Comparison of two electromyography-based neuromuscular monitors, AF-201P and TetraGraph, in rocuronium-induced neuromuscular block: A prospective comparative study

日本大学医学部麻酔科学系麻酔科学分野

佐藤　英恵

申請年　２０２２年

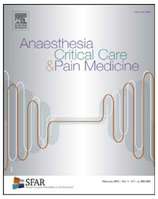
指導教員　鈴木　孝浩

Anaesth Crit Care Pain Med 41 (2022) 101145

Contents lists available at ScienceDirect

Anaesthesia Critical Care & Pain Medicine

journal homepage: www.elsevier.com



Original Article

Comparison of two electromyography-based neuromuscular monitors, AF-201P and TetraGraph, in rocuronium-induced neuromuscular block: A prospective comparative study

Hanae Sato [a], Hajime Iwasaki [a,*], Akira Doshu-Kajiura [a], Seidai Katagiri [a], Shunichi Takagi [a], Sarah Kyuragi Luthe [b], Takahiro Suzuki [a]

[a] *Department of Anesthesiology, Nihon University School of Medicine, 30-1 Oyaguchi, Kamicho, Itabashi-Ku, Tokyo 173-8610, Japan*
[b] *Department of Anesthesia, Indiana University School of Medicine, 1130 W. Michigan St., Fesler Hall 204, Indianapolis, IN 46202, USA*

ARTICLE INFO

Article history:
Available online 31 August 2022

Keywords:
AF-201P
Electromyography
Neuromuscular monitoring
Rocuronium
TetraGraph

ABSTRACT

Background: The study aimed to compare the responses obtained simultaneously from the newly developed electromyography (EMG)-based neuromuscular monitors, AF-201P and TetraGraph^{TM}, during rocuronium-induced neuromuscular block.

Methods: Twenty patients were enrolled in this study. During total intravenous general anesthesia, train-of-four (TOF) responses following 0.9-mg/kg-rocuronium administration were monitored at the abductor digiti minimi muscle with AF-201P and TetraGraph on the contralateral arms. Sugammadex 2 mg/kg was administered when both devices showed TOF counts (TOFC) = 2. The primary outcome was time from rocuronium administration to the first appearance of the post-tetanic count (PTC) response (first PTC). The secondary outcomes were supramaximal current, baseline compound muscle action potential, onset time, time to TOFC = 1, time to TOFC = 2, and time from sugammadex administration to TOF ratio ≥ 0.9. We used the paired *t*-test and Wilcoxon signed-rank test to analyze parametric and non-parametric data, respectively. $P < 0.05$ defined statistical significance.

Results: A total of 19 patients were analyzed. The supramaximal current was significantly lower with AF-201P than TetraGraph (31.7 ± 13.2 *vs.* 43.2 ± 8.2, $p = .002$). The time to first PTC (24.9 ± 9.4 *vs.* 27.3 ± 8.9 min, $p = .026$), time to TOFC = 1 (42.3 ± 9.0 *vs.* 45.1 ± 10.4 min, $p = .03$), and time to TOFC = 2 (52.0 ± 10.5 *vs.* 54.6 ± 11.7 min, $p = .014$) were significantly faster with AF-201P than with TetraGraph. There were no significant differences in the other outcomes between the devices.

Conclusions: AF-201P showed faster recovery of rocuronium-induced neuromuscular block compared with TetraGraph.

© 2022 Société française d'anesthésie et de réanimation (Sfar). Published by Elsevier Masson SAS. All rights reserved.

1. Introduction

Acceleromyography (AMG) has been used to objectively assess neuromuscular function for many years. However, it is limited by the need for normalization of the results to obtain a reliable measurement, since the baseline train-of-four (TOF) ratio often exceeds 100%, which is termed as "reverse fade" [1,2]. Although AMG results may be similar to mechanomyography (MMG) under some circumstances, under other circumstances there are significant differences; for this reason, AMG and MMG results should not be considered to be interchangeable [1].

Not all electromyography (EMG) monitors produce reliable results [3]. However, a properly functioning EMG monitor is considered by some experts to be the best alternative for routine neuromuscular monitoring [2,4]. In recent years, several manufacturers have introduced new EMG-based neuromuscular monitors [4–9]. AF-201P (Nihon-Kohden, Inc., Tokyo, Japan) and TetraGraph^{TM} (Senzime, Uppsala, Sweden) are clinically available EMG-based neuromuscular monitors that evoke and measure muscle compound action potentials via a single-use stimulating and sensing electrode. According to comparative studies between AMG and the two EMGs, AMG showed significantly faster recovery than TetraGraph [4,6,8], while AMG and AF-201P showed similar recovery [7]. Based on our clinical experience and these previous reports, we hypothesized that AF-201P would show faster recovery

---

[*] Corresponding author.
E-mail address: iwasaki.hajime@nihon-u.ac.jp (H. Iwasaki).

https://doi.org/10.1016/j.accpm.2022.101145
2352-5568/© 2022 Société française d'anesthésie et de réanimation (Sfar). Published by Elsevier Masson SAS. All rights reserved.

from the neuromuscular block as compared to TetraGraph. We, therefore, aimed to compare the two new EMG-based neuromuscular monitors, AF-201P and TetraGraph, during recovery of rocuronium-induced neuromuscular block.

