A MATCHED COMPARISON OF FOUR SUXAMETHONIUM ADMINISTRATION TECHNIQUES IN PATIENTS WITH STRABISMUS

D. A. COZANITIS, U. KARHUNEN, P. BRANDER AND J. D. MERRETT

SUMMARY

Four methods of administering suxamethonium were compared in patients undergoing surgery for strabismus who were matched for sex, age, weight and height. Pre-treatment with tubocurarine afforded the best control of suxamethonium-induced sequelae. Serum potassium remained within normal limits suggesting that individuals with strabismus behave differently from those free of this defect.

As advocated by Mayrhofer (1959), the administration of tubocurarine 0.05 mg kg⁻¹, if given 3 min (Takki, Kauste and Kjellberg, 1972) before suxamethonium 1.5 mg kg⁻¹ (Cullen, 1971) is capable of controlling the fasciculations of the depolarizing relaxant and affords satisfactory intubating conditions. The search continues for alternative methods to reduce the suxamethonium-induced sequelae. Diazepam has long been thought effective for this (Tonsa, 1966; Parada, 1968; di Giacomo, Beyer and Müller, 1970) but a more recent study reporting its benefits (Fahmy, Malek and Lappas, 1979) has been rebutted (Erkola, Salmenpera and Tammisto, 1980). Other compounds such as ascorbic acid (Gupte and Savant, 1971) and dantrolene (Collier, 1979; Plötz, Braun and Stallenberger, 1981) have been described as being, respectively, of no value (Wood et al., 1977) or unsuitable (Agoston, 1980).

Foldes (1973 and personal communication) and Baraka (1977) advocate "special handling" of suxamethonium for controlling the fasciculations so inherent with the i.v. injection. However, reports are conflicting (Mitchell and Brooks, 1978; Restelli et al., 1980; Wilson and Dundee, 1980).

The modification of Mayrhofer's technique mentioned earlier is our standard procedure when suxamethonium is given for endotracheal intubation. To determine if the methods of Foldes (1973) and Baraka (1977) would offer any advantages over this method, and using untreated suxamethonium as control, a study was designed involving matched groups of patients undergoing surgical correction for strabismus.

METHODS

Sixty patients undergoing anaesthesia and surgery for strabismus, of either sex, aged 6–56 yr and in good health were studied in 15 groups, each of four patients, matched for sex, age, weight and height. The limits of matching, except for children and adolescents, were within 15 years of age, 15 kg weight, and 15 cm height. Four methods of suxamethonium (Sx) administration for endotracheal intubation were allotted at random to the four members of each group.

The patients received atropine 0.01 mg kg⁻¹ and pethidine 1 mg kg⁻¹ i.m. 30–60 min before the start of anaesthesia. In the operating room, e.c.g. (precordial electrodes; lead II) was recorded on to an Elema Mingograph and a sphygmomanometer cuff was placed around the left forearm for arterial pressure measurement. The right cubital vein was cannulated and blood samples taken for serum creatine kinase (CK) and potassium (K) determinations. A buffered 5% glucose solution was connected to the cannula into which all drugs were given. The patients breathed oxygen from a facemask before thiopentone 5 mg kg⁻¹ was given over a period of 10 s.

The four i.v. methods of Sx administration, after the loss of verbal response to thiopentone, to enable endotracheal intubation are:

(I) Suxamethonium 1 mg kg⁻¹ given in 3 s.
(II) Suxamethonium 0.14 mg kg⁻¹ injected and after 45–60 s, Sx 1 mg kg⁻¹ administered over a 5-s period.
(III) Suxamethonium 0.6 mg kg⁻¹ given over 30 s into the fast running glucose solution. The
first one-third was injected in 15 s and the second two-thirds in the next 15 s.

(IV) Tubocurarine 0.05 mg kg\(^{-1}\) i.v. preceded thiopentone administration by 2.5 min. When 3 min had elapsed from the time of the tubocurarine injection, suxamethonium 1.5 mg kg\(^{-1}\) was given within 3 s.

After tracheal intubation the patients breathed, from a non-rebreathing system, nitrous oxide in oxygen (4:2) and 1% halothane. End-tidal carbon dioxide was maintained between 4.5 and 6% and recorded. Increments of pethidine were given i.v. to supplement anaesthesia.

