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# Comparison between cisatracurium and atracurium during general anaesthesia for abdominal surgery

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**Abstract**
**Background:** Neuromuscular blockers (NMB) are very important adjuvant to general anesthesia, Atracurium (benzyl isoquinoline NMB) and cisatracurium besylate (benzyl isoquinoline NMB) are intermediate acting non-depolarizing muscle relaxants. In a prospective randomized study we had compared both drug at a dose of 2xED95 for Atracurium and 6xED95 for Cisatracurium as regard the onset of action, intubating conditions, clinical duration, hemodynamic changes, and adverse effects.
**Method:** 60 patients, ASA I&II, 20-60 year old underwent elective abdominal surgerical procedure under general anesthesia (GA) were randomly assigned into 2 equal groups. Group A where 0.5mg/kg atracurium was given and Group C, where 0.3mg/kg cisatracurium was given. Neuromuscular monitoring was done by stimulating ulnar nerve and recording the action potential of adductor pollicis using TOF count. Standardized GA was given to all patients as follows, fentanyl 2mcg/kg, propofol 2mg/kg, followed by NMB agent of corresponding group at designated dose, patient will be ventilated till TOF count reaches 0, intubation was tried by the anaesthesiologist who was blind to the given NMB, intubation was done if the intubating condition was acceptable (excellent or good), and it was re-attempted every 30 sec if it was poor or inadequate. Anesthesia was maintained by $N_2O$, $O_2$ and sevoflurane to a total MAC 1, controlled ventilation was adjusted to normocarbia. Mean arterial blood pressure (MAP), heart rate, and intubating conditions were recorded. Interpretation of TOF count for the onset of action, clinical duration, recovery index was done.
**Results:** Clinically acceptable intubating conditions were achieved after 120 sec more frequently after Cisatracurium (85%) than after atracurium (0%) and after 180 sec Cisatracurium (100%) and atracurium (80%). Cisatacurium had a significant shorter onset time than atracurium (120±30 versus 180±30sec), Atracurium had a significant shorter duration of action than cisatracurium (30±5 versus 60±5min). There were no evidences of any significant clinical cardiovascular changes in both groups.
**Conclusion:** Cisatracurium has a rapid onset of action with good intubating conditions, atracurium has an intermediate duration of action, both are potent and safe with excellent cardiovascular stability.

**Keywords:** Atracurium, cisatracurium, muscle relaxant and TOF ratio

## Introduction
Neuromuscular blockers (NMB) have become essential parts of the anaesthetist armamentarium. They aid in endotracheal intubation, mechanical ventilation, reduce anaesthetic requirements, facilitate surgery for long hours and decrease oxygen consumption. An ideal neuromuscular blocking agent should have rapid onset of action, produce good intubating condition rapidly, intermediate to short duration of action, provide rapid airway control, lack of side effects, should provide cardiovascular stability and adequate recovery [1]. In the development of new neuromuscular blocking drugs, the anaesthesiologist is now provided with drugs that are almost free of unwanted effects, have a time course of action that allows great control of their activity and in most cases, allows the anaesthesiologist to substitute them for succinylcholine. In selecting a neuromuscular blocking agent, an anaesthetist strives to achieve three competing goals: rapid adequate muscle relaxation, hemodynamic stability, and predictable complete return of skeletal muscle function. Succinylcholine [2] reliably produces muscle relaxation within 60 seconds of its administration but it produces side effects such as bradycardia, hyperkalemia [3], masseter spasm [4], malignant hyperthermia and increase in intra ocular pressure [5].
To replace Succinylcholine, newer non-depolarizing muscle relaxants with intermediate action like atracurium and cisatracurium are being used.

Cisatracurium is a new benzylisoquinoline neuromuscular blocker. The generic name cisatracurium was conceived by scientists at Burroughs Wellcome [6] Co. by combining the name "atracurium" with "cis" because the molecule is one of the three cis-cis isomers comprising the ten isomers of the parent atracurium It has a intermediate duration non-depolarizing neuromuscular blocking drug that has recently been introduced into clinical practice and has a potency approximately three to four times at higher doses than atracurium. Cisatracurium besylate undergoes Hofmann elimination, a process dependent on pH and Temperature. Cisatracurium unlike atracurium is devoid of histamine induced cardiovascular effects.

