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Research Article

Kinemyography (KMG) versus Electromyography (EMG) neuromuscular monitoring in pediatric patients receiving cisatracurium during general anesthesia

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KEYWORDS

Kinemyography;
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Neuromuscular monitoring;
Cisatracurium

Abstract *Aim of the work:* To compare KMG versus EMG neuromuscular monitoring in pediatric patients receiving cisatracurium during general anesthesia.
Methods: After approval of the protocol by Ethics Committee 24 pediatric patients of both sexes aged 2–6 years, with a maximum weight 20 kg, were included in the study. Monitoring equipments (Datex-Ohmeda A/S 5™) were attached to the patient. The electromyogram was attached to one hand, while, KMG was attached to the other hand for simultaneous monitoring. Induction of anesthesia with fentanyl 2 μg/kg and propofol 2 mg/kg followed by endotracheal intubation. Anesthesia was maintained by end-tidal isoflurane 1.2%. Ventilation was kept by 50% oxygen in air and was adjusted to maintain end-tidal CO_2 in the range of 35–40 mm Hg. After a stable baseline period of at least 3 min, the 24 patients were received 0.1 mg/kg cisatracurium twice the 95% effective dose ($2 \times ED_{95}$). The following parameters were collected and compared; (1) lag time (time from start of muscle relaxant administration until the first measurable neuromuscular block (NMB), (2) onset time (time from start of muscle relaxant administration until maximal NMB), (3) assessing the recovery period by; train of four (TOF) 0.25, 0.50, 0.75 and 0.90 (time to reach a TOF ratio of 25%, 50%, 75% and 90%, respectively). No top-up doses of muscle relaxants were given.

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Results: There was no statistical difference between both studied groups as regard the demographic data of the patients, the lag time, the onset time, TOF 0.25, 0.5, 0.75 and 0.9 ratios using either EMG or KMG. In addition, there is excellent degree of agreement between EMG and KMG in measuring TOF ratio during both induction and recovery of muscle relaxants.
Conclusions: KMG showed an excellent degree of agreement with EMG for determination of onset and recovery of NMB in children.

1. Introduction

There are a limited number of studies compared KMG and EMG in clinical practice but none of these studies compared these two devices in children, or evaluated the effect of the type of the muscle relaxant on data obtained by KMG versus EMG.

This study was performed to determine whether data obtained from KMG can be interchanged with data obtained from EMG in children during general anesthesia. Adequate control of the duration and quality of neuromuscular blockade during surgery is essential for safe and successful surgery. Inadequate paralysis can endanger patients, particularly during thoracic and abdominal surgery [1–6]. Therefore, there is a growing understanding that more attention should be paid to objective monitoring of the degree of neuromuscular block during and after anesthesia and to the problems of residual curarization [7–12].

Electrical nerve stimulation is by far the most commonly used method in clinical practice. Available methods for objective neuromuscular monitoring is mechanomyography (MMG), EMG, KMG, phonomyography, and acceleromyography [13–15].

MMG has long been regarded as the gold standard of neuromuscular monitoring in that it measures the actual force created by muscle contraction. However, it has limitations. It was found that data obtained from EMG did not differ significantly from that obtained from MMG [16]. So EMG has replaced MMG as a standard neuromuscular monitoring in clinical practice [16].

KMG has been available for some years in the form of the NMT-Mechanosensor integrated in the Datex anesthetic machine. It consists of a molded plastic device which can be applied into the groove of the thumb and forefinger by use of adhesive tape. In addition, as known for other methods such as acceleromyography [17], attachment of the arm to an arm board may increase the precision of measurement. Some studies have shown that its agreement with MMG for scientific purposes might be limited with unacceptably wide limits of agreement [18] in clinical circumstances. It can be used reasonably well to detect time to tracheal intubation and recovery of NMB [18,19].

2. Patients and methods

After Ethics Committee approval parents written informed consent was taken this study was carried out on 24 pediatric patients of both sexes undergoing elective surgery under general anesthesia in Suez Canal University Hospital in the routine surgical lists. This study was a randomized, comparative clinical trial.

3. Patients

3.1. Inclusion criteria

ASA I and ASA II patients aged 2–6 years of both sexes with normal body mass index (BMI) (18–25 kg/m^2) who undergoing body surface operations, that do not require intense muscle relaxation.

