High concentration sevoflurane induction of anesthesia accelerates onset of vecuronium neuromuscular blockade

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Purpose: To investigate neuromuscular block using accelography after administration of vecuronium under sevoflurane 8% induction and maintenance with sevoflurane 2% in adults.

Methods: Patients were allocated to three groups: (1) group I: anesthesia was induced and maintained with propofol and fentanyl (n=15), (2) group II: anesthesia was induced with propofol and maintained with N₂O(66%)-O₂-sevoflurane 2% (n=15), (3) group III: anesthesia was induced with sevoflurane 8% using a vital capacity inhalation induction and maintained with N₂O(66%)-O₂-sevoflurane 2% (n=15). 0.1 mg·kg⁻¹ vecuronium was used for paralysis three minutes after anesthetic induction and reversed using intravenous 0.04 mg·kg⁻¹ neostigmine with 0.02 mg·kg⁻¹ atropine when the train-of-four (TOF) ratio returned to 25%.

Results: The onset time from initial administration of vecuronium to maximal block in the group III was shorter than that in the groups I and II (139 ± 35, 193 ± 35 and 188 ± 47s, respectively: *P* < 0.05). The clinical duration from maximal block to 25% recovery of TOF ratio in group II and III was longer than that in the group I (47 ± 15, 48 ± 14 and 36 ± 10 min, respectively: *P* < 0.05). The reversal times from administration of neostigmine to 75% of TOF ratio in groups II and III were longer than that in the group I (196 ± 53, 208 ± 64 and 136 ± 28s, respectively: *P* < 0.05).

Conclusions: Vital capacity inhalation induction of anesthesia with sevoflurane accelerates onset and prolongs duration of vecuronium neuromuscular block compared with propofol-fentanyl anesthesia.

Objectif : Étudier le blocage neuromusculaire à l'aide de l'accélographie après l'administration de vécuronium pendant l'anesthésie induite avec du sévoflurane à 8 % et maintenue avec du sévoflurane à 2 % chez des adultes.

Méthode : Les patients ont été répartis en trois groupes : le groupe I : l'anesthésie est induite et maintenue avec du propofol et du fentanyl (n=15); le groupe II : l'anesthésie est induite avec du propofol et maintenue avec N₂O(66 %)-O₂-sévoflurane 2 % (n=15); le groupe III : l'anesthésie est induite avec du sévoflurane à 8 % en utilisant la technique de la capacité vitale et maintenue avec N₂O(66 %)-O₂-sévoflurane 2 % (n=15). Une dose de 0,1 mg·kg⁻¹ de vécuronium a été utilisée pour provoquer le bloc, trois minutes après l'induction anesthésique. Ce bloc a été renversé avec une dose intraveineuse de 0,04 mg·kg⁻¹ de néostigmine avec 0,02 mg·kg⁻¹ d'atropine quand le train-de-quatre (TDQ) était revenu à 25 %.

Résultats : Le délai d'installation, de l'administration initiale de vécuronium jusqu'au bloc maximal, a été plus court dans le groupe III que dans les groupes I et II (139 ± 35, 193 ± 35 et 188 ± 47s, respectivement : *P* < 0,05). La durée clinique, du bloc maximal jusqu'à une récupération de 25 % du ratio du TDQ, a été plus longue dans les groupes II et III que dans le groupe I (47 ± 15, 48 ± 14 et 36 ± 10 min, respectivement : *P* < 0,05). Le temps de renversement du bloc, de l'administration de néostigmine jusqu'au retour de 75 % du ratio du TDQ, a été plus long dans les groupes II et III que dans le groupe I (196 ± 53, 208 ± 64 et 136 ± 28s, respectivement : *P* < 0,05).

Conclusion : L'induction de l'anesthésie par inhalation avec du sévoflurane, selon la technique de la capacité vitale, permet un début d'action plus rapide et prolonge la durée du bloc neuromusculaire réalisé avec du vécuronium comparé au mélange de propofol et de fentanyl.

VITAL capacity inhalation with a high concentration of sevoflurane has been described for the rapid induction of anesthesia.^{1,2} A vital capacity induction technique with approximately 8% sevoflurane provides more rapid induction and reduced side effects compared with other intravenous or inhaled anesthetics.¹⁻⁵

Since sevoflurane increases both intensity and duration of a non-depolarizing muscle relaxant,⁶⁻⁸ anesthetic induction with a high concentration of sevoflurane followed by maintenance with sevoflurane may induce a more rapid onset time and longer duration of action of non-depolarizing muscle relaxants.

The purpose of this study was to clarify the onset and duration of action of vecuronium after a high concentration sevoflurane induction of anesthesia using the vital capacity induction technique compared with the conventional techniques using propofol or propofol-sevoflurane anesthesia.