The same two anaesthetists undertook the study, one (PB) being in charge of grading the level of Sx-provoked fasciculations (0 = absent, 1 = mild, 2 = moderate, 3 = severe) and intubating conditions (0 = vocal cords abducted, no movement of diaphragm: 1 = vocal cords abducted, slight diaphragmatic movement: 2 = vocal cords slightly moving, gross movements of diaphragm: 3 = impossible to intubate). The second anaesthetist (UK) gave all the drugs during the study period and took the necessary blood samples. Care was taken that the first anaesthetist did not know what administration technique was used.

Blood was sampled with minimal or no stasis applied and no flushing of the cannula, which had been inserted into the great saphenous vein in the foot. If this cannula became occluded, the vein in the contralateral foot was used. Blood for serum K determination was taken before and at 1, 3, 5, 7, and 10 min after Sx administration and analysed immediately by a flame photometric technique. Blood for serum CK was collected just before anaesthesia, at 24 and 48 h later and stored at -20°C until measured according to the Recommendations of the Scandinavian Committee on Enzymes (Committee, 1976). The method is sensitive and eliminates the possibility of enzyme inactivation. In the laboratory here, 170 u. litre\(^{-1}\) and 220 u. litre\(^{-1}\) are the upper normal limits for females and males respectively.

During the 8-month period of investigation, 13 ampoules of suxamethonium used were at random returned to the manufacturer, who determined the activity of the relaxant according to the monograph for Succinylcholine Chloride Injection in the British Pharmacopoeia (BP) (1973).

The Friedman test and Cochran’s Q test were used for statistical handling of CK and fasciculation/intubation conditions respectively. These are non-parametric tests taking into account the matching. The former test permits the analysis of data which are not normally distributed. Mean serum K values of the four methods were compared by analysis of variance. Statistical significance was indicated by a probability value \(P < 0.05\).

RESULTS

The efficiency of matching of age, weight and height is shown in table I. Clearly, there are no large differences on average for any of the three variables.

Serum that yielded extraordinarily large CK values was re-examined about 1 week after the first measurements had been made. In all cases the repeat values were less than the first, indicating that CK activity decreased with storage. Where duplication was made, the first values were used for statistical analysis. As the delay in analysing the specimens occurred with similar frequency, it is reasonable to assume that the comparison of CK values is not confounded by this factor. CK concentrations before induction of anaesthesia were similar among the four methods. The mean ranks between the various techniques, that is within times, did not differ significantly (table II). On the other hand, when the mean ranks between times (within techniques) were studied, \(P = 0.01, 0.00, 0.06\) and \(0.04\) for methods I, II, III and IV respectively. The trends were upward from 0 to 24 h but then diminished from 24 to 48 h.

By examining the standard deviations in table II between the methods one could well consider these clinically important. In this respect, method IV had the least variation and method I the greatest.

Serum K concentrations remained well within normal limits over the 10-min sampling period. As there was no evidence that these values were not normally distributed, an analysis of variance was applied. This was used to reveal if there were method or time effects, or both, and whether these two factors, technique and time, interact. The means and standard deviations of the K values are seen in table III. An increasing trend with time was noted in all four methods, method IV resulting in the least change and that of method I, the greatest. Clinically, however, these alterations cannot be considered significant. Statistically, over all times combined, there were no significant differences between techniques \((F = 0.93: P > 0.05)\). There were, however, significant differences in the time means for all techniques combined \((F = 2.767: 0.05 > P > 0.025)\). Furthermore, there was no interaction between technique and time \((F = 0.77:\)
**Table I. Summary of the efficiency of matching**

<table>
<thead>
<tr>
<th>Method of suxamethonium administration</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (number of males)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Mean age (yr ± SD)</td>
<td>22.9±10.5</td>
<td>23.5±12.0</td>
<td>24.4±12.9</td>
<td>24.5±13.9</td>
</tr>
<tr>
<td>Mean weight (kg ± SD)</td>
<td>56.9±14.4</td>
<td>57.1±19.9</td>
<td>56.7±15.3</td>
<td>57.3±13.9</td>
</tr>
<tr>
<td>Mean height (cm ± SD)</td>
<td>161±15</td>
<td>160±18</td>
<td>162±14</td>
<td>162±19</td>
</tr>
</tbody>
</table>