2. Materials and methods

2.1. Study design

This study was approved by our Institutional Clinical Research Ethics Committee on the 11th of June 2021 (RK-210608-5). The trial was registered in the University Hospital Medical Information Network on the 22nd of June 2021 (registration number UMIN000044624, principal investigator: Hanae Sato). Written informed consent was obtained from all patients participating in the study. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.2. Study population

Patients aged $\geq$ 20 years old undergoing surgery under general anesthesia were enrolled in the study. We excluded patients with American Society of Anesthesiologists physical status class $\geq$ IV, a history of allergic reactions to neuromuscular blocking agents, hepatic disorders, and neuromuscular disorders. Additionally, patients receiving medications known to interfere with neuromuscular function were excluded.

2.3. Perioperative management

After arrival to the operating room, standard monitors (electrocardiogram, non-invasive blood pressure, and pulse oximetry) were applied to all patients. Intravenous access was established on the forearm or in the dorsal venous network of the hand. After preoxygenation, the patients were anesthetized using total intravenous anesthesia with propofol, remifentanil, and fentanyl, targeting a bispectral index of 40–50.

2.4. Neuromuscular management

AF-201P and TetraGraph were applied on contralateral arms after induction of anesthesia and prior to rocuronium administration. The monitor's location (dominant or non-dominant arm) was at the discretion of the attending anesthesiologist.

AF-201P was first placed on one arm (Fig.1A), following which TetraGraph was placed on the contralateral arm (Fig.1B). After cleansing the skin where the sensor will be attached using alcohol wipes, single-use surface electrodes for AF-201P (NM-345Y, Nihon–Kohden, Inc.) and TetraGraph (TetraSens™, Senzime) were placed to stimulate the ulnar nerve, with the sensing electrode component being placed on the abductor digiti minimi (ADM) muscle, according to the manufacturer's instructions. Calibration was performed after application of the device. TOF measurements were repeated at intervals of 15 s and 20 s with the AF-201P and TetraGraph, respectively.

After confirming stable baseline TOF responses for a few minutes, the baseline TOF ratio was recorded and rocuronium 0.9 mg/kg was administered. Post tetanic count (PTC) stimulations were performed every 6 min during a TOF count (TOFC) = 0. To prevent acceleration of TOF recovery [10], PTC stimulation was stopped once PTC responses appeared for each device. We measured spontaneous recovery of the rocuronium-induced neuromuscular block until three continuous TOF counts (TOFC) = 2 were observed with both devices. Additional doses of rocuronium 0.1 to 0.2 mg/kg were administered to maintain the TOFC $\leq$ 2 if necessary. At the end of the surgery, sugammadex 2 mg/kg was administered when three continuous TOFCs = 2 were observed with whichever device recovered later. TOF measurements were discontinued after confirming complete recovery of neuromuscular function (when twitch heights of TOF were stable and no further recovery was observed).

Intraoperatively, an upper body forced-air warming device was used throughout the surgery to ensure that core and peripheral temperatures were kept above 35 °C and 32 °C, respectively, and end-tidal carbon dioxide values were maintained at 35–40 mmHg.

