J Anesth (2004) 18:172–176
DOI 10.1007/s00540-004-0239-3

Journal of
Anesthesia

Duration of vecuronium-induced neuromuscular block can be predicted by change of skin temperature over the thenar muscles

Takahiro Suzuki, Osamu Kitajima, Aiko Watanabe, Hiroko Nonaka, Shigeru Saeki, and Setsuro Ogawa

Department of Anesthesiology, Surugadai Nihon University Hospital, 1-8-13 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8309, Japan

Abstract
Purpose. The purpose of this study was to clarify the relationship between skin temperature over the thenar muscles and the duration of action of vecuronium measured acceleromyographically at the thumb in anesthetized patients.
Methods. In 15 patients undergoing elective open abdominal surgery under propofol, fentanyl, and nitrous oxide anesthesia, train-of-four (TOF) stimuli were delivered over the ulnar nerve at 2 Hz every 15 s, and the degree of neuromuscular block was measured acceleromyographically at the thumb. Each patient received an intubating dose of vecuronium 0.1 mg·kg^{-1}, followed by maintenance doses of 0.02 mg·kg^{-1} administered repeatedly whenever the first twitch of TOF responses had recovered to 25% of control. The interval between maintenance doses was defined as the clinical duration (DUR25). The median values of skin temperature (ST) over the ipsilateral thenar muscles and esophageal temperature (ET) were recorded during the action of the first and all subsequent maintenance doses. The relationships between change in temperature and change in DUR25 were analyzed.
Results. Whereas ET showed only minor changes (median, −0.3°C), ST fluctuated markedly between +0.9° and −6.3°C (median, −1.4°C). Increase and decrease were also seen in a series of DUR25s, as expected from the changes in ST. The median values of DUR25 produced by the first and last maintenance vecuronium doses were 21.5 and 32.3 min, respectively. A negative linear correlation was found between the change in DUR25 and that in ST, demonstrating that DUR25 increased by 20% of baseline with each 1°C decrease in ST.
Conclusion. Our results show that peripheral ST decreases considerably during open abdominal surgery without reduction in core temperature, and the decrease contributes to the potentiation of neuromuscular block in the periphery during propofol, fentanyl, and nitrous oxide anesthesia.

Key words Hypothermia · Vecuronium · Neuromuscular block · Acceleromyography · Adductor pollicis muscle

Address correspondence to: T. Suzuki
Received: October 1, 2003 / Accepted: February 20, 2004

Introduction

The mechanical response of peripheral muscles, such as that of the adductor pollicis muscle evoked by ulnar nerve stimulation, is often monitored to assess the effect of neuromuscular blocking agents during general anesthesia. The temperature of the muscle should be maintained constant for an accurate evaluation of neuromuscular function, because a certain decrease in muscle temperature markedly augments neuromuscular block [1], and in addition it weakens muscle twitch tension without the use of a neuromuscular blocking agent [2–4]. Peripheral temperature often decreases with only minor changes in core temperature during many routine surgical procedures; therefore it should ideally be observed and kept constant throughout the neuromuscular monitoring. However, an invasive needle probe or intramuscularly implanted thermistor is required to measure muscle temperature, a method that is not well suited to the usual clinical settings. The previous study reported by Haler et al. [5] showed a linear correlation between changes in skin temperature and those in muscle temperature during peripheral hypothermia produced by active cooling of the lower extremity. We therefore anticipated that the same correlation of skin temperature with muscle temperature should be found in anesthetized patients. The purpose of this study is to evaluate whether the peripheral skin temperature on the monitored muscle, as an alternative to muscle temperature, would change without active cooling or warming during routine open abdominal surgery and could promptly estimate change in the duration of vecuronium-induced neuromuscular block.

