Research Article

Sevoflurane Induction Shortens the Onset of Vecuronium at the Corrugator Supercilii Muscles: A Randomized Comparison with Propofol Induction

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We evaluated if induction with sevoflurane shortened the onset of vecuronium-induced neuromuscular blockade at the corrugator supercilii muscles (which have a similar time course of neuromuscular blockade with laryngeal muscles). Thirty-two patients were randomly allocated to a sevoflurane or propofol group. Anesthesia was induced with 5% sevoflurane in oxygen (sevoflurane group, $n = 16$) or with propofol 2–2.5 mg kg⁻¹ (propofol group, $n = 16$), and vecuronium (0.1 mg kg⁻¹) was given in both groups. Evoked responses to train-of-four stimuli were measured by acceleromyography at the corrugator supercilii and adductor pollicis muscles. Sevoflurane induction, as compared with propofol, significantly shortened the onset time at the corrugator supercilii muscles from 138 ± 34 s to 107 ± 28 s ($P < 0.01$). Onset time at the corrugator supercilii was significantly shorter than at the adductor pollicis for both groups ($P < 0.01$). Our results suggest that induction with sevoflurane, as compared with propofol, shortened the onset time of vecuronium at laryngeal muscles.

1. Introduction

Induction and maintenance of anesthesia with sevoflurane has been used in adults owing to its low solubility and nonirritant properties upon the respiratory tract [1–3]. Inhalational anesthetics (including sevoflurane) increase the intensity and duration of nondepolarizing neuromuscular-blocking drugs [4–8]. It has been reported that the induction of general anesthesia with sevoflurane shortens the onset time of vecuronium at the adductor pollicis muscles [9]. However, during the induction of general anesthesia, it is important to know the degree of neuromuscular blockade at the laryngeal muscles.

Studies that have evaluated the effects of sevoflurane induction on the onset of nondepolarizing neuromuscular-blocking drugs at the laryngeal muscles (or other muscles having similar neuromuscular blocking profiles to the laryngeal muscles) are lacking. It has been reported that the time course of neuromuscular blockade at the corrugator

supercilii muscle is similar to that at the laryngeal muscles [10].

We aimed to evaluate if the induction of anesthesia with sevoflurane shortens the onset time of vecuronium 0.1 mg kg⁻¹ at the corrugator supercilii and adductor pollicis muscles compared with the conventional induction of anesthesia with propofol.

2. Materials and Methods

The study protocol was approved by the Institutional Review Board of Fukuoka University, Fukuoka, Japan (Chairperson, Professor R. Nishimura) and registered at the Japan Medical Association Clinical Trials Registry (which participates in the World Health Organization (WHO) International Clinical Trial Registry Platforms (Identification no., JMA-IIA00051)). Written informed consent was obtained from each patient.

We studied 32 patients classified as having physical status I-II as judged by guidelines set by the American Society

TABLE 1: Characteristics of patients.

	Sevoflurane group	Propofol group
Number (<i>n</i>)	16	16
Sex (male/female)	12/4	8/8
Age (years)	44.9 ± 13.5	42.8 ± 12.5
Height (cm)	157.8 ± 6.2	160.6 ± 7.5
Weight (kg)	55.4 ± 7.7	57.8 ± 10.7

Values are mean ± SD. No significant differences between the two groups were observed.

TABLE 2: Blood pressure and heart rate at the maximum blockade.

	Sevoflurane group	Propofol group
Number (<i>n</i>)	16	16
Systolic blood pressure (mmHg)	115 ± 21	113 ± 15
Diastolic blood pressure (mmHg)	75 ± 13	74 ± 12
Mean blood pressure (mmHg)	88 ± 15	87 ± 13
Heart rate (beats per min)	66 ± 13	73 ± 13

Values are mean ± SD. No significant differences between the two groups were observed.

of Anesthesiologists. They were aged 18–60 years, were within 20% of their ideal body weight, and were scheduled to undergo elective minor surgery. All patients were free from hepatic, renal, or neuromuscular disease. Patients were premedicated with diazepam (10 mg, p.o.) 90 min before the induction of anesthesia.