Atracurium is an intermediate-duration, nondepolarizing, skeletal muscle relaxant for intravenous administration. Drug is metabolized by two different pathways, ester hydrolysis and Hofmann elimination (90%) [7]. Hofmann elimination process is non-biologic and does not require renal, hepatic or enzymatic function and result in loss of the positive charges by molecular fragmentation to laudanosine (a tertiary amine) and a mono quaternary acrylate. Hofmann elimination takes place at pH (7.4) and Temperature (37.c) and slowed by a fall in pH (i.e. acidic condition) and especially by decrease in Temperature.

Thus, atracurium is metabolized at body Temperature and pH. Therefore, it is stored at 4 degree C and buffered to a pH of 3. At high Temperature potency of drug decreases. Laudanosine, the metabolite of drug is further metabolized by the liver and is eliminated in urine and bile. Ninety percent of drug may be destroyed in plasma, with 10% or less of the parent drug excreted in the urine. No biliary excretion of parent drug.

## Materials and Methods

This present study was designed as a prospective randomized comparative study on 60 ASA I & II patients undergoing elective surgical procedures under general anaesthesia. After obtaining prior institutional ethical committee clearance, the patients were visited preoperatively, full pre anaesthetic check-up was done. If the patient were found to be within the inclusion criteria of present study, informed consent were taken after explaining the procedure to be done and the effects of the drugs used.

Patients between 20 to 60 age group who are ASA I & II and elective surgeries under general anaesthesia were included in this study. Patient who are ASA III and above, pregnant females, patients with any hepatic or renal disease, history of any neuromuscular disorder and BMI >30 kg/m2 were excluded in this study.

All the patients were kept nil by mouth for 6 to 8 hrs. On arrival in the operation room, Standard monitors were attached and baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (spo2) were recorded. Neuromuscular monitors (TOF) were attached. Intravenous access was obtained with an intravenous cannula 18 G in the left upper limb.

All patients were preloaded with crystalloid Ringer lactate 8ml/kg. Patients were premedicated with Inj. Glycopyrolate 0.004mg/kg, Inj.Ondansetron 0.08 mg/kg. Inj. Midazolam 0.02mg/kg, Inj. Fentanyl 2 mcg/kg. and baseline TOF readings were taken. Patients were induced with standard dose of Inj.Propofol 2mg/kg. After confirming adequacy of ventilation, group C and group A received designated dose of their muscle relaxant. Both intubator and the patients were blind to this study. Patients were ventilated till the TOF count reached 0 in neuromuscular monitor. Intubation was attempted once the TOF reached 0 and intubating conditions were assessed using a four point scale during direct laryngoscopy (CL grade) [9] [excellent, good, poor, or inadequate]. If the intubating condition was excellent or good, tracheal intubation was performed with appropriate size cuffed endotracheal tube, and if it was poor or inadequate, intubation was postponed and re-attempted every 30 second. The time taken from induction dose of muscle relaxant to ideal condition for laryngoscopy was noted.

**Conditions for intubation are graded as follows [10]**

**Excellent:** Relaxed jaw, abducted immobile vocal cords, and no diaphragmatic movement.

**Good:** Relaxed jaw, abducted immo-bile vocal cords, and some diaphrag-matic movement (bucking).

**Poor:** Relaxed jaw, moving vocal cords, coughing on intubation.

**Inadequate:** Jaw is not relaxed, add-ucted vocal cords, and impossible intubation. Anaesthesia was maintained with $O_2$(1L/min), $N_2O$ (1L/min), Sevoflurane @ 1.0 MAC, maintenance dose of muscle relaxant based on TOF response, to maintain TOF % less than 30%.

