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A Comparative Study on the Efficacy of Atracurium and CIS Atracurium During General Anesthesia In Adult Surgical Patients

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Abstract

Atracurium an intermediate acting non depolarizing muscle relaxant is a benzylisoquinolinium compound that undergoes metabolism by Hoffman elimination reaction. It is therefore independent of hepatic and renal functions for its metabolism and excretion. Cisatracurium, the 1R-1'R cisisomer of atracurium, that is also metabolized by Hoffman elimination. It is four times more potent as Atracurium and does not cause histamine release.

With increasing number of patients with deteriorating hepatic and renal functions there is an imminent need to study the efficacy of Atracurium and Cisatracurium to improve the quality of patient care by using safer anesthetic technique.

Keywords: Atracurium, Cisatracurium, Neuromuscular Block.

Introduction

General anaesthesia is a balanced technique using muscle relaxation, sedation, and analgesia. Muscle relaxation is achieved with depolarizing and non-depolarizing muscle relaxants.

Atracurium[1] is a non-depolarizing neuromuscular blocking drug of the benzylisoquinolinium class[2]. It is a competitive antagonist of the alpha subunit of the postsynaptic nicotinic receptor at the neuromuscular junction.

Atracurium is indicated as an addition to general anesthesia to facilitate endotracheal intubation and provide skeletal muscle relaxation during surgery or mechanical ventilation[3].

Cisatracurium besilate[4] is a Bisbenzyl tetra hydroisoquin olinium that acts as a neuromuscular-blocking drug or skeletal muscle relaxant[5].

It is a non-depolarizing neuromuscular-blocking drug, used adjunctively in anesthesia to facilitate endotracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation. It shows intermediate duration of action.

Cisatracurium is one of the ten isomers of the parent molecule atracurium[6]. One of the metabolites of cisatracurium via Hofmann elimination is laudanosine[7].

The aim of the study is to compare the onset of action, condition at intubation, duration of action, hemodynamic effects, and signs of histamine release of Atracurium with Cisatracurium.

To compare the onset, condition at intubation, duration of action of Atracurium and Cisatracurium and to measure the hemodynamic parameters of systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate after administration of loading dose.

Materials and Methods

After approval from the institutional ethical committee, an observational study with 2 groups of patients undergoing general anesthesia.

Each group will have 30 patients each.

Group 1 patients will receive Atracurium at intubating dose of 0.5mg/kg and maintenance dose of 0.1mg/kg.

Group 2 patients will receive Cisatracurium at intubating dose of 0.15mg/kg and maintenance dose of 0.03mg/kg.

Preanesthetic evaluation will be done day before surgery. An informed consent will be taken. All patients will be kept fasting for eight hours before surgery and will be premedicated with tab.ranitidine 150mg and tab. Alprazolam 0.25mg on previous night and 2 hours before surgery.

Condition	Cisatracurim	Atracurim	Total
Excellent	27 (90%)	23 (76.6%)	50 (83.33%)
Good	3 (10%)	7 (23%)	10 (16.67%)

IV access secured before the procedure Intraoperative monitoring by,

Pulse oximetry

NIBP

ECG

Peripheral nerve stimulator

Baseline hemodynamic parameters (SBP, DBP, MAP, HR) recorded. All patients will be premedicated with injection midazolam 1mg IV. General anaesthesia will be induced in all patients with injection fentanyl (1.5mcg/kg), injection propofol (2mg/kg) IV. The muscle relaxant will be given for patients according to previously mentioned initial doses for each group.

After 2 min, endotracheal intubation will be done using proper size tube (male 8 – 8.5, female 7-7.5) and the condition of intubation will be assessed and recorded.

Excellent: Easy passage of the tube without coughing. Vocal cords relaxed and abducted.

Good: Passage of the tube with slight coughing and bucking. Vocal cords relaxed and abducted.

Poor: Passage of tubes with moderate coughing and/or bucking vocal cords moderately adducted.

Not possible: Vocal cords not relaxed, tightly adducted.

Onset of action is determined from the administration of initial dose of muscle relaxant until loss of TOF.

