EFFECT OF COMPETITIVE MYONEURAL BLOCKADE AND FENTANYL ON MUSCLE FASCICULATIONS CAUSED BY SUXAMETHONIUM IN CHILDREN

L. LINDGREN AND L. SAARNIVAARA

SUMMARY

The effects of tubocurarine 0.06 mg kg\(^{-1}\), alcuronium 0.03 mg kg\(^{-1}\), pancuronium 0.01 mg kg\(^{-1}\), and fentanyl 1 or 2 \(\mu\)g kg\(^{-1}\) on the muscle fasciculations associated with suxamethonium were studied in 171 children undergoing otolaryngological surgery. The mean fasculation index in all pretreatment groups was significantly smaller than in the control group. The most effective pretreatment was fentanyl 2 \(\mu\)g kg\(^{-1}\) followed, in order, by alcuronium, fentanyl 1 \(\mu\)g kg\(^{-1}\), tubocurarine and pancuronium. The rate of the onset of the fasciculations after the injection of suxamethonium ranged from 8 s after pancuronium to 20 s after tubocurarine. There was evidence of respiratory depression in the children receiving fentanyl 2 \(\mu\)g kg\(^{-1}\) if the duration of anaesthesia was less than 30 min.

It has been demonstrated in adults that those side-effects associated with suxamethonium, such as muscle fasciculations and muscle pain (Churchill-Davidson, 1954; Morris and Dunn, 1957; Takki, Kauste and Kjellberg, 1972; Collier, 1975, 1978; Fozard, Manford and Harris, 1977; Feingold and Velazquez, 1979; Bennetts and Khalil, 1981), an increase in intragastric pressure (La Cour, 1970; Miller and Way, 1971), an increase in serum potassium concentration (Stovner, Endresen and Bjelke, 1972; Bali, Dundee and Assaf, 1975; Gronert and Theye, 1975) and cardiac arrhythmia (Mathias, Evans-Prosser and Churchill-Davidson, 1970; Karhunen, Heinonen and Tammisto, 1972; Saarnivaara and Lindgren, 1983) can be treated successfully by the prior administration of small doses of competitive neuromuscular blocking drugs.

Salem, Wong and Lin (1972) reported that, in children, muscle fasciculations associated with suxamethonium were either absent or minimal although, more recently, we have described moderate or strong muscle fasciculations (Saarnivaara, 1977; Lindgren, Saarnivaara and Himberg, 1979, 1980).

The present study investigated the effect of tubocurarine, alcuronium, pancuronium and the opioid analgesic fentanyl, on muscle fasciculations caused by suxamethonium in children. Fentanyl was included in the study since it has been shown to protect against cardiac arrhythmia during the induction of anaesthesia in children and adults (Saarnivaara, Lindgren and Savolainen, 1981).

PATIENTS AND METHODS

Ethics Committee approval was obtained for this study in which 171 children were included (table I). Premedication consisted of triclofos 70 mg kg\(^{-1}\) plus atropine 0.03 mg kg\(^{-1}\) administered by mouth about 90 min before the induction of anaesthesia. Tubocurarine 0.06 mg kg\(^{-1}\), alcuronium 0.03 mg kg\(^{-1}\), pancuronium 0.01 mg kg\(^{-1}\), fentanyl 1 \(\mu\)g kg\(^{-1}\) or 2 \(\mu\)g kg\(^{-1}\) were injected (over 45 s) 2 min before thiopentone was administered i.v. The trachea was intubated, following suxamethonium 2 mg kg\(^{-1}\) in the children pretreated with non-depolarizing neuromuscular blocking drugs, and following suxamethonium 1.5 mg kg\(^{-1}\) in the remainder.

All the children were anaesthetized by one of the authors (L.L.) who assessed the onset, intensity and duration of muscle fasciculations without knowing the pretreatment. The intensity score is shown in table II. The fasciculation index was calculated as follows: the intensity score \(\times\) the duration of the fasciculations (s). Student's \(t\) test was used for the statistical analysis of the results.

