



# Pharmacokinetic simulation can detect erroneous TOF counts

Shinju Obara<sup>1</sup> · Ryota Suhara<sup>2</sup> · Masahiro Murakawa<sup>1,2</sup>

Received: 21 December 2023 / Accepted: 13 February 2024 / Published online: 2 March 2024  
© The Author(s) under exclusive licence to Japanese Society of Anesthesiologists 2024

**Keywords** Rocuronium · Pharmacokinetics · Train-of-four · Electromyography-based neuromuscular monitor

## Abbreviations

TOF Train-of-four

RoCE Rocuronium effect-site concentration

To the editor:

Monitoring the effects of muscle relaxants during anesthesia is clinically important to prevent adverse events [1], and is strongly recommended by clinical guidelines [2, 3]. Recently, electromyography-based neuromuscular monitors have become widely used in the clinical setting in Japan. This type of monitoring can be affected by various factors such as electrical noise conducted through the body. Thunderbeat (Olympus Medical Systems Corp., Tokyo, Japan) is a type of surgical scissors that can be used to perform both sealing and incision of vessels by simultaneously delivering bipolar and ultrasound energy. We herein report a case in which an erroneous train-of-four (TOF) count was displayed on a muscle relaxation monitor during surgery using Thunderbeat, although adequate muscle relaxation was achieved. Pharmacokinetic simulation of rocuronium was useful in discovering the error in the display.

A 52-year-old woman (body weight, 60 kg; height, 153 cm) with a history of depression was scheduled for laparoscopic hysterectomy. Before induction of anesthesia,

a disposable electromyogram electrode (NM-345Y, Nihon Kohden, Tokyo, Japan) was placed on the right arm according to the manufacturer's instructions. Standard vital signs were monitored with an integrated monitoring system (Lifescopre, Nihon Kohden). General anesthesia was induced with propofol 80 mg and fentanyl 0.1 mg. After calibration, intermittent monitoring of muscle relaxation was started using an electromyography-based neuromuscular monitor (AF-201P, Nihon Koden), followed by administration of rocuronium 50 mg. Anesthesia was maintained with sevoflurane and remifentanyl. Ultrasound-guided transversus abdominis plane and rectus sheath blocks were performed. The patient was placed in the lithotomy position. During surgery, 104 min after rocuronium administration an additional 10 mg of rocuronium was administered as the TOF count increased from 0 to 1. This response occurred when the simulated rocuronium effect-site concentration (RoCE), calculated using the Szenohradszky model [4] was 0.7 µg/mL. The TOF count subsequently returned to 0. In addition, 10 min later, the TOF count increased again to 1 while an incision was being made in the vagina. At that time, the RoCE was 1.7 µg/mL, which was considered too high for the TOF count to increase considering the previously recorded relationship between RoCE and muscle relaxation effect. When the Thunderbeat was activated (setting: Seal & Cut Level 1) during the TOF stimulation, the attending anesthesiologist observed that the stimulation response was interpreted as a myoelectric response. Consequently, the TOF count was displayed as 1 (Panel A in Fig. 1). When the Thunderbeat was not active, the TOF count was 0 (Panel B in Fig. 1). The patient's right arm was positioned parallel to her body, ensuring it remained uncompressed beneath the drapes. When the information window for the muscle relaxation monitor was opened, the monitor indicated that the signal was noise. (red arrow in Panel A). However, even when the window was closed, the TOF count persisted on the integrated monitor screen without the information that it was contaminated with noise while the Thunderbeat was

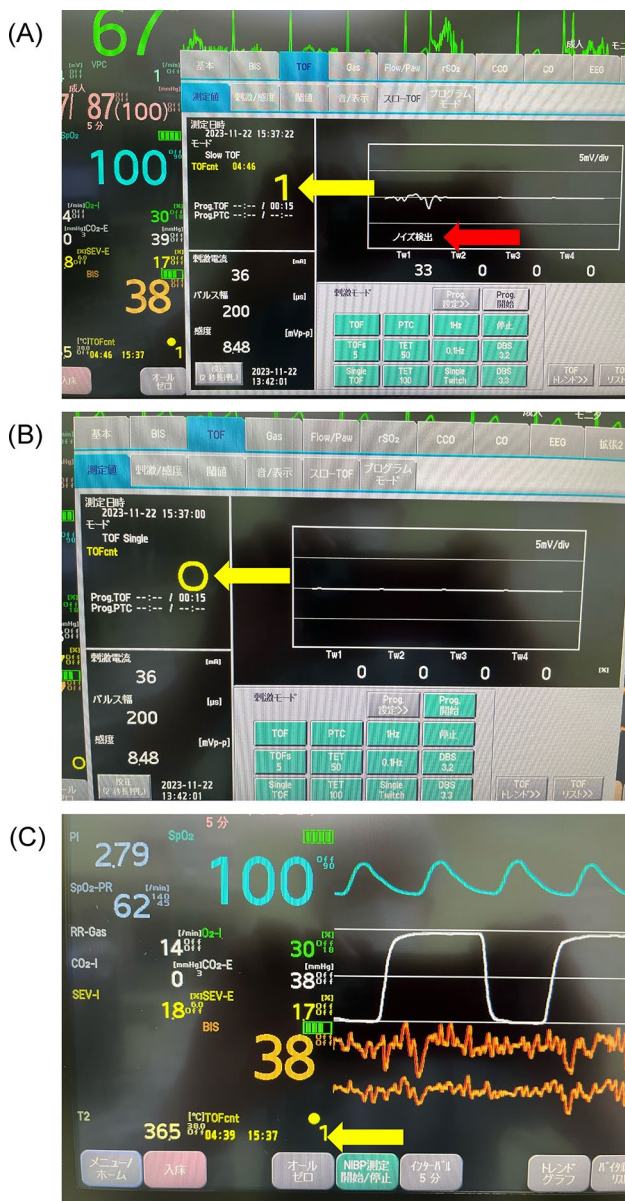
✉ Shinju Obara  
obashin99@gmail.com

Ryota Suhara  
srtjkrkhs0716@gmail.com

Masahiro Murakawa  
mamu\_ra\_3\_84@yahoo.co.jp

<sup>1</sup> Department of Anesthesiology, Center for Pain Management, Surgical Operation Department, Fukushima Medical University, Fukushima Medical University Hospital, 1 Hikarigaoka, Fukushima, Fukushima 960-1295, Japan

