Effect of isoflurane and sevoflurane on the magnitude and time course of neuromuscular block produced by vecuronium, pancuronium and atracurium

L. E. H. VANLINTHOUT, L. H. D. J. BOOIJ, J. VAN EGMOND AND E. N. ROBERTSON

Summary
We have compared the ability of equipotent concentrations of isoflurane and sevoflurane to enhance the effect of non-depolarizing neuromuscular blocking drugs. Ninety ASA I and II patients of both sexes, aged 18–50 yr, were stratified into three blocker groups (Vec, Pan and Atr), to undergo neuromuscular block with vecuronium (n = 30), pancuronium (n = 30) or atracurium (n = 30), respectively. Within each group, patients were allocated randomly to one of three anaesthetic subgroups to undergo maintenance of anaesthesia with: (1) alfentanil-nitrous oxide-oxygen (n = 10); (2) alfentanil-nitrous oxide-oxygen-isoflurane (n = 10); or (3) alfentanil-nitrous oxide-oxygen-sevoflurane (n = 10) anaesthesia. During maintenance of anaesthesia, end-tidal concentrations of isoflurane, sevoflurane and nitrous oxide were 0.95, 1.70 and 70%, respectively. Both the evoked integrated electromyogram and mechanomyogram of the adductor pollicis brevis muscle were measured simultaneously. In the Vec and Pan groups, a total dose of 40 μg kg⁻¹ of vecuronium or pancuronium, respectively, was given, and in the Atr group a total dose of atracurium 100 μg kg⁻¹. Each blocker was given in four equal doses and administered cumulatively. We showed that 0.95% isoflurane and 1.70% sevoflurane (corresponding to 0.8 MAC of each inhalation anaesthetic, omitting the MAC contribution of nitrous oxide) augmented and prolonged the neuromuscular block produced by vecuronium, pancuronium and atracurium to a similar degree. (Br J Anaesth 1996; 76: 389–395)

Key words

Various inhalation anaesthetics augment neuromuscular block produced by non-depolarizing neuromuscular blocking agents to a different degree. Although sevoflurane appears to increase both intensity and duration of neuromuscular block induced by vecuronium and pancuronium [1–4], the magnitude of this effect has not been quantified in a homogeneous population. Such information is clinically relevant; for example potentiation of blocker effect during administration of sevoflurane and reversal of this potentiation on withdrawal of this short-acting inhalation agent may reduce blocker dose requirements in the peroperative period and decrease the risk of residual curarization after operation.

Previous studies comparing the effects of isoflurane and sevoflurane on vecuronium block have produced inconclusive results. These studies were unable to show any significant difference for the effects of 1.15% isoflurane and 1.70% sevoflurane (both with 70% nitrous oxide [1, 2]) or for the effects of 1.15% isoflurane and 2.05% sevoflurane (both with 66% nitrous oxide [3]) on the block produced by vecuronium. Another interaction study, comparing opioid–nitrous oxide–oxygen and opioid–nitrous oxide–oxygen–sevoflurane anaesthesia, could not demonstrate any significant influence of sevoflurane with concentrations less than 2% on the duration of vecuronium-induced block [4].

In order to clarify the inconsistencies in the literature on the interactions between sevoflurane and neuromuscular blockers, we have compared the effect of equipotent concentrations of isoflurane and sevoflurane on non-depolarizing neuromuscular block in a carefully selected, homogeneous population of young adults. In this population the minimum alveolar concentrations (MAC) of isoflurane and sevoflurane in air–oxygen were found to be 1.15% [5] and 2.05% [6], respectively. The addition of 65–70% nitrous oxide reduces the MAC of both agents to 0.50% [5] and 1.10% [7], respectively.

Patients and methods
After obtaining approval from the Institutional Review Board and written informed consent, we studied 90 healthy adult patients, aged 18–50 yr, of both sexes, ASA I or II, undergoing elective surgical

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procedures of an anticipated duration of \( \geq 90 \) min under general anaesthesia. Patients were excluded if they had cardiac, pulmonary, renal, hepatic, neurological, psychiatric, muscular, inflammatory, malignant or endocrine diseases, as were pregnant women and patients with recent exposure (< 72 h) to medications known to interfere with neuromuscular transmission. Those more than 20% overweight, according to life insurance tables [8], or those with clinical laboratory abnormalities (i.e., serum electrolyte, creatinine, BUN, SGOT, LDH, alkaline phosphatase or GGT concentrations) were also excluded.

