ORIGINAL RESEARCH

Comparison of Atracurium versus Cisatracurium Regarding Onset Time, Intubating Conditions and Haemodynamic Parameters and Duration of Action

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ABSTRACT

Background:Endotracheal intubation is an integral part of the administration of general anesthesia during the surgery. Neuromuscular blocking agents facilitate general anaesthesia. cisatracurium having lack of histamine release, which provides better cardiovascular stability in comparison to atracurium. To compare of atracurium and cisatracurium onset time, intubation conditions, hemodynamics and duration of block.

Materials and Methods: The present study was a prospective randomize, conducted in the Department of Anaesthesia, Pacific medical college and hospital Udaipur, Rajasthan. Total 70 ASA Grade I/II patients in the age group of 18-60 years posted for elective surgery required general anesthesia were selected in this study. Patients were divided into two groups of 35 each. Group A patients received atacurium 0.5 mg/kg as loading dose while Group B cisatracurium 0.2mg/kg, The onset time,intubating conditions hemodynamic parameters and duration of action were noted.

Results: Cisatracurium have rapid onset ($p<0.001$) and long duration of action ($p<0.001$) and stable mean arterial pressure ($p<0.001$) and better intubating conditions ($p=0.04$.).

Conclusion: Cisatracurium provides rapid onset, excellent intubating conditions, long duration of action and good haemodynamic stability in comparision to atracurium.

Keywords: Cisatracurium, Atracurium, General Anaesthesia, Intubation.

INTRODUCTION

Endotracheal intubation is an integral part of the administration of general anesthesia during the surgical procedure. Succinylcholine, a depolarizing muscle relaxant with rapid onset of action and short duration is still the relaxant of choice to facilitate tracheal intubation. However, in addition to fasciculations, succinylcholine has many side effects such as bradycardia, dysrhythmias, increased release of potassium, post-operative myalgia, increased intra ocular pressure, intracranial tension, intragastric pressure, prolonged recovery in patients with pseudocholinesterase deficiency, masseter spasm, and triggering malignant hyperthermia.[1-6] Since these side effects are due to the depolarizing mechanism of action of succinylcholine, search has been focused onto find an ideal non-depolarizing muscle relaxant (NDMR) with rapid onset time and offering excellent intubating conditions.

Classification of non-depolarizing muscle relaxants:

	Long Acting>50min	Intermediate Acting20-50 Min	Short acting10-20 Min
Steroidal Compounds	Pancuronium	Vecuronium Rocuronium	
Benzylisoquinolinium Compounds	Tubocuraine	Atracurium Cisatracurium	Mivacurium

Cisatracurium is one of the 10 isomers of atracurium. The neuromuscular blocking potency of cisatracurium is approximately three-fold that of atracuriumbesylate. Cisatracurium has ED95 of 50 μg/kg and atracurium has ED95 of 0.2 mg/kg. The principal advantage of cisatracurium is lack of histamine release, which provides better cardiovascular stability in comparison to atracurium and other histamine-releasing neuromuscular blocking agents. Hence, these two drugs are compared in this study.

AIM AND OBJECTIVE

The aim of the study to compare the atracurium 0.5 mg/kg IV versus cisatracurium, i.e., 0.2mg/kg IV for intubation, with regard to

- Onset time for intubation
- Intubating conditions
- Duration of blockade
- Hemodynamic parameter

MATERIALS & METHODS

Adult patients of both sex in the age group of 18–60 years , (ASA) I/II posted for surgery requiring general anesthesia at pacific Medical College, Udaipur were taken up for the study. Our study was a prospective randomized study. The study was performed after obtaining the Institutional Ethical Committee approval.

Basis of sample size

Bruderer'sFormula:

$n= (Z_{\alpha} + Z_{(1-\beta)}) P(1-P) /E^2$

Where $Z\alpha$ =95% Confidence level equal to 1.96

$Z_{1-\beta}$ =80% power of study equals to 0.8413

Prevalence to be 90% margin of error to be 12% and 95% confidence level of study. Total of 67 or more study subjects will be considered in both groups. So we decided total of 70 patients, 35 each groups.

Pre-anaesthetic assessment done, procedure was explained and informed consent was taken. Patient having any Co morbid systemic conditions, i.e., cardiovascular system, hepatic, and renal impairment along with neuromuscular disorders, ASA grade III/ IV and anticipated difficult airway, Patients who are on amino glycosides, MgSO4, Known history of allergy to any of the study drugs, Pregnant women were excluded from our study. Patients randomly allocated into two groups based on computer-generated randomization.

Group A: Thirty five patients receiving Inj. atracuriumbesylate 0.5 mg/kg IV

Group B: Thirty five patients receiving Inj. cisatracuriumbesylate 0.2 mg/kg IV

On the day of surgery in operative room, IV line secured with 18G canula and

Monitors such as ECG, non-invasive blood pressure, SpO2, end-tidal carbon dioxide (EtCO2), and temperature were connected. All baseline parameters such as HR, SBP, DBP, MAP, and SpO2 were noted.