Materials and methods

After obtaining hospital ethics committee approval and informed consent, we studied 15 patients of both

sexes (11 men and 4 women), ASA physical status I or II, aged 30 to 65 years (mean, 53.5 ± 10.9 years), who were undergoing elective open abdominal surgery. All patients were free from neuromuscular, hepatic, renal, or endocrine disease or metabolic abnormalities, and were not taking drugs that might interfere with neuromuscular transmission. The patients were premedicated with pethidine 50 mg and atropine 0.5 mg i.m. approximately 45 min before the induction of anesthesia. On arrival at the operating room, monitors as appropriate for routine anesthetic care (electrocardiogram, noninvasive blood pressure, and pulse oximetry) were applied. An intravenous infusion line was kept in the right forearm, and acetated Ringer's solution was administered at an infusion rate of 8–10 $ml \cdot kg^{-1} \cdot h^{-1}$. Anesthesia was induced with fentanyl 2–4 $\mu g \cdot kg^{-1}$ and propofol 2–2.5 $mg \cdot kg^{-1}$ i.v. while the patient received 100% oxygen through an anesthesia face mask, and was maintained by continuous infusion of propofol 4–10 $mg \cdot kg^{-1} \cdot h^{-1}$, intermittent administration of fentanyl as required, and inhalation of nitrous oxide 67% in oxygen. Ventilation was adjusted to keep the end-tidal carbon dioxide within the range of 35–38 mmHg using a Capnomac Ultima (Datex, Helsinki, Finland).

Immediately after the induction of anesthesia, the left ulnar nerve was stimulated at the wrist with square-wave, automatically detected supramaximal stimuli of 0.2 ms duration, delivered in a train-of-four (TOF) mode at 2 Hz every 15 s, and contraction of the ipsilateral adductor pollicis muscle was measured using an accelerometer (TOFguard, Organon Teknika NV, Turnhout, Belgium). The skin temperature (ST) over the ipsilateral thenar muscle was recorded every 15 s throughout the experiment using a surface probe attached to the TOFguard. The monitoring arms were exposed to the theatre temperature (24°–25°C). After evoked responses had been stable for at least 10 min, all patients received vecuronium 0.1 $mg \cdot kg^{-1}$ via a running infusion. The patient's trachea was intubated when the maximum depression of the first twitch (T_1) of the TOF response had occurred. The esophageal temperature (ET) was observed and recorded every 1 min as a core temperature using Mon-a-Therm (Mallinckrodt, Anesthesia Products, St. Louis, MO, USA). The patient's body was warmed with a heating mattress and cotton.

Maintenance doses of vecuronium 0.02 $mg \cdot kg^{-1}$ were administered whenever T_1 recovered to 25% of control until the end of the surgical procedure. As shown in Fig. 1, the clinical duration from the administration of the first maintenance vecuronium dose to 25% recovery of T_1 ($DUR25_1$) was regarded as the baseline value and compared with $DUR25_{2\text{-}x}$ (x = total number of administrations of maintenance vecuronium) produced by the second and all subsequent doses in order. Each median value of ST and ET was calculated from the raw data that had been recorded during the action of the first maintenance vecuronium dose and was also regarded as the baseline value (ST_1 and ET_1). Changes in median $ST_{2\text{-}x}$ and $ET_{2\text{-}x}$, recorded in the same periods of $DUR25_{2\text{-}x}$, were observed throughout the study. The correlation between the DUR ratio ($DUR25_{2\text{-}x}$/$DUR25_1$) and delta ST ($ST_{2\text{-}x}$ minus ST_1) or delta ET ($ET_{2\text{-}x}$ minus ET_1) was evaluated. Least-squares linear regression analysis was applied to measure the correlation. Data are presented as median (range). Statistical analysis was performed by the Mann-Whitney U test. A P value less than 0.05 was considered to indicate statistical significance.