**Table II. Mean CK activity (u. litre⁻¹ ± SD). (Note that mean ranks shown can only be compared within a column and not within a row)**

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>0</th>
<th>24</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of Sx admin.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>81.3±40.7</td>
<td>413.4±611.1</td>
<td>282.5±378.5</td>
</tr>
<tr>
<td>Mean rank</td>
<td>2.40</td>
<td>2.87</td>
<td>2.83</td>
</tr>
<tr>
<td>II</td>
<td>83.5±39.8</td>
<td>306.0±365.8</td>
<td>198.3±193.2</td>
</tr>
<tr>
<td>Mean rank</td>
<td>2.63</td>
<td>2.47</td>
<td>2.40</td>
</tr>
<tr>
<td>III</td>
<td>93.0±46.9</td>
<td>216.1±223.0</td>
<td>175.2±131.5</td>
</tr>
<tr>
<td>Mean rank</td>
<td>2.83</td>
<td>2.57</td>
<td>2.73</td>
</tr>
<tr>
<td>IV</td>
<td>75.9±37.7</td>
<td>204.1±168.0</td>
<td>161.4±131.5</td>
</tr>
<tr>
<td>Mean rank</td>
<td>2.13</td>
<td>2.10</td>
<td>2.03</td>
</tr>
<tr>
<td>Chi square</td>
<td>2.46</td>
<td>2.70</td>
<td>3.54</td>
</tr>
<tr>
<td>d.f.</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>P</td>
<td>0.30–0.50</td>
<td>0.30–0.50</td>
<td>0.30–0.50</td>
</tr>
</tbody>
</table>

**Table III. Mean serum potassium values (mmol litre⁻¹ ± SD)**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>7</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of Sx admin.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4.11±0.35</td>
<td>4.11±0.23</td>
<td>4.13±0.21</td>
<td>4.11±0.23</td>
<td>4.15±0.22</td>
<td>4.22±0.23</td>
</tr>
<tr>
<td>II</td>
<td>4.08±0.28</td>
<td>4.15±0.29</td>
<td>4.11±0.26</td>
<td>4.12±0.23</td>
<td>4.11±0.27</td>
<td>4.16±0.23</td>
</tr>
<tr>
<td>III</td>
<td>4.08±0.16</td>
<td>4.23±0.23</td>
<td>4.12±0.25</td>
<td>4.17±0.24</td>
<td>4.16±0.19</td>
<td>4.21±0.23</td>
</tr>
<tr>
<td>IV</td>
<td>4.20±0.18</td>
<td>4.20±0.17</td>
<td>4.25±0.18</td>
<td>4.22±0.18</td>
<td>4.21±0.18</td>
<td>4.27±0.22</td>
</tr>
</tbody>
</table>
This latter result indicates that there were no significant differences, on average, between techniques at each time and that the overall trend in time means was consistent for each method.

Table IV summarizes the fasciculations and intubating conditions seen in the study. It is obvious that method I produced the greatest and method IV the least amount of fasciculations. As regards intubating conditions, methods I and IV provided the best situation. Statistically, because of the small number of patients in each group, a dichotomous classification, 0 and 1, was used, 1 being indicative of an adverse condition. Table IV shows the frequency (%) of adverse fasciculations and intubating conditions. Application of Cochran's $Q$ test, which takes into account the matching, shows that there are significant differences among the methods used as regards the frequency of adverse fasciculations, largely because of the lower frequency of fasciculations with method IV ($Q = 40.20; \text{d.f.} = 3; P < 0.001$). However, no significant differences were found in the frequency of adverse intubating conditions between the four techniques.

Methods II and III resulted in slowing of heart rates in 10 and three patients respectively. The decrease in the case of method II ranged from 8 to 50 (mean 26) beat min$^{-1}$ while in method III the range was 15–63 (mean 36) beat min$^{-1}$. The slowing of heart rate was noted when comparing the rates immediately before start of anaesthesia with those following suxamethonium, that is just before endotracheal intubation. During this time, the e.c.g. changes that occurred within the methods were: II, junctional wandering pacemaker 2, bigeminy 2; III, junctional wandering pacemaker 1, aberrations 2; IV, junctional wandering pacemaker 2.

