

Comparative study of Equipotent Dose of Cisatracurium and Atracurium in Patients Undergoing Abdominal Laparoscopic Surgeries

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Abstract:

Introduction: Cisatracurium is one of the ten stereoisomers of Atracurium and is devoid of histamine induced cardiovascular effects. The neuromuscular blocking potency of Cisatracurium is approximately three-fold that of Atracurium. Neuromuscular transmission was assessed by recording the muscle twitch response to train-of-four nerve stimulation.

Material and Method: This is a prospective study was conducted in the Department of Anesthesiology, Tertiary care Teaching Hospital over a period of 1 year among 140 patients aged between 20 and 45 years. Study was performed in 140 patients aged 20-45 years weighted 40-70 kilograms with ASA physical grading 1 and 2 of either sex scheduled for elective laparoscopic surgery. Monitoring – ECG, non-invasive blood pressure, pulse oximetry, temperature and capnography (EtCO₂). In operation theatre intravenous cannula of proper size was inserted into the largest vein on the forearm and an infusion of lactated ringer's solution was started at a rate of 5 ml/kg/hr. Induction – inj. Propofol 2 mg per kg. Patients were divided into 2 groups: Group 1 - 70 patients were given atracurium 0.5 mg per kg for induction. Group 2 - 70 patients were given cisatracurium 0.1 mg per kg for induction.

Results: The mean onset time was 5.12 ± 0.92 min vs. 6.03 ± 0.99 min for atracurium and cisatracurium respectively. The mean duration of action was 49.97 ± 2.86 min vs. 59.36 ± 7.8 min for atracurium and cisatracurium respectively ($p < 0.001$). Intubating conditions, hemodynamic changes, and safety profile were comparable between the groups.

Conclusion: Onset of action is faster with atracurium than cisatracurium, Duration of action of cisatracurium is longer than atracurium and Hemodynamic stability is more with cisatracurium than atracurium. So, we can say that efficacy of cisatracurium is more than atracurium.

Keywords: Atracurium, Cisatracurium, Neuromuscular monitoring, Propofol, Laparoscopic Surgery.

Introduction

Neuromuscular blockers (NMB) are very important adjuvant to general anesthesia. They aid endotracheal intubation, mechanical ventilation and facilitate surgery. The ideal neuromuscular blocking agent needs to take shortest time in endotracheal intubation, the best intubating condition and have the shortest duration of muscle paralysis.^[1]

Atracurium is a benzyl-isoquinolinium, non-depolarizing neuromuscular blocking agent of intermediate duration of action. Its introduction in early 1980's has revolutionized anesthetic practice by providing muscle relaxation with faster onset, a more rapid measurable recovery.^[2]

It is composed by a mixture of ten optical and geometrical isomers. Elimination of Atracurium from the plasma occurs by a number of mechanisms including ester hydrolysis as well as Hoffman elimination and organ dependent elimination.^[3]

Cisatracurium is a recently introduced benzyliisoquinolinium non-depolarizing neuromuscular drug which is a stereoisomer of Atracurium and constitutes about 15% of the commercially produced Atracurium and with a potency of three to four times greater than that of Atracurium with an ED95 of 0.05mg/kg.^[4]

Cisatracurium besylate is the purified form of one of the ten stereo-isomers of atracurium. It is eliminated by Hoffman degradation; it has one metabolite Laudanosine which does not trigger histamine release.

In clinical practice, tactile evaluation of the adductor pollicis response to Train-of-four (TOF) is observed. Stimulation of the ulnar nerve is the most common method used to evaluate neuromuscular block. The TOF count is often used in the guidelines for neostigmine induced reversal of neuromuscular block.^[5]

In addition, although a TOF ratio of 0.7 is the accepted norm for adequacy of reversal of neuromuscular block^[6] there is an increasing evidence that significant residual effects such as visual disturbances, decreased grip strength and depressed swallowing reflexes persists until the TOF ratio has reached 0.9.^[7]

Material and Methods

This is a prospective study was conducted in the Department of Anesthesiology, Tertiary care Teaching Hospital over a period of 6 months among 140 patients aged between 20 and 45 years.

Inclusion criteria

1. All patients >20 years and <45 years of age, undergoing elective laparoscopic surgery with ASA 1 or 2 physical status.
2. Mallampati grade 1 and 2.

Exclusion criteria

1. Patients undergoing any other surgery requiring general anesthesia.
2. <20 years and >45 years of age
3. ASA 3 or 4 physical status.
4. Patients having any neuromuscular disease and taking any medication which known to influence neuromuscular function
5. Patients having known allergy for neuromuscular blocking agents

Ethical approval was taken from the college ethics committee before starting the study. Study was performed in 70 patients aged 20-45 years weighted 40-70 kilograms with ASA physical grading 1 and 2 of either sex scheduled for elective laparoscopic surgery. Monitoring – ECG, non-invasive blood pressure, pulse oximetry, temperature and capnography (EtCO₂). In operation theatre intravenous cannula of proper size was inserted into the largest vein on the forearm and an infusion of lactated ringer's solution was started at a rate of 5 ml/kg/hr.

