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Effects of age on neuromuscular blockade by vecuronium as measured by accelography under sevoflurane anesthesia

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Abstract: We evaluated possible differential effects of age on a single bolus intravenous injection of vecuronium using accelography under sevoflurane anesthesia. Thirty anesthetized patients were divided into three groups of 10 patients as follows: group 1 = age 1–5 years; group 2 = age 20–40 years, and group 3 = age >70 years. Vecuronium 0.1 mg·kg^{-1} was given to facilitate tracheal intubation. Onset time, i.e., the time from the start of injection of the first dose of vecuronium to development of maximal twitch depression in group 1 was significantly shorter than those in groups 2 and 3 (103.5 ± 30.4 s, 166.5 ± 32.7 s, and 202.5 ± 56.7 s; mean ± SD; $P < 0.01$). Clinical duration, i.e., the time from completion of maximal block to 25% recovery of train-of-four (TOF) ratio in group 1 was significantly shorter than that in group 3 (43.6 ± 12.0 min and 67.3 ± 15.6 min; $P < 0.01$). The reversal time from 25% to 75% of the TOF ratio after the administration of neostigmine in group 1 was not significantly different from those in groups 2 and 3 (172.5 ± 73.9 s, 219.0 ± 59.7 s, and 222.0 ± 155.7 s). The authors conclude that the time to maximal twitch depression after the administration of vecuronium is significantly shorter in children than that in adults, and that the fastest recovery from vecuronium is also observed in children.

Key words: Sevoflurane, Accelography, Vecuronium, Age

Introduction

Age-related differences in the response to nondepolarizing muscle relaxants have been examined using various kinds of anesthetic agents. To date, however, no single study has compared such age-related differences with regard to nondepolarizing muscle relaxants administered under sevoflurane anesthesia. Sevoflurane causes a markedly greater potentiation of nondepolarizing muscle relaxants. To measure the age-related variations in response to nondepolarizing muscle relaxants, electromyography (EMG) has been used as a neuromuscular transmission monitor [1–3]. However, the smallness of the hands and arms of pediatric patients may make it technically more difficult to find a suitable position for attaching the electrodes [4]. Therefore, we used accelography to detect the degree of neuromuscular blockade after the administration of a nondepolarizing muscle relaxant. The accelograph was recently developed as a neuromuscular transmission monitor [5], and previous studies have demonstrated that accelography is a reliable way to evaluate the degree of neuromuscular blockade [6–9]. The purpose of this study is to compare age-related differences in the potency of vecuronium using accelography under sevoflurane anesthesia.

Materials and methods

Thirty patients of ASA physical status I or II who were scheduled to undergo elective surgery were studied after obtaining the approval of the Hospital Ethics Committee and the patients' or parents' informed consent. These patients were divided into three groups according to their age: group 1 (n = 10), age between 1 and 5 years; group 2 (n = 10), age between 20 and 40 years; and group 3 (n = 10), age more than 70 years. Patients with hepatic, renal, or neuromuscular disease were excluded from the study.

Children were premedicated with atropine 0.015 mg·kg^{-1} i.m. and adults were premedicated with atropine 0.5 mg·kg^{-1} i.m. 1 h before surgery. In children, anesthesia was induced with 50% nitrous oxide in oxygen and a progressively higher concentration of sevoflurane (maximum end-tidal concentration: 4%) using a face mask. In adults, anesthesia was induced with thiopental 5 mg·kg^{-1} i.v., and the patients were ven-

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tilated manually with 50% nitrous oxide in oxygen with sevoflurane (end-tidal concentration: 2%) using a face mask.

After anesthetic induction, the cutaneous electrodes of an Accelograph (Biometer, Copenhagen, Denmark) were applied to the right wrist to stimulate the ulnar nerve at a frequency of 2 Hz for train-of-four (TOF) stimulation every 15 s, with the positive electrode over the proximal part and the negative electrode over the distal part. The acceleration transducer was fastened to the thumb with adhesive tape. The apparatus was adjusted to supramaximal stimulation, and baseline response from the thumb was obtained in the transducer. Next, tracheal intubation was facilitated with a single bolus intravenous injection of vecuronium 0.1 mg·kg^{-1}, and anesthesia was maintained with 66% nitrous oxide in oxygen supplemented with sevoflurane (end-tidal concentration: 1.0%). Ventilation was controlled and end-tidal carbon dioxide tension was maintained between 32 and 38 mmHg. Paralysis was reversed using intravenous neostigmine 0.04 mg·kg^{-1} with atropine 0.02 mg·kg^{-1} when the TOF ratio returned to 25%.

We measured (1) the onset time, i.e., the time from the start of injection of the first dose of vecuronium to development of maximal twitch depression; (2) the clinical duration, i.e., the time from completion of maximal block to 25% recovery of TOF ratio; and (3) the reversal time from 25% to 75% of the TOF ratio after the administration of neostigmine.

Statistical comparisons in age and weight were performed with an unpaired Student's *t*-test. The Kruskal-Wallis test was used for statistical evaluation of the onset time, clinical duration, and reversal time; and Duncan's multiple range test was used to determine the statistical significance. Results are expressed as mean ± SD. The threshold for statistical significance was $P < 0.05$.

Results

The patients' demographic data are shown in Table 1. Significant differences in age and weight were observed between group 1 and the other two groups. However, there was no statistically significant difference in weight between groups 2 and 3.

