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Optimum priming dose of vecuronium for tracheal intubation

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Abstract: To determine the optimum priming dose of vecuronium, we divided 173 surgical patients into five groups according to priming dose (0, 2.5, 5.0, 7.5, and 10 $\mu g \cdot kg^{-1}$). For endotracheal intubation, we administered a priming dose of vecuronium, and then after 4 min, the remainder was injected for a total dosage of 0.15 $mg \cdot kg^{-1}$. Onset time was determined by a 95% depression of twitch height as shown by electromyography (EMG) of the hypothenar muscles. This was measured by repeating the train-of-four (TOF) stimulation. An increased priming dose shortened the onset time; however, this shortening rate diminished when the dosage was above 7.5 $\mu g \cdot kg^{-1}$. In the zero priming dose group there was a significant correlation between onset time and age, and between onset time and body mass index (BMI) in women (r = 0.62 and −0.45, respectively); however, this correlation was not observed in men. A priming dose of 10 $\mu g \cdot kg^{-1}$ showed a decrease of TOF ratio to 95% or less in 1 out of 25 cases. Although one-third of the patients in the 5 and 7.5 $\mu g \cdot kg^{-1}$ groups complained of clinical symptoms such as ptosis, this was clinically allowable. We conclude that the optimum priming dose of vecuronium is 7.5 $\mu g \cdot kg^{-1}$; however, in obese patients, a smaller dosage would be recommended.

Key words: Priming technique, Priming dose, Vecuronium, Body mass index, Onset time

Introduction

For quick and smooth tracheal intubation with vecuronium, many anesthesiologists have used large doses of vecuronium [1–2] or the so-called priming technique [3–5]. Although the former is simple and effective, it is not suitable for brief operations. Therefore, the priming technique has been practiced to reduce onset time. A priming dose of vecuronium of approximately 10 $\mu g \cdot kg^{-1}$ is recommended [3–5]. Mahajan and D'Honneur et al. recently reported, however, that 10 $\mu g \cdot kg^{-1}$ of vecuronium has caused impairment of pulmonary function [6], lowered glossal muscle activity on electromyography (EMG) [7], and resulted in swallowing difficulty in some cases [6]. We have tried to determine the ideal priming dose of vecuronium when a total dosage of 0.15 $mg \cdot kg^{-1}$ is used. We also studied the correlation between onset time of muscle relaxation and age, and between onset time and body mass index (BMI) without priming.

Patients and methods

A total of 173 patients (ASA physical status I or II) scheduled for elective surgery requiring neuromuscular blockade participated in this study. This study was approved by the Tokai University Hospital Ethics Committee, and oral informed consent was obtained from each patient. Patients were premedicated with pentobarbital 1 $mg \cdot kg^{-1}$ perorally, as well as pethidine hydrochloride 0.8–1 $mg \cdot kg^{-1}$ and atropine sulfate 0.01 $mg \cdot kg^{-1}$ subcutaneously, 1.5 and 0.5 h before induction of anesthesia, respectively. Some elderly patients were given a smaller dosage than usual, i.e., about half the usual dosage, depending on their physical status.

Upon arrival at the operating room, ECG, SpO_2, and arterial blood pressure were monitored. An intravenous infusion at the dorsal region of the hand was initiated with Ringer's lactated solution at a rate of 8–10 $ml \cdot kg^{-1} \cdot h^{-1}$. We divided the patients randomly into five groups according to priming dose of vecuronium (0, 2.5, 5.0, 7.5, and 10 $\mu g \cdot kg^{-1}$). Each priming group consisted of 85, 20, 21, 22, and 25 patients, respectively. Surface electrodes were pasted on the forearm for

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ulnar-nerve supramaximal stimulation, and over the hypothenar muscles for EMG monitoring using a Relaxograph (NMT 100, Datex, Helsinki, Finland). After the administration of fentanyl 2 μg·kg^{-1} and midazolam 0.02 mg·kg^{-1}, the electrical response to train-of-four (TOF) stimulation (2 Hz) for control was recorded. We injected a priming dose corresponding with the above dosage, and recorded twitch heights every 20 s. After 4 min following the priming we rapidly injected an intubation dose of vecuronium to make a total dosage of 0.15 mg·kg^{-1} and 2–3 mg·kg^{-1} of thiopental. When T_1 (first twitch height) decreased to 5% or less of the control value, the trachea was intubated.