Patients were stratified into one of three blocker groups (Vec, Pan, and Atr) consisting of 30 patients each. Within each blocker group, patients were allocated randomly to one of three anaesthetic subgroups, to undergo maintenance of anaesthesia with either: (1) alfentanil-nitrous oxide-oxygen (non-halogenated anaesthetics group (NHA)) \( (n = 10) \); (2) alfentanil-nitrous oxide-oxygen-isoflurane (isoflurane group (Iso)) \( (n = 10) \); or (3) alfentanil-nitrous oxide-oxygen-sevoflurane (sevoflurane group (Sey)) \( (n = 10) \).

After an overnight fast, patients were premedicated with diazepam 0.1 mg kg\(^{-1}\) orally, 60–90 min before induction of anaesthesia. Before this, patients were given Ringer’s solution 1.5 ml kg\(^{-1}\) per hour of fasting. Alfentanil 100 \( \mu \)g kg\(^{-1}\) was administered as a bolus i.v. followed by a variable rate infusion of alfentanil 0.5–1.5 \( \mu \)g kg\(^{-1}\) min\(^{-1}\). Three minutes after the alfentanil infusion was started, anaesthesia was induced with propofol 3.5–5 mg kg\(^{-1}\) i.v. in divided doses. The trachea was intubated without neuromuscular block. Anaesthesia was maintained with the anaesthetic technique selected during the randomization procedure. End-tidal concentrations of isoflurane, sevoflurane and nitrous oxide were targeted at 0.95%, 1.70% and 7.0%, respectively. For the population studied, the MAC values of isoflurane and sevoflurane in air–oxygen were defined as 1.15% [5] and 2.05% [6], respectively. The contribution of nitrous oxide to the MAC value of the inhalation agent was calculated applying the concept of additivity of MAC fractions, where the individual MAC values of each gas (in this case nitrous oxide and sevoflurane or isoflurane) are summated to find the MAC value of the combination [9]. Equi potency concentrations of isoflurane and sevoflurane were defined as equal fractions of the MAC of either volatile anaesthetic without the MAC contribution of nitrous oxide [10].

After 40 min of stable end-tidal anaesthetic concentrations (within 5% of the target values), an end-tidal carbon dioxide partial pressure of 4.7–5.3 kPa, stable haemodynamics with a systolic arterial pressure > 100 mm Hg and a stable baseline neuromuscular transmission recording, the blocker was administered i.v. in a cumulative manner, as described below. During the procedure both central and thenar skin temperatures were maintained between 35.5 and 36.5 °C using surface heating.

ECG monitoring of lead II was performed continuously and arterial pressure was measured intermittently by automated sphygmomanometry (Dinamap, Criticon, Tampa, USA). The arterial pressure cuff was placed on the arm opposite to the site where neuromuscular transmission was assessed. Thenar skin temperature was monitored using a thermocouple placed on the dorsum of the hand from which the response to ulnar nerve stimulation was recorded. Central temperature was measured using a rectal probe. The end-tidal concentrations of carbon dioxide, nitrous oxide, isoflurane and sevoflurane were measured continuously and displayed by a multiple gas analyser (Capnomac Ultima, Datex). This gas analyser was calibrated once every week using a calibrating gas (Quick Cal, Datex).

Neuromuscular transmission was evaluated using both the evoked integrated electromyogram (IEMG) and the mechanomyogram (MMG) of the ipsilateral adductor pollicis muscle. The stimulating current, consisting of supramaximal rectangular pulses (duration 100 \( \mu \)s) into a train-of-four (TOF) pattern (frequency 2 Hz), was generated by the stimulating unit of the Datex Relaxograph and delivered every 20 s (0.05 Hz) to the ulnar nerve at the wrist via s.c. 27-gauge steel needle electrodes, placed 30 mm apart. The hand and forearm were immobilized in supination and abduction on a splint and the fingers were strapped in extension. The thenar electromyographic signal was detected using gelled silver–silver chloride skin electrodes. These were placed over the belly of the adductor pollicis muscle (the active recording electrode), at the distal phalanx of the second finger (the reference recording electrode) and midway between the stimulating and recording electrodes (grounding electrode). The force transducer was mounted so that the thumb was exposed to a preload of 200 g, measured continuously and recorded. During the study, a preload of 100–300 g was accepted.