3.2. Exclusion criteria

Patients with any disorders of the cardiovascular, hepatic, renal, small joint arthritis or neuromuscular systems known from history or clinical examination and investigations, patients who had taken, anticonvulsants or oral muscle relaxants, medication known to interact with neuromuscular blocking drugs, e.g. antibiotics (aminoglycosides, tetracyclines), antiarrhythmics (calcium channel blockers, quinidine) and magnesium sulfate .patients in whom difficult intubation was expected, and major operations, upper limb or thoracic operations were excluded from the study.

4. Methods

Pre-operative assessment was carried out in the pre-operative outpatient anesthesia clinic in Suez Canal University Hospital, The patient's age, sex, BMI & ASA status and type of surgery were recorded.

4.1. Anesthesia protocol

All patients were premedicated using 0.5 mg/kg midazolam per os 30–60 min preoperatively in the pre-operative holding area. Thereafter, cannulation of the patient by 22 or 20 gauge cannula was performed. Monitoring equipments (Datex-Ohmeda A/S 5™) were attached to the patient including 3 leads ECG, automatic non-invasive blood pressure, pulse oximetry; anesthetic gas monitoring and temperature probe after induction of anesthesia.

Both arms were comfortably positioned on arm boards. The area overlying the ulnar nerve at the wrist, where the electrodes to be placed, is cleaned by alcohol swap to ensure adequate contact. The stimulating electrodes (Ag/AgCl ECG electrodes for children) were stuck to the skin, which had been

cleaned. The electromyogram was attached to one hand, while the kinetomyogram was attached to the other hand for simultaneous monitoring.

The stimulating electrodes were placed over the ulnar nerve, which is found directly radially from the tendon of the flexor carpi ulnaris muscle as it ends in the pisiform bone of the hand.

The NMT mechano-sensor consists of two quick-fit malleable plastic semicircular rings for the thumb and index finger with an interconnecting bending strip. The piezoelectric sensor pad, embedded in the bending strip, lies over the metacarpophalangeal joint of the thumb at the angle between the index finger and thumb. It is aligned with the ideal plane of the opposition movement of the thumb to the index finger. A narrow adhesive tape was used to fix the middle portion of the strip in place. The ring over the thumb was also tapped. This should not interfere with the free thumb movement.

The electromyogram electrodes were placed for stimulation of the ulnar nerve and for recording of the compound action potential from adductor pollicis previs muscle, using a second Datex-Ohmeda A/S 5 monitor.

Preoxygenation with 100% oxygen for 3 min. Induction of anesthesia with fentanyl 2 μg/kg and propofol 2 mg/kg followed by endo-tracheal intubation.

Anesthesia was maintained by isoflurane 1.2%. Ventilation by 50% oxygen in air, ventilation was adjusted to maintain end-tidal CO_2 in the range of 35–40 mm Hg. Patients were warmed to keep the temperature of both hands constant at $\geqslant 32$ °C and the core temperature $\geqslant 35$ °C by means of warmed IV fluids and warming blankets.

Readings of the heart rate (HR), arterial blood pressure (ABP), oxygen saturation (SpO_2), temperature (body core temperature through nasopharyngeal probe and skin temperature) and neuromuscular transmission sensors were continuously displayed in the monitors.

Neuromuscular monitoring was carried out by supramaximal TOF stimuli up to 80 mA from Datex-Ohmeda NMT sensor (2 Hz/0.5 s; pulse width 0.2 ms) every 10 s to stimulate the ulnar nerve via surface electrodes.

After a stable baseline period for at least 3 min, the 24 patients were randomly allocated into one of two groups, KMG group and EMG group using closed envelope method and received cisatracurium 0.1 mg/kg twice the 95% effective dose ($2\times ED_{95}$). The drug was prepared in a fixed volume of 5 ml.

The following parameters were collected and compared:

Lag time: time from start of muscle relaxant administration until the first measurable block TOF ratio 90%.
Onset time: time from start of muscle relaxant administration until maximal neuromuscular block.

Assessing the recovery period by:

TOF 0.25 = time to reach a TOF ratio of 25%.
TOF 0.50 = time to reach a TOF ratio of 50%.
TOF 0.75 = time to reach a TOF ratio of 75%.
TOF 0.90 = time to reach a TOF ratio of 90%.
Spontaneous recovery index (dur TOF 0.25–TOF 0.9).
No top-up doses of muscle relaxants were given.

Patients were allowed to recover spontaneously from the neuromuscular block until a stable recovery signal occurred, defined as TOF ratio of $\geqslant 0.9$ with response variation $\leqslant 5\%$ for 2 min.

