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Original Research Article

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

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Abstract:

Background: Muscle relaxant makes an important part of the balanced anesthesia, especially for abdominal surgery. Over a period of time, newer relaxants have been developed with lower side effects and better recovery profile. This study compared two relaxants – cisatracurium and atracurium, as a part of general anesthesia for the laparoscopic medical procedures. Cisatracurium is comparatively a newer agent and there is still a limited experience in its use in various fields of surgery, including laparoscopic abdominal interventions in which short-term blockade of neuromuscular conduction is usually required. It is the R-cis isomer of atracurium carrying 3-4 times more potency. Unlike atracurium, it has significantly less histamine-releasing effect and creates better hemodynamic stability. These distinctive qualities are the most significant, and according to many publications, these two muscle relaxants practically are not distinguishable from each other.

Materials and Methods: This prospective, randomized study was conducted at Prakash Institute of Medical Sciences and research for the period of February 2023 to July 2023 included 60 patients, aged from 18 to 60 y, ASA I-III class, who underwent laparoscopic abdominal surgery. Patients were randomly divided into two groups; Group C received cisatracurium 0.1 mg/kg as muscle relaxant and Group A received atracurium 0.3 mg/kg IV. The mean onset time and duration of action for the two groups was done by Stockholm rules of the pharmacodynamic investigations of muscle relaxants activity. Intubating conditions, hemodynamic changes, and safety profile were noted.

Result: The mean onset time and duration of action for cisatracurium were 6.48 ±0.49 minutes, 52.12 ±7.5 minutes while, for atracurium, the values were 5.18 ±0.28 minutes, 43.05 ±2.74 minutes respectively ($p < 0.001$). Intubating conditions, haemodynamic changes, and safety profile were comparable between the groups. Recovery time following administration of cholinesterase inhibitors in the cisatracurium and atracurium group were 4.88 ±0.29 and 5.74 ±0.28 minutes respectively ($p < 0.001$).

Conclusion: Cisatracurium(0.2mg/kg) provides better intubating conditions, stable hemodynamic status and no signs of histamine release as compared to atracurium(0.5mg/kg). Thus, cisatracurium appears a better alternative for preventing undesirable effects of atracurium.

Keywords: Cisatracurium, Atracurium, Neuromuscular Blockade, Neuromuscular Monitoring.

Introduction

The concept of balanced anesthesia, with induced muscle paralysis with relaxant drugs is one of the foundations of the current anesthetic practice. [1]

Muscle relaxation not only provides a comfortable environment for the surgeons, but also allows for effective and safe management of gas exchange, circulation and metabolism of the patient. [2] The use of muscle relaxants has not only revolutionized anesthesiology, but also marked the beginning of the modern era in surgery. [3]

Cisatracurium is comparatively a newer agent and there is still a limited experience in its use in various fields of surgery, including laparoscopic abdominal interventions in which short-term blockade of neuromuscular conduction is usually required. [4] It is the R-cis isomer of atracurium

carrying 3-4 times more potency. [5] Unlike atracurium, it has significantly less histamine releasing effect and creates better hemodynamic stability. These distinctive qualities are the most significant, and according to many publications, these two muscle relaxants practically are not distinguishable from each other. [6] In separate studies, it has been shown that the pharmacodynamic characteristics of cisatracurium and atracurium at equipotent doses are also very close to each other. [7]

However, despite the fact that cisatracurium is a more potent muscle relaxant, its ED95 is 0.05 mg/kg compared to 0.2 mg/kg that of atracurium, otherwise the pharmacodynamics in many ways are similar. Some studies have shown a slower onset of neuromuscular block (NMB) with cisatracurium compared to atracurium. [8]

Few comparative assessments of the action of both muscle relaxants have been presented under the same conditions. [9] We conducted this study to have a comparative assessment of cisatracurium and atracurium for endotracheal anesthesia for abdominal laparoscopic surgery.

Materials and Methods

This prospective, randomized study was conducted at Prakash Institute of Medical Sciences and research for the period of February 2023 to July 2023 included 60 patients, aged from 18 to 60 y, ASA I-III class, who underwent laparoscopic abdominal surgery. The expected duration of surgery was 25-35 min. Written and informed consent was obtained from each of the patients. Patients on medications, which could significantly affect neuromuscular conduction (e.g., carbamazepine, aminoglycosides, lincosamides and diuretics), patients with pathology of the nervous system, kidney or liver disease, were excluded from the study. Patients for whom additional doses of muscle relaxants were required, or an unstable control of neuromuscular transmission was observed, were also excluded from the study.

