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Acute Steroid Therapy Does Not Alter Nondepolarizing Muscle Relaxant Effects in Humans

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Several investigators have described an interaction between muscle relaxants and acutely administered corticosteroids in different animal species.[1–4] Some have provided evidence of antagonism between these two drugs. Arts and Oosterhuis found that prednisolone given sc to mice before treatment with *d*-tubocurarine (*d*Tc) improved their ability to walk a treadmill.[1] In the rat sciatic nerve–tibialis anterior muscle preparation, Leeuwin and Wolters were able to antagonize the effects of hemicholinium-3 with dexamethasone (DX) and prednisolone.[2] In addition, Leeuwin *et al.* showed that ip-administered dexamethasone significantly increased the LD_{50} of *d*Tc in the rat.[3]

There is also evidence of an enhancement of muscle relaxant effects with acute corticosteroid therapy. In the cat, Durant *et al.* reported a significant potentiation of steady-state pancuronium (PCN) neuromuscular blockade with iv hydrocortisone (HC), 7 mg/kg.[4] Leeuwin *et al.*, using the rat sciatic nerve–tibialis anterior muscle preparation, showed antagonism of *d*Tc blockade with DX at a dose of 40 μg/kg, but enhancement of blockade with DX at 160 μg/kg.[3]

The method of Durant *et al.* was used as a model for this study to determine if the acute administration of corticosteroid at a clinically relevant dose would alter the neuromuscular blockade of the most commonly used nondepolarizing muscle relaxants in humans.

METHODS

This study was approved by the Institutional Review Board, and informed consent was obtained from all 25 participating patients. Patients with evidence of hepatic, renal, or adrenocortical dysfunction or with histories of previous corticosteroid therapy were excluded. All study subjects were scheduled for lumbar laminectomy and were premedicated and monitored according to departmental guidelines. They were given PCN, metocurine (MTc), or *d*Tc 1, 2, or 3 mg, iv, respectively, depending on the muscle relaxant being studied. Anesthesia was induced with thiopental 4–6 mg/kg iv and 1.0% halothane in oxygen. For patients receiving PCN, MTc, or *d*Tc, succinylcholine 1.5 mg/kg was used for endotracheal intubation. For those receiving vecuronium (VCN), muscle relaxation for intubation was accomplished with a single dose of VCN, 0.1 mg/kg. Anesthesia was maintained in all patients with 60% nitrous oxide and halothane, 0.6–1.0% inspired concentration, in oxygen. Patients were ventilated to maintain an end-tidal CO_2 tension of 25–32 mmHg. Esophageal temperature was maintained at 35–36.3° C with warming blankets. Neuromuscular transmission was assessed by measuring twitch of the thumb adductor with a Grass® force–displacement transducer (FT-10) in response to 0.15 ms supramaximal stimuli administered at a rate of 0.1 Hz, using needle electrodes applied at the wrist in the vicinity of the ulnar nerve (Grass® Model S-8 stimulator). After recovery from succinylcholine blockade, as judged by twitch tension, and 10 to 15 min of halothane administration, one or two small boluses of the muscle relaxant to be studied were administered iv to hasten the establishment of a steady-state neuromuscular blockade. The bolus dosages were approximately .03 mg/kg for PCN, 0.1 mg/kg for MTc, and 0.15 mg/kg for *d*Tc. A continuous iv infusion of either PCN, MTc, or *d*Tc was then started to maintain a constant level of neuromuscular blockade. For VCN, an infusion was begun immediately after endotracheal intubation. The doses were chosen with the aim of producing a continuous twitch tension at 50% of that prior to nondepolarizing neuromuscular blockade. Actual levels of blockade ranged between 38–56%. The steady-state twitch height during infusion of the relaxant prior to corticosteroid administration was used as control.

After at least 20 min of steady-state neuromuscular blockade, patients received either HC, 10 mg/kg, or DX, 0.4 mg/kg, iv. The muscle relaxant infusion rate remained constant, and twitch height was monitored for at least 34 min after the administration of the corticosteroid.

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The twitch heights at 5, 10, 15, and 30 min after the injection of the corticosteroid were compared with their respective control values. Repeated-measures analysis of variance was employed to determine the significance of any changes in twitch height following steroid injection. $P < 0.05$ was considered significant.

Results

A summary of the results is shown in table 1. Twitch tension, shown 5, 10, 15, and 30 min after corticosteroid administration, is expressed as a per cent of the preadministration value. With none of the relaxants studied did the acute iv administration of a corticosteroid significantly alter the steady-state twitch tension.

TABLE 1. Twitch Height Following Injection of Corticosteroid*

	5 min	10 min	15 min	30 min
PCN + HC	100	100	98.0 ± 2.7	95.6 ± 5
PCN + DX	100	100	100	102.4 ± 7.7
MTc + DX	100	100	100.4 ± 0.9	99.8 ± 3.5
*d*Tc + DX	100	100	100	99.2 ± 1.8
VCN + DX	98.4 ± 3.6	101.4 ± 3.1	102.0 ± 3.1	101.6 ± 4.3

n = 5 for each group.
PCN = pancuronium; HC = hydrocortisone; DX = dexamethasone; MTc = metocurine; *d*Tc = *d*-tubocurarine; VCN = vecuronium.
* Control twitch height taken as 100%.

Discussion

The successful treatment of myasthenia gravis with corticosteroids probably first aroused interest in the effects of these drugs on the neuromuscular junction. Wilson *et al.*, using microelectrode recording techniques, showed that prednisolone facilitated the release of acetylcholine in the rat phrenic nerve–diaphragm preparation. This was manifested by a reversible increase in miniature end plate potential (MEPP) frequency.[5] Wilgenburg, using a similar preparation, confirmed this finding and demonstrated an increase in MEPP amplitude with prednisolone.[6] In a later study, Wilgenburg *et al.*, using electron microscopy, showed an increase in the size of rat phrenic nerve synaptic vesicles when treated with prednisolone or DX.[7]

Corticosteroids have been shown to affect neuromuscular function. The Durant *et al.* study in cats implied that potentiation of a nondepolarizing neuromuscular blockade by corticosteroids was a possibility in humans.[4] In this study, we were unable to document a significant change in neuromuscular function, despite a dose of corticosteroid exceeding that used in nearly all clinical situations. Thus, in humans, acutely administered corticosteroids neither potentiate nor antagonize a nondepolarizing neuromuscular blockade.

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