At the end of surgery inhalational anesthesia was omitted, patient ventilated with 50% oxygen in air and the patient was extubated when TOF ratio $\geqslant 0.9$. Any unwanted events were recorded.

At the post anesthesia care unit, the patient was monitored for heart rate, blood pressure, oxygen saturation, conscious level and activity.

5. Results

5.1. Demographic data

The mean age of the patients was 3.71 ± 1.15 years. Regarding the weight of the patients, the mean weight of the patients was 15.84 ± 2.86 kg. Regarding sex distribution, the frequency of male patients was 14 (58.33%) and the frequency of female patients was 10 (41.67%). As regarding ASA state of the patients, ASA I patients represented about 62.5%, while ASA II patients represented about 37.5%.

Pharmacodynamic time variables using EMG and KMG in both studied groups (in seconds):

There was no statistical difference between both groups using EMG or KMG (Table 2). This was confirmed by a strong degree of agreement between KMG and EMG in both groups using correlation coefficient test.

5.1.1. Onset phase

After cisatracurium administration, the TOF ratio of both monitors started to decrease simultaneously. There was no significant difference in the lag and onset times measured by the two monitors. Full block was reached in all patients independent of the monitoring technique.

5.1.2. Recovery phase

Both monitors detected the start of recovery from NMB as well as TOF 0.25, 0.50, 0.75 and 0.90 with excellent limits of agreement (Table 2).

During recovery from NMB, the plotting of difference and mean of the two monitors in TOF 0.90 showed in Fig. 1. The correlation coefficient for the strength of agreement between both monitors was 0.992 (Table 1).

The plotting of difference and mean of the two monitors in TOF 0.75 showed in Fig. 2. The correlation coefficient for the

Table 1 Comparison between the two studied groups regarding the operative data.

	Patients	
	No.	%
ASA state		
ASA I	15	62.50
ASA II	9	37.50
Type of operations		
General surgery	6	25.00
Plastic surgery	2	8.33
ENT	11	45.83
Orthopedic	5	20.83

Table 2 Pharmacodynamic time variables (in seconds) using EMG and KMG in both studied groups.

	EMG		KMG		Mean difference	Mean (EMG + KMG)/2	*t*	*p* Value	α *c*
	Mean	SD	Mean	SD					
Lag time	48.8	15.4	52.5	17.0	−3.70	50.65	0.8	0.43	0.958
Onset time	186.3	54.1	191.3	55.5	−5.01	188.8	0.3	0.77	0.995
TOF 0.25	25.4	3.4	25.8	3.5	−0.40	25.63	0.4	0.69	0.986
TOF 0.50	45.5	4.6	45.8	4.9	−0.24	45.63	0.36	0.72	0.990
TOF 0.75	55.14	5.47	55.63	5.27	−0.48	55.38	0.4	0.68	0.978
TOF 0.90	66.62	6.60	67.17	6.82	−0.55	66.90	0.3	0.67	0.992
Dur TOF 0.25–TOF 0.9	30.60	2.50	30.50	1.80	0.10	30.55	0.76	0.47	–

EMG = Electromyography, KMG = Kinemyography.
Insignificant *p*-value > 0.05.
α *c* = Correlation coefficient description for strength of agreement: <0.6 = unsatisfactory; 0.6–0.9 = satisfactory; 0.91–1 = excellent.

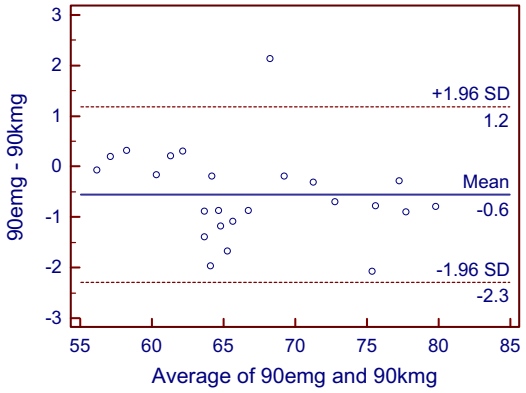

Figure 1 Bland and Altman scatter-plot of the difference between the TOF 0.90 of the EMG and KMG against the mean of the two measurements during recovery from NMB. The middle dotted line represents the bias.

