TITLE: NEUROMUSCULAR PHARMACOLOGY OF SUCCINYLCHOLINE IN THE FERRET
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Succinylcholine (SDC) is the most commonly used depolarizing neuromuscular blocker in humans and animals. In this study, we describe the atypical neuromuscular effects of SDC in the ferret. The study was prompted by the high cost of dogs ($400-$500 ea) and cats ($100-$200 ea) in our institution and many others, and by a desire to substitute these popular animals with less popular farm-raised species for pharmacological research.

With institutional approval, six ferrets were anesthetized with pentobarbital 30 mg/kg i.p. Ventilation was controlled via tracheostomy to maintain normocarbia. External jugular vein and carotid artery cannulations were done for i.v. access and blood pressure monitoring. Supramaximal train-of-four (TOF) sciatic nerve stimulation was applied every 10 seconds for electromyographic (EMG) and mechanomyographic (MMG) responses of the tibial anterior muscle. Normothermia was maintained. Following the i.v. injection of the first dose of SDC (0.15 mg/kg, which approximates the ED_{95} in this species), the following neuromuscular responses were observed and recorded: (1) fasciculation, increase in muscle tone, or increase in twitch, if any, and (2) TOF ratio during onset. This was immediately followed by a brief infusion of SDC to maintain a 50% block for evaluation of tetanic and post-tetanic (PTT) responses, and then a 60-70% block for evaluation of the reversibility of the block with 0.3 mg/kg of edrophonium i.v. upon termination of the infusion. The total duration of infusion was limited to 5-8 min. The total dose of SDC infused was 0.42 ± 0.08 mg/kg.

The data in the table show that SDC (1) does not produce fasciculation, increase in resting muscle tone or increase of twitch force before it blocks, (2) produces clear TOF and tetanic fade on first sign of block, and (3) manifests post-tetanic facilitation during block. Its neuromuscular effect is reversible with edrophonium.

"Nondepolarizing" features of neuromuscular block occur on exposure to the first ED_{95} dose of SDC in the ferret. Whereas recent observations have shown that ferrets may serve as a useful model for studying nondepolarizing neuromuscular blockers, they are not suitable for the study of depolarizing blockers.

Neuromuscular Effect of SDC in the Ferret (N=6)

Fasciculation	absent
TOF ratio (T_4/T_1) at	
88% T_1 block in onset phase	0.62 ± 0.02
50% T_1 block in recovery phase	0.53 ± 0.04
Tetanic fade at 50% T_1 block (% faded)	83.2 ± 4.5
PTT (% increased)	14.4 ± 5.0
Reversibility *	yes

* Neuromuscular block of T_1 reduced from 65.6 ± 7.3% of control to 43.2 ± 8.2% of control by edrophonium 0.3 mg/kg

A874

TITLE: REVERSAL OF PIPECURONIUM AND PANCURONIUM INDUCED NEUROMUSCULAR BLOCK BY EDROPHONIUM AND PYRIDOSTIGMINE
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Pipecuronium (Pi) is effectively antagonized with neostigmine.[1] We compared its reversibility with that of pancuronium (Pa) using edrophonium (E) and pyridostigmine (Py).

With Human Subjects Committee approval and written consent, 32 ASA I-II patients of both sexes, and free of hepatic, renal or neuromuscular diseases were studied. Anesthesia was induced with thiopental Na and maintained with N_2O/O_2 (60/40%) + halothane (0.5-1.0% end tidal) + narcotics. Normocarbia and normothermia were maintained. Neuromuscular function was monitored (1) mechanomyographically (MMG) [thumb adductor m. contractile responses to a) TOF stimuli (left hand), b) tetanic stimuli 50 Hz (right hand)] and (2) electromyographically (EMG) (left hand) with a Datex Relaxograph (TOF stimuli each 20 seconds). After obtaining control responses, equipotent doses of Pa (0.1 mg/kg) or Pi (0.07 mg/kg) were first administered. T_1 responses subsequently were kept at 75% block level by infusion or by small bolus doses. Reversal was started at 75% T_1 block level (25% of baseline) with a) E 0.5 mg/kg + glycopyrrolate (0. 005 mg/kg) or b) Py 0.3 mg/kg + glycopyrrolate and was observed for 15 min. Additional assessment of the reversal was made at the PACU (head lift test). Results are shown in Fig. 1.

We conclude that Py effectively antagonizes the NMB produced by Pi. This finding is based on full reversal of T_1 response, restoration of the MMG and EMG T_4/T_1 ratio to 0.7 or above, reversing tetanic fade by > 50%, and positive head lift sign. E reversed the clinically relevant T_4/T_1 ratios less than Py ($p < .05$ between the ratios at peak reversal). The degree of Py reversal was slowly developing. It approached but often did not reach maximum in 15 min; however, the reversal with E was maximal, yet incomplete (for the T_4/T_1 ratios) already after 2 min. The results support former observations showing less than optimal reversal by E against longer acting NMB agents.[2]

References

1. Anesth Analg 69:734-739, 1989
2. Anesthesiology 50:139-142, 1979