In the other study we observed clinical symptoms such as heavy eyelids, dyspnea, and drowsiness for 4 min following the administration of the priming dose of 5 μg·kg^{-1} (n = 31) or 7.5 μg·kg^{-1} (n = 37) without sedation.

Statistical analysis

We used multiple regression analysis to find the correlation between onset time and age, and between onset time and BMI. Significant differences in age, height, weight, BMI, and onset time between each priming dose group were analyzed by Student's t-test after using one-way analysis of variance (ANOVA). The frequency of train-of-four ratio (TOFR) depression was analyzed by the chi-squared test. $P < 0.05$ was considered statistically significant. All values are expressed as means ± SD.

Results

In the zero priming dose group (n = 85) we determined the correlation between onset time and age, and between onset time and BMI. There were a total of 41 men (54.3 ± 14.4 years of age, BMI 22.0 ± 2.5, height 165.1 ± 7.1 cm, weight 59.9 ± 6.2 kg), and 44 women (57.5 ± 14.8 years of age, BMI 22.9 ± 4.0, height 151.9 ± 5.7 cm, weight 52.6 ± 9.6 kg). Partial correlation coefficients between onset time and age, and between onset time and BMI were 0.18 and −0.22, respectively, in male patients, and 0.62 ($P < 0.01$) and −0.45 ($P < 0.01$) in female patients (Table 1). To compare the onset time among the five groups we selected patients between 40 and 70 years of age whose BMI were between 17 and 28 (n = 130). Demographic data of the patients in each priming group are shown in Table 2. Age, height, weight, and BMI were not significantly different among the five groups. The onset times of vecuronium in the 0, 2.5, 5.0, 7.5, and 10 μg·kg^{-1} priming dose groups were 144 ± 39, 134 ± 33, 123 ± 40, 113 ± 30, and 108 ± 27 s, respectively (Fig. 1). As the priming dose was incrementally increased by 2.5 μg·kg^{-1} from a level of zero to 7.5 μg·kg^{-1}, the mean onset time became shorter by approximately 10 s for every incremental increase. However, from 7.5 to 10 μg·kg^{-1}, the onset shortening rate diminished to 5 s. The differences of onset time between the group without priming (zero priming dose group) and the groups with a priming dose of 7.5 or 10 μg·kg^{-1} were statistically significant, but no significant differences between a priming dose of zero, 2.5, or 5.0 μg·kg^{-1} were observed.

The percentage of patients in each priming group whose TOFR decreased to 95% or less within 4 min after priming is shown in Table 3. Age, height, weight, and BMI were not significantly different among all four groups. Although TOFR depression was observed in 1 (4%) out of 25 patients in the 10 μg·kg^{-1} group, it was not observed in the 7.5, 5, and 2.5 μg·kg^{-1} groups.

Four (27%) of 15 male and 6 (38%) of 16 female patients in the 5 μg·kg^{-1} priming dose group, and 5

Table 1. Partial correlation between onset time of vecuronium 0.15 mg·kg^{-1} (without priming) with age and BMI

	Men (n = 41)	Women (n = 44)
Onset time vs age	r = +0.18 (N.S.)	r = +0.62 ($P < 0.01$)
Onset time vs BMI	r = −0.22 (N.S.)	r = −0.45 ($P < 0.01$)

BMI (body mass index) = weight (kg)·height(m)$^{-2}$ N.S., not significant.

