Title: COMPARATIVE PHARMACOLOGY OF SUCCINYLCHOLINE ON JAW, EYE AND TIBIALIS MUSCLE.

Authors: SJ Pryn, FFARCS, APL van der spek, MD

Affiliation: Anesthesia Dept, University of Michigan, Ann Arbor, MI 48109

Introduction: Masseter muscle rigidity (MMR) in children occurs frequently, yet has been associated with MI susceptibility (1). Subjects who develop MMR do not necessarily show the same response on repeated exposure to succinylcholine. Jaw closure and an increased resistance to mouth opening has been shown in normal children (2) and in cats (3) after IV succinylcholine (SuX). We postulated that catecholamines augment normal contractures of jaw muscles to SuX in children. This study tested this hypothesis in the cat model.

Methods: Halothane anesthesia was induced in cats and a tracheotomy was performed. Arterial blood and end-tidal gases, temperature and acid base balance were maintained constant. The tibia was fixed; the tibialis (TA) tendon was attached to a force transducer. The head was bolted to a frame, its right eye encapsulated, and the superior oblique eye muscle's (EOM) force was transduced. The mandible (JAW) was opened to 3 cm and its force transduced. The trochlear, tibial and the sciatic nerves were stimulated supramaximally at 0.15 Hz and 0.2 ms. SuX dose–response (twich & contracture) curves were constructed by nonlinear regression. Tachyphylaxis of contractures to SuX was demonstrated, thus, for this study a single dose (2×ED-95) technique was used. Cats received either 150 μg/kg SuX or 150 μg/kg SuX preceded by 1 μg/kg epinephrine (EPI), IV. Contractures were recorded, and after recovery, the doses were repeated to record twitch depression.

Analysis: Contractures were normalized for their muscle's twitch height. Comparisons between groups made by ANOVA.

TABLE: DESFLURANE VERSUS ISOFLURANE: DOSE-RESPONSE RELATIONSHIPS OF PANCURONIUM AND SUCCINYLCHOLINE

AUTHORS: J.E. Caldwell, FFARCS, T. Magorian, M.D., D.P. Lynam, M.D., V. Segredo, M.D., E.L. Egger II, M.D., R.D. Miller, M.D.

AFFILIATION: Anes. Dept, University of California, San Francisco, CA 94143

Desflurane is a new volatile anesthetic which depresses neuromuscular function. To determine the interaction of desflurane with neuromuscular blocking drugs, we compared the influence of desflurane vs. suxamethonium on the dose–response relationships of pancuronium and succinylcholine.

Following approval from our Committee on Human Research, and obtaining informed consent, we studied 27 adult surgical patients, ASA P.S. I or II. Anesthesia was induced with sodium thiopental, 0.5-2 mg/kg, IV, nitrous oxide 60%-70% and maintained with 1.25 MAC concentrations of desflurane, 5.5-9.5%, or isoflurane, 1.5–1.7% (end-tidal concentrations). Nitrous oxide was discontinued prior to tracheal intubation. Mechanical ventilation was adjusted to maintain normocapnia. The evoked twitch tension of the adductor polloss, in response to train–of–four stimulation of the ulnar nerve, was measured with a force transducer. The amplitude of the first response (T1) in the train immediately preceding the initial administration of pancuronium or succinylcholine was the the control to which subsequent T1 responses were compared.

In the pancuronium group, a standard cumulative dose–response curve was generated by administering repeated boluses of 5 μg/kg IV until T1 depression was >90%. In the succinylcholine group, we used a modification of the method of Miller et al. Each patient received, in order, IV boluses of 40, 80, 160, 200, 300 or 400 μg/kg. Recovery was allowed between each dose, and increasing doses were administered until the T1 depression was >90%. Dose–response curves were generated by linear regression of the logarithm of each dose versus the probit transform of the T1 depression which it produced. The slopes of the dose–response curves, and the calculated ED50 and ED90 values were compared by Mann-Whitney U test. P < 0.05 was considered significant.

During anesthesia with desflurane, the dose–response relationships of pancuronium and succinylcholine were not different to those during isoflurane anesthesia (see below).

Results: SuX induced contractures in all 3 muscle groups with a peak 10-20s after injection. Increased jaw tone lasted in excess of 1h; EOM tone reached baseline in 10-20min, while TA tone reached it in 60s. The TA twitch had been abolished a significant jaw force was still present. Epinephrine increased the force (TA & JAW) and duration of all contractures.

CONTRACTURES AS % OF ITS MUSCLE TWITCH, mean ± SD

<table>
<thead>
<tr>
<th></th>
<th>EOM</th>
<th>TA</th>
<th>JAW</th>
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</thead>
<tbody>
<tr>
<td>SuX 150μg/kg n=4</td>
<td>158 ± 28</td>
<td>3 ± 2</td>
<td>23 ± 14</td>
</tr>
<tr>
<td>SuX 150μg/kg Epi 1μg/kg n=4</td>
<td>199 ± 47</td>
<td>8 ± 4</td>
<td>150 ± 109</td>
</tr>
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</table>

ANOVA NS p < 0.05 p < 0.05

Conclusions: Epinephrine markedly potentiates SuX-induced contractures in cat jaw muscles. This suggests a mechanism for MMR in normal humans, unrelated to MI; MMR may represent an exaggerated "jaw contracture" after SuX administration in children with high endogenous catecholamine levels.


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PANCURONIUM

Desflurane (n = 8) 4.1±0.9 10.5±2.6 22.6±6.9
Isoflurane (n = 8) 5.0±1.0 12.3±0.5 22.4±8.7
SUCINYLCHOLINE

Pancuronium (μg/kg) 132±76 233±100
Isoflurane (μg/kg) 6.1±1.7 214±78

(Values are mean ± S.D.)

We anticipate that desflurane will significantly augment the action of all clinically used neuromuscular blocking drugs, and predict that the interaction of desflurane with neuromuscular blocking drugs will be similar to that of isoflurane.