

Title: IS THE DURATION OF ACTION OF SUCCINYLCHOLINE PROLONGED FOLLOWING ANTAGONISM OF NEUROMUSCULAR BLOCKADE BY EDROPHONIUM?

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**Introduction.** The duration of succinylcholine (SCh) action is prolonged 2 and 3 times if administered following antagonism of neuromuscular blockade by pyridostigmine and neostigmine respectively.<sup>1</sup> The effect on SCh was attributed in part to inhibition of plasma cholinesterase by these antagonists. Pharmacokinetics and dynamics of edrophonium as an antagonist of neuromuscular blockade are similar to those of neostigmine and pyridostigmine. Will the duration of action of SCh be prolonged following edrophonium administration? To determine this we compared the duration of SCh neuromuscular blockade before and after edrophonium. We also measured the degree of cholinesterase inhibition following edrophonium.

**Methods.** We studied 6 surgical patients (23-77 yr) after informed consent approved by our Committee on Human Research. Anesthesia was induced with thiopental (2-4 mg/kg) and maintained with nitrous oxide (60%) and halothane (0.5-0.7% end-tidal concentration) as measured by mass spectrometry. The force of thumb adduction in response to supramaximal ulnar nerve stimulation (0.2 msec at 0.15 Hz) was quantified and recorded. SCh (0.5 mg/kg) was then administered. Following recovery from SCh pancuronium (0.05 mg/kg) was administered. When muscle twitch had recovered to 20% of control edrophonium (0.5 mg/kg) was administered in combination with atropine (0.5 mg). SCh (0.5 mg/kg) was administered again five minutes following edrophonium. We measured the onset (time from SCh injection until complete neuromuscular blockade), duration (time to complete recovery of muscle twitch tension) and recovery time (from 25 to 75% recovery of muscle twitch tension) for SCh before and after edrophonium. In addition venous blood was sampled at 1, 2, 4, 6, 8, 10, 15, 30 and 60 minutes following edrophonium administration. To determine the degree of cholinesterase inhibition we measured the rate of hydrolysis of <sup>3</sup>H-acetylcholine and compared this to that prior to edrophonium administration. Data were analyzed by Student's t test for paired comparisons with differences considered significant at  $p < 0.05$ .

**Results.** Following edrophonium the onset, duration and recovery time of SCh neuromuscular blockade were significantly prolonged (Fig. 1). Inhibition of cholinesterase activity was maximal at one minute following edrophonium and decreased rapidly towards control by 15 minutes (Table 1).

**Discussion.** The duration of SCh neuromuscular blockade was prolonged 1.6 times following edrophonium administration. However, this prolongation was much less than that reported following neostigmine and pyridostigmine.<sup>1</sup> Although neostigmine and pyridostigmine are kinetically similar to edrophonium the duration of cholinesterase inhibition produced by them is much longer (up to 4 hours).<sup>2</sup> The reversible nature of cholinesterase inhibition produced by edrophonium would explain this difference. At the time SCh was administered following edrophonium the

degree of cholinesterase inhibition was minimal (15-20%). This amount of inhibition may be inadequate to result in the prolongation of response on the basis of impaired SCh hydrolysis. Perhaps an interaction at the neuromuscular junction may better explain observed results. We conclude that SCh administration following antagonism of non-depolarizing neuromuscular blockade with edrophonium results in prolongation of the SCh reponse which is significantly less than seen following neostigmine or pyridostigmine.

Figure 1. Onset, duration and recovery of SCh before and after edrophonium. Values are means  $\pm$  SD.

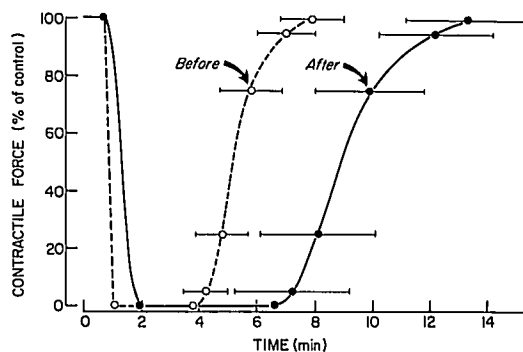


Table 1. Inhibition of cholinesterase after edrophonium (% , means  $\pm$  SD).

minutes		minutes	
1	47 $\pm$ 3.7	8	19 $\pm$ 3.9
2	29 $\pm$ 3.9	15	11 $\pm$ 2.1
4	19 $\pm$ 3.0	30	7 $\pm$ 5.1

#### References.

1. Sunew KY, Hicks RG: Effects of neostigmine and pyridostigmine on duration of succinylcholine action and pseudocholinesterase activity. *Anesthesiology* 49: 188-191, 1978
2. Mirakhur RK, Lavery TD, Briggs LP and Clark RSJ: Effects of neostigmine and pyridostigmine on serum cholinesterase activity. *Can Anaesth Soc J* 29:55-58, 1982