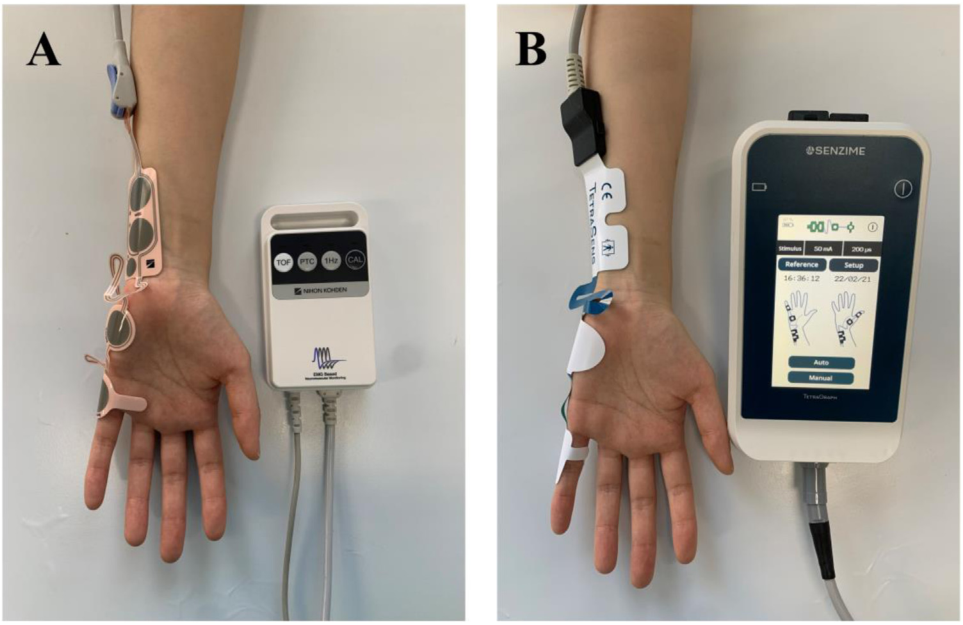


Fig. 1. Setup of the two devices for monitoring neuromuscular block at the abductor digiti minimi muscle. (A) AP-201P. (B) TetraGraph™.

Table 1
Results of the primary and secondary outcomes of the study.

Outcomes	AF-201P	TetraGraph	Mean difference	95% CI	*P* value
Supramaximal current (mA)	31.7 ± 13.2	43.2 ± 8.2	11.4	4.86 to 48.0	.002
Baseline compound muscle action potential (mV)	11.9 ± 3.2	10.6 ± 4.2	−1.3	−2.79 to 0.19	.083
Onset time (s)	83 (65−201)	81 (49−219)	NA	NA	.83
Time to first PTC (min)	24.9 ± 9.4	27.3 ± 8.9	2.44	0.33 to 4.55	.026
Time to TOF count = 1 (min)	42.3 ± 9.0	45.1 ± 10.4	2.74	0.3–5.17	.03
Time to TOF counts = 2 (min)	52.0 ± 10.5	54.6 ± 11.7	2.65	0.61 to 4.7	.014
Time to TOF ratio ≥ 90% (s)	78.0 (36−197)	82.0 (43−184)	NA	NA	.73

Results are expressed as mean ± SD or median (range). We used the paired t-test for parametric data and Wilcoxon signed-rank test for non-parametric data.
CI, confidence interval; NA, not applicable; TOF, train-of-four; PTC, post-tetanic count.

2.5. Outcomes of the study

The study's primary outcome was time from administration of rocuronium to the first appearance of the PTC response (first PTC). The secondary outcomes were supramaximal current, baseline compound action potential, time from administration of rocuronium to TOFC = 0 (onset time), time from administration of rocuronium to the first reappearance of TOFC = 1 (time to TOFC = 1), time from administration of rocuronium to the first reappearance of TOFC = 2 (time to TOFC = 2), and time from sugammadex administration to TOF ratio ≥ 90%.

2.6. Sample size and statistical analysis

To estimate sample size, we used previous first PTC appearance data of 25.4 ± 8.6 min, which is the average ± standard deviation (SD) time for the first appearance of PTC following 0.6-mg/kg-rocuronium administration [11]. We considered a 30% difference in the first reappearance time (difference of approximately three cycles of PTC stimulation) observed between the two monitors to be clinically significant. To provide adequate power (80%) with an alpha error of 5%, it was necessary to include 19 patients in this study. We determined our sample size to be 20 patients in anticipation of dropouts. Parametric and non-parametric data are expressed as mean ± SD and median (range), respectively.

We used the D'Agostino–Pearson omnibus test to determine whether the data were normally distributed. The paired *t*-test was used for parametric data and Wilcoxon signed-rank test was used for non-parametric data, to analyze differences in outcomes between the two devices. To assess the agreement between the two devices, we used Bland-Altman analysis [12] and the biases and limits of agreement for onset and recovery times were calculated. All statistical analyses were performed using GraphPad Prism® version 7.03 (GraphPad Software, Inc., La Jolla, CA), and a *P*-value of <.05 was considered statistically significant.

3. Results

A total of twenty patients (aged 22–59 years) were enrolled in this study between June 2021 and November 2021. One patient who progressed from PTC = 0 to TOFC = 1 within 6 min (during the interval of PTC stimulation) was excluded from the analysis. Data from 19 patients (females/males: 14/5) were included in the analysis. Patients' characteristics of age, weight and body mass index were 35.3 ± 11.9 years, 57.2 ± 11.2 kg and 21.3 ± 3.3 kg/m^2, respectively. The types of surgeries included oral surgery (n = 11), otolaryngology surgery (n = 4), orthopedic surgery (n = 3) and gynecological surgery (n = 2). The median duration of surgery was 116.5 min (43–214).