RESULTS

None of the children complained spontaneously of any adverse effects after any pretreatment. Indeed,
TABLE I. Characteristics of different treatment groups. Mean value ± SD. Number of children in parentheses

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Male</th>
<th>Age (yr) ± SD</th>
<th>Weight (kg) ± SD</th>
<th>Haemoglobin concn (g litre⁻¹) ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pretreatment (41)</td>
<td>31</td>
<td>5.6 ± 1.5</td>
<td>21.4 ± 4.8</td>
<td>130 ± 5.9</td>
</tr>
<tr>
<td>Tubocurarine 0.06 mg kg⁻¹ (30)</td>
<td>19</td>
<td>6.4 ± 3.0</td>
<td>23.3 ± 9.5</td>
<td>129 ± 8.9</td>
</tr>
<tr>
<td>Alcuronium 0.03 mg kg⁻¹ (30)</td>
<td>14</td>
<td>5.1 ± 3.0</td>
<td>19.5 ± 7.8</td>
<td>131 ± 9.2</td>
</tr>
<tr>
<td>Pancuronium 0.01 mg kg⁻¹ (30)</td>
<td>18</td>
<td>5.9 ± 2.9</td>
<td>20.6 ± 6.7</td>
<td>131 ± 6.9</td>
</tr>
<tr>
<td>Fentanyl 1 µg kg⁻¹ (20)</td>
<td>13</td>
<td>5.3 ± 2.4</td>
<td>19.5 ± 4.6</td>
<td>130 ± 8.2</td>
</tr>
<tr>
<td>Fentanyl 2 µg kg⁻¹ (20)</td>
<td>15</td>
<td>6.2 ± 2.7</td>
<td>21.8 ± 6.2</td>
<td>129 ± 9.2</td>
</tr>
</tbody>
</table>

TABLE II. Intensity score of visible muscle fasciculations caused by suxamethonium. Mild = 1; Moderate = 2; Violent = 3

<table>
<thead>
<tr>
<th>Score Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Small fine movements around eyes and fingers</td>
<td>1</td>
</tr>
<tr>
<td>Reasonable movements in face, neck, fingers and trunk</td>
<td>2</td>
</tr>
<tr>
<td>Vigorous movements in trunk and extremities</td>
<td>3</td>
</tr>
</tbody>
</table>

the pretreatments often seemed to have a calming effect especially on the younger children. On the basis of the fasciculation index, all the pretreatments decreased the fasciculations significantly compared with the control group (fig. 1). The most effective pretreatment was fentanyl 2 µg kg⁻¹ followed by alcuronium, fentanyl 1 µg kg⁻¹, tubocurarine and pancuronium. The rate of onset of the fasciculations ranged from 8 s after pancuronium to 20 s after tubocurarine, the latter differing significantly from all the other pretreatments and from the control group (10 s) (table III). In the control group the mean duration of fasciculations was 25 s and, after pretreatment with tubocurarine, alcuronium, pancuronium, fentanyl 1 µg kg⁻¹ and 2 µg kg⁻¹, was 13, 12, 5, 5 and 3 s, respectively. Although fentanyl 2 µg kg⁻¹ was the most effective pretreatment, there was evidence of respiratory depression if the duration of anaesthesia was less than 30 min.

FIG. 1. Visible muscle fasciculations after suxamethonium i.v. in children following various pretreatments. Intensity score: mild = 1; moderate = 2; violent = 3. Mean intensity index ± SEM. Number of children in parentheses. • P < 0.001 from the group without pretreatment; * P < 0.01; **P < 0.001 from the group pretreated with pancuronium. △P < 0.05 from the group pretreated with fentanyl 2 µg kg⁻¹.
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TABLE III. Rate of onset (s) of visible muscle fasciculations and percentage exhibiting fasciculations after the injection of suxamethonium i.v. in children following various pretreatments. Mean values ± SEM. Number of children in parentheses. *P < 0.001 from the other groups.

