A Comparative Evaluation of Pretreatment with Nondepolarizing Neuromuscular Blockers Prior to the Administration of Succinylcholine

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The interaction of subparalyzing doses of nondepolarizing neuromuscular blockers and paralyzing doses of depolarizing neuromuscular blockers is intriguing and mystifying. The use of a small dose of a nondepolarizing neuromuscular blocking agent prior to the administration of succinylcholine (SCh) has become routine anesthetic practice in the United States. Reasons for pretreating with a nondepolarizer prior to SDC include: prevention of increased intragastric pressure, attenuation of potassium release, attenuation of increased intraocular pressure, decreased incidence of postoperative myalgia, and obliteration of fasciculations.1–6

The purpose of this study was to compare four commonly used nondepolarizing neuromuscular blockers (d-tubocurarine, gallamine, metocurine, pancuronium) as pretreatment agents. Metocurine has not been previously studied as a pretreatment drug and we attempted to determine the optimum dosage of metocurine for this purpose.

METHODS

Human Subjects Committee approval and informed consent was obtained from 80 adult patients (ASA I–II), requiring general anesthesia with endotracheal intubation. Consecutive patients were randomly assigned to eight groups of ten patients each. Six of the eight groups were given a selected dose of a nondepolarizing neuromuscular blocker as “pretreatment” and two groups were not pretreated and served as controls. Pretreatment regimens consisted of 20 mg gallamine, 3 mg d-tubocurarine, 0.5 mg pancuronium, and 1, 1.5, and 2.0 mg metocurine (DMT), intravenously. No patients were chronically receiving any medication known to have an effect upon neuromuscular blocking agents.

Immediately after pretreatment, 100 per cent oxygen was administered for 3 min and then anesthesia was induced with 4 to 6 mg/kg thiopental intravenously. Force of thumb adduction in response to supramaximal ulnar nerve stimulation (0.25 Hz) was recorded using needle electrodes at the wrist and a Grass S88 stimulator as previously described.7 When a satisfactory, stable twitch response was obtained (15–20 s), 1.5 mg/kg SCh was given intravenously to all pretreated patients and one group of control patients. Another group of control patients received 1.0 mg/kg SCh. Since prior studies have shown 1.5 mg/kg SCh in association with pretreatment to be equivalent to 1.0 mg/kg SCh without pretreatment, we elected to study these two doses as control groups.8

When twitch response was abolished, the trachea was intubated. Nitrous oxide-narcotic or nitrous oxide-enflurane was used for maintenance of anesthesia. Nitrous oxide administration (65 per cent) commenced shortly after intubation of the trachea and narcotic or enflurane was added 2–10 min later (in most cases after the twitch response had started to return to the control level).

Time to abolition of twitch following administration of SCh and time to 10, 50, and 90 per cent recovery of control twitch height were measured.

Intubating conditions and clinical relaxation were evaluated using the following scale:

4 = cords abducted, jaw well-relaxed, optimum intubating conditions;
3 = no muscular response to intubation but jaw not totally relaxed and/or cords not totally abducted;
2 = poor jaw relaxation, slight cough, contraction of diaphragm, cords not abducted;
1 = vigorous cough, contraction of the diaphragm and trunk muscles, jaw not relaxed, cords not abducted;
0 = unable to intubate because of poor relaxation.

The presence and degree of fasciculations was assessed as follows:

3 = vigorous contractions of trunk, face, and extremities;
2 = minimal contraction of trunk, face, and extremities;

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Received from the Department of Anesthesiology, University of Arizona, Health Sciences Center, 1501 North Campbell Avenue, Tucson, Arizona 85724. Accepted for publication June 3, 1981. Supported in part by a grant from Eli Lilly Company.

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Key words: Neuromuscular relaxants: d-tubocurarine; gallamine; metocurine; pancuronium; succinylcholine. Muscle, skeletal: fasciculation. Complications: myalgia.