For each blocker group, a cumulative dosing regimen was designed in which all patients undergoing maintenance of anaesthesia with different anaesthetic techniques were given the same amount of neuromuscular blocking agent. In the Vec and Pan groups, a total dose of 40 \( \mu \)g kg\(^{-1}\) of vecuronium or pancuronium, respectively, was given and in the Atr group a total dose of atracurium 100 \( \mu \)g kg\(^{-1}\) was given. Each blocker was injected in four equal doses and administered cumulatively. For vecuronium and pancuronium, an initial dose of 10 \( \mu \)g kg\(^{-1}\) and three increments of 10 \( \mu \)g kg\(^{-1}\) each were administered. For atracurium, an initial dose of 25 \( \mu \)g kg\(^{-1}\) and three increments of 25 \( \mu \)g kg\(^{-1}\) each were administered. Each dose of neuromuscular blocking agent was injected as an i.v. bolus over < 5 s into a rapidly running infusion.

As soon as the patient was anaesthetized, baseline evaluations of neuromuscular transmission were started and continued for 40 min before administration of the neuromuscular blocking agent. The mean of 10 first twitch (T1) responses, immediately preceding the first administration of neuromuscular blocking agent, became the control to which all subsequent T1 responses were compared. Each dose increment was given (at times t1, t2 and t3, respectively) only after the effect of the previous dose had reached a stable response, defined as three equal
(± 1 %) consecutive IEMG or MMG T1 responses, or when 7 min had passed with no decrease in T1 from control.

DATA ANALYSIS

Age, weight and percentage of ideal weight for height between the nine subgroups were compared using one-way analysis of variance (ANOVA). The Ryan–Einot–Gabriel–Wesch multiple range test (REGW test) [11] was applied subsequently to identify eventual sources of difference.

Within each blocker group, the time schedule in which the four doses of the neuromuscular blocking agents were administered was compared between the three anaesthetic subgroups, by comparing the times to injection of the first (t1), second (t2) and third (t3) increments after administration of the initial dose, using one-way ANOVA. The REGW test was applied subsequently to identify eventual sources of difference.

The individual dose–effect relationship was examined by plotting the logarithm of the dose against the logit transformation of T1 depression relative to control

\[ \text{Logit}(E) = \alpha \times \log \frac{D}{E_{\text{max}} - E} - \beta \]

where \( \text{Logit}(E) = \log \frac{E}{(E_{\text{max}} - E)} \); \( E = T1 \) depression relative to control (%); \( E_{\text{max}} = \) maximal effect, that is 100%; \( D = \) dose, administered cumulatively; \( \alpha = \) steepness coefficient; and \( \beta = \) intercept.

Because logit 0 and logit 1 do not exist, 0% and 100% T1 depression were considered as missing values. Lines of best fit were computed using linear least squares regression. The doses required for 50%, 90%, and 95% T1 depression (ED50, ED90, and ED95, respectively) were calculated from the regression line.

The regression lines were tested to determine if they deviated from parallelism [12]. If they did not, ED50, ED90, and ED95 values were compared between the subgroups. Parallelism was tested using one-way ANOVA and subsequent REGW test of the steepness coefficients of the regression lines (\( \alpha \)). Comparison of the ED50, ED90, and ED95 values between subgroups was performed using one-way ANOVA and subsequent REGW test.

Duration of action was defined as the interval between injection of the last neuromuscular blocking agent increment to 90% T1 recovery (T90) and to 70% T4/T1 recovery (TTOF70). T90 and TTOF70 were calculated on both the IEMG and MMG by linear interpolation between the nearest neighbour measuring points [13].

In the current study, significant baseline drift with time was defined as failure of the IEMG T1 to recover to ≥ 90% of the pre-blocker T1 reference level, with T4/T1 > 0.90. In patients showing significant baseline drift with time, the IEMG–based T90 was considered as a missing value.

If, within the blocker groups, administration of the neuromuscular blocking agent was the same in each of the anaesthetic subgroups, T90 and TTOF70 values were compared between the anaesthetic subgroups by means of one-way ANOVA. The REGW test was applied subsequently to identify the source of difference.

Within the anaesthetic subgroups, IEMG–based ED50, ED90, ED95, T90 and TTOF70 values were compared with the corresponding MMG–based variables using the two-tailed paired Student’s t tests.