Anesthesia is maintained with a mixture of 50% nitrous oxide in oxygen, isoflurane (1-1.5 MAC), boluses of muscle relaxant with 25% recovery of TOF and ventilation controlled by DATEX OHMEDA ventilator which will adjust end tidal CO2 (30 to 35 mmhg). Neuromuscular blockade after induction will be monitored every 5minutes by supramaximal TOF.

The duration of action of muscle relaxant (time from the end of injection of the drug until 25% recovery of TOF) will be recorded.

Hemodynamic parameters (SBP, DBP, MAP, HR, SPO2) will be recorded at regular intervals of 5mins during the surgery.

Patients will also be monitored for signs of histamine release through changes in hemodynamic parameters, bronchospasm, or skin changes like flush (if redness lasted more than 120secs), erythema or wheals.

At the end of surgery with 25% recovery from TOF, reversal will be achieved by administering (2.5mg neostigmine and 0.4mg glycopyrrolate) through slow IV injection.

All hemodynamic parameters were monitored at regular intervals. Data collection was done using a proforma and Data will be analysed by SPSS (Statistical Package for Social Sciences) software. Unpaired t-Test (13) will be applied for onset and duration of action and hemodynamic parameters. P value of less than 0.05 will be considered statistically significant.

Results

The studied patients were matched regarding age and sex with no statistically significant difference being recorded.

Condition at Intubation

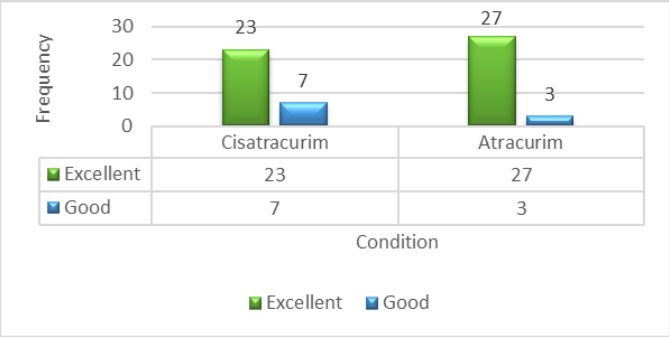


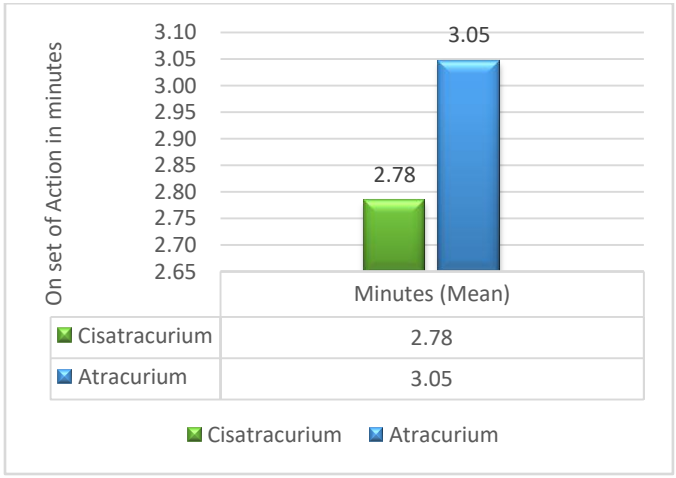
Chart showing condition at Intubation.

Statistical Analysis: Excellent condition at intubation was observed in 90% with cisatracurium and 76% with Atracurium. Good conditions at intubation were observed in 10%in Cisatracurium and 23%with Atracurium.

Onset of Action

Onset of Action (n=30)

Group	Minutes (Mean)	P Value
Cisatracurium	2.78 ± 0.45	0.030
Atracurium	3.05 ± 0.34	



Statistical Analysis: The onset of action was compared and found to be 2.78+_0.45 seconds in group Cisatracurium and 3.05+_0.34 in group Atracurium. This was found to be statistically significant with a p value of 0.030.

