fentanyl/*n* 20 anesthesia." Revealed similarly the intubating conditions to be 97.7% satisfactory in Group C and 96.4% in Group V respectively.[10]

Time taken for 25% recovery following First Dose and Subsequent Doses was longer for Group C than Group V. However, the time taken to 25% recovery of t1/tc following Last Vose was shorter in Group C patients as compared to Group V. Thus, duration of action of Group C was longer than Group V. C Melloni has made the similar observation in his study while comparing cisatracurium and vecuronium in the above parameters.[10]

The return of t4/t1 ratio of 0.8-spontaneous recovery at end of operation for Group C was shorter than Group V in our study. Hence, forth proving that recovery from Group C was speedy than Group V in similar conditions. "Cisatracuriumbislate, a review of its pharmacology and clinical potential in anesthetic practice" entitled study by Bryson HM concluded similarly that cisatracurium was associated with significantly faster recovery offered more predicitive recovery profile after continuous infusion than vecuronium.[11]

Moreover, cisatracurium as well as vecuronium demonstrated hemodynamic and cardiovascular stability in all patients.[10,12] Bencini stated that: The short duration of vecuronium may be due to its rapid distribution kinetics such that recovery occurs largely during distribution phase, in contrast to which cisatracurium rapidly degrades by pathway which is independent of hepatic and renal and thus its pharmacological recovery occurs during the elimination phase of the drugs metabolism. The above reason could thus explain the faster recovery of ciatracurium as compared to vecuronium at the end of operation in our study.[13]

Wright P et al. mentioned in his research that cisatracurium would be superior to vecuronium as it does not exhibit even the slightest or minimal trend towards the minimal accumulation as evidenced by atracurium and prolonged effect of vecuronium prior to recovery might be due to its accumulation of metabolites which possess NMB properties on repeated subsequent doses.[14] This observation was supported by studies of Hughes MA and positively explains the results of our study also.[15]

AMEl-Kasaby studied "Cisatracurium in different doses *versus* atracurium during general anesthesia for abdominal surgery" and observed that cisatracurium at larger doses (4*ED95) as compared to atracurium doses had slow onset time as compared to atracurium but possessed longer duration of action and excellent intubating condtions at 2 mins with stable hemodynamic profile."[16]

Conclusion

Both the compared drugs were safe and effecacious under the conditions of the study. In a nutshell cisatracurium is the latest intermediate onset nondepolarizing muscle relaxant devoid of histamine release with longer duration of action and faster recovery.

Key Messages

Thus, Cisatracurium is latest intermediate acting nondepolarizing muscle relaxant preffered now-a-days for induction and maintenance in general anesthesia.

Abbreviations

ASA - American Society of Anesthesiologists

IPPV - Intermittent Positive Pressure Ventilation

SBP - Systolic Blood Pressure

DBP - Diastolic Blood Pressure

$EtCO_2$ - End Tidal CO_2

NMB - Neuromuscular Blocking

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