Results of the primary and secondary outcomes of the study are shown in Table 1. Recovery time from rocuronium administration to the first PTC appearance ($p = .026$), TOFC = 1 ($p = .03$), and TOFC = 2 ($p = .014$) were significantly faster with AF-201P than with TetraGraph. There were no significant differences in onset and recovery times from the administration of sugammadex to a TOF ratio ≥ 90% between AF-201P and TetraGraph. The supramaximal current was significantly lower with AF-201P than TetraGraph ($p = .002$). There were no significant differences in baseline compound muscle action potentials between the devices.

Results of Bland-Altman analyses and scatter plot of individual values are shown in Fig. 2. Bland–Altman analyses showed acceptable ranges of limits of agreement (difference calculated by AF-201P subtracted by TetraGraph) of the two devices. The biases and limits of agreement [95% confidence interval] were −3.7 ± 36.8 [−75.8–68.3] for the onset, −2.4 ± 4.4 [−11.0–6.1] for the time to first PTC, −2.9 ± 5.3 [−13.3–7.5] for the time to TOFC = 1,

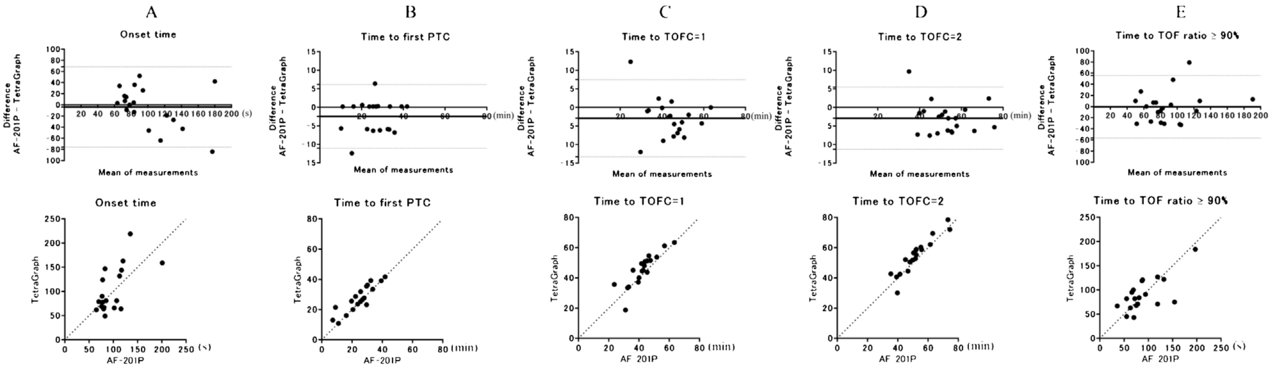


Fig. 2. Upper panel: Bland–Altman plot illustrating the differences (difference calculated by AF-201P subtracted by TetraGraph) of (A) onset time, (B) time to first post-tetanic count (PTC) response, (C) time to train-of-four count (TOFC) = 1, (D) time to TOFC = 2, and (E) time to TOF ratio ≥ 90% recovery time between the two devices. Solid horizontal line represents the bias, and dotted horizontal lines represent the upper and lower limits of agreement with 95% confidence intervals. Lower panel: Scatter plot of individual values. A linear regression slope of 1 is represented by a dotted line.

−2.9 ± 4.3 [−11.3–5.5] for the time to TOFC = 2, and −0.4 ± 28.6 [−56.5–55.7] for the recovery time to TOF ratio ≥ 90%, respectively.

4. Discussion

This comparative clinical trial found that AF-201P showed significantly faster recovery than TetraGraph in all patients in terms of the time to first PTC appearance, time to reappearance of TOFC = 1, and time to TOFC = 2. A recent comparative study between AF-201P and the conventional AMG-based monitor TOF-Watch® SX demonstrated that AF-201P showed slightly faster recovery than the TOF-Watch® SX during profound neuromuscular block [7]. On the other hand, comparative studies between TetraGraph and TOF-Watch® SX demonstrated that the TOF-Watch® SX overestimated recovery from neuromuscular block compared with TetraGraph [4,8]. The results of these previous studies are consistent with our results of faster recovery with AF-201P than TetraGraph. However, the observed mean differences of approximately 2.5 min in recovery time during profound and moderate neuromuscular block between the two devices in our study might not be clinically significant.

