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Original research article

COMPARISON OF THE VARIABILITY OF RECOVERY PROFILE AND HEMODYNAMIC EFFECTS OF NEUROMUSCULAR BLOCKADE WITH CISATRACURIUM VERSUS ATRACURIUM

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Abstract: *A randomized controlled trial was conducted at the Main Operation Theatre of Jinnah Postgraduate Medical Centre (JPMC) in Karachi to compare the recovery profile and hemodynamic effects of cisatracurium and atracurium among patients undergoing laparoscopic cholecystectomy. The study was conducted from 20th July 2019 to 19th January 2020 and included 68 patients aged between 20 to 50 years undergoing elective laparoscopic cholecystectomy under general anesthesia. Patients with a history of allergy to the study drugs, neuromuscular, pulmonary, renal, or hepatic diseases, smoking, pregnancy, or breastfeeding, and those on preoperative medication such as antipsychotics, aminoglycosides, steroids, or neuroleptics were excluded. The patients were randomly divided into two groups. In Group 1, comprising 34 patients, cisatracurium (0.2 mg/kg) was administered, whereas in Group 2, also with 34 patients, atracurium (0.5 mg/kg) was given. Neuromuscular blocking agents were administered three minutes before intubation. The primary outcomes measured were the recovery profile and hemodynamic effects. In Group 1 (cisatracurium), the baseline mean arterial pressure (MAP) was recorded as 98.40 ± 8.02 mmHg, which increased to 112.20 ± 8.88 mmHg before intubation, resulting in a change of 13.56 ± 5.59 mmHg. In contrast, in Group 2 (atracurium), the baseline MAP was 94.10 ± 7.91 mmHg, which rose to 109.07 ± 8.35 mmHg before intubation, indicating a change of 16.50 ± 4.38 mmHg. The study concluded that cisatracurium is more effective in exhibiting neuromuscular blocking properties than atracurium in patients undergoing laparoscopic cholecystectomy under general anesthesia.*

Keywords: tracheal intubation, neuromuscular blocking agent, recovery profile.

Introduction

In addition to analgesia, amnesia, and areflexia, muscular relaxation is vital to a well-rounded anesthetic. Anesthesia and surgery entered a new era with the development of muscle relaxants and better knowledge of their pharmacology (Foldes et al., 1952). In the neuromuscular junction, non-depolarising muscle relaxants cause paralysis by binding competitively to the alpha subunit of acetylcholine receptors (Bowman, 2013). There was a revolution in anesthesia thanks to the development of long-acting relaxants like pancuronium (used by Baird WL and Reid AM) and intermediate-acting drugs like vecuronium and atracurium (Baird and Reid, 1967; Stenlake et al., 1983). The ability to monitor neuromuscular activity is a significant step forward for muscle relaxants. Because of the wide diversity of reactions to relaxants and the small effective dosage ranges (Padmaja and Mantha, 2002), it is advised by the authors. Up to 42% of patients exhibit evidence of insufficient reversal in the recovery room without neuromuscular monitoring (VIBY-MOGENSEN et al., 1980). Atracurium was introduced to the medical community as early as 1980 (Stenlake et al., 1983). One way to eliminate this substance is by Hofmann degradation; it's a bis benzyl tetrahydroisoquinoline. The commercially available substance includes ten different isomers, including cis-cis, cis-trans, and trans-trans forms, all of which are possible configurations. Safety in elderly and organ failure patients is a significant benefit of atracurium over competing neuromuscular blocking medicines because of its spontaneous disintegration and non-organ dependent excretion. Nevertheless, its primary limitations include histamine release and hemodynamic instability (Elbradie, 2004; Grattan and Marsland, 2016). Nevertheless, cisatracurium, launched in 1995, has a lower tendency to produce histamine and more excellent autonomic stability. It generates a block three to four times as powerful as atracurium and accounts for 15% of the commercially available atracurium combination (Bluestein et al., 1996). The study examined the differences between cisatracurium and atracurium regarding recovery profile and hemodynamic consequences in laparoscopic cholecystectomy patients.