Intra operative monitoring included hemodynamic monitoring i.e, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure oxygen saturation and neuromuscular monitoring i.e, Train of Four (TOF) [11]. At the end of surgery, administration of all anaesthetic agents were stopped and reversal attempted with Inj. Neostigmine 0.05mg/kg and Inj. Glycopyrolate 0.008mg/kg. Reversal was given after TOF count raised to 4 and TOF % >90%. Extubation was done after full reversal.

## Observation and Results

### Statistical analysis

The statistical analysis was done by using SPSS-2. The statistical analysis was done by calculating mean and standard deviation. For detail analysis, Chi-square test, unpaired t test and Mann-Whitney test were used to calculate the P value and to establish correlation between study groups. A p value < 0.001 was considered highly significant statistically, a p value <0.05 was considered significant, whereas a p value > 0.05 was considered insignificant.

## Results

60 patients were recruited in the study, the patients were randomly divided in two groups of 30 patients. The current study showed no significant differences in demographic data that included age, gender and also with regards to ASA.

**Table 1: Shows in**Demographic data that included age, gender and also with regards

| | Group A (n=30) | Group C (n=30) |
|---|---|---|
| Age (year) | 42.23 ± 11.44 | 42.20 ± 11.73 |
| Gender (M/F) | 16/14 | 14/16 |
| Body Weight (kg) | 54.9 ± 5.14 | 53.96 ± 5.46 |
| ASA ( I/II) | 17/13 | 20/10 |

Values are expressed in terms of mean±SD. No significant differences were found between the two groups. ($P$>0.05), SD= Standard deviation with regards to vital signs and hemodynamic stability pre operatively and intra operatively the recorded HR, MAP showed no statistically significant difference between both the groups.

Figure 1 shows distribution of heart rate among two groups ie, baseline, induction, starting from 0 min of administration of muscle relaxant till end of surgery. Mean value for baseline HR for group C and group A were 83.10 ± 7.462 and 87.20.

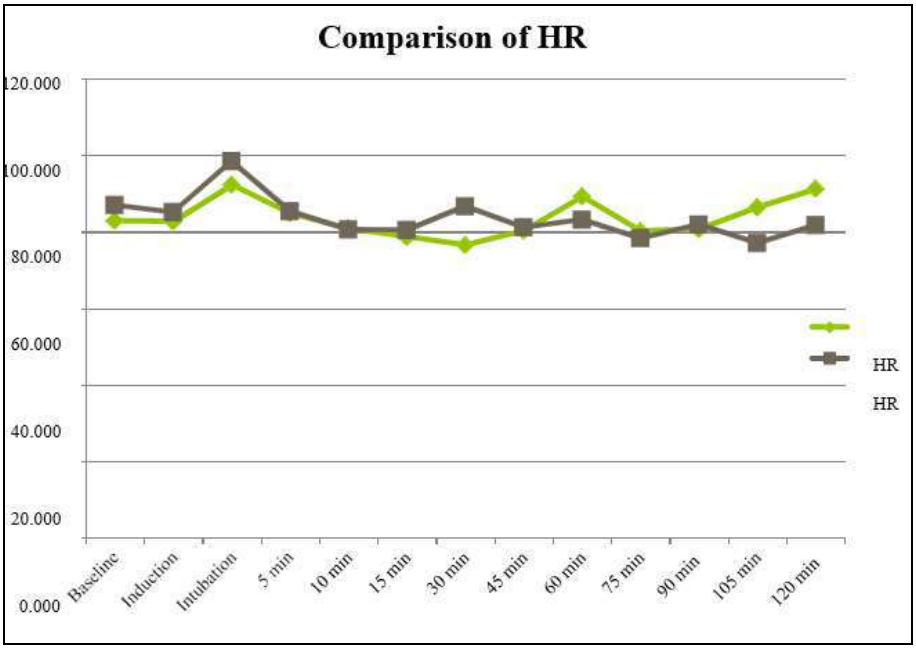


**Fig 1:** Comparison of HR

Figure 2 shows distribution of mean arterial blood pressure among two groups ie, baseline, induction, starting from 0 min of administration of muscle relaxant.