Premedication was given Inj. Glycopyrrolate(0.005 mg/kg IV), Inj. Ondansetron(0.1 mg/kg IV), Inj. fentanyl 2μg/kg. Preoxygenation was done with 100% O2 for 3 min.

• TOF–nerve stimulator was attached. Calibration and baseline responses obtained before administering the neuromuscular blocking drug (NMBD). Randomization was done on computer generated lottery method. All patients received priming dose (1/10th of the bolus dose) of the study drug according to the allocated group just before induction to shorten the onset time.

• Group A: Received priming dose of atracurium (i.e., 0.05 mg/kg)

• Group B: Received priming dose of cisatracurium (i.e., 0.02 mg/kg)

Induction of general anesthesia was done with Inj. Propofol 2mg/kg with loss of eyelash reflex/loss of verbal response was considered to be the endpoint of induction. Patient was checked for mask ventilation and remaining dose of muscle relaxant was given.

• Group A received remaining bolus of an intubating dose of atracurium (0.45 mg/kg)

• Group B received remaining bolus of an intubating dose of cisatracurium (0.18 mg/kg)

TOF ratio as percentage and results was recorded at 30 s interval. Time to maximum blockade was noted. Time interval between administration of the dose of relaxant and disappearance of all four twitches was noted .This was considered as a onset time. Intubating conditions and time required for intubation was noted. Patient requiring intubating time more than 30 second was excluded from study.

Assessment of intubation was done by following,[7]

1) Excellent: Easy passage of the tube without coughing. Vocal cord relaxed and abducted.
2) Good: Passage of tubes with slight coughing and bucking. Vocal cord relaxed and abducted.
3) Poor: Passage of tubes with moderate coughing and bucking. Vocal cord is moderately adducted.
4) Not possible: Vocal cords not relaxed, tightly adducted

Intubation was confirmed by EtCO2 and connected to a ventilator for intermittent positive pressure ventilation until completion of surgery. Maintenance of anaesthesia was done with N2 O 60% and Sevoflurane. Hemodynamic parameters such as HR, SBP, DBP, and MAP were recorded before induction, immediately after tracheal intubation.

Duration from intubating dose of NMBD to 25% recovery of TOF was recorded. This was considered as duration of action. At the end of surgery when TOF recovery was 25% from the last dose, after completion of surgery, reversal (neostigmine (0.05 mg/kg) and glycopyrolate (0.01 mg/kg)) was given. Adequate reversal was assessed by sustained head lift, leg lift, and hand grip for 5 seconds, eye opening, protrusion of tongue, adequate tidal volume confirmed and patient was extubated and shifted to ward.

RESULTS

All demographic data (age and weight), duration of surgery and duration of anaesthesia were compared and there were no statistical significant difference were noted ($p>0.05$), [Table 1] Baseline haemodynamic variables were comparable in both groups but after intubation and extubationMAP was significantly high in atracurium group.($p>0.05$),Table 2. Intubating conditions shows statistically significant difference ($p=0.03$), Graph 1. There were excellent intubating conditions in cisatracurium group than atracurium group. Cisatracurium group also have early onset and long duration of action. ($p<0.05$). [Table 3]

Table 1: Comparison of demographic data, duration of anaesthesia and duration of surgery between study groups

	Group BMean±Sd	**Group AMean±Sd**	**P Value**
Age	32.57±12.02	31.94±11.24	0.822
Weight	67.06±10.63	66.17±10.21	0.723
Duration of Surgery	121.23±28.63	126.57±33.13	0.473
Duration of Anaesthesia	138.83±31.86	141.29±33.05	0.473

Table 2: Comparison of haemodynamic parameters before intubation, after intubation and after extubation between study groups

Before Intubation	Haemodynamic	Group B	Group A	P Value
	Pulse Rate	78.29±6.55	76.97±6.60	0.406
	MAP	91.83±6.01	93.40±5.04	0.406
	SPO2	98.43±1.09	98.43±1.09	1.00
After Intubation	Pulse Rate	88.94±8.53	91.00±7.29	0.282
	MAP	103.91±10.38	115.29±2.28	<0.001
	SPO2	99.6±0.6	99.6±0.6	1.00
After Extubation	Pulse Rate	92.60±6.22	94.77±8.43	0.225
	MAP	110.03±10.63	116.23±3.44	<0.001
	SPO2	98.37±1.06	98.37±1.06	1.000

Table 3: comparison of onset time and duration of action in study groups

	Group B	Group A	P Value
Onset Time (S)	94.77±2.89	137.43±3.50	<0.001
Duration of Action(Min)	47.77±1.65	35.66±3.53	<0.001