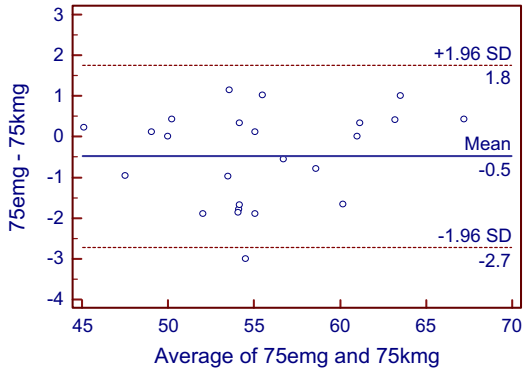

Figure 2 Bland and Altman scatter-plot of the difference between the TOF 0.75 of the EMG and KMG against the mean of the two measurements during recovery from NMB. The middle dotted line represents the bias.

strength of agreement between both monitors was 0.978 (Table 2).

The plotting of difference and mean of the two monitors in TOF 0.50 showed in Fig. 3. The correlation coefficient for the strength of agreement between both monitors was 0.990 (Table 2).

The plotting of difference and mean of the two monitors in TOF 0.25 showed in Fig. 4. The correlation coefficient for the strength of agreement between both monitors was 0.986 (Table 2).

6. Discussion

Monitoring the action of NMB drugs is one of the essential components in the practice of anesthesiology. In this study, the lag time for cisatracurium was 48.8 ± 15.4 s when monitored with the EMG and 52.5 ± 17 s when monitored with the KMG, with no statistical difference between the two monitors. In addition, there was a strong agreement between the KMG and EMG in detecting the lag time of cisatracurium using correlation coefficient test (α *c* = 0.95).

The lag time for cisatracurium in the presenting study was comparable to that of the study by Carroll et al. [20] in comparing the NMB effects and reversibility of cisatracurium

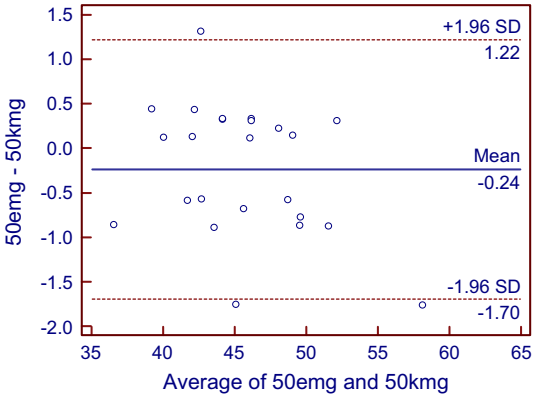

Figure 3 Bland and Altman scatter-plot of the difference between the TOF 0.50 of the EMG and KMG against the mean of the two measurements during recovery from NMB. The middle dotted line represents the bias.

and atracurium. They found that the median lag time of cisatracurium 0.1 mg/kg was 48 s with a range from to 30 to 60 s. These findings were supported also by results of Kim et al. [21] where the lag time of cisatracurium 0.1 mg/kg was 42 (36–48) seconds. Naguib et al. [22] also compared the clinical

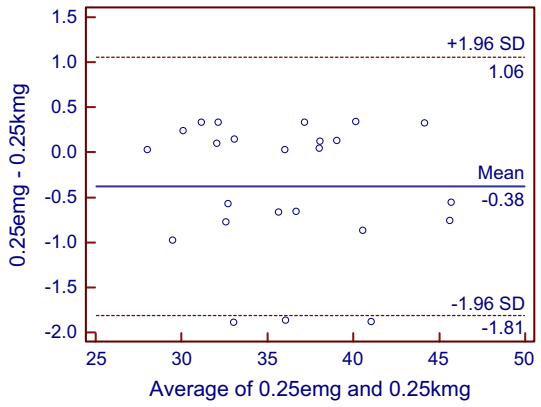

Figure 4 Bland and Altman scatter-plot of the difference between the TOF 0.25 of the EMG and KMG against the mean of the two measurements during recovery from NMB. The middle dotted line represents the bias.

pharmacology of cisatracurium and rocuronium and found that the lag time of cisatracurium 0.1 mg/kg was 45 ± 12 s.

When comparing the EMG and KMG in detecting the lag time of cisatracurium, there was no statistical difference between the two monitors. In addition, there was a strong degree of agreement between KMG and EMG in detecting the lag time of cisatracurium using the correlation coefficient.