The mean baseline MAPs were almost similar in both groups (Group C = 92.800 ±10.548 mmHg and Group A = 96.588 ± 6.365 mmHg). There was no statistical difference between the group with respect to mean baseline MAPs as their p value was > 0.05.

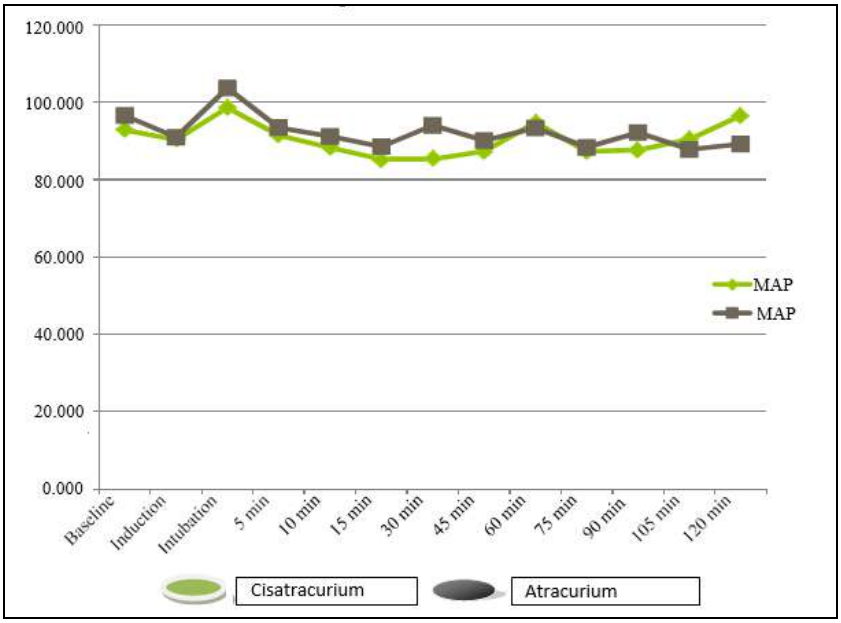


**Fig 2:** Comparison of MAP

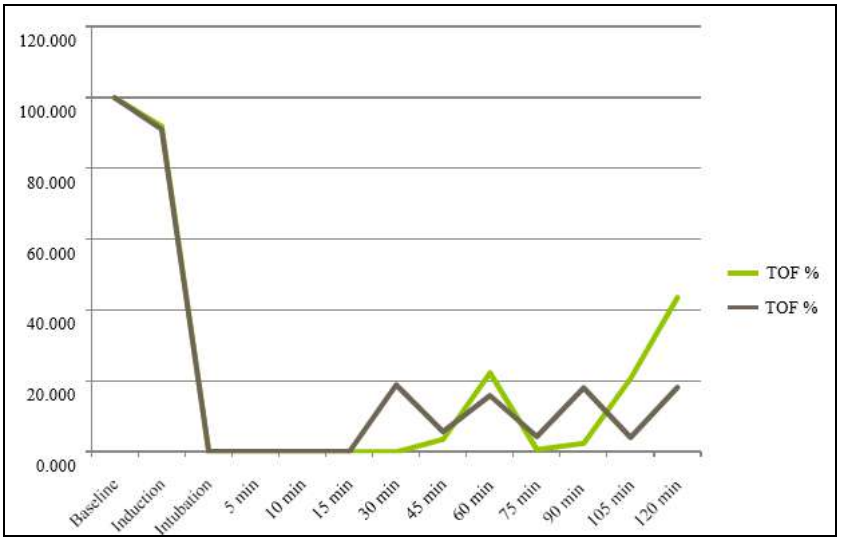


**Fig 3:** Comparison of TOF % at various time intervals.

The Mean baseline TOF % in Group C was 100.00 ± 0.000 and in Group A was 99.93 ± 0.365. There was no significant difference between the two groups with respect to baseline TOF % as p value was > 0.05.

