

# Randomized Controlled Trial to Evaluate Efficacy of Atracurium and Cis-Atracurium in Patients in Laparoscopic Surgery at Tertiary Care Center

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## Abstract

**Background:** Muscle relaxants are used routinely during intubation to relax muscles in the neck and throat, which reduces the risk of injury. They may also be used to relax the chest muscles when an endotracheal tube is used to help mechanical ventilation. This study is designed to compare the efficacy of atracurium and cisatracurium by the means of: Onset of action, Hemodynamic stability and Duration of action. **Subjects and Methods:** Present Experimental Randomized controlled trial was done at the Department of Anaesthesiology, GMERS Medical College, Sola, Ahmedabad from July 2018 to July 2020 in 80 patients aged between 20 and 45 years. Study was performed in 80 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 (EtCO<sub>2</sub>). 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 - 40 patients were given atracurium 0.5 mg per kg for induction. Group 2 - 40 patients were given cisatracurium 0.1 mg per kg for induction. **Results:** No significant difference was found in both of the groups in measures of age, sex and weight. Onset of atracurium's action is 3 minutes where as 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. **Conclusion:** This randomized control study of 80 patients with 40 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.

**Keywords:** Atracurium, Cisatracurium, Muscle relaxants, Propofol.

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## Introduction

Laparoscopic surgeries are done very commonly nowadays in every part of the world. They have many advantages compared to an open procedure like less surgical trauma, less intra-operative and post-operative pain, early discharge and above all cosmetic benefit. Endotracheal intubation is an integral part of the administration of general anesthesia during the laparoscopic surgical procedure.<sup>[1-4]</sup>

Muscle relaxants are used routinely during intubation to relax muscles in the neck and throat, which reduces the risk of injury. They may also be used to relax the chest muscles when

an endotracheal tube is used to help mechanical ventilation. The first successful administration of a neuromuscular blocker (curare) to produce surgical relaxation in an anesthetized patient occurred in 1912, when Arthur L awen, a German surgeon from Leipzig, used a partially purified preparation of the substance. Muscle relaxants rapidly became a routine part of the anaesthesiologist's drug arsenal.<sup>[5-7]</sup>

Succinylcholine, introduced by Thesleff and associates in 1952, a depolarizing muscle relaxant with rapid onset of action and short duration is still the relaxant of choice to facilitate tracheal intubation.<sup>[8]</sup> However, in addition to fascicu-

lation, succinylcholine has many side effects such as bradycardia, dysrhythmias, increased release of potassium, post-operative myalgia, increased intraocular pressure, intracranial tension, intragastric pressure, prolonged recovery in patients with pseudo-cholinesterase deficiency, masseter spasm, and triggering malignant hyperthermia. 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 and offering excellent intubating conditions.<sup>[9,10]</sup>

This study is designed to compare the efficacy of atracurium and cisatracurium by the means of: Onset of action, Hemodynamic stability and Duration of action.

## Subjects and Methods

Present Experimental Randomized controlled trial was done at the Department of Anaesthesiology, GMERS Medical College, Sola, Ahmedabad from July 2018 to July 2020 in 80 patients aged between 20 and 45 years.

### Inclusion criteria

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

### Exclusion criteria

- Patients undergoing any other surgery requiring general anaesthesia
- <20 years and >45 years of age
- ASA 3 or 4 physical status.
- Patients having any neuromuscular disease and taking any medication which known to influence neuromuscular function
- 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 80 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 (EtCO<sub>2</sub>). 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.

Group 1 - 40 patients were given atracurium 0.5 mg per kg for induction

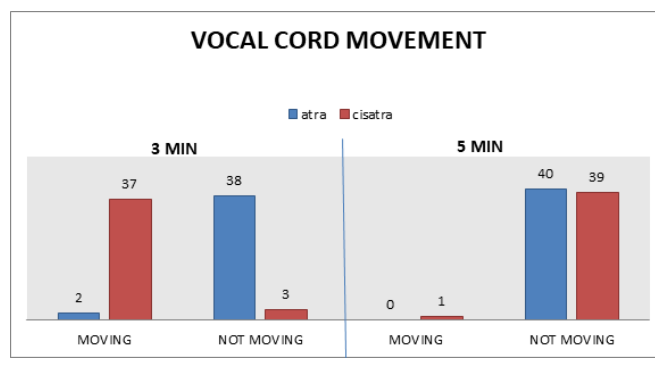
Group 2 - 40 patients were given cisatracurium 0.1 mg per kg for induction