0003-3022/81/12/0687 $00.65 © The American Society of Anesthesiologists, Inc.
TABLE 1. Times to Disappearance and Recovery of Twitch for All Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>SCH (mg/kg)</th>
<th>Pretreatment</th>
<th>Time (s) to Disappearance of Twitch</th>
<th>Time to 10 Per Cent Recovery of Twitch (s)</th>
<th>Time to 50 Per Cent Recovery of Twitch (s)</th>
<th>Time to 90 Per Cent Recovery of Twitch (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5</td>
<td>metocurine, 2.0 mg</td>
<td>91.1 ± 9.7</td>
<td>207 ± 30</td>
<td>348 ± 41</td>
<td>419 ± 50</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>metocurine, 1.5 mg</td>
<td>90.3 ± 7.6</td>
<td>257 ± 39</td>
<td>458 ± 69</td>
<td>585 ± 118</td>
</tr>
<tr>
<td>3</td>
<td>1.5</td>
<td>metocurine, 1.0 mg</td>
<td>75.0 ± 5.3</td>
<td>305 ± 47</td>
<td>467 ± 60</td>
<td>557 ± 78</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>d-tubocurarine, 3 mg</td>
<td>76.0 ± 6.8</td>
<td>253 ± 39</td>
<td>452 ± 74</td>
<td>549 ± 92</td>
</tr>
<tr>
<td>5</td>
<td>1.5</td>
<td>gallamine, 20 mg</td>
<td>84.9 ± 6.7</td>
<td>340 ± 47</td>
<td>496 ± 55</td>
<td>586 ± 65</td>
</tr>
<tr>
<td>6</td>
<td>1.5</td>
<td>pancuronium, 0.5 mg</td>
<td>74.3 ± 11.0</td>
<td>343 ± 36</td>
<td>535 ± 48</td>
<td>612 ± 29</td>
</tr>
<tr>
<td>7</td>
<td>1.0</td>
<td>none</td>
<td>82.3 ± 5.0</td>
<td>335 ± 35</td>
<td>548 ± 53</td>
<td>652 ± 63</td>
</tr>
<tr>
<td>8</td>
<td>1.5</td>
<td>none</td>
<td>67.1 ± 5.4</td>
<td>483 ± 48*</td>
<td>752 ± 62*</td>
<td>906 ± 76*</td>
</tr>
</tbody>
</table>

All values are means ± SEM. N = 10 for all groups.

*P < 0.05.

1 = very fine muscular movements; 0 = no visible fasciculations.

Patients were questioned for myalgia 24 hours post-operatively by an observer not acquainted with the treatment regimen. The following interview sequence was used: the patient was asked, “Do you have any pain?” If the response to this question was affirmative, location and severity of pain were determined. If the response was negative, the patients were again asked, “Are you sore anywhere?” We attempted to separate surgical incisional pain from “other pain” by questioning. If non-incisional pain was discovered, we attempted to determine the involvement of a muscle mass. Particular attention was directed to the neck, shoulder and back areas.

All data were analyzed by a one-way analysis of variance (ANOVA) and P < 0.05 was selected to represent significant differences between groups.

RESULTS

Data revealed homogeneity of all eight groups with regard to age, sex, weight, and induction medications. Times to disappearance of twitch following administration of SCH as well as times to 10, 50, and 90 percent recovery of control twitch height were not different among any groups except for the group that received 1.5 mg/kg SCH without pretreatment (control group—#8). Recovery time was significantly prolonged in these patients (P < 0.05) (table 1).