Statistical calculations were performed with the Statistical Applications Software of the SAS Institute (SAS/STAT Release 6.03, SAS Institute Inc, Cary, USA). All statistical tests were two-sided. \( P < 0.05 \) was considered to indicate statistical significance.

Results

We studied 108 patients, but the results from 18 were excluded because of measurement errors, technical failures or deviations from the study procedure. Within the blocker groups, there were no significant differences in age, weight, percentage of ideal weight for height or sex distribution between the anaesthetic subgroups (table 1).

The mean concentrations of isoflurane (n = 30) and sevoflurane (n = 30) were calculated to be 0.82 (SEM 0.01) MAC and 0.83 (0.01) MAC, omitting the MAC contribution of nitrous oxide, and 1.49 (0.02) MAC and 1.50 (0.01) MAC, respectively, including the MAC contribution of 70% nitrous oxide.

Within the blocker groups, the times of administration of the first (t1), second (t2) and third dose (t3) increments did not differ significantly between the anaesthetic subgroups (table 2).
Table 2  Times (mean (pooled SEM)) to cumulative dose administration after the initial dose: increments 1, 2 and 3 were injected at times T1, T2 and T3, respectively, in the different anaesthetic subgroups within the vecuronium, pancuronium and atracurium groups. NHA = No halogenated anaesthetic (n = 10), Iso = isoflurane (n = 10), Sev = sevoflurane (n = 10). Within the three blocker groups, there were no significant differences between the subgroups NHA, Iso and Sev for t1, t2 or t3.

<table>
<thead>
<tr>
<th>Group</th>
<th>Anaesthetic technique</th>
<th>t1  (min)</th>
<th>t2  (min)</th>
<th>t3  (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vecuronium</td>
<td>NHA</td>
<td>5.8 (0.2)</td>
<td>9.8 (0.3)</td>
<td>12.9 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>6.1 (0.2)</td>
<td>10.0 (0.3)</td>
<td>13.2 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>6.2 (0.2)</td>
<td>10.4 (0.3)</td>
<td>13.5 (0.3)</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>NHA</td>
<td>6.2 (0.1)</td>
<td>10.0 (0.1)</td>
<td>13.2 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>6.3 (0.1)</td>
<td>10.4 (0.1)</td>
<td>13.9 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>6.0 (0.1)</td>
<td>10.2 (0.1)</td>
<td>13.4 (0.2)</td>
</tr>
<tr>
<td>Atracurium</td>
<td>NHA</td>
<td>6.0 (0.1)</td>
<td>10.0 (0.2)</td>
<td>13.4 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>6.0 (0.1)</td>
<td>10.1 (0.2)</td>
<td>13.6 (0.2)</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>6.1 (0.1)</td>
<td>10.4 (0.2)</td>
<td>13.9 (0.2)</td>
</tr>
</tbody>
</table>

Table 3  Steepness coefficients (mean (pooled SEM)) in the different anaesthetic subgroups within the vecuronium, pancuronium and atracurium groups. NHA = No halogenated anaesthetic (n = 10), Iso = isoflurane (n = 10), Sev = sevoflurane (n = 10). The steepness coefficients are the slopes of the regression lines, representing the relationship between the logit transformation of neuromuscular block and the logarithm of the dose. Neuromuscular block was assessed using either integrated electromyography (IEMG) or mechanomyography (MMG) as an effect variable. Within the three blocker groups, there were no significant differences between the subgroups NHA, Iso and Sev in steepness coefficients, as determined by either IEMG or MMG.

<table>
<thead>
<tr>
<th>Group</th>
<th>Anaesthetic technique</th>
<th>Steepness coefficient</th>
<th>IEMG</th>
<th>MMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vecuronium</td>
<td>NHA</td>
<td>4.2 (0.2)</td>
<td>4.3 (0.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>4.4 (0.2)</td>
<td>3.8 (0.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>4.2 (0.2)</td>
<td>3.7 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Pancuronium</td>
<td>NHA</td>
<td>4.8 (0.2)</td>
<td>4.2 (0.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>4.4 (0.2)</td>
<td>3.7 (0.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>4.5 (0.2)</td>
<td>3.6 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Atracurium</td>
<td>NHA</td>
<td>5.1 (0.3)</td>
<td>4.8 (0.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>4.6 (0.3)</td>
<td>4.3 (0.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>4.3 (0.3)</td>
<td>4.1 (0.4)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4  Cumulative dose–response data for vecuronium, pancuronium and atracurium in the different anaesthetic subgroups. NHA = No halogenated anaesthetic (n = 10), Iso = isoflurane (n = 10), Sev = sevoflurane (n = 10). ED50, ED90 and ED95 = doses producing 50%, 90% and 95% neuromuscular block, respectively, using either integrated electromyography (IEMG) or mechanomyography (MMG) as an effect variable. Within the three blocker groups, there were no significant differences between subgroups NHA, Iso and Sev. There were no significant differences between subgroups Iso and Sev; there were no significant differences between IEMG- and MMG-based variables.