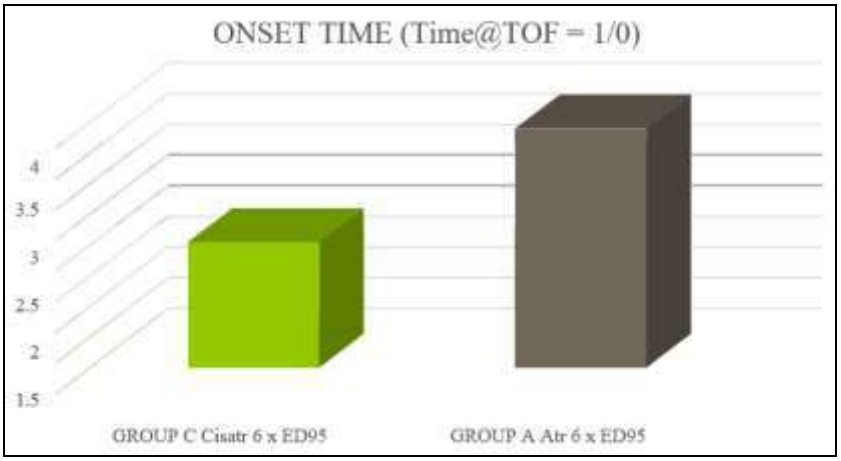


**Fig 4:** Onset of Action

In our study, the onset of action was considered when TOF % was 0 or TOF Count was 1.

In our study the onset of action of Group C was found to be 2.050 ± 0.3037 mins and the onset of action of Group A was found to be 3.90 ± 0.242 mins which on comparison was found to be statistically highly significant as p value was < 0.05.

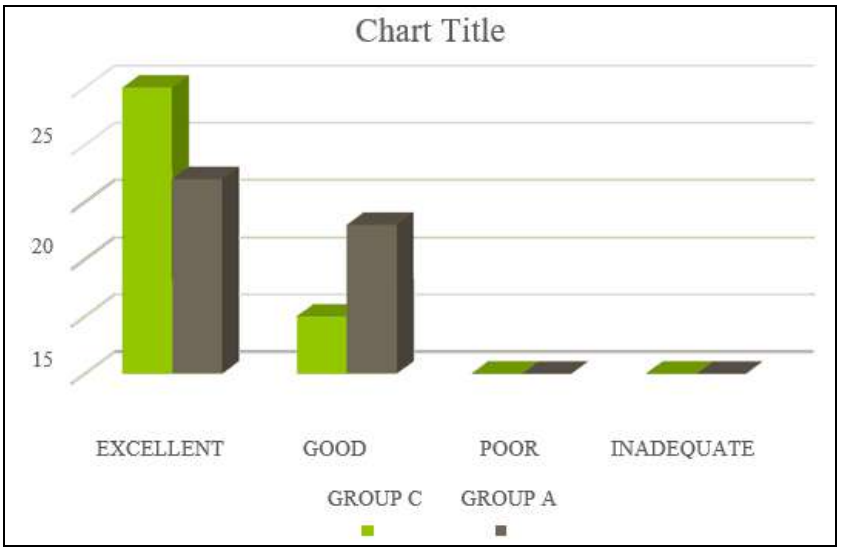


**Fig 5:** Intubating Conditions

In our study, in Group C 25 patients out of 30 patients had excellent intubating conditions and 5 patients out of 30 patients had good intubating conditions while in Group A 17 patients out of 30 patients had excellent intubating conditions and 13 patients out of 30 patients had good intubating condition.

## Discussion

Neuromuscular blockers (NMB) are very important adjuvant to general anesthesia. During general anaesthesia, after induction endotracheal intubation is facilitated by either depolarizing or non-depolarizing neuromuscular blocking agent. Succinylcholine is undoubtedly the ultra-short acting muscle relaxant with rapid onset but it has many side effects such as increase in IOP, intragastric pressure, myalgia, bradycardia and cardiac arrest. Hence globally there was search for an alternative for succinylcholine which has rapid onset and less side effects. In 1983 atracurium was introduced in clinical practice having advantage that this new drug is extensively metabolized in such a way that its pharmacokinetics are independent of renal and hepatic function, although less than 10% excreted unchanged by renal and biliary routes.