No differences between groups were observed regarding intubating conditions (table 2). All patients in non-pretreated groups exhibited fasciculations to varying de-

TABLE 2. Comparisons of Intubation Conditions and Fasciculations

<table>
<thead>
<tr>
<th>Group Number</th>
<th>Pretreatment</th>
<th>Number of Patients</th>
<th>Intubation Conditions</th>
<th>Fasciculations</th>
<th>Postoperative Myalgia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Score†</td>
<td>Score‡</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>metocurine, 2.0 mg</td>
<td>9</td>
<td>4</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>metocurine, 1.5 mg</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>metocurine, 1.0 mg</td>
<td>9</td>
<td>4</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>d-tubocurarine, 3 mg</td>
<td>8</td>
<td>4</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>gallamine, 20 mg</td>
<td>2</td>
<td>2</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>pancuronium, 0.5 mg</td>
<td>4</td>
<td>4</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>none (control, 1.0 mg SCH)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>none (control, 1.5 mg SCH)</td>
<td>9</td>
<td>4</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

* A score of 4 is given for the best conditions for intubation and 0 for the worst conditions for intubation.
† A score of 0 is no fasciculations, and 3 is marked fasciculations.
greeks. Three patients in the pancuronium pretreatment group (#6) had fasciculations and one patient in the 2 mg metocurine pretreatment group (#1) had fasciculations (table 2). The only statistical significance achieved regarding fasciculations compared the pretreated groups in the aggregate (no fasciculations) versus nonpretreated groups in the aggregate (P < 0.001). Only one patient in our study was found to have a postoperative myalgia (incidence 1.25 percent) and this patient was in the 1.5 mg/kg SCh nonpretreated group (#8).

DISCUSSION

Attenuation or obliteration of fasciculations represents the most common indication for the use of a small dose of a nondepolarizing muscle relaxant prior to SCh and fasciculations have come to be regarded as aesthetically undesirable. The patient with a full stomach who requires a “rapid sequence of induction of anesthesia and endotracheal intubation” needs the optimum combination of depolarizing and nondepolarizing relaxants to permit a rapid, reliable and profound neuromuscular block. The time to “SCh-onset of action” in these patients is critical. Our results show that all of the pretreatment regimens we studied are acceptable and indistinguishable from each other for use in a “rapid anesthesia-intubation sequence.” The higher doses of metocurine (1.5 and 2.0 mg) appear to increase the time of “SCh-onset of action” but this difference was not statistically significant. All pretreatment regimens virtually eliminated fasciculations but pancuronium did not appear to be as effective in this regard.

The incidence of postoperative myalgias is remarkably variable in published studies.3,5,7,8 Our incidence of 1.25 per cent is at the lower range of previously reported values and may be related to our studying patients in whom the likelihood of muscle pain was not high.

Cullen has reported that 20 mg gallamine prior to 1.5 mg/kg SCh is associated with the most rapid “SCh-onset of action.”12 He reported that this time to complete relaxation from SCh (after gallamine) was 60 (±5.2 SEM) seconds and additionally he found the time to onset of action of 1.5 mg/kg SCh after 3 mg d-tubocurarine was 94 (±10 SEM) seconds. This compares with SCh-onset of action of 85 seconds (±6.7 SEM), and 76 seconds (±6.8 SEM) for gallamine and d-tubocurarine pretreatment, respectively, in our study. Our data are statistically different and conflict with the information previously reported by Cullen. Cullen used a Block-Aid® nerve stimulator and visually observed abolition of twitch response. Our stimulating device (Grass S 88) and measurement devices (force displacement transducer and recorder) could be responsible for the differences in the two studies.

We have shown 1.0 mg metocurine to be an effective pretreatment agent and it may be associated with less undesirable autonomic side effects (even at pretreatment dosages) than other nondepolarizing muscle relaxants.13 Because there is no significant difference in “SCh-onset of action” or other variables evaluated in this study following pretreatment with either 1.0 mg metocurine, 20 mg gallamine, or 3 mg d-tubocurarine (in a 70-kg adult), these three drugs may be used interchangeably as pretreatment drugs.

REFERENCES

1. Miller RD, Way WL: Inhibition of succinylcholine-induced increased intragastric pressure by nondepolarizing muscle relaxants and lidocaine. ANESTHESIOLOGY 34:185-188, 1971
7. Lamoreux LF, Urbach KF: Incidence and prevention of muscle pain following the administration of succinylcholine. ANESTHESIOLOGY 21:394-396, 1960