<table>
<thead>
<tr>
<th>Group</th>
<th>Anaesthetic technique</th>
<th>ED50 (µg kg⁻¹)</th>
<th>ED90 (µg kg⁻¹)</th>
<th>ED95 (µg kg⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IEMG</td>
<td>MMG</td>
<td>IEMG</td>
<td>MMG</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vecuronium</td>
<td>NHA</td>
<td>23.9 (1.7)</td>
<td>24.8 (2.0)</td>
<td>41.6 (3.4)</td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>16.5 (1.7)*</td>
<td>16.9 (2.0)*</td>
<td>29.1 (3.4)*</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>15.0 (1.7)*</td>
<td>14.4 (2.0)*</td>
<td>25.8 (3.4)*</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>NHA</td>
<td>31.7 (1.3)</td>
<td>29.0 (1.4)</td>
<td>49.9 (1.7)</td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>20.7 (1.3)*</td>
<td>20.3 (1.6)*</td>
<td>34.7 (1.7)*</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>21.3 (1.3)*</td>
<td>21.3 (1.4)*</td>
<td>35.0 (1.7)*</td>
</tr>
<tr>
<td>Atracurium</td>
<td>NHA</td>
<td>117.0 (4.3)</td>
<td>112.4 (4.9)</td>
<td>187.0 (8.0)</td>
</tr>
<tr>
<td></td>
<td>Iso</td>
<td>67.8 (4.3)*</td>
<td>66.8 (4.9)*</td>
<td>109.6 (8.0)*</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>65.0 (4.3)*</td>
<td>66.5 (4.9)*</td>
<td>108.9 (8.0)*</td>
</tr>
</tbody>
</table>
For the blocker groups, the slopes of the cumulative dose–response curves did not differ significantly between the anaesthetic subgroups (table 3). The ED$_{50}$, ED$_{90}$ and ED$_{95}$ values, calculated for the subgroups Iso and Sev, were not significantly different. There was a significant difference in ED$_{50}$, ED$_{90}$ and ED$_{95}$ values ($P < 0.01$) between the subgroups receiving halogenated volatile anaesthetics (Iso and Sev) and the subgroup receiving opioid–nitrous oxide–oxygen anaesthesia (NHA) (table 4, fig. 1). There were no significant differences between the ED$_{50}$, ED$_{90}$ and ED$_{95}$ values determined using the IEMG or MMG.

In the blocker groups, T90 and TTOF70, measured for the subgroups Iso and Sev, were not significantly different. There was a significant difference in T90 and TTOF70 ($P < 0.01$) between the subgroups receiving the halogenated volatile anaesthetics and the subgroup receiving opioid–nitrous oxide–oxygen anaesthesia (table 5).

Fourteen patients exhibited significant IEMG baseline drift with time. Within the blocker groups, there were no significant differences between IEMG- and MMG-based T90 values for the patients exhibiting no significant baseline drift with time. Also, there were no significant differences between IEMG- and MMG-based TTOF70 values in all patients.

Discussion

We have demonstrated that equipotent concentrations of isoflurane and sevoflurane (i.e. 0.95% and 1.70% respectively) augmented and prolonged vecuronium-, pancuronium- and atracurium-induced neuromuscular block to a similar degree compared with opioid–nitrous oxide anaesthesia. The concentrations of isoflurane and sevoflurane corresponded to 0.8 MAC, omitting the MAC contribution of nitrous oxide, and to 1.5 MAC, including the MAC contribution of 70% nitrous oxide.

The current interaction study differed from previous ones [1–4] in that anaesthetic-related effects on neuromuscular blocking agents were compared within a carefully selected homogeneous population of young adults, using IEMG and MMG responses of the adductor pollicis brevis muscle simultaneously.