<sup>2</sup> Iwase General Hospital, 20 Kitamachi, Sukagawa, Fukushima 962-8503, Japan



**Fig. 1** **A** Integrated monitor screen with a pop-up window displaying muscle relaxation monitor data. Although noise is detected (red arrow), the TOF count is 1 (yellow arrow). **B** When the Thunderbeat is turned off, the TOF count returns to 0 (yellow arrow). **C** Default screen of the monitor, displaying the erroneous TOF count (yellow arrow). There is no indication of the potential effect of the noise on the screen

in use (Panel C in Fig. 1), and this data was also transmitted to, and recorded in, the electronic anesthesia record. Subsequently, the stage of the surgery that required the Thunderbeat was completed. Fifty-six minutes after the second administration of rocuronium, the TOF count increased from 0 to 1, when the RoCE was 0.7  $\mu\text{g}/\text{mL}$ . Twenty-two minutes later, the surgery was finished without any problems. The muscle relaxant effect was antagonized with 120 mg of

sugammadex, and the patient successfully recovered from anesthesia. There were no anesthesia-related complications.

In the present case, there were no malfunctions in any of the devices used; however, the electromyography-based neuromuscular monitor detected noise although the electrode site was distant from where the Thunderbeat was used. The noise detection information is not displayed on the default screen (Panel C in Fig. 1); it can only be confirmed by actively opening the pop-up window (Panels A, B in Fig. 1). Therefore, there must be a trigger to suspect that the TOF count might be abnormal; in the present case, the pharmacokinetic simulation served as that trigger. If activation of the Thunderbeat and the increase in TOF count occur simultaneously, it is necessary to check the pop-up window, where the noise detection is displayed. It is advisable to repeat TOF measurement when the Thunderbeat is not activated. By monitoring muscle relaxation and observing the time course with RoCE along with its corresponding muscle relaxation effect, we were able to avoid unnecessary additional administration of rocuronium. This was achieved by not relying solely on the erroneously displayed TOF counts.

In the present case, even though rocuronium was administered correctly and showed sufficient muscle relaxation effects, the TOF count increased due to noise. Conversely, if rocuronium is not properly administered intravenously, possibly due to spillage or accidental extravascular administration, the TOF count is expected to increase despite a high simulated RoCE, indicating insufficient muscle relaxation. In this scenario, in addition to pharmacokinetic simulation, confirmation that the TOF measurement is not affected by electrical noise would become a key piece of information to indicate that rocuronium was not administered intravenously correctly. Thus, anesthesiologists must be aware that the values displayed on the monitor may be incorrect in some situations.

The combination of AF-201P and NM-345Y can be affected by the use of the Thunderbeat. To assess the reliability of displayed values, simulation of the effect-site concentration of muscle relaxants is effective.

For this case report, written informed consent was obtained from the patient.

**Acknowledgements** We would like to thank the Scientific English Editing Section of Fukushima Medical University for editing a draft of this manuscript.

**Author contributions** SO treated the patient and wrote the manuscript. RS and MM helped treated the patient and revised the manuscript. All authors reviewed and approved the final draft.

**Funding** The authors declare no funding for this report.

**Data availability** Not applicable.

## Declarations

**Conflict of interest** The author declares that there is no conflict of interest regarding the publication of this article.

**Ethics approval and consent to participate** In our institutions, IRB approval is not required for a case report.

**Consent for publication** Written informed consent was obtained from the patient for publication of this case report.

## References

1. Dong Y, Li Q. Phonomyography on perioperative neuromuscular monitoring: an overview. *sensors* (Basel, Switzerland). 2022;22:2448. <https://doi.org/10.3390/s22072448>
2. Japanese Society of Anesthesiologists. Standards and guidelines: monitoring during anesthesia (in Japanese). 2019. [https://anesth.or.jp/files/pdf/monitor3\\_20190509.pdf](https://anesth.or.jp/files/pdf/monitor3_20190509.pdf). Accessed 20 Jan 2024.
3. Thilen SR, Weigel WA, Todd MM, Dutton RP, Lien CA, Grant SA, Szokol JW, Eriksson LI, Yaster M, Grant MD, Agarkar M, Marbella AM, Blanck JF, Domino KB. 2023 American Society of anesthesiologists practice guidelines for monitoring and antagonism of neuromuscular blockade: a report by the american society of anesthesiologists task force on neuromuscular blockade. *Anesthesiology*. 2023;138:13–41.
4. Szenohradszky J, Fisher DM, Segredo V, Caldwell JE, Bragg P, Sharma ML, Gruenke LD, Miller RD. Pharmacokinetics of rocuronium bromide (ORG 9426) in patients with normal renal function or patients undergoing cadaver renal transplantation. *Anesthesiology*. 1992;77:899–904.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.