In the current study, the onset time for cisatracurium was 186.3 ± 54 s when monitored with EMG, and 191 ± 55.5 s when monitored with KMG, with no statistical difference between the two monitors in detecting the onset time of cisatracurium. Moreover, there was a strong degree of agreement between KMG and EMG in detecting the onset time of cisatracurium since the correlation coefficient (α *c*) was 0.995.

These finding were supported by results of Carroll et al. [20] during comparing the neuromuscular blocking effects and reversibility of cisatracurium and atracurium where the median onset time of cisatracurium 0.1 mg/kg was 162 s with a range from to 114 to 246 s.

Also, Mellinghoff et al. [23] compared the cisatracurium and atracurium, and found that the onset time of cisatracurium 0.1 mg/kg was 186 ± 60 s. In a further study done by Imbeault et al. [24] that assessed the pharmacokinetics and pharmacodynamics of a 0.1 mg/kg cisatracurium in children during N_2O/O_2/propofol anesthesia, the onset time was 150 ± 48 s. This shorter onset time may be due to the use of higher dose of induction agent, propofol up to 4 mg/kg, and N_2O/O_2 (70:30) and may be explained also by use of different measuring tool, where they used the MMG in form of relaxometer.

However in the study of Kim et al. [21] the onset time of cisatracurium 0.1 mg/kg was 234 (180–288) seconds [mean (95% confidence intervals)]. The short onset time of cisatracurium in the present study could be attributed to a more rapid distribution of cisatracurium in children than in adult. Therefore, the peak concentration and maximal blocking effect of cisatracurium and the short onset time were produced sooner in children than in adults.

In this study, the time to reach a TOF ratio of 25% for cisatracurium was 35.8 ± 4.9 min when monitored with EMG and 36.4 ± 5.0 min when monitored with KMG, with no statistical difference between the two monitors in detecting the time to reach a TOF ratio of 25% of cisatracurium .

This result was supported by the findings of Lepage et al. [25] as they studied the pharmacodynamic dose–response and safety of cisatracurium in adult surgical patients during N_2O–O_2–opioid anesthesia, where the median time taken for 25% recovery of 0.1 mg/kg cisatracurium was 33 min with the range of 22–50 min. Also, Imbeault et al. [24] found that the recovery of cisatracurium 0.1 mg/kg to T25% time was 37.6 ± 10.2 min.

However, Carroll et al. [20] during studying the NMB effects and TOF fade of cisatracurium compared with other non-depolarizing relaxants, found that the median time from 0.1 mg/kg cisatracurium injection to the recovery of a TOFR of 0.25 was 41 (20.6–50.0) min.

In addition, Hans et al. [26] during comparing the recovery from NMB after an intubating dose of cisatracurium and rocuronium in adults found that the time from 0.1 mg/kg cisatracurium injection to the recovery of a TOFR of 0.25 was 49.8 ± 5.3 min. In their study, anesthesia was induced with IV sufentanil 0.15 μg kg^{-1}, ketamine 0.15 mg kg^{-1} and propofol 2 mg kg^{-1} and maintained with sevoflurane (1.5–2% end tidal) and 60% nitrous oxide in oxygen. Neuromuscular transmission was monitored at the wrist by accelerometry using the TOF-Guard monitor.

In the present study, the time to reach a TOF ratio of 50% for cisatracurium was 45 ± 4.6 min when monitored with EMG, and 47.8 ± 4.8 min when monitored with KMG, with no statistical difference between the two monitors in detecting the time to reach a TOF ratio of 50% of cisatracurium.

Similar results were recorded by Imbeault et al. [24] since they found that the mean time from injection of cisatracurium to recovery of the TOF ratio to 0.4 were 42.6 ± 8.3 min.

However, Hans et al. [26] in studying the recovery from neuromuscular block after an intubating dose of cisatracurium and rocuronium in adult patients found that the time from 0.1 mg/kg cisatracurium injection to the recovery of a TOFR of 0.5 was 61 ± 6.2 min. In their study, anesthesia was induced with IV sufentanil 0.15 μg kg^{-1}, ketamine 0.15 mg kg^{-1} and propofol 2 mg kg^{-1} and maintained with sevoflurane (1.5–2% end tidal) and 60% nitrous oxide in oxygen. Neuromuscular transmission was monitored at the wrist by accelerometry using the TOF-Guard monitor.

In this study, the time to reach a TOF ratio of 75% for cisatracurium was 55.0 ± 5.4 min when monitored with EMG, and 55.6 ± 5.3 min when monitored with KMG, with no statistical difference between the two monitors in detecting the time to reach a TOF ratio of 75% of cisatracurium.