Premedication – inj. Glycopyrrolate 0.004 mg per kg, Inj. Ondansetron 0.15 mg/kg IV, inj. Midazolam 0.01 mg per kg and inj. Fentanyl 1 microgram per kg intravenously. Pre-oxygenation with 100% oxygen was given for 3 minutes.

Induction – inj. Propofol 2 mg per kg. Patients were divided into 2 groups.

1. Group 1 - 70 patients were given atracurium 0.5 mg per kg for induction.
2. Group 2 - 70 patients were given cisatracurium 0.1 mg per kg for induction

Mask ventilation was continued for 3 minutes. Following which endotracheal tube was inserted, fixed and confirmed. Maintenance – 50% O₂, 50% N₂O and Sevoflurane.

Titration of inhalational agents was targeted to maintain MAP within 20% of baseline values. Neuromuscular block was monitored with TOF guard by using train of four stimulation and curare cleft in capnography. Group 1 patients were given atracurium 0.1 mg per kg for maintenance. Group 2 patients were given cisatracurium 0.03 mg per kg for maintenance. The volatile anesthetic agent was discontinued at the beginning of skin closure up till the last skin suture. Reversal – inj. Glycopyrrolate 0.008 mg per kg and inj. Neostigmine 0.05 mg per kg. After watching adequate tidal exchange and return of protective reflexes, patients were extubated and observed till full recovery. Adequacy of reversal was assessed. Vitals were noted every 15 minutes. Operating time was asked beforehand surgery. Surgeries more than 120 minutes were not included in the study.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2017) and then exported to data editor page of SPSS version 25. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Result

Demographic data (e.g., age, gender, weight, stature, and BMI) were comparable between the groups. The majority of the patients underwent laparoscopic cholecystectomy. Type of surgery, mean duration of anesthesia, and mean duration of surgery were comparable. The volume of intravenous fluid administered was comparable between the two groups. Intraoperative core temperature was comparable in both the groups. The preoperative vitals i.e. pulse rate, BP (systolic, diastolic, and mean), SpO₂, were also comparable among the two groups.

Table 1: Characteristic of Demographic

Variable	Group A Mean±SD or n (%)	Group C Mean±SD or n (%)	p-value
Age (y)	36.27 ± 10.12	37.41 ± 9.69	0.251
sex (m: f)	32:38	32:38	
BMI (kg/m ²)	24.24 ± 1.41	25.43 ± 1.79	0.051

Table 2: Surgical and anaesthesia data

Variable		Group A Mean±SD or n (%)	Group C Mean±SD or n (%)	p-value
Type of surgery	Cholecystectomy	49 (70%)	48 (68.5%)	
	Inguinal hernia repair	15 (21.4%)	17 (24.2%)	
	Ventral hernia repair	6 (8.5%)	5 (7.14%)	
Duration of surgery		64.15 ± 4.34	70.27 ± 08.13	0.197
Duration of anaesthesia		67.39 ± 5.13	70.34 ± 08.46	0.198
Intraoperative fluid used		693 ± 5.51	764 ± 109.4	0.192

Temperature	31.36 ± 0.02	32.64 ± 0.02	0.416
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Table 3: Neuromuscular blocking properties of cisatracurium and atracurium

Parameter	Group A (Mean ± SD)	Group C (Mean ± SD)	p-value
Onset of full relaxation	5.12 ± 0.92	6.03 ± 0.99	< 0.001
Duration	49.97 ± 2.86	59.36 ± 7.8	< 0.001
Recovery Time	5.74 ± 0.93	4.67 ± 0.97	< 0.001
No. of patients receiving top-up doses	12	12	

Table 4: Mean hemodynamic parameters following injection in both groups

Time	Mean pulse rate (beats/min)		Mean MAP (mmHg)	
	Group A	Group C	Group A	Group C
Preoperative	80	82	99	99
1 Min	75	77	92	96
2 Min	72	78	95	91
6 Min	79	76	99	96
10 Min	78	81	98	98
After Intubation	96	98	120	122

The onset time in the Group A was significantly short in comparison to Group C (5.12 ± 0.92 vs. 6.03 ± 0.99 min, $p < 0.001$). Also, the duration of action in the Group A was significantly short compared to Group C (49.97 ± 2.86 vs. 59.36 ± 7.8 min, $p < 0.001$). The recovery times were between the two groups (5.74 ± 0.93 min in Group A vs. 4.67 ± 0.97 min in Group C ($p < 0.001$), and the difference was significant. Grading of intubating conditions accomplished by the senior anesthesiologist (blinded to the learning), showed excellent intubating conditions in all the patients in both groups.