Methodology

After the approval from the ethical review committee, this randomized controlled trial was performed at the Main operation theatre, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from 20th July 2019 to 19th January 2020. Through non-probability consecutive sampling, patients between the ages 20-50 years, of both genders, with ASA grade I and II, undergoing elective laparoscopic cholecystectomy under general anesthesia were included in

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the present study. Patients with ASA grade III and IV, with drug allergy, pregnancy, smoking history, neuromuscular pulmonological, hepatic, or renal disease were excluded from the present study. Patients' personal information (such as gender, age, weight, height, and ASA classification) was gathered using a pre-anesthesia proforma. Two groups of 34 patients were randomly selected and placed into Group 1 and Group 2, respectively. Patients in Group 1 were administered Cisatracurium (0.2mg/kg), whereas those in Group 2 were given Atracurium (0.5mg/kg). The patient was attached to various monitors in the operating room to track things like their heart rate, non-invasive blood pressure, oxygen saturation, and exhaled carbon dioxide levels (capnography). A Train of Four (TOF) monitor was used to track the progress of the neuromuscular block. Fundamental vital indicators such as heart rate, systolic pressure, diastolic pressure, and mean arterial pressure were obtained in a questionnaire before induction (baseline hemodynamic). Before tracheal intubation, the patient's hemodynamics were also documented.

After establishing intravenous (I/V) access, fluids were administered. Before induction, 10 mg of Metaclopromide was administered as premedication. Propofol (2mg/kg), Nalbuphine (0.1mg/kg), and either Cisatracurium (0.2mg/kg) or Atracurium (0.5mg/kg) were used to produce standard general anesthesia. As the time of expiration (TOF) count reached zero (Onset), direct laryngoscopy was performed, and an endotracheal tube of the appropriate size was passed orally while the patient was on intermittent positive pressure ventilation (IPPV) with a bag mask on 100% Oxygen. Patients in this trial were given 100% oxygen while receiving regulated mechanical ventilation (CMV) at a volume of 8-10 mm/kg and a respiratory rate of 10-12/min through anesthesia machines. Isofluorane was employed during surgery because of its high anesthetic depth and consistent hemodynamic impact. After a TOF count of one was reached, maintenance doses equal to 10% of the loading dosage were administered once more (duration of action). After the final maintenance dosage of the neuromuscular blocker, the blockade was reversed when the TOF Ratio (TOFR) reached 75%. (Recovery index). Extubation of the trachea occurred when a TOFR of 0.9 was reached. Data was analyzed using SPSS 23.0, the latest version of the Statistical Package for the Social Sciences. Mean and standard deviation (mean, standard deviation) were used to show quantitative. T-test was used to compare onset time, action time, and recovery index for hemodynamics across the study groups. Quantitative information was shown as frequencies and percentages, whereas qualitative information was shown as frequencies and percentages. Using a stratified version of the Independent t-test, we could account for potential confounding factors such as age, gender, ASA status, and body mass index. A significance level of ≤0.05 was used to conclude.

Results

A total of 68 patients were included in the present study. Table 1 shows the clinical and demographic parameters of the study participants. The mean age of the participants in the present study was 36.68 ± 8.12 years. The mean age of patients in groups 1 and 2 was 36.99 ± 7.92 and 36.60 ± 9.23 years. Most of the patients, 39 (57.35%), were between 36 to 50 years of age. Out of 68 patients, 31 (45.59%) were males, and 37 (54.41%) were females, with a female ratio of 1:1.3. The onset time, duration, and recovery index with Cisatracurium was found to be 166.66 ± 5.64 seconds, 36.22 ± 2.12 minutes and 13.90 ± 1.61 minutes. With Atracurium, they were recorded to be 185.54 ± 5.13 seconds, 42.84 ± 2.50 minutes and 15.43 ± 1.72 minutes respectively. In group 1, the baseline, before intubation and change in HR, was 79.90 ± 10.47, 102.10 ± 10.20, and 21.69 ± 10.24 bpm, respectively, while in group 2, it was 82.50 ± 10.23, 108.43 ± 6.26 and 26.47 ± 7.57 bpm respectively. In group 1, the baseline, before intubation and change in MAP, was 98.40 ± 8.02, 112.20 ± 8.88, and 13.56 ± 5.59 mmHg, respectively, while in group 2, it was 94.10 ± 7.91, 109.07 ± 8.35 and 16.50 ± 4.38 mmHg respectively (Table II). The stratification of time of onset, duration of action, recovery index, and change in HR and MAP in terms of age, gender, ASA, and BMI are shown in Table III-VII