Although AF-201P and TetraGraph use the same electromyographic technologies, the devices have several differences. First, TetraGraph has a fixed noise filter threshold of 1 mV [4], while AF-201P has a default threshold of 0.7 mV. For AF-201P, the noise filter threshold is configurable from 0.3 to 3.0 mV only when it is connected to a specific display unit VA-201R (Nihon–Kohden, Inc.). The lower detection threshold with AF-201P as compared to TetraGraph might explain the significantly faster recovery during profound and moderate neuromuscular block in our study. However, management of noise is critical because if the noise filter threshold is too low, the noise can be misinterpreted as a correct muscle action potential. On the other hand, if the noise filter reduction is too high, compound muscle action potentials might be lost along with noise, causing the monitor to underestimate twitches [13]. Therefore, we believe the noise filter should be set at the threshold recommended by the manufacturer when using EMG.

Second, the calibration algorithm (setup of the supramaximal stimulation current) is different between the devices. According to manufacturer instructions of AF-201P, the calibration sequence starts at 30 mA and increases or decreases the current by 3 mA until the response does not show a more than 10% difference. It then sets the supramaximal current 3 mA higher. In contrast, according to the manufacturer instructions of TetraGraph, the calibration sequence starts at 10 mA and increases the current in 5 mA increments. It then sets the supramaximal current 20% higher than the current at which the response does not increase by more than 10%. The difference in the calibration sequence between the devices might explain the significantly higher supramaximal current with TetraGraph than AF-201P in our study. However, despite the difference in supramaximal current between the two devices, there were no differences in baseline compound muscle action potentials in our study.

Our study has several limitations. First, the two EMG monitors used in our study have not been previously compared to MMG, which is the “gold standard” of neuromuscular monitoring. Therefore, it is impossible to know whether the differences in the results from the two monitors are in the direction of being more correct or less correct. Second, we only compared the two devices based on the time required to reach a PTC = 1, a TOFC = 1, a TOFC = 2, and a TOF ratio ≥ 0.9. We did not compare the devices at PTC > 1, at TOFC of 3 or 4, or at TOF ratio less than 0.9. Therefore, our comparison of the performance of the two devices is limited to specific points in time, rather than over the full range of PTC, TOFC and TOF ratio. Third, the noise filter threshold was different between the devices. Although the threshold is configurable with AF-201P, we used the default threshold of 0.7 mV, as clinicians typically do not change the threshold setting. Further studies are required to confirm whether there is a difference between the devices when the same noise filter threshold of 1 mV is used. Forth, although we applied two monitors to the same patient, the location of the devices was at the discretion of the attending anesthesiologist and was not randomized to the dominant and non-dominant arms. However, according to previous reports [14–16], dominance/non-dominance and location of intravenous catheters and non-invasive blood pressure cuffs do not affect measurements of neuromuscular block. Finally, the two devices have different TOF stimulation intervals. Although the repeat interval of AF-201P is adjustable, we used the default setting of TOF stimulation interval (AF-201P: 15 s and TetraGraph: 20 s), as clinicians are unlikely to adjust the setting. This could potentially affect the results of onset and reversal times. According to a previous study, longer TOF stimulation intervals resulted in significantly slower onset times [17]. However, since there were no significant differences in onset times between the devices in our study, differences in TOF stimulation intervals might have had little impact on our study outcomes.

5. Conclusions

In conclusion, AF-201P showed faster recovery of rocuronium-induced neuromuscular block compared with TetraGraph in this study. Although it is essential to understand the different characteristics of these EMG-based monitors, the clinical significance may be limited.

Author’s contributions

Study design: HS, HI, ST, and TS.
Data collection: HS, HI, ADK, and SK.
Data analysis: HS, HI, and SKL.
Manuscript preparation: HS, HI, ADK, SK and SKL.
Editing the manuscript: ST and TS.
All authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

Hajime Iwasaki has received speaker fees from MSD, Inc., Japan, Nihon-Kohden, Inc., Japan and Fukuda-Denshi, Inc., Japan. Shunichi Takagi and Takahiro Suzuki have received speaker fees from MSD, Inc., Japan and Nihon-Kohden, Inc., Japan. Hanae Sato, Akira Doshu-Kajiura, Seidai Katagiri and Sarah Kyuragi Luthe have no competing interests.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. We would like to thank FORTE (https://www.forte-science.co.jp/) for English language editing. We also would like to thank Dr. Yohei Kawasaki PhD, Faculty of Nursing, Japanese Red Cross College of Nursing, Tokyo, Japan, for his support on statistical analyses.

