TITLE: EFFECTS OF THIOPENTAL AND d-TUBOCURARINE ALONE AND COMBINED AT THE NEUROMUSCULAR JUNCTION.

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The ability of potent inhalation anesthetics but not thiobarbiturates to augment the effects of non-depolarizing neuromuscular blocking drugs has been long recognized. Both types of anesthetics have similar effects on the receptor activated ion channel suggesting that this is not the site of the potentiation. We therefore studied the combined effects of thiopental (PENT) and d-tubocurarine (DTC) on the nerve terminal.

Methods: All studies were performed using the in vitro frog (R. Pipeins) sciatic nerve sartorius muscle preparation. The two microelectrode voltage clamp was used to study the effects of DTC and PENT on the endplate current (EPC). Briefly, a recording microelectrode is inserted into the muscle cell in the endplate region. If acceptable miniature endplate currents are seen a second (current passing) electrode is inserted into the same cell within 100μm of the first. EPC's were recorded before and after the application of the drug or drug combination being studied. The sciatic nerve was stimulated at frequencies of 0.4 and 40 Hz to evaluate effects on quantum content and rundown respectively. EPC's were evaluated for amplitude, tau (time constant of decay of the rising limb) and extent of rundown with rapid rates of stimulation.

Results: When PENT 150 μM was applied EPC amplitude remained at 100 + 17% of the control value with slow rates of stimulation. After the application of PENT rundown was 10% greater than that seen without PENT. With the addition of PENT, tau decreased to 80.4% of the control value. When DTC 10^{-6}M alone was added to the bath, amplitude and tau decreased to 44 and 82% of control respectively. With the addition of PENT, amplitude increased to 100% of control while there was a continued decrease of tau to 71% of control. With tetanic stimulation DTC alone caused an 11% decrease in amplitude while tau decreased 5%. When PENT was added to DTC there was a further 10% decrease in amplitude and 5% decrease in tau.

Discussion: PENT alone appears to have little effect on the amplitude of the EPC elicited at both slow and fast frequencies of stimulation while tau is moderately decreased. Application of DTC caused a significant decrease in amplitude and a modest decrease in tau. When PENT was applied in combination with DTC amplitude increased to about the control value while there was a slight further decrease in tau. These results suggest that PENT, in this preparation, antagonizes the depressant effects of DTC on neuromuscular transmission by increasing evoked neurotransmitter release.

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TITLE: SUCCINYLCHOLINE ACTIONS IN PLASMA FROM PATIENTS WITH AND WITHOUT BURNS

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Clinically, patients with burns have abnormal responses to neuromuscular blocking drugs. Previous work shows that plasma from burned patients can decrease the potency of nondepolarizing blockers in vitro (1). One possible mechanism for this resistance to competitive acetylcholine receptor antagonists is that burn plasma increases the muscle sensitivity to acetylcholine. This possibility was tested by comparing an agonist action of succinylcholine (SCh) on phrenic nerve-diaphragm preparations bathed in either burn or control plasma. The agonist action examined was contracture. Additionally, the neuromuscular blocking actions of SCh in burn and control plasma were compared.

Preparations were initially bathed in a modified Krebs solution (37°C), stimulated supramaximally (0.2 Hz), and resting length was adjusted for maximal isometric twitch tension. Krebs was replaced with plasma (obtained after informed consent and IRB approval by Dr. J.A.J. Martyn, Harvard) from burned patients (BP) or control patients (CP). Train-of-four stimulation (4 pulses at 2 Hz every 11.5 sec) was then applied and SCh (50 μM) administered.

Results are presented (mean of 6) in the Table. CP and BP did not differ in size of contracture, peak block, time to peak block, or spontaneous recovery from block. The time to reach 50% spontaneous recovery from block was significantly different between CP and BP.

Thus, in contrast to results with nondepolarizing blockers, burn plasma does not acutely alter the magnitude of SCh actions on the neuromuscular junction. Further, the decreased potency of nondepolarizing blockers in burn plasma is not associated with an increased potency of agonists. The difference in time to recovery from SCh block indicates that plasma cholinesterase (which hydrolyzes SCh) may differ between burns and controls.

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	Control mean (SEM)			Burn mean (SEM)	
Peak contracture (g)	1.6	(.40)		1.9	(.23)
Peak block (%)	85	(8.8)		93	(1.7)
Time to peak block (s)	39	(6.2)		34	(5.6)
Recovery from block (%)	102	(2.0)		89	(8.5)
Min. to 50% recovery	2	(.21)	*	10	(3.0)

* = $P < 0.05$, t-Test