Table 2. Demographic data of the patients* in each priming dose group

Priming dose	Number (M/F)	Age (years)	Height (cm)	Weight (kg)	BMI
0 μg/kg	25/25	55.7 ± 8.3	158.8 ± 9.3	57.0 ± 7.8	22.7 ± 2.7
2.5 μg/kg	10/10	57.3 ± 7.9	157.4 ± 9.0	56.1 ± 8.4	22.6 ± 2.6
5.0 μg/kg	10/10	57.3 ± 8.8	157.0 ± 7.3	55.0 ± 6.7	22.4 ± 2.8
7.5 μg/kg	10/10	56.9 ± 7.8	159.6 ± 9.4	55.9 ± 7.0	22.0 ± 2.1
10.0 μg/kg	10/10	57.4 ± 7.0	159.0 ± 7.2	57.1 ± 9.7	22.5 ± 2.7

* Aged between 40 and 70 years, with a BMI between 17 and 28.
Data are means ± SD.
BMI (body mass index) = weight·(height/100)$^{-2}$.

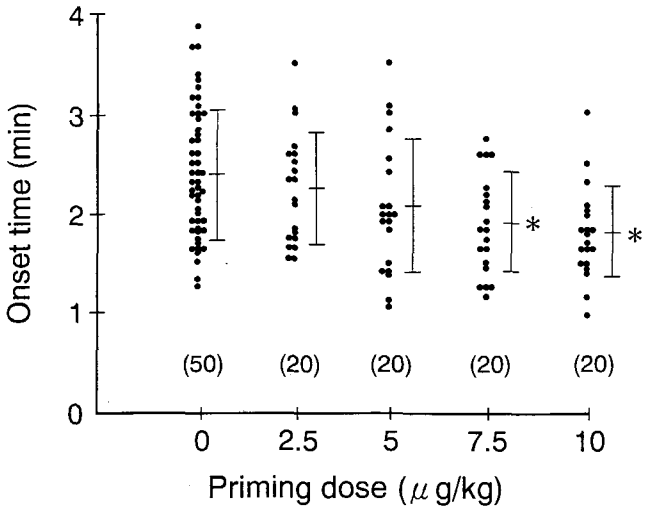

Fig. 1. Onset time of muscle relaxation with vecuronium 0.15 mg·kg^{-1} and priming dose of vecuronium. Onset time is the interval from the administration of vecuronium to 95% depression on T_1 in train-of-four stimulation. *Numbers in parentheses* indicate the number of patients in each group. Values are expressed as the means ± SD. *$P < 0.01$ compared with zero priming dose group

(29%) of 17 male and 7 (35%) of 20 female patients in the 7.5 μg·kg^{-1} group had clinical symptoms such as heavy eyelids following the administration of priming doses. Age and BMI did not differ between the 2 male groups. In women, BMI was not significantly different between the 2 groups; however, age was significantly higher in the 7.5 μg·kg^{-1} group (44.4 ± 13.1 *vs* 53.4 ± 10.7 years).

One patient in the 7.5 μg·kg^{-1} priming dose group complained of slight difficulty in breathing.

Discussion

To date, two different opinions concerning the onset of muscle relaxation in proportion to vecuronium dosage when administered in a single bolus have existed. According to one opinion, onset time becomes shorter as the dosage increases between 0.1 and 0.3 mg·kg^{-1} [1,2,8]. The other opinion holds that this shortened onset time is only observed under 0.15 mg·kg^{-1}, and a further shortening of onset time is not expected beyond this dosage [9]. At the same time, it is recognized that the duration of action of vecuronium relates positively to its dosage [1,2]. Therefore, we have chosen 0.15 mg·kg^{-1} as the ideal intubation dosage at which onset was expected to occur relatively quickly and the duration of action would not be of an exceedingly long duration.

The mean onset time with a single bolus injection of vecuronium 0.15 mg·kg^{-1} was 144 s in this study. We utilized the priming technique to speed up onset of muscle relaxation. The speed of onset increased in a dose-dependent manner between zero to 7.5 μg·kg^{-1} of the priming dose, but this shortening rate diminished at doses above 7.5 μg·kg^{-1}.