References

[1] Iwasaki H, Nemes R, Brull SJ, Renew JR. Quantitative neuromuscular monitoring: current devices, new technological advances, and use in clinical practice. Curr Anesthesiol Rep 2018;8(2):134–44.

[2] Naguib M, Brull SJ, Kopman AF, Hunter JM, Fülesdi B, Arkes HR, et al. Consensus statement on perioperative use of neuromuscular monitoring. Anesth Analg 2018;127(1):71–80.

[3] Bussey L, Jelacic S, Togashi K, Hulvershorn J, Bowdle A. Train-of-four monitoring with the twitchview monitor electctromyograph compared to the GE NMT electromyograph and manual palpation. J Clin Monit Comput 2021;35(6):1477–83.

[4] Nemes R, Lengyel S, Nagy G, Hampton DR, Gray M, Renew JR, et al. Ipsilateral and simultaneous comparison of responses from acceleromyography- and electromyography-based neuromuscular monitors. Anesthesiology 2021;135(4):597–611.

[5] Bowdle A, Bussey L, Michaelsen K, Jelacic S, Nair B, Togashi K, et al. A comparison of a prototype electromyograph vs. a mechanomyograph and an acceleromyograph for assessment of neuromuscular blockade. Anaesthesia 2020;75(2):187–95.

[6] Iwasaki H, Yamamoto M, Sato H, Doshu-Kajiura A, Kitajima O, Takagi S, et al. A comparison between the adductor pollicis muscle using TOF-watch SX and the abductor digiti minimi muscle using TetraGraph in rocuronium-induced neuromuscular block: a prospective observational study. Anesth Analg 2022;135(2):370–5.

[7] Takagi S, Suzuki T, Nakatsuka H, Sasakawa T, Iwasaki H, Kotake Y, et al. Comparison of a new EMG module, AF-201P, with acceleromyography using the post-tetanic counts during rocuronium-induced deep neuromuscular block: a prospective, multicenter study. J Clin Monit Comput 2021. In press.

[8] Giudici G, Piccioni F, Proto P, Valenza F. A comparison of accelerometric monitoring by TOF Watch® SX and electromyographic monitoring by Tetragraph® for recovery from neuromuscular blockade. J Clin Anesth 2021;75110481.

[9] Iwasaki H, Sato H, Takagi S, Kitajima O, Luthe SK, Suzuki T. A comparison between the adductor pollicis muscle and the abductor digiti minimi muscle using electromyography AF-201P in rocuronium-induced neuromuscular block: a prospective comparative study. BMC Anesthesiol 2022;22(1):117.

[10] Brull SJ, Silverman DG. Tetanus-induced changes in apparent recovery after bolus doses of atracurium or vecuronium. Anesthesiology 1992;77(4):642–5.

[11] Kameyama Y, Takagi S, Seto K, Kajiwara I, Goto M, Kitajima O, et al. Efficiency of the TOF-Cuff™ for the evaluation of rocuronium-induced neuromuscular block and its reversal with sugammadex: a comparative study vs. acceleromyography. J Anesth 2019;33(1):80–4.

[12] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1(8476):307–10.

[13] Bowdle A, Michaelsen K. Quantitative twitch monitoring: what works best and how do we know? Anesthesiology 2021;135(4):558–61.

[14] Jeong JS, Kim KS, Lee HJ, Shim JC, Lee JC, Lee JH. The effect of hand dominance on neuromuscular monitoring at the adductor pollicis muscle. Korean J Anesthesiol 2013;65(1):33–6.

[15] Merle JC, Jurczyk M, D'Honneur G, Ruggier R, Duvaldestin P. Onset of neuromuscular block is the same if the ipsilateral or contralateral limb to the injection site is used for monitoring. Br J Anaesth 1995;74(3):333–4.

[16] Claudius C, Skovgaard LT, Viby-Mogensen J. Arm-to-arm variation when evaluating neuromuscular block: an analysis of the precision and the bias and agreement between arms when using mechanomyography or acceleromyography. Br J Anaesth 2010;105(3):310–7.

[17] Meretoja OA, Taivainen T, Brandom BW, Wirtavuori K. Frequency of train-of-four stimulation influences neuromuscular response. Br J Anaesth 1994;72(6):686–7.