**Magnitude of Block**

If administered in equipotent concentrations, inhalation anaesthetics enhanced vecuronium-, pancuronium- and atracurium-induced neuromuscular block to an approximately equal extent. The IEMG and MMG tend to detect similar magnitudes of block after administration of either vecuronium, pancuronium or atracurium. Similar observations have been made previously with tubocurarine [14]. The results of the current study are at variance with those of Engbæk and Roed [15] using pancuronium. Their findings may be explained by different conditions of anaesthesia, or recording electrode positioning [16] and stimulation frequency, or both [17].

The MMG-based potency estimates, assessed in the current study with an opioid–nitrous oxide–oxygen anaesthetic, were consistent with previously determined values for vecuronium [18, 19], pancuronium [20] and atracurium [18, 19] using the cumulative dose technique.

Our conclusions regarding the effect of isoflurane and sevoflurane on non-depolarizing neuromuscular block are in keeping with those of Morita and co-workers [3] who were unable to detect any significant difference between the potentially effects of 1.15% isoflurane and 2.05% sevoflurane in 66% nitrous oxide (i.e. 1 MAC of either vapour in oxygen–air without the MAC contribution of nitrous oxide) on neuromuscular block produced by vecuronium. However, the ED$_{50}$, ED$_{90}$ and ED$_{95}$ values calculated, using the single dose technique, were less than the current cumulative dose values. Redistribution between successive cumulative doses may explain the greater ED$_{50}$, ED$_{90}$ and ED$_{95}$ estimates in the current study. Moreover, the end-tidal concentrations of isoflurane and sevoflurane in their study (1.15 and 2.05%, respectively) were approximately 20% lower than those used in the current study.
higher than those used in the current study (0.95 and 1.70 %, respectively). Additionally, there may be other factors (i.e. anthropometric, ethnic [21] or environmental [22]) that could have affected the sensitivity to vecuronium.

The cumulative dose technique, used in the current study, may underestimate the potency of the neuromuscular blocking agent with rapid distribution and elimination. However, administration of a neuromuscular blocking agent was consistent throughout the study and the volatile agent was chosen randomly; thus the degree of redistribution would have been similar in all patients within a blocker group undergoing maintenance of anaesthesia with different techniques. Additionally, the aim of the current study was to determine anaesthesia-related effects on non-depolarizing neuromuscular block and not to provide absolute potency estimates.

**DURATION OF ACTION**

In equipotent concentrations, both inhalation anaesthetics prolonged vecuronium-, pancuronium- and atracurium-induced neuromuscular block to a similar degree. The IEMG- and MMG-based TTOF70 values may be used interchangeably for the three neuromuscular blocking agent studied. Similar findings have been shown previously for atracurium [23] and tubocurarine [14]. However, during offset of neuromuscular block, IEMG T1 should be interpreted with caution as it may be unstable with time. The MMG-based T90 values assessed in the current study were comparable with previously published MMG T90 values during opioid–nitrous oxide–oxygen anaesthesia for vecuronium [24, 25], pancuronium [26] and atracurium [27] and during opioid–nitrous oxide–isoflurane anaesthesia for atracurium [27, 28].

Recent studies on the effect of sevoflurane on duration of vecuronium-induced neuromuscular block yielded data that showed wide variation on the extent of prolongation [2–4]. However, there were several methodological differences compared with our study. First, in these studies, patient ages ranged from 22 to 77 yr [2], 22 to 62 yr [3] and 25 to 75 yr [4], respectively. Second, offset of neuromuscular block was measured using the evoked IEMG, which was shown to be unreliable in 5–42 % (18% in the current study) of patients [29]. As advancing age is associated with a greater incidence of slow recovery after vecuronium [5], and because the IEMG is unreliable during offset of non-depolarizing neuromuscular block [30], considerable between-patient variability in duration of neuromuscular block may have been produced within the populations studied. In the investigation of Saitoh, Toyooka and Amaha [2], the scatter in the duration of neuromuscular block, after the same dose of vecuronium (0.2 mg kg  –1 ) was so large that significant differences in the duration of neuromuscular block with opioid–nitrous oxide and opioid–nitrous oxide–isoflurane (end-tidal isoflurane concentration = 1.15 %) anaesthesia could not be demonstrated. Therefore, comparison of such inaccurately determined recovery variables between these heterogeneous populations produces results that should be interpreted with caution.

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