

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

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Introduction: Masseter muscle rigidity (MMR) in children occurs frequently, yet has been associated with MH susceptibility (1). Subjects who develop MMR do not necessarily show the same response on repeated exposure to Sux. 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 tracheostomy was performed. Arterial blood & 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 enucleated, 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, mandibular and the sciatic nerves were stimulated supramaximally at 0.15 Hz and 0.2 ms. Sux dose-response (twitch & 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 µ/kg Sux or 150 µ/kg Sux preceded by 1 µ/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.

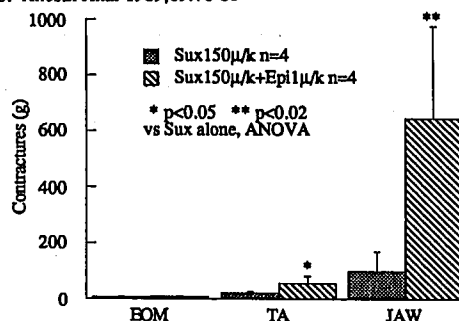
Results: Sux induced contractures in all 3 muscle groups with a peak 10-20s after injection. Increased jaw tone lasted in excess of 1h; EOM tone reached baseline in 10-20min, while TA tone reached it in 60s. When the TA twitch had been ablated a significant jaw force was still present. Epinephrine increased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

CONTRACTURES AS % OF ITS MUSCLE TWITCH, mean ± SD.

	EOM	TA	JAW
Sux 150µ/k n=4	158 ± 28	3 ± 2	23 ± 14
Sux 150µ/k Epi 1µ/k n=4	199 ± 47	8 ± 4	150 ± 109
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 MH; MMR may represent an exaggerated "jaw contracture" after Sux administration in children with high endogenous catecholamine levels.

References: 1. Can J Anaesth 1990;37:31-5; 2. Br J Anaesth 1990;64:21-27; 3. Anesth Anal 1989;69:76-80



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

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Desflurane is a new volatile anesthetic which depresses neuromuscular function.¹ To determine the interaction of desflurane with neuromuscular blocking drugs, we compared the influence of desflurane vs isoflurane on the dose-response relationships of pancuronium and succinylcholine.

Following approval from our Committee on Human Research, and after obtaining informed consent, we studied 27 adult surgical patients, ASA P.S. I or II. Anesthesia was induced with sodium thiopental, 0.5 mg/kg, iv, nitrous oxide 60-70% and maintained with 1.25 MAC concentrations of desflurane,² 8.5-9.5%, 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 pollicis, 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 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.*³ 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).

	Slope	ED50 (µg/kg)	ED90 (µg/kg)
PANCURONIUM			
Desflurane (n = 8)	4.1±0.9	10.5±2.8	22.6±6.9
Isoflurane (n = 8)	5.0±1.0	12.3±5.0	22.4±8.7
SUCCINYLCHOLINE			
Desflurane (n = 5)	5.3±1.9	132±76	233±100
Isoflurane (n = 6)	6.1±1.7	123±36	210±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.

References
1. Anesth Analg 70:S47,1990 2. ANESTHESIOLOGY 71:A269, 1989 3. ANESTHESIOLOGY 36:509-514, 1971