The ampoules of suxamethonium analysed contained hydrolysis products well within the limits of the Assay for Succinylcholine Injection in the British Pharmacopoeia. The fasciculations therefore could not have been affected by the relaxant, per se.

**DISCUSSION**

The study was limited to patients with strabismus on the basis of a hypothesis originating here which proposes that such persons, because of a defect in their skeletal muscle biochemistry, respond differently to suxamethonium (Tammisto et al., 1970). It is well known that the greater the skeletal muscle trauma, the greater are the concentrations of CK. As surgery for squint would produce limited injury, changes in CK would be more indicative of those evolving from Sx-induced fasciculations and their subsequent "damage" or "strain", or "increased outflux" of the affected muscle part. Matching was done to give a more sensitive statistical comparison of the techniques as it reduced the random variation between groups.

The size of the standard deviations of CK provide valuable information. Method IV gave a more limited range of change than did the others. This correlates well with the level of fasciculations, which were minimal with this method.

The behaviour of serum K is particularly surprising in that, even in method I, the electrolyte remained within normal limits. This finding disagrees with that of Berkebile, Pfaffle and Smith (1973), who noted a statistically significant increase after Sx administration in seven patients with squint. Our finding seems to add support to the hypothesis of Tammisto and others (1970).

The most apparent e.c.g. finding was the slowing of heart rate in 10 patients who received suxamethonium according to method II. This technique is one of intermittent administration, the second dose provoking the slowing. Junctional wandering pacemaker seen in all but method I is obviously an escape rhythm resulting from the slowing of the rapid rate. Perhaps the changes in e.c.g. could have been prevented had a potent antimuscarinic drug such as glycopyrrolate been given i.v. just before start of anaesthesia (Cozanitis, Dundee and Khan, 1980).

The results of this investigation suggest that "special handling" of Sx (methods II and III) do not offer any advantages over the injection of tubocurarine 0.05 mg kg$^{-1}$ 3 min before the administration of Sx 1.5 mg kg$^{-1}$ for controlling the sequelae of i.v. injected Sx. Failure of serum K to increase in patients with squint after untreated Sx indicates that these individuals should be studied further.
REFERENCES


Collier, C.B. (1979). Dantrolene and suxamethonium Anesthesiology, 34, 152


ETUDE COMPARATIVE DE QUATRE TECHNIQUES D'ADMINISTRATION DU SUXAMETHONIUM CHEZ DES PATIENTS SOUFFRANT DE STRABISME

RESUME

Quatre méthodes d'administration du suxaméthonium ont été comparées chez des patients subissant une chirurgie du strabisme et de sexe, d'âge, de poids et de taille comparables. C'est avec un traitement préalable par la tubocurarine que l'on obtenait la meilleure prévention des séquelles dues au suxaméthonium. La kaliémie restait dans les limites de la normale, ce qui suggère que les individus porteurs d'un strabisme ont un comportement différent de celui des individus normaux.

EIN PASSENDER VERGLEICH VON VIER VERABREICHUNGSTECHNIKEN VON SUXAMETHONIUM-BEI PATIENTEN MIT STRABISMS

ZUSAMMENFASSUNG

Vier Verabreichungsformen von Suxamethonium wurden bei Patienten verglichen, die sich einer Strabismus-Operation unterziehen mußten und die in Bezug auf Geschlecht, Alter, Gewicht und Größe vergleichbar waren. Durch Vorbehandlung mit Tubokurarin konnten die auf Suxamethonium folgenden Nebenwirkungen am besten beherrscht werden. Das Serumkalium blieb im Normbereich, was darauf hinweist, daß Individuen mit Strabismus sich hier anders verhalten als jene ohne diesen Defekt.

UNA COMPARACIÓN CONTRAPUESTA DE CUATRO TÉCNICAS DE ADMINISTRACIÓN DEL SUXAMETONIO EN PACIENTES CON ESTRABISMO

SUMARIO

Se llevó a cabo una comparación de cuatro métodos de administración del suxametoniño en pacientes sometidos a cirugía para estrabismo que tenían la misma edad, el mismo sexo, peso y altura. El pre-tratamiento con tubocurarinina permitió el mejor control de las consecuencias inducidas por el suxametoniño. El potasio en el suero se mantuvo dentro de límites normales, lo que hace pensar que los individuos afectados por el estrabismo se comportan de manera distinta de los que no padecen de dicho defecto.