Glossary

ADM: abductor digiti minimi
AMG: acceleromyography
EMG: electromyography
MMG: mechanomyography
PTC: post tetanic count
SD: standard deviation
TOF: train-of-four
TOFC: train-of-four count

主論文の要約

氏名：佐　藤　英　恵
博士の専攻分野の名称：博士（医学）
論文題名：Comparison of two electromyography-based neuromuscular monitors, AF-201P and TetraGraph, in rocuronium-induced neuromuscular block: A prospective comparative study
（電位感知型筋弛緩モニタ AF-201P と TetraGraph を用いた小指外転筋のロクロニウム筋弛緩回復過程の比較）

【はじめに】非脱分極性筋弛緩薬のロクロニウムは、気管挿管時や手術中の患者不動化のために使用される。ロクロニウムの効果は個人差が大きいため、定量的筋弛緩モニタに基づき、ロクロニウムを投与することで適切な筋弛緩状態を得ることが可能となり、さらに拮抗薬であるスガマデクスの至適量を滴定し、投与することで筋弛緩状態からの確実な回復を観察できる。スガマデクスの不適切な使用による残存筋弛緩や再クラーレ化は、抜管後の上気道閉塞による低酸素血症や咽喉頭機能低下による誤嚥などの重篤な呼吸器合併症を引き起こすため、定量的筋弛緩モニタによる評価は患者の安全管理のために重要である。これまで筋弛緩モニタには筋張力感知型や圧感知型など様々な測定方法が使用されてきたが、その中でも汎用性、簡便性、適応性などの観点より、加速度感知型モニタ（acceleromyography: AMG）が臨床麻酔において長年に渡り使用されてきた。AMG の場合、信頼できる測定結果を得るためには、装着時のコントロールデータによる標準化や preload としての手指の固定が必要となり、また測定部位への接触だけで測定不良となる等の欠点があった。近年、新たに電位感知型（electromyography: EMG）筋弛緩モニタが上市され、筋弛緩状態評価のためのデータの精確性とともに、AMG の問題点を補うことが可能となった。EMG 筋弛緩モニタにも数種の機種が存在する中、これまで機種間のデータの比較はされたことがなかった。先行研究において、AMG は Tetragraph™ より早い回復、AF-201P™ と同等の回復を示している。先行研究の結果と臨床経験より、AF-201P™ が Tetragraph™ よりも早い回復を示すという仮説を立てた。本研究は、EMG 筋弛緩モニタである AF-201P™ と TetraGraph™ で得られる筋弛緩反応を比較することを目的としたものである。

【方法】それぞれのモニタの専用電極（刺激電極および感知電極一体型）を左右の手関節付近で尺骨神経と小指外転筋上に装着し、全静脈麻酔下に尺骨神経に最大上刺激による 2Hz 四連（train-of-four: TOF、各刺激の名称：T1、T2、T3、T4）電気刺激を 15 秒ごとに加え、小指外転筋複合筋活動電位を導出した。ロクロニウム 0.9 mg/kg を単回静脈内投与し、TOF 反応が消失後は、6 分ごとにポストテタニックカウント（post-tetanic counts: PTC、TOF 刺激に反応しない深部遮断状態で、5 秒間の 50Hz テタヌス刺激を加え、その 3 秒後より 1Hz 単収縮刺激を連続して加えると、post-tetanic facilitation の原理により一時的に反応が認められ、その反応数をカウントする方法）を評価した。筋弛緩状態からの回復時、両モニタで TOF カウント＝2（T1、T2 に対する反応のみ確認された時点）が得られた時点で、スガマデクス 2 mg/kg を投与した。主要評価項目は、ロクロニウム投与から PTC が最初に出現するまでの時間とし、副次的評価項目は、最大上刺激電流値、複合筋活動電位コントロール値、ロクロニウムの作用発現時間、ロクロニウム投与から TOF カウント＝1 と 2 までの作用持続時間、スガマデクス投与から TOF 比≧0.9 までの回復時間とした。統計には対応のある t 検定とウィルコクソンの符号順位検定を使用し、$P<0.05$ を有意差ありと定義した。

【結果】本研究に登録した 20 名のうち、19 名のデータを分析した。

主要評価項目

初めて PTC が出現するまでの時間は、AF-201P™ で TetraGraph™ より有意に速かった。（24.9±9.4 分 vs. 27.3±8.9 分，P＝0.026）。

副次的評価項目

① 最大上刺激電流値：AF-201P™ で TetraGraph™ より有意に低値であった（31.7±13.2 mA vs. 43.2±8.2 mA, P=0.002）。

② 複合筋活動電位コントロール値: AF-201P™ と TetraGraph™ 間で有意差はなかった（11.9±3.2 mV vs. 10.6±4.2 mV, P=0.082）。

③ ロクロニウムの作用発現時間：AF-201P™ と TetraGraph™ 間で有意差はなかった（83[65-201]秒 vs. 81[49-219]秒, P=0.83）。