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>Rate of onset of fasciculation (s)</th>
<th>Children with fasciculations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pretreatment (41)</td>
<td>10.4 ± 0.8*</td>
<td>80</td>
</tr>
<tr>
<td>Tubocurarine 0.06 mg kg⁻¹ (30)</td>
<td>20.0 ± 0.8*</td>
<td>40</td>
</tr>
<tr>
<td>Alcuronium 0.03 mg kg⁻¹ (30)</td>
<td>10.2 ± 0.8</td>
<td>43</td>
</tr>
<tr>
<td>Pancuronium 0.01 mg kg⁻¹ (30)</td>
<td>8.1 ± 0.8</td>
<td>73</td>
</tr>
<tr>
<td>Fentanyl 1 μg kg⁻¹ (20)</td>
<td>8.8 ± 0.4</td>
<td>45</td>
</tr>
<tr>
<td>Fentanyl 2 μg kg⁻¹ (20)</td>
<td>9.5 ± 0.5</td>
<td>20</td>
</tr>
</tbody>
</table>

DISCUSSION

All the pretreatments decreased markedly the muscle fasciculations caused by suxamethonium. The most effective pretreatment was fentanyl 2 μg kg⁻¹ followed, in order, by alcuronium, fentanyl 1 μg kg⁻¹, tubocurarine and pancuronium. The dose ratio (6:3:1) between tubocurarine, alcuronium and pancuronium was considered to be equipotent (Schuh, 1981).

Since muscle fasciculations were observed visually the method may not seem to be especially sensitive. However, Jansen and Hansen (1979) found a good correlation between an objective method for the measurement of fasciculations and visually observed effects. In addition, the reliability of the method was increased by the use of a well-defined rating scale.

The result that competitive myoneural blockade inhibited muscle fasciculations in children agrees well with the results obtained in adults (Cullen, 1971; Durant and Katz, 1982). In the present study pancuronium was inferior to tubocurarine and, even more so, to alcuronium. This result agrees with observations in adults (Cullen, 1971; Damaoal, Weniger and Wolfson, 1975). The rate of onset of fasciculations following pretreatment with tubocurarine was significantly slower than that following pretreatment with other drugs. Whether this was a result of normal variability among individuals or had some clinical importance remains to be seen. The most marked and unexpected result was that fentanyl decreased the muscle fasciculations effectively.

Muscle fasciculations occur during the onset of the neuromuscular block with suxamethonium and they are associated with the initial depolarization of the muscle fibres (Durant and Katz, 1982). On the basis of the present study the exact site and mechanism of the action of fentanyl remain completely unexplained. There is, however, evidence that opioids have neuromuscular effects. Both morphine and nalorphine inhibit neuromuscular transmission in mammalian and amphibian neuromuscular preparations apparently as a result of the impairment of the acetylcholine release (Frederickson and Pinsky, 1971; Pinsky and Frederickson, 1971). Resting tension of the indirectly stimulated rat hemidiaphragm increases slowly in the presence of high concentrations of morphine and is further augmented by nalorphine (Pinsky and Frederickson, 1971). This result supports the view that high concentrations of opioids may affect the contractile mechanism of the mammalian muscle. Furthermore, fentanyl inhibits in a dose-dependent manner the contraction of the cat nictitating membrane to sympathetic nerve stimulation and an increase of plasma calcium concentration prevents the inhibitory effects of fentanyl (Roquebert and Demichel, 1981). However, fentanyl does not seem to decrease the frequency of muscle fasciculations associated with suxamethonium in adults (Saarnivaara, Lindgren and Savolainen, 1981). This difference in effect remains to be explained.

We have found recently that competitive myoneural blockade (Saarnivaara and Lindgren, 1983) and fentanyl (Saarnivaara, Lindgren and Savolainen, 1981) also decreased the frequency of cardiac arrhythmia associated with suxamethonium in children. The other side-effects of suxamethonium such as postoperative muscle pain seem to be of minor clinical significance (Fozard, Manford and Harris, 1977). Salem, Wong and Lin (1972) found that muscle fasciculations and the
increase in intragastric pressure were minimal in children. In their study, anaesthesia for 70% of the children was induced with halothane and for the remainder with thiopentone. Thus, the intensity of muscle fasciculations may have been decreased since halothane inhibits suxamethonium-induced depolarization at the muscle endplate (Kennedy and Galindo, 1975). In the present study, anaesthesia for each child was induced with thiopentone and moderate or even violent fasciculations following suxamethonium were seen in 80% of the children in the control group. Therefore, more data are required before we can evaluate the side-effects of suxamethonium, such as increased intragastric pressure and hyperkalaemia (Durant and Katz, 1982), in children. Consequently the role of neuromuscular blocking drugs, and fentanyl, on these effects remains to be investigated in children.