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Table I: clinical and demographic parameters of the study participants

Parameters	**Group 1 (n=34)**	**Group 2 (n=34)**
Age	36.99±7.92	36.68±8.12
20-35 years	14(41.18%)	15 (44.12%)
36-50 years	20 (58.82%)	19 (55.88%)
Gender		
Male	16 (47.06%)	15 (44.12%)
Female	18 (52.94%)	19 (55.8%)
ASA grade		
I	17 (50%)	15 (44.12%)
II	17 (50%)	19 (55.8%)
BMI (kg/m^2)	29.57±3.34	29.93±3.04
≤30	14 (41.18%)	12 (35.29%)
>30	20 (58.82%)	22 (64.71%)

Table II: Comparison of the recovery profile and hemodynamic effects of cisatracurium and atracurium among laparoscopic cholecystectomy patients

Outcome	**Group 1 (n=34)**	**Group 2 (n=34)**	**p-value**
Time of onset (sec)	166.66 ± 5.64	185.54 ± 5.13	0.0001
Duration of action (min)	36.22 ± 2.12	42.84 ± 2.50	0.0001
Recovery index (min)	13.90 ± 1.61	15.43 ± 1.72	0.0001

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Change in heart rate (bpm)	21.69 ± 10.24	26.47 ± 7.57	0.0001
Change in MAP (mmHg)	13.56 ± 5.59	16.50 ± 4.38	0.0001

Table III: Stratification of onset time concerning age, gender, ASA, and BMI.

Effect modifiers		Time of onset (sec) Mean ± SD		P-value
		Group 1 (n=34)	Group 2 (n=34)	
Age (years)	20-35	167.14± 6.06	183.41 ±4.74	0.0001
	36-50	166.33 ±5.38	187.13 ±4.88	0.0001
Gender	Male	166.15±5.57	184.13 ±4.62	0.0001
	Female	167.14±5.74	186.73 ±5.29	0.0001
ASA	I	167.77 ±5.82	185.87 ±5.38	0.0001
	II	165.48 ±5.27	185.27 ±4.96	0.0001
BMI (kg/m^2)	≤30	169.17 ±5.41	183.30 ±3.43	0.0001
	>30	164.79 ±5.10	186.69 ±5.50	0.0001

Table IV: Stratification of Duration of action concerning age, gender, ASA, and BMI.

Effect modifiers		Duration of action (sec) Mean ±SD		P-value
		Group 1 (n=34)	Group 2 (n=34)	
Age (years)	20-35	36.04 ±2.41	42.21 ±2.86	0.0001
	36-50	36.35 ±1.92	43.31 ±2.10	0.0001
Gender	Male	36.03 ±2.43	42.29 ±2.51	0.0001
	Female	36.40 ±1.80	43.30 ±2.43	0.0001
ASA	I	36.34 ±1.98	42.94 ±2.49	0.0001
	II	36.09 ±2.28	42.76 ±2.53	0.0001
BMI (kg/m^2)	≤30	37.03 ±1.74	44.30 ±1.33	0.0001
	>30	35.61 ±2.20	42.09 ±2.63	0.0001

Table V: Stratification of Recovery index concerning age, gender, ASA, and BMI.

Effect modifiers		Recovery index (min) Mean ±SD		P-value
		Group 1 (n=34)	Group 2 (n=34)	
Age (years)	20-35	13.96 ±1.37	15.10 ±1.78	0.0001
	36-50	13.85±1.78	15.67 ±1.66	0.0001
Gender	Male	14.03 ±1.45	15.16 ±1.57	0.0001
	Female	13.77 ±1.77	15.65 ±1.83	0.0001
ASA	I	13.86 ±1.51	15.45 ±1.65	0.0001
	II	13.94 ±1.73	15.41 ±1.80	0.0001
BMI (kg/m^2)	≤30	14.14 ±1.71	15.65 ±1.56	0.0001
	>30	13.72 ±1.54	15.31±1.81	0.0001

Table VI: Stratification of Change in heart rate concerning age, gender, ASA, and BMI.