The mean values (±SD) obtained from the acceleration transducer are shown in Table 2. The onset time in group 1 was the shortest, and statistically significant differences were observed compared with the other two groups. The clinical duration in TOF stimulation was the shortest in group 1. There was a significant difference between groups 1 and 3. The reversal time from 25% to 75% in group 1 was the shortest. However, there were no significant differences among the three groups.

Discussion

The accelograph is a newly developed neuromuscular transmission monitor, and previous studies have demonstrated that the single-twitch response and TOF ratio as determined by accelography correlate well with those obtained with the traditional method of measuring twitch tension [6–9]. We prefer to use the accelograph with children because it is easy to set up and operate. Attaching the acceleration transducer and the stimulation electrodes requires only a few seconds [5]. Additionally, since the transducer is only 0.5 cm × 1 cm in size and weighs only 20 g, it works well on a child's thumb.

This study demonstrated age-related differences in the potency of vecuronium using accelography under sevoflurane anesthesia. Sevoflurane exerts the most potent effect for a nondepolarizing muscle relaxant in volatile anesthetics [10]. In our study, the time to maximal twitch depression after the administration of vecuronium in children was shorter than that in adults and the elderly. This result was similar to that of Fisher and Miller, who used EMG as a neuromuscular transmission monitor under halothane anesthesia [11]. They suggested that the higher cardiac output during infancy causes vecuronium to be delivered to the neuromuscular junction more rapidly. The method of anesthetic induction was different for children and adults in this study. In children, anesthesia was induced with 50% nitrous oxide and sevoflurane by a face mask. In adults, anesthesia was induced with thiopental 5 mg·kg^{-1} intravenously, and then sevoflurane was introduced with a face mask. Since volatile anesthetics affect the onset of nondepolarizing muscle relaxants, these methods of anesthetic induction may affect the onset time after the administration of vecuronium. When anesthesia is induced with a progressively higher concentration of sevoflurane in children, vecuronium may therefore be administered in smaller doses compared to the dose for adults.

With respect to clinical duration, some investigators have reported that children are more sensitive to nondepolarizing muscle relaxants than adults [11–13]. However, Goudsouzian et al. [14] reported that children were more resistant to d-tubocurarine than adults.

Table 1. Patients' demographic data

	Group 1 (age 1–5 yrs)	Group 2 (age 20–40 yrs)	Group 3 (age >70 yrs)
Age	2.6 ± 1.4 yrs	31.4 ± 5.7 yrs	73.4 ± 3.5 yrs
Sex	M6/F4	M6/F4	M6/F4
Body weight	13.3 ± 2.9 kg	56.8 ± 5.9 kg	52.3 ± 9.2 kg

M, male; F, female.
Values expressed as mean ± SD.

Table 2. Variables obtained from accelography in children, adults, and elderly patients

	Group 1 (age 1–5 yrs)	Group 2 (age 20–40 yrs)	Group 3 (age >70 yrs)
Onset time (s)	103.5 ± 30.4	166.5 ± 32.7*	202.5 ± 56.7**
Clinical duration (min)	43.6 ± 12.0	54.4 ± 12.4	67.3 ± 15.6**
Reversal time from 25% to 75% of TOF (s)	172.5 ± 73.9	219.0 ± 59.7	222.0 ± 155.7

TOF, train-of-four.
Values expressed as mean ± SD.
* $P < 0.01$. Significant difference between groups 1 and 2.
** $P < 0.01$. Significant difference between groups 1 and 3.

Matteo et al. [15] reported that there was no difference in sensitivity to d-tubocurarine between children and adults. There are still many discrepancies in the literature, so further studies on vecuronium are necessary. Our results suggest that the clinical duration in children was the shortest among the three groups and was significantly shorter than that in the elderly. D'Hollander et al. [16] reported that the dose of vecuronium and rate of recovery of twitch height are age-dependent, and that there is a need to decrease the maintenance dose of vecuronium in the elderly. Matteo and Ornstein [17] have pointed out that the clinical duration of vecuronium in the elderly is prolonged because of decreased hepatic elimination. As another reason, the characteristics of limb musculature motor units change significantly with age. The difference between children and the elderly may consist in different proportions of muscle fibers. They are histochemically classified into fast-twitch fibers and slow-twitch fibers as they differ in the activities of myosin ATPase [18]. An adductor pollicis muscle electrically stimulated by an accelograph was shown to contain 80.4% slow-twitch fibers and 19.6% fast-twitch fibers [19]. Nondepolarizing muscle relaxants affect slow-twitch fibers more than fast-twitch fibers [20,21]. Dubowitz [22] reported that muscle in children shows a pattern of differentiation similar to that of mature adult muscle, with an approximately equal proportion of fast-twitch and slow-twitch fibers. The elderly, however, may have a greater proportion of slow-twitch fibers in the adductor pollicis muscle, as fast-twitch fibers atrophy with age [23]. Therefore, the clinical duration in the elderly may be longer than that in children.

The reversal time after the administration of neostigmine was shorter in children than that in adults. However, there was no significant difference between them. Intravenous administration of neostigmine $0.04\,mg \cdot kg^{-1}$ at 25% of TOF ratio was effective as an antagonist in both children and adults.

In conclusion, this study demonstrates that the onset time after a single bolus intravenous injection of vecuronium in children is shorter than that in adults and that the clinical duration in children is also shorter than that in the elderly.

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