REFERENCES
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EFFET D’UN BLOC NEUROMUSCULAIRE COMPETITIF ET DU FENTANYL SUR LES FASCICULATIONS MUSCULAIRES INDUITES PAR LE SUXAMETHONIUM CHEZ L’ENFANT

RESUME
Les effets de tubocurarine $0.06 \text{ mg kg}^{-1}$, de l’alcuronium $0.03 \text{ mg kg}^{-1}$ et pancuronium $0.01 \text{ mg kg}^{-1}$ et de fentanyl 1 ou $2 \mu\text{g kg}^{-1}$ sur les fasciculations musculaires induites par le suxaméthonium ont été étudiées chez 171 enfants subissant des actes de chirurgie ORL. L’index moyen de fasciculation, dans tous les groupes ayant reçu un traitement préliminaire, était significativement inférieur à celui de groupe témoin. Le prétraitement le plus efficace était le fentanyl $2 \mu\text{g kg}^{-1}$, suivi de l’alcuronium, du fentanyl $1 \mu\text{g kg}^{-1}$, de la tubocurarine et du pancuronium, dans cet ordre. Le délai d’apparition des fasciculations après l’injection de suxaméthonium allait de 8 s après pancuronium à 20 s après tubocurarine. Les enfants qui avaient reçu fentanyl $2 \mu\text{g kg}^{-1}$ présentaient des signes de depression respiratoire si la durée de l’anesthésie était inférieure à 30 min.

WIRKUNG VON KOMPETITIVEN MUSKELRELAXANTEN UND FENTANYL AUF DURCH SUXAMETHONIUM VERURSACHTE MUSKELFASZIKULATIONEN BEI KINDERN

ZUSAMMENFASSUNG
Bei 171 Kindern während HNO-Operation wurde die Wirkung von Tubocurarin $0.06 \text{ mg kg}^{-1}$, Alcuronium $0.03 \text{ mg kg}^{-1}$, Pancuronium $0.01 \text{ mg kg}^{-1}$ und Fentanyl 1 oder $2 \mu\text{g kg}^{-1}$ auf Suxaméthonium bedingte Muskelfascikulationen untersucht. Der mittlere Faszikulationsindex war bei allen Gruppen mit Prämiedikation niedriger als in der Kontrollgruppe. Am wirksamsten erwies sich Fentanyl $2 \mu\text{g kg}^{-1}$, dann Alcuronium, Fentanyl $1 \mu\text{g kg}^{-1}$, Tubocurarine und Pancuronium. Der Beginn der Faszikulationen lag zwischen 8 Sekunden nach Suxaméthoniumgabe bei Pancuronium und 20 Sekunden bei Tubocurarine. Bei den Kindern, die Fentanyl $2 \mu\text{g kg}^{-1}$ erhalten hatten, war bei unter 30 Minuten Narkosedauer eine postoperative Atemdepression zu beobachten.

EFECTO DEL FENTANILO Y DEL BLOQUEO MIONEURAL COMPETITIVO SOBRE LA SEPARACION DE LAS FIBRAS MUSCULARES OCASIONADA POR EL SUXAMETONIO EN LOS NIÑOS

SUMARIO
Se estudiaron en 171 niños sometidos a intervención quirúrgica otorrinolaringológica, los efectos de $0.06 \text{ mg kg}^{-1}$ de tubocurarina, $0.03 \text{ mg kg}^{-1}$ de alcuronium, $0.01 \text{ mg kg}^{-1}$ de pancuronio y de $0.02 \mu\text{g kg}^{-1}$ de fentanilo, sobre la separación de las fibras musculares asociada con el suxametonio. El índice medio de separación de las fibras musculares, en todos los grupos antes de recibir el tratamiento, fue significativamente menor que en el grupo de control. El pretratamiento más efectivo fueron $2 \mu\text{g kg}^{-1}$ de fentanilo, seguidos, por orden, de alcuronium, fentanilo ($1 \mu\text{g kg}^{-1}$), tubocurarina y pancuronio. El régimen de iniciación de la separación de las fibras musculares, después de la inyección de suxametonio, osciló entre 8 segundos, después del pancuronio y 20 segundos, después de la tubocurarine. Se observó evidencia de depresión respiratoria en los niños que recibieron $2 \mu\text{g kg}^{-1}$ de fentanilo si la duración de la anestesia fue inferior a 30 minutos.