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TITLE: A HIGH DOSE REGIMEN OF TRIAMCINOLONE INDUCES RESISTANCE TO VECURONIUM NEUROMUSCULAR BLOCK IN CATS

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The synthetic glucocorticoid, triamcinolone, enhances a facilitatory function of cat motor nerve endings. The posttetanic repetitive activity of soleus motor nerve endings in the cat is provoked a much lower tetanic frequencies (1). Vecuronium, a relative short acting muscle relaxants, suppresses this repetitive activity.(2) This study was undertaken to determine if neuromuscular transmission was affected by glucocorticoid treatment.

The Institutional Research Review Board approved the experimental protocol and all animal housing and handling met NIH requirements. Cats were placed on an regimen of triamcinolone, 8 mg/kg/day, for 7 days. On the 8th day, an in vivo soleus nerve-muscle preparation was made. Atropine, 0.5 mg/kg, was administered and then the cats were anesthetized with 4 L/min 2% halothane in 100% oxygen mixture. Heart rate, blood pH, and blood gases were monitored. The isometric contractile responses of the soleus muscle were recorded on a Grass polygraph using a Grass FT10C force transducer. The soleus nerve was continuously and supramaximally stimulated at 0.4 Hz. except when interrupted for 10 sec trains of100 HZ. Vecuronium was administered intravenously in single doses from 5 to 50 μg/kg. Neuromuscular block, and the times from injection to peak effect (onset) and to 90% recovery (total duration) were measured. A single dose of edrophonium, 125 μg/kg, was administered to reverse a neuromuscular block of 90%. Neuromuscular function was allowed to recover completely between doses and was considered recovered when the response to 100 HZ tetanic stimulation showed no fade. Data were analyzed using a Mann-Whitney rank test with significance at $p \leq .05$.

In the triamcinolone treated cats, the vecuronium dose response regression was significantly shifted to the right. The control ED50 dose was 10 μg/kg; in the triamcinolone treated animals the ED50 was 30 μg/kg. At equipotent doses, there was no significant differences in onset time or total duration. In control cats at 90% block, edrophonium restored neuromuscular transmission to 63±8.1%. In the triamcinolone cats, edrophonium completely restored transmission.

The results of the present study demonstrate that neuromuscular transmission in triamcinolone treated cats is resistant to vecuronium block and is more easily reversed.

References: 1. Riker WF, Baker T, Okamoto M: Arch Neurol 32:688-694, 1975
2. Baker T, Aguero A, Stanec A, Lowndes HE: Anesthesiology 65: 480-484, 1986

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POTENTIATION OF NEUROMUSCULAR BLOCKADE BY CYCLOSPORINE IS NOT MEDIATED BY PRE OR POST-SYNAPTIC MEMBRANE EFFECTS

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INTRODUCTION: Cyclosporin (CYC) is an important immunosuppressive agent. Recent clinical reports have implicated CYC in prolonging neuromuscular blockade post-operatively.[1,2] Animal studies have confirmed the augmentation by CYC of a relaxant induced neuromuscular blockade.[3] Therefore, we wished to determine the mechanism of action of CYC upon neuromuscular blockade by studying the effect of CYC infusion upon miniature end-plate potentials (mepps). Changes in the frequency and/or amplitude of mepps during CYC infusion would indicate a direct effect upon the pre- and/or post-synaptic membrane of the neuromuscular junction.
METHODS: With Animal Care Council approval, 4 adult New Zealand white rabbits were studied. Under isoflurane and oxygen/nitrous oxide anesthesia, a tracheostomy was performed. Positive pressure ventilation (#6025 cat/rabbit ventilator) was used to maintain normocapnia (Nellcor capnograph). A 22 GA catheter was then placed in an ear artery and vein for blood pressure measurement and drug infusion, respectively. During steady-state anesthesia, (end-tidal 1.0%) mepps were recorded for 15 min from the gastrocnemius using a concentric needle electrode (type DFC25, Teck Corp) and a Clark-Davis Advantage monitoring unit. A continuous CYC infusion (vehicle: cremaphor/ethanol 94%) was then started at 0.375 mg/kg/hr; a dose shown to augment neuromuscular blockade in the rabbit during a vecuronium infusion as measured by electromyography. After 15 min the dose was increased 10 fold to 3.75 mg/kg/hr for 15 min, then increased 25 fold to 9.375 mg/kg/hr for 15 min, with continuous recording of the mepps. Both frequency and mean amplitude of the mepps were measured before and during the different doses of CYC infusions.
RESULTS: Two mepps (arrows) recordings are shown below prior to (B) and during CYC (C) infusion. The infusion of CYC did not effect the frequency or amplitude of the mepps compared to baseline.
DISCUSSION: The inability of high dose CYC to effect the mepps indicates there is no direct effect of CYC upon the pre- or post-synaptic membrane of the neuromuscular junction. This suggests the augmentation by CYC of a relaxant induced neuromuscular blockade is through indirect mechanisms.

REFERENCES: 1) Can J Anaesth 37:543-8, 1990
2) Can J Anaesth 36:358, 1989
3) Br J Anaesth 58:1149-55, 1986