Effect modifiers		Change in heart rate (bpm) Mean ±SD		P-value
		Group 1 (n=34)	Group 2 (n=34)	
Age (years)	20-35	23.96 ±8.01	27.34 ±6.95	0.0001
	36-50	20.10 ±11.38	25.82 ±8.03	0.0001
Gender	Male	21.30 ±9.24	27.13 ±6.09	0.0001
	Female	22.06 ±11.23	25.92 ±8.66	0.0001
ASA	I	22.09 ±13.14	27.29 ±7.99	0.0001
	II	21.27 ±5.97	25.78 ±7.23	0.0001
BMI (kg/m^2)	≤30	20.66 ±9.92	26.87 ±7.11	0.0001
	>30	22.46 ±10.54	26.27 ±7.86	0.0001

Table VII: Stratification of Change in MAP concerning age, gender, ASA, and BMI.

Effect modifiers		Change in MAP (mmHg) Mean ±SD		P-value
		Group 1 (n=34)	Group 2 (n=34)	
Age (years)	20-35	16.04 ±4.86	15.72 ±4.29	0.678
	36-50	11.83 ±5.46	17.08 ±4.42	0.0001
Gender	Male	13.15 ±5.97	17.16 ±4.12	0.0001
	Female	13.94 ±5.26	15.95 ±4.57	0.0001
ASA	I	12.66 ±5.93	17.26 ±3.48	0.0001
	II	13.94 ±5.26	15.86 ±4.97	0.0001
BMI (kg/m^2)	≤30	13.38 ±5.53	17.35 ±4.01	0.0001
	>30	13.69 ±5.70	16.07 ±4.54	0.0001

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Discussion

A plethora of non-depolarizing neuromuscular blocking medications have been brought to clinical practice. Still, concerns about adverse effects such as cardiovascular instability, the possibility of recurrence, and the persistence of paralysis have limited their usage. Treatments for renal and liver failure often include atracurium, a combination of 10 optical isomers of a medium-acting NDMR. Histamine release causes hypotension and anaphylaxis, although it is metabolized via Hoffmann elimination and nonspecific ester hydrolysis (Bartkowski et al., 1993; Yazdanian et al., 2008). Cisatracurium, a pure version of one of Atracurium's ten stereoisomers, is about 3-4 times as potent as Atracurium but is not linked to dose-dependent histamine release in humans. The amount of laudanosine produced by metabolism is five times lower (Bergeron et al., 2001; ShangGuan et al., 2008). Nevertheless, intubating circumstances similar to those obtained with equipotent dosages of Atracurium may not be achieved with cisatracurium. Cisatracurium intubation dosage is 3ED95 (Smith et al., 1997). This investigation compared the hemodynamic effects of cisatracurium and atracurium in patients undergoing laparoscopic cholecystectomy and their respective recovery profiles. With Cisatracurium, 23 measured an onset time of 166.66±5.64 seconds, 36.22±2.12 minutes, and a recovery index of 13.90 1.61 minutes; for Atracurium, I reported 185.54 5.13 seconds; a length of 42.84±2.50 minutes; and a recovery index of 15.43±1.72 minutes. Group 2 had a baseline HR of 82.50±10.23, pre-intubation HR of 108.43±6.26, and post-intubation HR of 26.47±7.57 bpm, whereas Group 1 had HR values of 79.90±10.47, 102.10±10.20, and 21.69±10.24. Comparing groups 1 and 2, we observed that the baseline, pre-intubation, and post-intubation MAP values were 98.40±8.02, 112.20±8.88, and 13.56±5.59 mmHg, whereas in group 2, they were 94.10±7.91, 109.07±8.35, and 16.50±4.38 mmHg. One research indicated that Cisatracurium's onset time was 168.60±13.44 seconds, duration was 37.12±7.62 minutes, and recovery index was 14.63±1.84 minutes, whereas Atracurium's values were 181.03±21.76 seconds, length was 40.37±7.04 minutes, and recovery index was 15.30±1.96 minutes (Bluestein et al., 1996). ASA physical status I or II patients (aged 18 to 70) were randomly allocated to one of four groups in a study by Bluestein and colleagues (MELLINGHOFF et al., 1997). (A-D). Cisatracurium was administered to group A at 0.1 mg/kg (2xED95), whereas atracurium was administered at 0.5 mg/kg (2xED95) to group B. Cisatracurium was administered at a dose of 0.2 mg/kg (4xED95) to patients in group C and at a dose of 0.15 mg/kg (3xED95) to patients in group D., They looked at how long it took for symptoms to start, how long they lasted, and whether or not intubation was necessary. Their findings were consistent with ours on the median start and duration of therapeutic effectiveness. They found that a rise in the starting dosage of cisatracurium (from 0.1 to 0.15 and 0.2 mg/kg) shortened the average onset time (from 4.6 to 3.4 and 2.8 min, respectively) and lengthened the average duration of its clinical effects (45 to 55 and 61 min, respectively).