Upon arrival in the operating room, pulse oximetry, electrocardiography, and noninvasive monitoring of arterial blood pressure were instituted. Patients were randomly allocated to the sevoflurane group or propofol group with the use of a random number list generated by a computer. In both groups, before induction of anesthesia, 50–100 µg of fentanyl was given. In the sevoflurane group ($n = 16$), general anesthesia was induced with 5% sevoflurane in oxygen via a facemask. Patients were breathing room air before the induction of anesthesia. The anesthetic circuit was primed with sevoflurane 5% in oxygen at 6 L min⁻¹ fresh gas flow for 30 s. Patients were asked to take deep breaths after fitting of the facemask. The end-tidal concentration of sevoflurane was monitored continuously with an anesthetic gas monitor (AS/3, Datex-Ohmeda, Helsinki, Finland). In the propofol group ($n = 16$), general anesthesia was induced with propofol 2–2.5 mg kg⁻¹ and maintained with 10 mg kg⁻¹ h⁻¹ of propofol. In both groups, artificial ventilation was applied with the facemask in all patients to maintain end-tidal carbon dioxide tension (P_{ETCO_2}) between 35 mmHg and 40 mmHg. After loss of consciousness, vecuronium 0.1 mg kg⁻¹ was given over 5 sec in both groups. Blood pressure was monitored every 2.5 min. If systolic blood pressure fell below 80 mmHg, ephedrine (4 mg, i.v.) was administered.

The neuromuscular monitoring was started 5 min before induction of anesthesia. Evoked responses to train-of-four (TOF) stimuli were measured by acceleromyography (TOF-Guard; Organon Instruments, Boxtel, The Netherlands) at

the corrugator supercilii and adductor pollicis muscles. The temporal branch of the facial nerve was stimulated supramaximally every 15 s at the external part of the superciliary arch, and an acceleration transducer was fixed to the left medial eyebrow [10]. Another pair of electrodes was applied to stimulate the ulnar nerve supramaximally every 15 s at the left wrist. The acceleration transducer was fixed to the volar side of the distal phalanx of the left thumb. Signals from the corrugator supercilii muscle were amplified five times because of the low responses of this muscle. Onset time was defined as the time from the end of vecuronium injection until 95% T1 depression. The trachea was intubated, and, after intubation, anesthesia was maintained with sevoflurane 1.5–2.5% in oxygen and air or 6–10 mg kg⁻¹ h⁻¹ propofol with controlled ventilation. Fentanyl was given intermittently at the discretion of each anesthesiologist in charge. Times to 25% recovery of T1 at both muscles between the groups were also compared. Incremental doses of vecuronium were administered at the discretion of anesthesia staff. Neuromuscular monitoring was continued until the end of anesthesia.

3. Statistical Analyses

For the analysis of patient characteristics, a Chi-squared test and analysis of variance (ANOVA) were used. Differences in onset time as well as times to 25% recovery of T1 between sevoflurane and propofol groups induced by vecuronium at each muscle were compared using ANOVA. Differences in onset time, times to 25% recovery of T1, and recovery of train-of-four ratio between the adductor pollicis and the corrugator supercilii muscles in each group were compared using repeated-measures ANOVA (Stat View 5.0 software for Windows; SAS Institute, Cary, NC, USA). All tests were two sided; $P < 0.05$ was considered significant.

From our pilot study, we found that the standard deviation of onset time with vecuronium (0.1 mg kg⁻¹) at the corrugator supercilii muscles was 28 s. This indicated that a sample size of 14 patients per group was needed to detect a 30 s difference in onset time at a 5% significance level with a power of 80%.

4. Results

There were no statistically significant differences between the groups with regard to sex ratio, age, height, and weight (Table 1). End-tidal concentrations of sevoflurane at the time of loss of consciousness and at the time of maximum blockade in the sevoflurane group were $3.1 \pm 0.4\%$ and $3.9 \pm 0.3\%$, respectively. Differences in mean arterial blood pressure and heart rate at the nearest measuring point from maximal blockade were similar between the sevoflurane group and propofol group (Table 2).

The neuromuscular effects of vecuronium are summarized in Table 3. The onset time after administration of vecuronium (0.1 mg kg⁻¹) was significantly shorter in the sevoflurane group than in the propofol group at the corrugator supercilii and adductor pollicis muscles ($P < 0.01$).

TABLE 3: Neuromuscular effects of vecuronium.

	Sevoflurane group	Propofol group
Onset(s)		
Adductor pollicis	127 ± 29* (112–143)	155 ± 27 (140–169)
Corrugator supercilii	107 ± 28* [#] (92–122)	138 ± 34 [#] (120–156)
T1 recovery to 25% of control (min)		
Adductor pollicis	51.5 ± 10.9* (44.9–58.0)	37.6 ± 6.4 (33.8–41.5)
Corrugator supercilii	38.5 ± 4.2 ^{†#} (36.0–41.1)	33.8 ± 6.4 [#] (30.0–37.7)
Train-of-four ratio at the end of anesthesia		
Adductor pollicis	0.97 ± 0.06 (0.93–1.01)	0.97 ± 0.05 (0.93–1.00)
Corrugator supercilii	1.12 ± 0.12 [#] (1.05–1.20)	1.01 ± 0.17 (0.91–1.13)

Values are mean ± SD; 95% confidence interval is given in parentheses. * $P < 0.01$, [†] $P < 0.05$ compared with the propofol group. [#] $P < 0.01$, compared with the adductor pollicis muscle.