There was a reduction in mean heart rate and mean blood pressure after administration of the muscle relaxants in comparison to the baseline values in both the groups. All these hemodynamic parameters increased following intubation. There was neither any apparent signs of histamine release nor any episode of bradycardia or hypotension or hypertension in any patient.

Discussion

While selecting neuromuscular agent for tracheal intubation or skeletal muscle relaxation, main aim of an anesthesiologist is to select an agent with rapid onset, longer clinical duration of action, better intubating conditions, better hemodynamic stability and good spontaneous reversal, and minimal adverse events.^[8-14]

No significant difference was found in both of the groups in measures of age, sex and weight. (P value >0.05) The results of our study, clearly showed that, onset of atracurium's

action is 3 minutes (after pre-oxygenation of 3 minutes) whereas that is 5 minutes for cisatracurium.

Using the Cooper's scoring system, we can easily state that vocal cord movement was still present after 3 minutes of administration of cisatracurium whereas it was absent after 3 minutes of administration of atracurium. Cisatracurium required 5 minutes for complete cessation of movement of vocal cord. Not only was the movement of vocal cord but position also better with atracurium after 3 min of administration. Bucking was not seen after 3 minutes and 5 minutes from administration atracurium and cisatracurium, respectively.

Anesthesiologists' satisfaction using between cisatracurium and rocuronium for the intubation in the anesthesia induced by remifentanyl and propofol Hyunjung Lee stated Despite fundamentally slower onset time, ^[15] cisatracurium can provide quite good intubating conditions, which were comparable to those achieved with equipotent doses of rocuronium, which is more expensive in anesthesia induced with remifentanyl and propofol. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery AM El-Kasaby. ^[16] They had 70 total patients in group of 24s. They studied different doses of cisatracurium with atracurium. We here studies one decided dose of cisatracurium 0.1 mg per kg for intubation and 0.03 mg per kg for maintenance. For the same dose of our study and group of 24 in this reference study, had same results. So, we are having group of 70 instead of 24. They concluded no difference in effect of atracurium and cisatracurium. We found significant difference on p value of <0.0001.

Lien et al et al, ^[17] concluded that the maximal MABP and HR changes of patients receiving cisatracurium were small and similar to those observed in patients receiving two times the ED 95 of atracurium. Study from 1995, also supports our results. A comparison of cisatracurium and atracurium: onset of neuromuscular block after bolus injection and recovery after subsequent infusion. H Mellinghoff ^[18] concluded that time profiles for neuromuscular block of both muscle relaxants, when given in equipotent doses, are not different. They suggested slower onset of cisatracurium compared to atracurium, but longer duration of action with cisatracurium. ^[19]

Comparison of the neuromuscular blocking effect of cisatracurium and atracurium on the larynx and the adductor pollicis K Kirov. ^[20] Also said the same thing about cisatracurium, 0.1mg per kg dose is sufficient for intubating conditions but it is taking 1 more minute to relax vocal cords as atracurium. Comparative Evaluation of Cisatracurium and Atracurium Action as Components of Endotracheal Anesthesia in Laparoscopic Surgeries according to Lipnitski AL et al. ^[21] According to this one, they were having faster onset of action of cisatracurium than atracurium in same sample size.

Hemodynamic stability with cisatracurium was very regular, as we can see only around 90 minutes i.e. time of 1st maintenance dose of cisatracurium; the lines were near to atracurium. Otherwise from post-intubation vitals to pneumoperitoneum vitals were far more under control. Lien et al ^[17] concluded that the maximal MABP and HR changes of patients

receiving cisatracurium were small and similar to those observed in patients receiving two times the ED₉₅ of atracurium.

We found that, appearance of curare cleft was a bit behind of hemodynamic changes in atracurium, whereas it was preceding in case of cisatracurium. This would be advantageous in setups with capnography, as we could save hemodynamic instabilities. Hemodynamic effects of atracurium and cisatracurium and the use of diphenhydramine and cimetidine according to Correa et al, ^[22] concluded that, hemodynamic stability is better with cisatracurium compared to atracurium as use of antihistaminic drugs affects hemodynamic profile more in atracurium group. Cisatracurium group has more stability even without diphenhydramine and cimetidine.

Conclusion

This randomized control study of 140 patients with 70 in each group was performed to evaluate efficacy of atracurium and cisatracurium in patients in laparoscopic surgery. From our results, we can conclude that, Onset of action is faster with atracurium than cisatracurium, Duration of action of cisatracurium is longer than atracurium and Hemodynamic stability is more with cisatracurium than atracurium. So, we can say that efficacy of cisatracurium is more than atracurium.

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