Researchers Mellinghoff et al.(Carroll et al., 1998) evaluated the onset of the neuromuscular block between cisatracurium (n=40) and atracurium (n=20) in a study involving 80 participants. Our findings were consistent with those of Mellinghoff et al. Onset timings were predicted to be 3.1 +/- 1.0 min with cisatracurium and 2.3 +/- 1.1 min with atracurium (P = 0.008). It took 1.5 +/- 0.4 micrograms per minute to achieve a 95% +/- 4% neuromuscular block and 6.6 +/- 1.7 micrograms per minute for cisatracurium. When comparing atracurium and cisatracurium in terms of their active cations, atracurium has 3.3 times more kinetic energy per unit time, expressed as kg1.min1. The 25%-75% spontaneous recovery times were reduced from 18 +/- 11 minutes for cisatracurium and atracurium to 5 +/- 2 minutes and 4 +/- 3 minutes following neostigmine infusion (P = 0.896 and P = 0.921, respectively).

Comparisons were made between cisatracurium (0.1 or 0.15 mg.kg-1) and atracurium (0.5 mg.kg-1) for their neuromuscular blocking effects and reversibility under propofol, nitrous oxide, and isoflurane anesthesia. The adductor pollicis muscle's mechanomyographic response was recorded to detect the presence of neuromuscular block during train-of-four stimulation. Either 10% or 25% recovery of the initial twitch of the train-of-four was used to oppress the block with 50 micrograms.kg-1 of neostigmine. With cisatracurium 0.1 and 0.15 mg.kg-1 and atracurium 0.5 mg.kg-1, the median times to maximal block were 2.7 and 2.2 minutes, respectively. The median time for the train-of-four ratio to return to 0.8 ('adequate recovery') after 0.1 mg. kg of cisatracurium was 74 minutes during spontaneous recovery, 48 minutes after reversal with neostigmine when the first twitch had returned to 10% of control, and 50 minutes after reversal when the first twitch had returned to 25% of control. Ninety minutes, 66 minutes, and 57 minutes were recorded for 0.15 mg of cisatracurium per kilogram of body weight, whereas 75 minutes, 56 minutes, and 54 minutes were recorded for 0.5mg of atracurium per kilogram. Nevertheless, there were no statistically significant differences between the groups of patients administered neostigmine at 10% or 25% recovery of the initial twitch of the train-of-four, suggesting that neostigmine's effect was similar for both neuromuscular blocking medications (Amini et al., 2011).

Researchers AminiShahram et al. found that the mean clinical duration of action (recovery of the evoked response to 25% 0f control) with 0.15 mg/kg was 44.93±5.40 minutes. In contrast, with 0.2 mg/kg, it was 57.03±4.21 minutes when studying the effects of different doses of cisatracurium on the appropriate time for endotracheal intubation and hemodynamic changes during anesthesia. 65 The mean clinical duration of effect with 0.15 mg/kg body weight was 58.9±10.4 minutes, according to research by Luc Bergeron et al. (Bergeron et al., 2001).

Conclusion

Cisatracurium was more effective as a neuromuscular blocking drug than atracurium in patients undergoing general anesthesia. To reduce onset time and improve intubating circumstances, we advocate for the regular administration of Cisatracurium in all patients having surgery under general anesthesia.

Declarations

Data Availability statement

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All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department Concerned.

Consent for publication

Approved

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Conflict of interest

The authors declared an absence of conflict of interest.

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Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript
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