Methods

After obtaining approval of the hospital ethics committee and informed consent, 45 patients, aged 30-59 yr old, ASA 1 or 2, scheduled for elective surgery were studied. The surgical procedures were otorhinolaryngologic, oral or orthopedic and involved minimal blood loss. Patients were within 15% of ideal body weight and those with hepatic, renal or neuromuscular disease were excluded. In addition, none had received any medication that might potentiate the action of neuromuscular blocking drugs. The study was randomized and double-blind. Observations were made by a single-blinded anesthesiologist and induction of anesthesia was performed by an anesthesiologist familiar with the vital capacity induction technique.

Patients were premedicated with 0.5 mg atropine and 50 mg hydroxyzine one hour before surgery. After arriving in the operating room, the cutaneous electrodes of an accelerograph (TOF-Guard®, Organon Teknika B.V., Netherlands) were applied to the right wrist and the acceleration transducer was fastened to the right thumb. Venous cannulation was performed on the dorsum of the left hand. Indirect arterial blood pressure and pulse oximetry were monitored in the left arm. Electrocardiography, capnography and rectal temperature were also used as monitors.

Patients were randomly allocated to three groups (Table I). In the propofol-sevoflurane and sevoflurane 8% groups, the circle system of the anesthetic machine (A-VSEVO; Aladin Cassette for Sevoflurane with Quik Fil™, Datex-Omeda, Sweden) was primed for five minutes with sevoflurane 2 or 8% in oxygen mixture at 6 l·min⁻¹ fresh gas flow, respectively.

In the propofol and propofol-sevoflurane groups, anesthesia was induced by intravenous injection of propofol and standard controlled ventilation was performed with a face mask in oxygen 100%. In the sevoflurane 8% group, patients were breathing room air before induction of anesthesia. They were instructed to breathe out to residual volume and then the face mask was fitted tightly. They took a vital capacity breath of sevoflurane 8% in oxygen 100% which they held as long as possible.³ When they could no longer hold their breath, they were allowed to breathe normally. After loss of consciousness, assisted ventilation was started with a face mask, and then we performed standard controlled ventilation after breathing stopped.

The ulnar nerve was stimulated at a frequency of 2 Hz in trains lasting two seconds every 15 sec. The train-of-four (TOF) stimulus was used to give single twitch height. The accelerograph was adjusted to supramaximal stimulation and the baseline response was obtained three minutes after the start of anesthetic induction in the three groups. Immediately after obtaining the baseline value, 0.1 mg·kg⁻¹ vecuronium was administered intravenously in all groups. Ventilation was controlled after tracheal intubation, and P_{ET}CO₂ was maintained between 35 to 40 mmHg during the study.

Neuromuscular block was reversed using 0.04 mg·kg⁻¹ neostigmine with 0.02 mg·kg⁻¹ atropine when the TOF ratio had returned to 25%.

Measurements were made of (1) onset time (T₀) from initial administration of vecuronium to maximal block, (2) clinical duration (T_{2/3}) from maximal block to 25% recovery of the twitch height, and (3) reversal time (TOF₂₅₋₇₅) from the administration of neostigmine to 75% of the TOF ratio.

Data were expressed as mean ± SD. Statistical analysis of the data was performed using one-way ANOVA, followed by Bonferroni correction. Statistical significance was assumed at *P* < 0.05.

Results

No demographic differences were found among the three groups (Table II). No patient experienced hypothermia during anesthesia.

Onset time in the sevoflurane 8% group was shorter than in the other groups. There was no difference between the propofol and propofol-sevoflurane groups. Clinical duration and reversal time in both sevoflurane 8% and propofol-sevoflurane groups were longer than those in the propofol group (Table III).

Discussion

A high concentration of sevoflurane is the most suitable for inhalation induction.^{3,9-11} A vital capacity

TABLE I Methods of anesthetic induction and maintenance in three groups

Group	Induction	Maintenance
1. Propofol group (n=15)	2 mg·kg ⁻¹ propofol with 2 µg·kg ⁻¹ fentanyl <i>iv</i> in oxygen 100%	continuous infusion of 10 to 4 mg·kg ⁻¹ ·hr ⁻¹ propofol and 0.5 µg·kg ⁻¹ fentanyl <i>iv</i> every 30 min in 34% oxygen
2. Propofol-sevoflurane group (n=15)	2 mg·kg ⁻¹ propofol <i>iv</i> followed by inhalation of sevoflurane 2% in oxygen 100%	nitrous oxide 66% and 2% sevoflurane 66% (dial setting) in oxygen 34%
3. Sevoflurane 8% group (n=15)	sevoflurane 8% in oxygen 100% using vital capacity inhalation induction	66% nitrous oxide and 2% sevoflurane (dial setting) in oxygen 34%

TABLE II Demographic data.