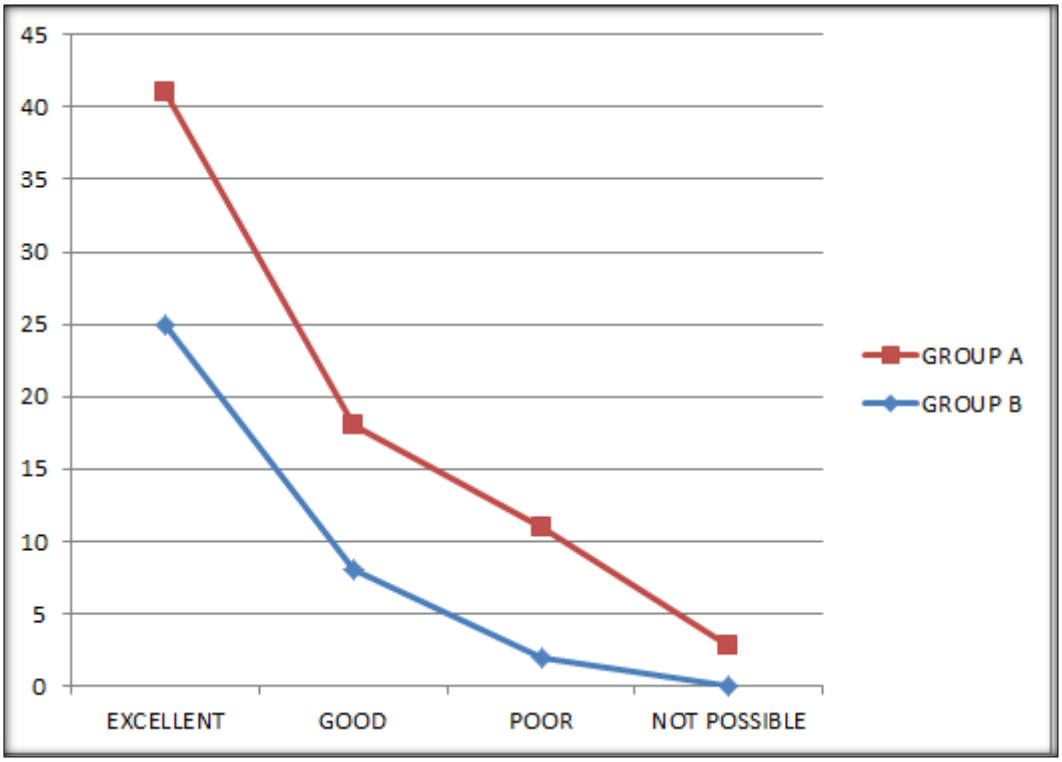

Figure 1: Intubating Conditions

DISCUSSION

Choice of an anaesthesiologist for selecting neuromuscular blocking agent for tracheal intubation or skeletal muscle relaxation depends on these properties, Rapid onset; longer clinical duration of action; better hemodynamic stability and Good spontaneous reversal. In present study, we compared cisatracurium and atracurium for their onset time, intubating conditions, duration of action and hemodynamic stability. Various studies have been conducted earlier on cisatracurium and atracurium to determine pharmacokinetics, pharmacodynamics, safety and efficacy. To reduce the onset time priming technique has been

used, priming is a small, subparalyzing dose of the non-depolarizer muscle relaxant (10% of the intubating dose) is administered 2–4 min before the intubating dose of the compound. This procedure accelerates the onset of blockade for most non-depolarizing NMBDs only by 30–60 s, thereby indicating that intubation can be performed within 90 s of the second dose. Hence, in this study, we also introduced priming dose of NMBD before administrating intubating dose. Athaluri et al,[8] also administered priming dose of NMBD before administrating intubating dose.

Athaluri et al,[8]also compared atracurium andcisatracurium regarding onset,intubating conditions and haemodynamic parameters during genralanaesthesia. They concluded that Cisatracurium 0.15 mg/kg provides excellent intubating conditions with rapid onset of action, with longer duration of action and no adverse effect.

AminiShahram et al,[9] studied effects of different doses of cisatracurium on appropriate time for endotracheal intubation and hemodynamic changes during anaesthesia and found that the mean clinical duration of action with 0.15 mg/kg was 44.93±5.40 minutes while with 0.2 mg/kg was 57.03±4.21 minutes.As seen with other nondepolarising neuromuscular agents, increasing the dose decreases the time of onset of block at the expense of prolonging the time to spontaneous recovery. Prabhudevkailash et al,[10] found that increasing the dose of cisatracurium from 0.15 to 0.2 increases the duration of action and excellent intubating conditions and both provides hemodynamic stability without an side effect.

Kasaby et al,[11] studied different doses of cisatracurium versus atracurium during general anaesthesia for abdominal surgery They compared between atracurium ($2\times ED_{95}$) and different doses of cisatracurium ($2\times ED_{95}$, $4\times ED_{95}$, $6\times ED_{95}$) regarding onset time, duration of action, condition of intubation, hemodynamic effects, and sings of histamine release clinically. They observed that small changes occurred in mean blood pressure and heart rate post induction and post intubation but these changes were not statistically and clinically significant at higher doses of cisatracurium and so hemodynamic stability were more evident among higher doses of cisatracurium (4 × ED95, 6× ED95).

Jammar et al,[12]studid two intubating dose of cisatacurium. They concluded that 4×ED95 dose of cisatracurium provides longer duration of action and more stable hemodynamic status than 3×ED95. No associated signs of histamine release were detected clinically.

CONCLUSION

Cisatracurium provides rapid onset, excellent intubating conditions,long duration of action and haemodynamic stability in comparision to atracurium.

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