④ TOF カウント＝1 までの作用持続時間: AF-201P™ が TetraGraph™ より有意に速かった（42.3±9.0 分

vs. 45.1±10.4分, P=0.03)。

⑤ TOFカウント＝2までの作用持続時間: AF-201P™がTetraGraph™より有意に速かった（52.0±10.5分 vs. 54.6±11.7分, P=0.014)。

⑥ スガマデクス投与からTOF比≧0.9までの回復時間：AF-201P™とTetraGraph™間で有意差はなかった（78.0[36-197]秒 vs. 82.0[43-184]秒, P=0.73)。

【考察】本研究では、今後臨床麻酔で多用されるであろう２つのEMGモニタのデータを比較する目的で行ったが、AF-201P™でより早い回復を示すとの仮説のとおり、深部遮断を示すPTCや中等度筋弛緩状態を示すTOFカウント1-2までの回復時間において、同じEMG機種でありながら約2.5分の差を示した。Bland-Altman分析では、ほとんどのデータが誤差の許容範囲内に入り、2つのモニタの相関性が認められたが、バイアス値は小さいものの、AF-201P™が早期回復を示す結果となった。このTetraGraph™よりもAF-201P™において、ロクロニウム筋弛緩からの回復が早いというバイアスは、機種ごとの反応検出閾値や最大上刺激設定のためのキャリブレーションアルゴリズムの違い、TOF刺激頻度による影響が考えられる。反応検出閾値は、AF-201P™の方が低い（0.7mV vs. 1mV）ため、より早く複合筋活動電位を検出した可能性がある。キャリブレーションアルゴリズムの違いから、Tetragraph™がより大きい最大上刺激電流値を示したが(AF-201P™：31.7mA vs. Tetragraph™ ：43.2mA)、両機種とも同じ刺激電流値で測定した場合には、AF-201P™での検出が早まり、回復時間の差がさらに広がることも予想される。またTOF刺激頻度は、AF-201P™では15秒ごと、Tetragraph™では20秒ごとであり、AF-201P™でTOF刺激の頻度が高いため、その分、筋血流が増加、筋弛緩薬の排泄が増加し、筋弛緩からの回復が早まったとも考えられる。

本研究では、PTC回復時間あるいはTOFカウント1または2までの回復時間における平均差で2.5分前後の差を認めた。この差により、術中に深い筋弛緩状態を維持する場合と、筋弛緩の拮抗をする時点において、ロクロニウムやスガマデクスの投与量に違いが生じる可能性があるため注意が必要である。良好な手術ワーキングスペースを要する内視鏡手術などで、PTCを維持するような深い筋弛緩管理を維持する場合、AF-201P™モニタリングでは、TetraGraph™と比べて、ロクロニウム投与量が増加することが考慮され、過量投与や筋弛緩の遷延に繋がる可能性に留意が必要である。また今回の結果からは、AF-201P™でTOFカウント2に回復した場合、同時期のTetraGraph™ではTOFカウント1以下を示すことが推定され、その場合にはスガマデクスの投与量を4mg/kgに増加せねばならない。今回の研究では、遅く回復するTetraGraph™でTOFカウント2を示した際に、スガマデクス2mg/kgを投与しているため、全例で至適回復が得られているが、先述したような状況、つまりAF-201P™でTOFカウント2の際にスガマデクスを投与した場合、TetraGraph™側では過少投与となり得ないか、至適拮抗されるかを今後検討する必要があると考えられた。

本研究にはいくつかのリミテーションがある。まずは先述した機種ごとの反応検出閾値や最大上刺激、TOF刺激頻度が異なる点である。これを同一にした場合のデータを検証する必要がある。さらに本研究で使用されたEMG機器と、歴史的に筋弛緩モニタリングのゴールドスタンダードである力感知型筋弛緩モニタ（MMG）との比較がされていない。すでにMMG機種がなくなっている現状では解決できないが、歴史的にはMMGとEMGのデータには互換性があるとされてきた。先行研究でのEMGとAMGとの差を鑑みても、今回の結果はMMGに近い値を示しているものと考えている。また本研究ではPTC=1、TOFC=1、TOFC=2、TOF比≧0.9に達するまでの時間のみの比較であり、この特定の時点に限定されていることである。TOFカウント3以降の浅い筋弛緩状態での自然回復も比較する必要がある。左右の上肢で筋量や筋の運動性が異なれば、EMG測定に影響することが推定されるが、今回の研究ではこれら左右差を考慮していないことが挙げられる。AMGにおける筋弛緩モニタリングでは、血圧測定や静脈内カテーテル留置の左右差に対する影響はないといわれているが、EMGでの比較をすべくさらなる研究が必要である。

【結論】AF-201P™はTetraGraph™と比較して、ロクロニウム筋弛緩からの回復をより早く示す。