Mask ventilation was continued for 3 minutes. Following which endotracheal tube was inserted, fixed and confirmed. Maintenance – 50% O<sub>2</sub>, 50% N<sub>2</sub>O 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 0.03mg per kg for maintenance. The volatile anaesthetic 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 15minutes. 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 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

## Results

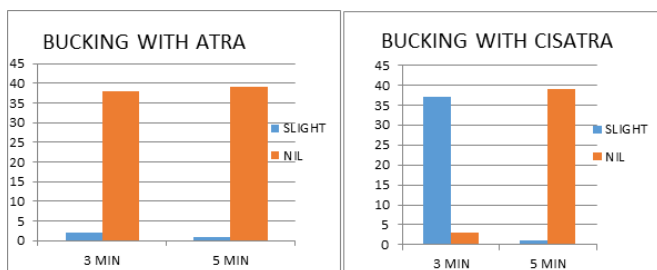
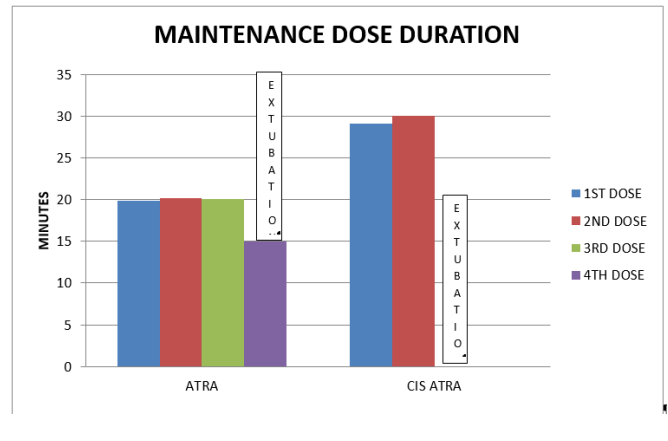
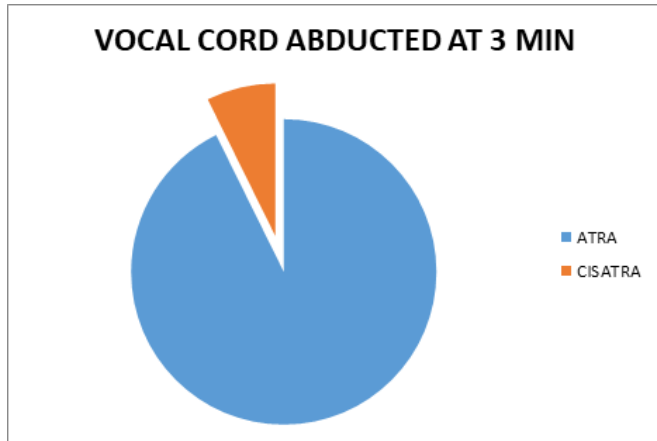


**Table 1: Age Distribution Among Study Participants**

Group 1 (ATRA)	Group 2 (CISATRA)	P value
34.3+- 2(6.92)	32.25+- 2(6.73)	0.0901

**Table 2: Sex Distribution Among Study Participants**

Sex	Male	Female
ATRA	13	27
CISATRA	14	26



The ulnar nerve was stimulated transcutaneously at the wrist with supramaximal stimuli of 0.2ms duration in a train-of-four (TOF) mode at 2Hz every 12sec. The force of contraction of the adductor pollicis was measured and recorded using a force displacement transducer and a neuromuscular function analyser. When TOFR is between 0.4 – 0.9 maintenance dose was given.

## Discussion

While selecting neuromuscular agent for tracheal intubation or skeletal muscle relaxation, main aim of an anaesthesiologist 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.<sup>[10]</sup>

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) where as 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.