The onset time was significantly shorter at the corrugator supercilii muscles than at the adductor pollicis muscles for both groups ($P < 0.01$). The times to 25% recovery of T1 were significantly longer in the sevoflurane group than in the propofol group at both muscles ($P < 0.05$, $P < 0.01$). The times to 25% recovery of T1 were significantly shorter at the corrugator supercilii muscles than at the adductor pollicis muscles for both groups ($P < 0.01$).

5. Discussion

Compared with the propofol group, the sevoflurane group had a shorter onset time and a delayed recovery of neuromuscular blockade induced by vecuronium at the corrugator supercilii and adductor pollicis muscles. We measured neuromuscular blockade at these two muscles because (i) the time course of neuromuscular blockade at the corrugator supercilii muscles is similar to that at laryngeal muscles and (ii) the adductor pollicis is a useful and convenient site for anesthesiologists to monitor the effects of neuromuscular-blocking drugs [10]. A shorter onset time at the corrugator supercilii muscle indicates a shorter onset time at the laryngeal muscles during sevoflurane induction than during propofol induction.

The effects of sevoflurane on the onset of neuromuscular-blocking drugs have been studied only at adductor pollicis muscles. Yamaguchi et al. evaluated the effects of inhalation of sevoflurane as an induction agent on the onset time of neuromuscular-blocking drugs [9]. They reported that induction with 8% sevoflurane accelerated the onset time of 0.1 mg kg⁻¹ vecuronium compared with induction with propofol [9]. Conversely, using intravenous agents for the induction of general anesthesia, several authors reported that the onset time of nondepolarizing neuromuscular-blocking

drugs was not shortened by sevoflurane at concentrations <2%. Suzuki et al. administered vecuronium during general anesthesia with 1.7% sevoflurane after induction with intravenous agents. They demonstrated that sevoflurane did not shorten the onset time of vecuronium 0.1 mg kg⁻¹ compared with balanced anesthesia using propofol or midazolam [6]. Lowry et al. reported that, for those aged 18–65 years, after induction with propofol, the onset times of rocuronium 0.6 mg kg⁻¹ during maintenance with a 1.5 minimum alveolar concentration (MAC) of sevoflurane or with propofol were similar [7]. They also reported that, after the induction of general anesthesia with propofol, 1.5 MAC of sevoflurane did not shorten the onset of mivacurium [11]. High concentrations of sevoflurane used for the induction of general anesthesia in the present study and those in the study of Yamaguchi et al. may be the reason for accelerated onset time despite the relatively short duration of exposure time to sevoflurane. Concentration-dependent inhibition of neuromuscular transmission by sevoflurane has been reported in animal and human studies [12, 13].

Pharmacokinetic factors may also have been involved in the accelerated onset by sevoflurane in the present study. Induction with a high concentration of sevoflurane compared with propofol has been shown to have a strong dilatory effect on peripheral vessels during the induction of general anesthesia [14]. Ogawa et al. evaluated the effects of autonomic circulatory control during induction with 5% sevoflurane and propofol and showed that, although the reduction in autonomic nervous modulation of the heart was similar, the reduction in sympathetic modulation of peripheral vessels was greater in the sevoflurane group [14]. Circulation time, cardiac output, and regional blood flow affect the onset time of neuromuscular-blocking drugs [15–17]. We did not measure hemodynamic parameters such as cardiac output and systemic vascular resistance. The precise pharmacokinetic mechanisms that affect the onset of vecuronium need further investigation.

In the present study, the times to 25% recovery of T1 were significantly longer in the sevoflurane group than in the propofol group at the corrugator supercilii and adductor pollicis muscles. This is in accordance with a study using a similar concentration of sevoflurane for maintenance of general anesthesia examined at the adductor pollicis muscles. Suzuki et al. demonstrated that, after an intubating dose of vecuronium (0.1 mg kg⁻¹), the duration of incremental doses of vecuronium (0.02 mg kg⁻¹) was prolonged by 1.7% sevoflurane compared with anesthesia induced by propofol or midazolam [6].

In conclusion, induction with sevoflurane resulted in accelerated onset and delayed recovery of neuromuscular blockade induced by vecuronium at the corrugator supercilii and adductor pollicis muscles.

Conflict of Interests

The authors declared that there is no conflict of interests.

Acknowledgments

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