This finding was in accordance with the results Lepage et al. [25] in studying pharmacodynamic dose–response and safety study of cisatracurium in adult surgical patients during N_2O–O_2–opioid anesthesia, where the median time taken for TOF 0.7 recovery of 0.1 mg/kg cisatracurium was 53 min with the range of 32–72 min. Also, Meretoja et al. [27] in assessing cisatracurium during halothane and balanced anesthesia in children found that the median time of 0.1 mg/kg cisatracurium to the recovery of TOF ratio to 0.7 was 56.5 (38.3–61.2) min.

In addition, Jellish et al. [28] agree with the present result in studying the recovery from neuromuscular blockade after both bolus and prolonged infusions of cisatracurium or rocuronium, where they established the median time to recovery of

TOF ratio to 0.75 was 50.1 (31.4–59.5) min after bolus injection of 0.1 mg/kg cisatracurium.

However, Imbeault et al. [24] found that the recovery to TOF ratio to 0.7 was 49.1 ± 9.2 min for cisatracurium 0.1 mg/kg dosage. Meretoja et al. [27] in assessing cisatracurium during halothane and balanced anesthesia in children found that the median time of 0.1 mg/kg cisatracurium to the recovery of TOF ratio to 0.7 was 56.5 (38.3–61.2) min. Further, Maybauer et al. [29] in studying the incidence and duration of residual paralysis at the end of surgery after multiple administrations of cisatracurium and rocuronium, the recovery time of 0.1 mg/kg cisatracurium till TOFR of 0.7 was 44 ± 8 min. Also, Amin et al. [30] in a comparative study of neuromuscular blocking and hemodynamic effects of rocuronium and cisatracurium under sevoflurane or total intravenous anesthesia, found that the time till recovery of 0.1 mg/kg cisatracurium till TOF 0.75, was 44 ± 6.4 min.

Moreover, Maybauer et al. [29] in evaluating the incidence and duration of residual paralysis at the end of surgery after multiple administrations of cisatracurium and rocuronium, the recovery time of T4/T1 to 0.7 was 58 ± 28 min following 0.6 mg/kg rocuronium.

In this study the time to reach a TOF ratio of 90% for cisatracurium was 66.4 ± 6.6 min when monitored with EMG, and 67.0 ± 6.8 min when monitored with KMG, with no statistical difference between the two monitors in detecting the time to reach a TOF ratio of 90% with cisatracurium.

This result was supported by Barrio et al. [31] in studying the neuromuscular recovery of rocuronium and cisatracurium after early, late or no reversal with neostigmine, the recovery of TOF ratio to 0.9 was 62.2 ± 8.8 min. Additionally, Carroll [20] in assessing the neuromuscular blocking effects and train-of-four fade with cisatracurium, supported our results as the time to TOF 0.8 after cisatracurium 0.1 mg/kg was 65 (39.6–77.7).

Imbeault et al. [24] in 2005 found that the recovery to TOF ratio to 0.9 was 56.6 ± 11 min of cisatracurium 0.1 mg/kg. In their study, the mean age of subjects was 3.7 years and anesthesia was induced with a bolus dose of fentanyl (1–2 μg/kg) and propofol (2–4 mg/kg) as well as maintained with propofol (150 μg/kg/min) and N_2O/O_2 (70:30).

Moreover, Maybauer et al. [29] found that the recovery time of 0.1 mg/kg cisatracurium till TOFR of 0.9 was 51 ± 8 min. Anesthesia was induced with propofol (1.5–2.5 mg/kg) and fentanyl (4–8 μg/kg), and was maintained with propofol (5–10 mg/kg/h) and remifentanil (0.05–2 μg/kg/min). They use repeated doses of cisatracurium rather than a single bolus dose.

Furthermore, Carroll et al. [20] in 1998 compared the NMB effects and reversibility of cisatracurium and atracurium where the median recovery time to TOF 0.8 after cisatracurium 0.1 mg/kg was 74 min with a range from 62 to 86 min. However there was some limitations in our study, first was that we compared KMG versus EMG using the same NMT module for Datex ohmeda monitor that may explain the excellent degree of agreement between the two sensors. Second limitation was that the use of pediatric KMG sensor is limited to patient not more than 20 kg, according to the manufacture guide so in using KMG in clinical practice we cannot use pediatric sensor in patients heavier than 20 kg till adult age group where adult sensor is used.

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