	Propofol group	Propofol-sevoflurane group	Sevoflurane 8% group
Age (yr)	43 ± 14	42 ± 12	44 ± 11
Sex	Male 8, Female 7	Male 8, Female 7	Male 8, Female 7
Height (cm)	160 ± 9	163 ± 9	164 ± 11
Body weight (kg)	57 ± 8	57 ± 14	60 ± 11

Values expressed as mean ± SD.

induction technique with high concentration of sevoflurane produces a more rapid induction, reduced adverse airway events and decrease of cardiovascular instability than conventional inhalation induction technique with gradual increases of the concentration.¹¹ We used sevoflurane 8% concentration as an inhalation induction according to Hall *et al.*¹ They showed that the times to loss of eyelash reflex and jaw relaxation under 8% sevoflurane in 100% oxygen were 71 sec and 169 sec, respectively.¹ Therefore, vecuronium was administered three minutes after inhalation induction of sevoflurane 8% in oxygen 100% and the onset time of vecuronium neuromuscular block was accelerated compared with conventional induction techniques using propofol-fentanyl or propofol-sevoflurane anesthesia in the present study. A vital capacity induction technique with a high concentration of sevoflurane may produce conditions for tracheal intubation rapidly. Our results may be added to highlight the advantages of vital capacity rapid inhalation induction with sevoflurane.

TABLE III Neuromuscular measurement

	Propofol group	Propofol-sevoflurane group	Sevoflurane 8% group
Time to maximal block (sec)	193 ± 35*	188 ± 47*	139 ± 35
Clinical duration from maximal block to 25% twitch height spontaneously (min)	36 ± 10	47 ± 15†	48 ± 14†
Reversal time from 25% to 75% of TOF ratio (sec)	136 ± 28	196 ± 53†	208 ± 64†

Values expressed as mean ± SD.

TOF; train-of-four; **P* < 0.05 vs sevoflurane 8% group; †*P* < 0.05 vs propofol group.

Inhalation anesthetics enhance the potency of non-depolarizing muscle relaxants to a different degree. Sevoflurane appears to increase both intensity and duration of neuromuscular block induced by non-depolarizing muscle relaxants. However, Ahmed *et al.*⁶ reported that the maximum onset time produced by vecuronium was not shortened by an increase of sevoflurane exposure time under sevoflurane 2%. Lowry *et al.*⁷ reported that with 1.5 MAC sevoflurane the maximum onset time after administration of mivacurium did not differ from that during propofol infusion. Furthermore, Lowry *et al.*⁸ reported that intubating conditions after 0.6 mg·kg⁻¹ rocuronium following anesthetic induction with a vital capacity induction technique with sevoflurane 8% in oxygen 100% or intravenous administration of 2-3 mg·kg⁻¹ propofol were similar. They assessed intubating conditions one minute after intravenous rocuronium and patients received only two to three minutes of sevoflurane inhalation. In this study, we administered vecuronium intravenously three minutes after the start of anesthetic induction with sevoflurane, and the end-tidal concentration of sevoflurane was reached between 6 to 7% in the sevoflurane 8% group. Tracheal intubation could be performed approximately two minutes after administration of vecuronium. The time from the start of anesthesia to tracheal intubation in the present study was almost double that of Lowry *et al.*⁸ A longer duration of anesthetic induction with a high concentration of sevoflurane may induce easier intubating conditions. The speed of onset of paralysis after intravenous injection of a non-depolarizing muscle relaxant is related to age, circulation time, cardiac output and regional muscle blood

flow.¹²⁻¹⁶ A high concentration of volatile anesthetics may also be associated with the onset time of non-depolarizing muscle relaxants.

Anesthetic induction with sevoflurane 8% and maintenance with sevoflurane 2% induced the prolonged duration of action of vecuronium and a longer reversal time compared with intravenous anesthesia with propofol and fentanyl. However, there were no differences in recovery time or the reversal time between the propofol-sevoflurane group and the sevoflurane 8% group. This suggests that anesthetic induction with a high concentration of sevoflurane followed by maintenance of sevoflurane does not induce a longer duration of action of a non-depolarizing muscle relaxant and prolonged reversal time compared with a conventional technique using propofol and sevoflurane.

In conclusion, a vital capacity anesthetic induction technique with sevoflurane 8% may induce a more rapid onset time and may not prolong the duration of action of vecuronium compared with conventional techniques using propofol-sevoflurane anesthesia.

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