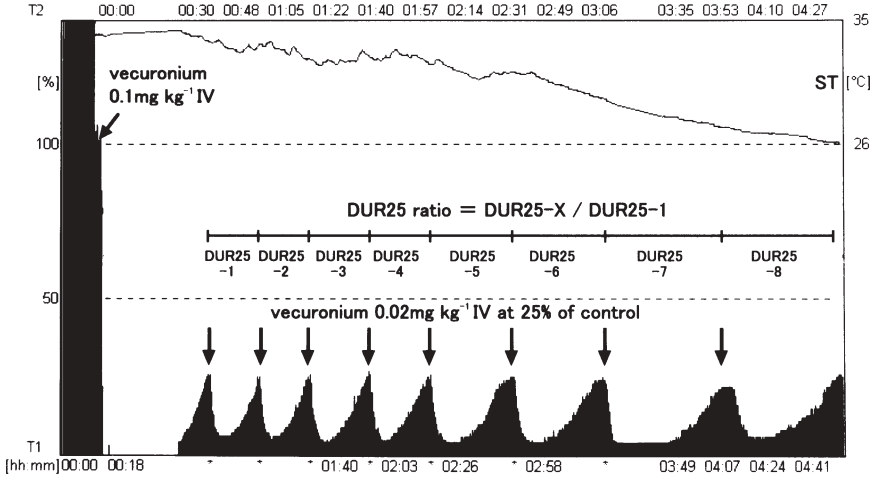

Fig. 1. Serial recording of acceleromyographic responses measured at the thumb and skin temperature over the thenar muscles

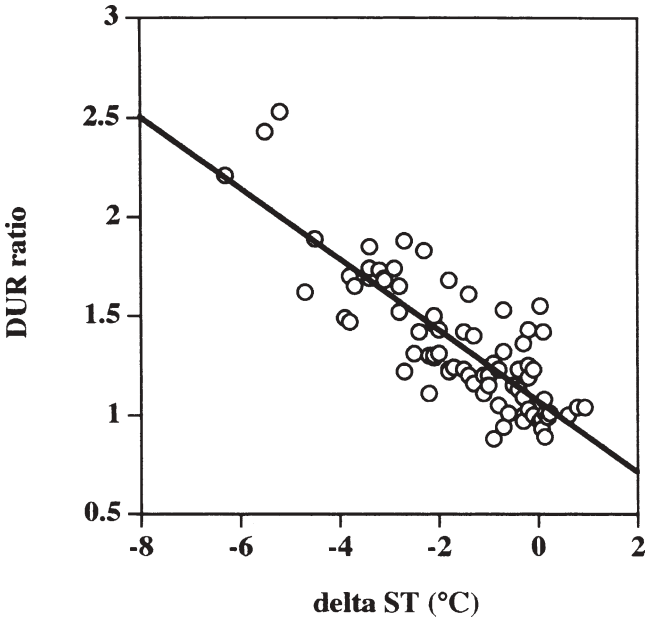

Fig. 2. Relationship between duration (*DUR*) ratio and delta skin temperature (*ST*). The regression line including individual data points is presented ($Y = -0.18X + 1.07$, $r = 0.829$, $n = 80$, $P < 0.01$), and a significant correlation is shown between variables

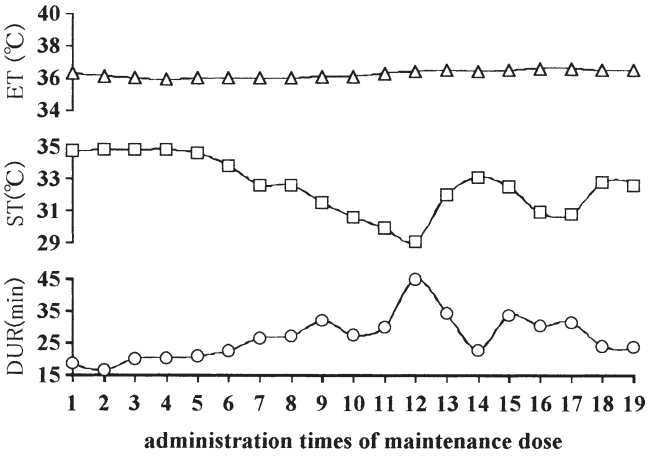

Fig. 3. Successive recording of *DUR*, *ST*, and esophageal temperature (*ET*) in a patient receiving 19 doses of maintenance vecuronium during long-lasting open abdominal surgery