Cisatracurium is a new benzyl isoquinoline neuromuscular blocker which has intermediate action. It is one of the 10 stereoisomers of atracurium and has a potency approximately three to four times at higher doses than atracurium. It is used in different doses 0.1 mg/kg, 0.2mg/kg, 0.3 mg/kg. It has longer onset of action which makes it less suitable for rapid sequence intubation. In the current study we decided to compare Atracurium and Cisatracurium for onset of action, intubating condition and hemodynamic changes in patients posted for elective abdominal surgeries under general anaesthesia.

M. EI-Kasaby *et al*, [8] 2010 studied that Onset time was found to be significantly lower with 2×ED95$^{95}$ dose of atracurium (3.24±0.55 min) than with the same dose of cisatracurium (4.37±0.46 min). At the same time, higher doses of cisatracurium (4×ED$^{95}$ and 6×ED$^{95}$) (2.9±1.4 min and 2±1.2 min) showed onset time and longer duration of action that was significantly lower than with atracurium and with lower dose of cisatracurium (2×ED$^{95}$).

Bluestein LS1 *et al*, [9] 1996 found that with increasing dose of cisatracurium from 0.1 mg/kg (2 x ED$^{95}$) to 0.15 mg/kg (3 x ED$^{95}$) and 0.2mg/kg (4 x ED$^{95}$), decreased mean time of onset from 4.6 to 3.4 and 2.8 min, respectively. The findings of the above studies correlated with our study

Admus M *et al*, [10] 2006 observed in their study that clinical durations were 42 ± 7 min, 52 ± 7 min with 0.1mg/kg (2 x ED$^{95}$) and 0.15 mg/kg (3 x ED$^{95}$) dose cisatracurium respectively.

Bluestein LS1 *et al*, [9] 1996 found that with increasing dose of cisatracurium from 0.1mg/kg (2 x ED$^{95}$) to 0.15 mg/kg (3 x ED$^{95}$) and 0.2 mg/kg (4 x ED$^{95}$), increased mean time of clinically effective duration (from 45 to 55 and 61 min respectively).

Zha Y *et al*, [11] 2006 studied that the duration of action were 35.7 ± 11.6 min, 35.2 ± 13 min with 0.1mg/kg (2 x ED$^{95}$) and 0.15 mg/kg (3 x ED$^{95}$) dose cisatracurium respectively. The findings of the above studies correlated with our study.

Bluestein *et al*, [9] 1996 reported that intubation conditions were good or excellent in over 90% of patients in all treatment groups (2 min after approximately 2×ED$^{95}$ doses of cisatracurium or atracurium and 1.5 min after 3× and 4×ED$^{95}$ doses of cisatracurium).

Schmautz E *et al*, [12] 1994 found in their study that one of two intubating doses of cisatracurium may be chosen based on the desired time of intubation and the anticipated length of surgery. Doses of 0.15 mg/ kg (3×ED$^{95}$) and 0.2 mg/kg (4×ED$^{95}$) of cisatracurium, as components of a propofol /nitrous oxide/oxygen induction intubation technique, may produce generally good or excellent conditions of intubation in 2.0 and 1.5 min, respectively.

Belmont MR *et al*, [13] 1995 observed in their study that cisatracurium dose of 0.15 mg/kg (3×ED$^{95}$) is higher than the dose of atracurium 0.5 mg/kg (2×ED$^{95}$) required to produce clinically acceptable intubation conditions after 120 s. The findings of the above studies correlated with our study.

Lien *et al*. [13] in the year 1995 conducted study on cardiovascular effects and histamine releasing properties of cis-atracurium and 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. The findings of the above studies correlated with our study.

## Conclusion

From the present study, we concluded that the patients receiving 6 x ED$^{95}$ dose of Cisatracurium provided better outcome as compared to patients receiving 2 x ED$^{95}$ dose of Atracurium in rapid onset of action, excellent intubating conditions, better hemodynamic stability, longer duration of action and no any adverse reaction.

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