With a priming of 10 μg·kg^{-1}, one patient, a 53-year-old woman with a BMI of 28.5, experienced TOFR depression. This did not occur with a priming of 7.5, 5, or 2.5 μg·kg^{-1}. We therefore consider that the optimum priming dose of vecuronium is 7.5 μg·kg^{-1}. Clinical symptoms such as heavy eyelids were observed in 32% of the 7.5 μg·kg^{-1} and 32% of the 5 μg·kg^{-1} groups; however, these were mild and clinically allowable. Engbæk and Viby-Mogensen reported a case where a patient's twitch height decreased to 25% of the control at 4 min after the administration of 5 μg·kg^{-1} vecuronium [10], but we have never encountered such a case.

While many drugs affect the neuromuscular blockade with nondepolarizing neuromuscular blocking drugs (NMBD), fentanyl and midazolam, which we administered before recording the control twitch height, have little influence on the action of NMBD [11,12]. A clinical dose of thiopental has only slight effects on the neuromuscular blockade [11]. We strived to keep patients' blood circulation as stable as possible by administering the minimal effective dosage of thiopental which would cause patients to sleep.

It is known that a 95% depression of twitch height is adequate for tracheal intubation under light anesthesia [13]. Therefore, we intubated the trachea when the T_1 of hypothenar muscles was depressed by 95% or more. Although muscle relaxation was not as strong as that induced by suxamethonium, it was satisfactory for tracheal intubation in most cases. A few patients exhibited signs of incomplete muscle relaxation such as partial opening of vocal cords or diaphragmatic movement following the intubation.

In obese patients, the speed of onset was expected to be faster because of a smaller distribution volume per body weight [14]. The multiple regression analysis in this study demonstrated that this prediction was correct,

Table 3. Percentage of patients in each priming dose group whose train-of-four ratio (TOFR) decreased to 95% or less within 4 min after the administration of a priming dose of vecuronium

Priming dose	Male	Female	Overall
2.5 μg/kg	0/10	0/10	0/20
5.0 μg/kg	0/11	0/10	0/21
7.5 μg/kg	0/10	0/12	0/22
10.0 μg/kg	0/13	1/12 (8%)	1/25 (4%)

Denominator is total number in each group.
Numerator is number of patients whose TOFR decreased to 95% or less.

especially in the case of female patients. The administration of a dose based upon body weight probably leads to an overdose in these patients [14]. This fact indirectly indicates that the onset of vecuronium speeds up in a dose-dependent manner when administered in dosages greater than $0.15\,mg \cdot kg^{-1}$. This finding disagrees with an earlier report by Casson and Jones [9] who observed a faster onset time as the dosage increased in cases when the dose was less than $0.15\,mg \cdot kg^{-1}$. This perhaps could be because their patient groups differed with regard to age, gender, and BMI. Factors such as gender, age, and BMI influence onset time to some extent [15–17], which was confirmed in this study. Consequently, these factors should be taken into account whenever the onset time of vecuronium is studied.

At the present time three different and useful techniques for tracheal intubation with vecuronium have been recognized, i.e., large dose administration, the timing principle [8], and the priming technique. Each technique has its own shortcomings; e.g., administration of a large dose is accompanied by a long duration of muscle relaxation. In the timing principle technique, choosing the best time to administer the intravenous hypnotic agent is difficult, as is predicting the optimal priming dose in the priming technique. In most prolonged operations, a large dose can be administered for tracheal intubation; however, the priming technique would be more appropriate for brief surgery. If the priming technique is used for an emergency operation, we suggest that a smaller dosage than $7.5\,\mu g \cdot kg^{-1}$ be administered for priming because there is some possibility that patients have low blood volume, and/or their stomach is full.

In conclusion, the optimum priming dose of vecuronium is $7.5\,\mu g \cdot kg^{-1}$ in most cases; however, in obese patients, a smaller priming dose would be recommended.

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