Duration of Action

Group	Mean	P Value
Cisatracurium	56.10 ± 4.40	0.000
Atracurium	38.40 ± 3.11	

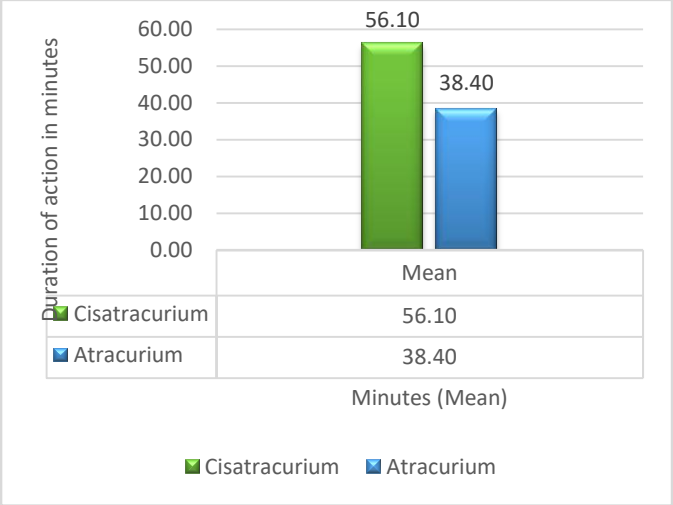
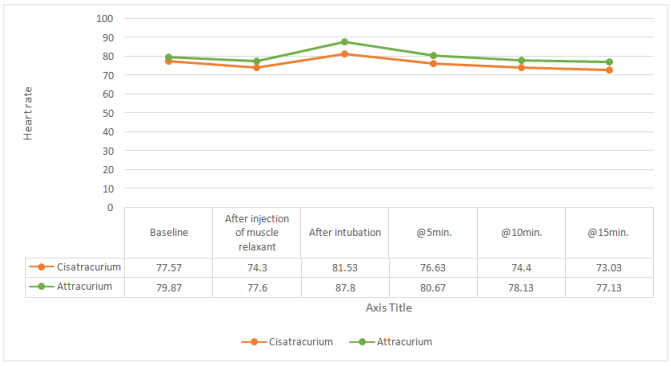


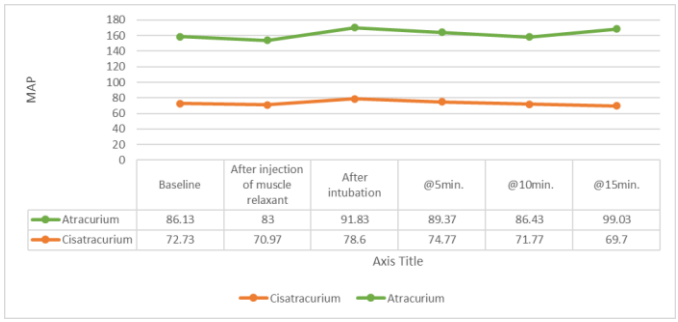
Chart showing duration of action.

Statistical analysis: The Duration of action was compared and that of cisatracurium was found to be 56.10+_4.40and Atracurim was found to be 38.40+_3.11.

This was found to be statistically significant with p value of 0.00.



There is significant Heart rate variability between the group Atracurium and cisatracurium after intubation with p value of 0.00 and at 5min post intubation with p value of 0.02 .At 10 min post intubation the p value is 0.01.At 15min post extubation the p values is 0.01.



Sample Analysis: There is significant MAP variability between the group Cisatracurium and Atrcurium, after attempt of intubation p value is 0.00, after 5 minutes p value is 0.00,at 10 minutes is 0.00 and at 15 minutes is 0.00.

Discussion

Neuromuscular blocking drugs are the most widely used drugs in our daily anesthetic practice while intubating patients.

Drugs like Atracurium and Cis atracurium with their unique metabolic properties are useful for use in patients with impaired renal and hepatic functions. Cisatracurium being an almost Ideal Muscle relaxant with properties similar to atracurium but with faster onset and no signs of histamine release.

Laudanosine production is much less with Cisatracurium.

This study was an observational study done with comparison group carried out in 60ASA1 and ASA2 patients scheduled for elective surgical procedures undergoing general anaesthesia with controlled ventilation.

Patients having hepatic, renal or neuromuscular disease, asthma, COPD, cardiovascular diseases and difficult airway were excluded.