Results

The time from administration of the intubating dose of 0.1 mg·kg^{-1} vecuronium to 25% recovery of T_1 was 45.8 min (33.0–75.0 min). Subsequently, 3 to 19 doses (median, 5 doses) of maintenance vecuronium were administered during each surgical procedure. The median values of DUR25 produced by the first ($DUR25_1$) and the last ($DUR25_x$) maintenance dose were 21.5 min (13.8–44.8 min) and 32.3 min (18.8–56.3 min), respectively; a statistically significant difference was found between the median values ($P < 0.01$). ST fluctuated markedly between +0.9° and −6.3°C (median, −1.4°C), and ST_x was significantly lower than ST_1 [30.8°C (25.2°–35.0°C) vs 32.1°C (30.5°–34.7°C), $P < 0.01$]. Figure 1 shows a serial recording of DUR25 and ST. In the earlier part of the recording, both DUR25 and ST are kept stable; however, DUR25 shows a gradual prolongation associated with a marked decrease in ST in the later part. There was a statistically significant correlation between DUR ratio and delta ST ($Y = -0.18X + 1.07$, Y; DUR ratio, X; delta ST, $r = 0.829$, $n = 80$, $P < 0.01$, Fig. 2), although the minor changes in ET observed in the study [ET_1: 35.9°C (35.6°–37.2°C), ET_x: 35.5°C (34.4°–37.3°C)] did not influence DUR25 ($Y = -0.01X + 1.35$, $r = 0.018$, $n = 80$, $P > 0.05$). Figure 3 shows a considerable fluctuation in ST even when ET is kept stable and normal in a patient receiving 19 doses of vecuronium. The variation in DUR25 is likely to be in inverse relation to that in ST.

Discussion

The present study found that the peripheral ST over the thenar muscles decreased significantly with minor or no decreases in core temperature in anesthetized patients, and was a reliable and useful index for estimating the degree of prolonged vecuronium-induced neuromuscular block.

It is well known that the effect of neuromuscular blocking agents is potentiated by hypothermia [1,6–8]. Muscle temperature is generally thought to be one of the very important factors influencing the extent of neuromuscular block during hypothermia [1–3]. However, it is difficult to measure muscle temperature routinely in clinical settings. We therefore observed the time course of ST over the thenar muscles contracted by ulnar nerve stimulation and evaluated the relationship between ST and vecuronium-induced block in this study. The results suggested that DUR25 produced by vecuronium was extremely sensitive to changes in ST. On the basis of the relationship observed between the DUR ratio and delta ST (DUR ratio $= -0.18 \cdot$ delta ST $+ 1.07$), it is estimated that the duration of action of vecuronium increases by 20% of the baseline with every 1°C decrease in ST. We did not evaluate muscle temperature concurrently in the present study; however, variations in ST were expected to reflect those in thenar muscle temperature. This assumption is supported by the report of Halar and colleagues [5]. They measured intramuscular temperature in the lower extremity when ST was re-

duced from the average (32.2°C) at ambient temperature to 30°, 28°, and 26°C by artificial surface cooling in healthy subjects, and found a linear correlation between ST and muscle temperature. Eriksson and colleagues [2] also demonstrated a correlative decrease of temperatures in hypothermic arms of patients receiving an opioid-based nitrous oxide anesthesia. They reported that over an ST range of 32.0°–27.0°C maintained by progressive cooling of a forearm, muscle temperature showed a range of 34.5 ± 0.3 to 30.8 ± 0.4°C, and a close relationship [muscle temperature (°C) = 0.75·ST (°C) + 10.9] was found. The results indicate that ST is a reliable index for the assessment of muscle temperature change. In the usual clinical setting, ST can be easily observed as an alternative to muscle temperature and can exactly predict a certain fluctuation of vecuronium-induced neuromuscular block.

