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TITLE: BRETYLIUM TOSYLATE AND NEUROMUSCULAR TRANSMISSION

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Introduction: Bretylium tosylate is a bromobenzyl quaternary ammonium compound which has been shown to inhibit release of norepinephrine from adrenergic nerve endings. Initially bretylium was used for treatment of hypertension, but, was discontinued because of poor oral absorption. Recently, it has been released for the treatment of ventricular arrhythmias. Because it is a quaternary ammonium compound, we decided to examine the effect of bretylium tosylate on neuromuscular transmission.

Methods: Isolated guinea pig nerve-lumbrical muscle preparations were made by dissecting the intact nerve and lumbrical muscle from guinea pigs weighing between 300 and 400 gm. The preparations were placed in oxygenated Krebs'-Hensleit solution at 37°C. and stimulating electrodes were attached to the nerve. Stimulating impulses were administered one every ten seconds, and the intensity adjusted to produce a maximal twitch height. The bathing solution was changed every 30 minutes. After the preparation had stabilized, bretylium tosylate was added and the resulting steady state depression of the twitch response was determined. The bretylium dose-response curve in the presence of tubocurarine was also determined.

Results: Bretylium depressed the twitch response in a graded dose-dependent fashion. However, the time necessary to reach steady state was much longer than seen with tubocurarine. Washing out bretylium resulted in prompt recovery of the twitch response. In the presence of 0.4 μM tubocurarine, a concentration that did not reduce the twitch response, the ED50 of bretylium was reduced.

Discussion: As anticipated from structure, bretylium produced a neuromuscular block. The ED50 is higher than would be anticipated during daily use. However, in the presence of a level of tubocurarine not sufficient to produce observable neuromuscular block (i.e. a level that might be present in the recovery room), the ED50 for bretylium was markedly reduced. Thus, bretylium administration for postoperative arrhythmias might compromise neuromuscular transmission in patients with an appreciable residual load of a competitive neuromuscular blocking agent.

References:

1. Koch-Weser, J: Bretylium. NEJM 300:473-477, 1979.