Hence 60 patients were divided equally and recruited to two groups –group Cis atracurium and group Atracurium having 30 patients each.

Studies have been conducted on many doses of the two muscle relaxants. The usual dose for intubation is usually twice the ED95 dose but for Cisatracurium 3ED95 dose is used that is 0.15mg/kg whereas 2ED95 dose of atracurium ie; 0.5mg/kg is used.

The sex distribution in the study were Males 30 (50%) and Females 30(50%).In group Atracurium,males 19 (63%)and females 11(36%).In group Cisatracurium , the number of males 11(36%) and females 19(63%) .

Even though the male to female ratio is not equal it is not statistically significant.

Neuromuscular monitoring was done using train of four monitoring at the adductor pollicis muscle, to assess the response and recovery from neuromuscular blockade. Train of four is a reliable indicator of the neuromuscular function.

In our study the mean ±SD time onset of action of group Cis Atracurium was 2.78 ± 0.45minutes and in group Atracurium 3.05 ± 0.34 minutes. This was statistically significant with a p value of 0. 030.Hence onset of action with 3ED95 Cisatracurium was much faster than Atracurium.

Similar findings were reported by Mohanty et al [8]while comparing the two-intubating doss of cisatracurium with atracurium found that cisatracurium at 3ED95 dose produced more rapid onset of action than atracurium at 0.5mg/kg.

Bakshi et al[9] also concluded that as the dose of Cisatracurium increased the onset of action was reduced compared to Atracurium at 0.5mg/kg.

El kasaby et al[10] concluded that as the intubating dose of Cisatracurium increased (2ED95, 3ED95, 4ED95) the onset of action became shorter when compared to 2ED95 dose of Atracurium.

Bluestien et al[11] also concluded that as the dose of Cisatracurium is increased to 3ED95 and 4ED95 the onset to action is less than Atracurium 2ED95.

MT caroll et al[12] also had similar findings.

The condition at intubation was excellent in 90% of patients who received Cisatracurium and 76%of patients of group Atracurium.

Condition at intubation was Good in 10%patients of group Cisatracurium and 23%patients of group Atracurium.

This was similar to findings of Mohanty et al where 3 ED95 dose of Cisatracurium had better intubating condition compared to 2ED95 doses of Cisatracurium and Atracurium.

El kasaby et al also had similar findings as the ED95 dose of Cisatracurium increased, so did the condition at intubation improve compared to Atracurium 2ED95dose.

Bluestein et al also had similar findings regarding condition at intubation.

The mean ±SD duration of action of intubating dose in our study for Group Cisatracurium was found to be 56.10±4.4min and for group Atracurium 38.4±3.11 min.

Bakshi et al also concluded that with cisatracurium 0.2mg/kg was 61.50min, while with Atracurium 0.5mg/kg it was 38.57min.

Mohanty et al had observed a mean ±SD duration of action of intubating dose in g Atracurium 0.5mg/kg was 43.0+2.27 min,Cisatracurium 0.1mg/kg was 43.2+2.72 min and in Cisatracurium 0.15mg/kg was 64.6±4.83 min.

Bluestein and colleagues also observed that increasing the dose of cisatracurium from 0.1 to 0.15 to 0.2mg/kg) lead to an subsequent increase in the duration of action to 45 to 55 to 61 min respectively El kasaby et al also had similar findings.

The mean and standard deviation of baseline MAP, MAP at different time intervals at 5,10,15mins after intubation among three groups were compared.

The results obtained from the analysis shows that there was an increase in MAP compared to baseline in all the three groups after intubation and at 5 mins which gradually returned to baseline at 15mins but there was no statistically significant difference.

Conclusion

Thus by our study, we conclude that the mean ±SD time onset of action of group Cis Atracurium was 2.78 ± 0.45minutes and in group Atracurium 3.05 ± 0.34 minutes. This was statistically significant with a p value of 0. 030.Hence onset of action with 3ED95 Cisatracurium was much faster than Atracurium.

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Condition at intubation was Good in 10%patients of group Cisatracurium and 23%patients of group Atracurium. This is statistically significant.

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