The prolonged DUR25 accompanying lowered ST is probably caused by the impairment of neuromuscular transmission. It has been reported that a progressive and statistically significant decrease in mechanical twitch tension of the adductor pollicis muscle and TOF ratio without the use of neuromuscular blocking drugs is seen when ST is peripherally cooled below 32.0°C [2]. Peripheral hypothermia reduces nerve conduction velocity [5], mobilization and release of presynaptic acetylcholine [9], and muscular twitch tension [10,11]. These mechanisms may contribute to the prolongation of DUR25 during peripheral hypothermia.

Simultaneous measurement of ST and ET in this study revealed that the peripheral temperature frequently decreased with minor or no changes in core temperature during long-lasting open abdominal surgery. During induction of anesthesia, blood flow into the adductor pollicis muscle was demonstrated to increase up to 10 times the baseline value [12]. The peripheral temperature, which is initially increased by the increased circulation, tends to decrease gradually when the patient's body is exposed to lower ambient room temperature. In this situation, peripheral vasoconstriction may occur to maintain a stable core temperature. A pharamacokinetic factor, the reduction in the amount of vecuronium eliminated from the neuromuscular junction caused by the decrease in blood flow, may also contribute to the prolongation of the action of vecuronium [13]. We anticipate that the change in peripheral temperature may be dependent on the type of surgical procedure and the duration of surgery, and that marked reduction in the temperature will be observed particularly in long-lasting open abdominal surgery because of the large area of the internal organs exposed to the ambient temperature. Further investigations specifically comparing recovery from neuromuscular block in various surgical situations may be warranted.

Figures 1 and 3 show the marked increase in DUR25 associated with decreased ST. We have to consider the possibility that vecuronium and its metabolites may accumulate following repetitive administration and contribute to the prolonged DUR25 during long-lasting surgery. Eriksson et al. [14] reported that in 15 patients, DUR25 after 10 supplementary doses of 0.02 mg·kg^{-1} vecuronium administered at every 25% recovery of T_1 showed minor or no variations (2nd dose, 22.4 ± 5.1 min; 6th dose, 22.8 ± 5.9 min; 10th dose, 23.4 ± 6.9 min) under neuroleptanesthesia. There is another report that showed no accumulation even after 71 supplementary doses of 0.02–0.04 mg·kg^{-1} vecuronium and 22 h of neuroleptanesthesia [15]. Figure 3 shows that marked increases and decreases were observed in a series of DUR25s during a long-lasting surgery, and that in the latter part of this case the temporarily prolonged DUR25 tended to recover to the baseline. It is therefore suggested that accumulation of vecuronium is unlikely to contribute to our results.

The anesthetics used in this study, such as propofol, fentanyl, and nitrous oxide, have only a minor inhibitory effect on neuromuscular transmission [16], whereas it is well known that potent volatile anesthetics potentiate the action of neuromuscular blocking drugs [16–18] and that the degree of potentiation is dependent on the time of exposure to the anesthetics [17,18]. If we use sevoflurane to maintain general anesthesia in the study protocol, there is a possibility that DUR25 would be prolonged time-dependently without any changes in ET and ST. However, previous studies [17,18] indicate that 30 min of exposure to sevoflurane anesthesia is sufficient to achieve a stable potentiating effect on vecuronium. Therefore, sevoflurane has probably minor or no influence on the variations in DUR25s produced by repeated administration of vecuronium after 30 min of inhalation.

We conclude that ST on the thenar muscles decreases considerably in patients undergoing open abdominal surgery under propofol, fentanyl, and nitrous oxide anesthesia, even when the core temperature is kept normal. Under these conditions, the peripheral muscles are becoming more sensitive to neuromuscular blocking drugs than the central muscles. Therefore, the peripheral temperature should be monitored and maintained actively for a reliable evaluation of neuromuscular blockade.