Patients were randomly divided into 2 groups using a computer-generated program, each group consisting of 70 patients. Patients in Group A received cisatracurium in a loading dose of 0.1 mg/kg, and Group B received atracurium 0.3 mg/kg. Eight patients required additional doses of muscle relaxants due to prolonged operating time, and 2 patients had unstable control of neuromuscular transmission, so were excluded from the study.

As a result, 60 patients completed the study in each group. During anesthesia and surgery, standard monitoring was used, and non-invasive blood pressure, heart rate, pulse oximetry, capnography and ECG were recorded at the following stages: 1st; before the start of anesthesia (patient on the operating table), 2nd; –5 min after surgery started, 3rd;10 min after the surgery started, 4th; 20-30 min after surgery started; (the main stage operations), 5th; at the suturing the skin; and 6th–5 min after extubation.

Premedication and induction of anesthesia was performed similarly in all patients. All patients received inj. glycopyrrolate 0.2 mg IV and inj. diphenhydramine 10 mg IV, 30 min before the onset of anesthesia. Induction consisted of sequential administration of fentanyl 0.1 mg, propofol 1.5-2.0 mg/kg. Muscle relaxation either with cisatracurium or atracurium was done as per the study protocol.

The start time of intubation was determined by clinical signs and significance of TOF (Train-of-four). The conditions for intubation were assessed by an experienced anesthesiologist; the criteria included ease of laryngoscopy, location and/or movement of vocal cords, and the patient's response to intubation. Maintenance of anesthesia was carried out with sevoflurane (0.8-1.0 MAC in oxygen-air mixture (50:50) and an additional bolus of fentanyl. Mechanical ventilation during anesthesia was carried out by the Workstation. Inhalational agent was discontinued before the end of anesthesia. The suitability of extubation was determined by monitoring neuromuscular conduction and clinical signs of recovery: e.g., eye opening, the ability to raise and hold the head above the operating table for 5 sec, and the strength of the handshake. Anaesthesia was reversed using inj. neostigmine 0.05mg/kg IV and inj. glycopyrrolate 0.01 mg/kg IV.

Statistical Analysis

All data obtained were noted in a performa with an interval of 5 min. The data was tabulated on Microsoft Excel Sheet. Student T Test was applied on all parametric data and Chi-Square test was applied on NonParametric data. A $p < 0.05$ was considered as statistically significant.

Results

BMI were comparable between the groups. The majority of the patients underwent laparoscopic cholecystectomy. Type of surgery, mean duration of anaesthesia, and 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 (Table1). The preoperative vitals i.e. heart rate, blood pressure (systolic, diastolic, and mean), SpO2, were also comparable between the two groups.

Table 1: Demographic Data

		Group A	Group B	P-Value
Age(Years)		42.99± 15.05	44.58± 14.78	0.341
Gender(M:F) BMI(Kg/M^2)		11:14 29.63±4.79	11:14 30.95±5.12	 0.063
Type of surgery	Cholecystectomy	22	25	
	Inguinal Hernia Repair	6	5	
	Ventral Hernia Repair	2	0	
Duration of surgery		70.41± 13.75	67.88±8.15	0.175
Duration of Anaesthesia		76.38± 14.72	73.38±9.33	0.159
Intraopfluidused		806 ± 120.5	776± 9.05	0.133
Temperature		38.79±0.05	38.71±0.06	0.015

The onset time was significantly longer in the cisatracurium ($p<0.001$) in comparison to atracurium (6.48 ±0.49 vs. 5.18 ±0.28 minutes, $p<0.001$). Cisatracurium took 41% more time to achieve TOF 0 in contrast to atracurium. But, the duration of action was longer in the cisatracurium group to that of the atracurium group (52.12 ±7.5 vs. 43.05 ±2.74 minutes) which was highly significant ($p<0.001$) (Table 2, figure 2). Grading of intubating conditions was carried out by the senior anaesthesiologist (blinded to the study), showed excellent intubating conditions in all the patients from both drug groups.

Table 2: Neuromuscular Blocking Properties of Cisatracurium (Group A) and Atracurium (Group B)

	Group A		Group B		P-Value
	Mean	±SD	Mean	±SD	
Onset	6.48	0.49	5.18	0.28	<0.001
Duration	52.12	7.5	43.05	2.74	<0.001
Recovery	4.88	0.29	5.74	0.28	<0.001
Numberofpatients Receivingtop-Up Dose	8		10		

Body mass index; ECG: Electrocardiogram; ED: Effective dose; MAC: Minimum alveolar concentration NIBP: Non-invasive blood pressure; NMBD: Neuromuscular blocking drug; NMJ: Neuromuscular junction; TOF: Train-of-four

There was a decrease in mean pulse rate, systolic, diastolic, and mean blood pressure after administration of the muscle relaxant in comparison to the baseline values in both the groups.