Anaesthesiologists’ satisfaction using between cisatracurium and rocuronium for the intubation in the anesthesia induced by remifentanil and propofol Hyunjung Lee, Sinho Jeong,

**Table 3: Comparison Of Heart Rate Among Study Participants**

Group	Pre Intubation	Post Intubation	15 Min	30 Min	45 Min	60 Min	75 Min	90 Min	105 Min	120 Min
ATRA										
MEAN	79.20	99.20	89.20	87.20	89.20	85.20	83.20	85.20	91.38	99.97
SD	8.56	8.56	8.56	8.56	8.56	8.56	8.56	8.56	9.18	9.03
CIS ATRA										
MEAN	79.20	89.2	85.20	83.20	81.20	85.20	79.20	85.20	86.32	82.32
SD	8.37	8.37	8.37	8.37	8.37	8.37	8.37	8.37	8.05	8.05
P Value	0.5000	0.0001	0.0174	0.0174	0.0001	0.0174	0.0174	0.5000	0.0044	0.0001

**Table 4: Mean Arterial Blood Pressure (Map)**

Group	Pre Intubation	Post Intubation	15 Min	30 Min	45 Min	60 Min	75 Min	90 Min	105 Min	120 Min
ATRA										
MEAN	91.18	98.52	99.18	95.18	96.18	95.18	95.18	95.18	97.52	106.46
SD	7.43	7.43	7.43	7.43	7.43	7.43	7.43	7.43	7.43	7.43
CIS ATRA										
MEAN	90.8	94.13	94.80	91.51	91.51	94.80	91.39	94.80	93.28	91.28
SD	7.29	7.29	7.29	6.84	6.84	7.29	6.76	7.29	7.49	7.49
P Value	0.4090	0.0039	0.0039	0.0110	0.0018	0.0091	0.0087	0.4090	0.0055	0.0001

**Table 5: Duration Of Action Of Loading Dose**

	Mean	SD
ATRA	45.05 Minutes	1.06
CISATRA	60.03 Minutes	2.19

**Table 6: Maintenance Dose Timings**

		ATRA		CISATRA		P VALUE
		MEAN	SD	MEAN	SD	
1 <sup>st</sup>	Maintenance Dose	45.05	1.06	60.03	2.18	0.0001
2 <sup>nd</sup>	Maintenance Dose	64.83	1.15	29.06	5.68	0.0001
3 <sup>rd</sup>	Maintenance Dose	84.95	1.08	–	–	0.0001
4 <sup>th</sup>	Maintenance Dose	105.00	0.93	–	–	0.0001

Cheolhun Choi, Hyejin Jeong, Seongheon Lee, Seongwook Jeong. Despite fundamentally slower onset time,<sup>[10]</sup> cisatracurium can provide quite good intubating conditions, which were comparable to those achieved with equipotent doses of rocuronium, which is more expensive in anesthesia inducted with remifentanyl and propofol. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery AM El-Kasaby, HM Atef, AM Helmy, M Abo El-Nasr. They had 64 total patients in group of 16s. 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 16 in this reference study, had same results. So we are having group of 40 instead of 16. They concluded no difference in effect of atracurium and cisatracurium. We found significant difference on p value of <0.0001. Other differences were age group of patients and male to female ratio.

Lien et al., and Basta et al, 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 1, L Radbruch, C Diefenbach, W Buzello 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.<sup>[11]</sup>

Comparison of the neuromuscular blocking effect of cisatracurium and atracurium on the larynx and the adductor pollicis K Kirov, C Motamed, F Decailliot, N Behforouz, P Duvaldestin.<sup>[12]</sup> 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 A.L. Lipnitski, A.V. Marochkov.<sup>4,7,9,10</sup> According to this one, they were having faster onset of action of cisatracurium then atracurium in same sample size.

Hemodynamic stability with cisatracurium was very regular, as we can see only around 90 minutes i.e. time of 1<sup>st</sup> 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,<sup>[12]</sup>and Basta et al., 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.

We found that, appearance of curare cleft was a bit behind of hemodynamic changes in atracurium, whereas it was pre-

ceding 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 Claudia Maria Nogueira Correa et al,<sup>[13]</sup> 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.

Hosking MP,<sup>[14]</sup> Combined H1 and H2 receptor blockade attenuates the cardiovascular effects of high dose atracurium for rapid sequence endotracheal intubation. In this study, they concluded that combined H1 and H2 receptor blockade attenuates cardiovascular effects associated with large doses of atracurium in humans. Histamine-releasing agents may be contraindicated in patients subject to chronic H2 receptor blockade.<sup>[13-18]</sup> In our study, we had noticed that, change in hemodynamic parameters were higher in atracurium than in cisatracurium immediately after intubation. But we didn't observed histamine concentration in the blood and there was no skin flushing in any of our patient after administration of atracurium or cisatracurium, it is hard to comment on histamine release.

## Conclusion

This randomized control study of 80 patients with 40 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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