References

1. Eriksson LI, Viby-Mogensen J, Lennmarken C (1991) The effect of peripheral hypothermia on a vecuronium-induced neuromuscular block. Acta Anaesthesiol Scand 35:387–392
2. Eriksson LI, Lennmarken C, Jensen E, Viby-Mogensen J (1991) Twitch tension and train-of-four ratio during prolonged neuro-

muscular monitoring at different peripheral temperatures. Acta Anaesthesiol Scand 35:247–252
3. Heier T, Caldwell JE, Sessler DI, Kitts JB, Miller RD (1989) The relationship between adductor pollicis twitch tension and core, skin, and muscle temperature during nitrous oxide-isoflurane anesthesia in humans. Anesthesiology 71:381–384
4. Buzzelo W, Pollmaecher T, Schluermann D, Urbanyi B (1986) The influence of hypothermic cardiopulmonary bypass on neuromuscular transmission in the absence of muscle relaxants. Anesthesiology 64:279–281
5. Halar EM, DeLisa JA, Brozovich FV (1980) Nerve conduction velocity: relationship of skin, subcutaneous and intramuscular temperatures. Arch Phys Med Rehabil 61:199–203
6. Buzello W, Schluermann D, Schindler M, Spillner G (1985) Hypothermic cardiopulmonary bypass and neuromuscular blockade by pancuronium and vecuronium. Anesthesiology 62:201–204
7. Buzzelo W, Schluermann D, Pollmaecher T, Spillner G (1987) Unequal effects of cardiopulmonary bypass-induced hypothermia on neuromuscular blockade from constant infusion of alcuronium, d-tubocurarine, pancuronium, and vecuronium. Anesthesiology 66:842–846
8. Thornberry EA, Mazumdar B (1988) The effect of changes in arm temperature on neuromuscular monitoring in the presence of atracurium blockade. Anaesthesia 43:447–449
9. Hubbard JI, Jones SF, Landau EM (1971) The effect of temperature change upon transmitter release, facilitation and post-tetanic potentiation. J Physiol 216:591–609
10. Ricker K, Hertel G, Stodieck G (1977) Increased voltage of the muscle action potential of normal subjects after local cooling. J Neurol 216:33–38
11. Harris JB, Leach GDH (1968) The effect of temperature on end-plate depolarization of the rat diaphragm produced by suxamethonium and acetylcholine. J Pharm Pharmacol 20:194–198
12. Abdulatif M, Hegazy M (1994) Thenar muscle blood flow and neuromuscular effects of vecuronium in patients receiving balanced or isoflurane anesthesia. Br J Anaesth 72:650–653
13. Caldwell JE, Heier T, Wright PMC, Lin S, McCarthy G, Szenohradszky J, Sharma ML, Hing JP, Schroeder M, Sessler DI (2000) Temperature-dependent pharmacokinetics and pharmacodynamics of vecuronium. Anesthesiology 92:84–93
14. Eriksson LI, Staun P, Cederholm I, Lennmarken C, Löfström JB (1988) Experience with vecuronium during long-lasting surgery. Acta Anaesthesiol Scand 32:619–622
15. Staun P, Lennmarken C (1988) Experience of multiple supplementary doses of vecuronium. Acta Anaesthesiol Scand 32:156–157
16. Suzuki T, Munakata K, Watanabe N, Katsumata N, Saeki S, Ogawa S (1999) Augmentation of vecuronium-induced neuromuscular block during sevoflurane anaesthesia: comparison with balanced anaesthesia using propofol or midazolam. Br J Anaesth 83:485–487
17. Suzuki T, Iwasaki K, Fukano N, Hariya S, Saeki S, Ogawa S (2000) Duration of exposure to sevoflurane affects dose-response relationship of vecuronium. Br J Anaesth 85:732–734
18. Ahmed AAK, Kumagai M, Otake T, Kurata Y, Amaki Y (1999) Sevoflurane exposure time and the neuromuscular blocking effect of vecuronium. Can J Anaesth 46:429–432