All these haemodynamic parameters increased following intubation (figure 3). There was neither any apparent signs of histamine release nor any episode of bradycardia or hypotension or hypertension in any patient. Recovery time after administration of cholinesterase inhibitors (from TOF2 to TOF4) was faster in the cisatracurium group in comparison to atracurium group (4.88 ±0.29 vs. 5.74 ±0.28 minutes, $p<0.001$).

Discussion

The demographic parameters of the patients including age, weight, sex and ASA status were comparable in both groups (p value > 0.05). There was statistically no significant difference between group 1 and group 2 as far as type of surgeries was concerned. In our study intubating conditions were assessed using jaw relaxation, vocal cord position and intubating response as per the Cooper's Criteria. It was found that intubating conditions were most favourable in group 2 followed by group 1. Our results were in accordance to Athaluri VV et al., 20196 who found excellent intubating conditions with rapid onset of action with cisatracurium (0.15mg/kg) as compared to cisatracurium (0.1mg/kg) and atracurium (0.5mg/kg) and El kasaby AM et al., 20105 who found excellent intubating conditions of cisatracurium in higher doses (0.2mg/kg, 0.3mg/kg) versus 2ED95 dose of cisatracurium (0.1mg/kg) and atracurium(0.5mg/kg). [10, 11]

On intergroup comparison it was found that difference in Heart rate was statistically significant at 1 and 3 minutes after intubation. Group 1 produced a more significant increase in heart rate as compared to group 2 whereas on intragroup comparison, the difference in heart rate from the baseline was greatest in group 1 than group 2 at 1 minute and 3 minutes after intubation which was statistically significant. Our results were in accordance with Thukral S et al., (2018) who compared cisatracurium (0.2mg/kg) with atracurium (0.5mg/kg) and concluded that cisatracurium has a faster onset, good intraoperative hemodynamic parameters and better recovery profile. [12] Kaur H et al., 2018 studied recovery profile and haemodynamic profile of atracurium (0.5mg/kg) versus cisatracurium (0.1mg/kg) and reported that there was no statistically significant difference in heart rate. [13] Our results are in contrary to this study as the dose

of cisatracurium taken in this study was 0.1 mg/kg which was less than that taken in our study. On intergroup comparison we found that group 1 produced a more significant increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure as compared to group 2 after 1 minute and 3 minutes after intubation whereas on intragroup comparison, statistically significant difference in systolic blood pressure, diastolic blood pressure and mean arterial pressure from baseline was seen at 1 minute and 3 minutes after intubation in both groups which were greatest in group 1 than group 2. However, the HR, systolic blood pressure, diastolic blood pressure and mean arterial pressure returned to baseline at 5 minutes after intubation and thereafter till 60 minutes. Change in HR, SBP, DBP, MAP was considered significant only when there is >20% deviation from baseline values. The more significant increase in HR, SBP, DBP, MAP in group 1 than group 2 might be because we had not taken equipotent doses i.e. 2ED95 of atracurium (0.5mg/kg) and cisatracurium (0.1mg/kg) in which the results are insignificant. The dose we had taken in our study was 2ED95 (0.5mg/kg) of atracurium and 4ED95 (0.2mg/kg) of cisatracurium. As we increase the dose of drug the cardiovascular stability also increases. Our results were also in accordance with that of Teymourian H et al., 2014 who found that the same dose (2ED95) atracurium is more effective neuromuscular blocking agent than cisatracurium, but higher doses of cisatracurium 4ED95 and 6ED95 provide more effective, more rapid neuromuscular blocking with longer duration of action and stable hemodynamic status. [14] Bhagat M et al., 2018 concluded that atracurium and cisatracurium had similar safety profile. [15] Oxygen saturation, ETCO2, signs of histamine release like erythema, wheal and flush were comparable in both groups which was statistically insignificant. The syndrome becomes clinically evident when doses of 0.5 mg/kg (two times ED95) or more are injected rapidly Basta SJ et al.,1992. [16] Our study was in accordance with Mohanty AK et al., 2018 who compared cisatracurium and atracurium and found that cisatracurium had no signs of histamine release. [17] Similarly Kopman AF et al., 2000 reported that cisatracurium is 3-4 times more potent than atracurium and it did not release histamine. [18] Jammar P et al., 2017 evaluated two intubating doses of cisatracurium during general anaesthesia and stated that 0.2mg/kg of cisatracurium provides longer duration of action and more stable hemodynamic status than 0.15mg/kg. No associated signs of histamine release were detected clinically. [19]

Conclusion

We concluded that cisatracurium (0.2mg/kg) provided better intubating conditions, stable hemodynamic status and no signs of histamine release as compared to atracurium(0.5mg/kg).

Thus cisatracurium appears a better alternative for preventing undesirable effects of atracurium.

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