Title: Dose Response Curves for Succinylcholine: Single versus Cumulative Techniques.

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Introduction: The construction of dose response curves for muscle relaxants using cumulative dose techniques (CD) has several advantages compared with single dose (SD) methods: fewer patients are required to produce statistically reliable results, and the problem of whether to include or reject 0 and 100% responses is avoided. Long acting relaxants have been accurately studied using CD because drug elimination is negligible during administration of incremental doses (1). It follows that CD may underestimate potency for short acting relaxants and that its accuracy may be improved by the addition of an infusion to replace eliminated drug. The present study was designed to determine dose response relationships for succinylcholine with SD, CD and CD with an infusion (CDI).

Methods: After approval of the Hospital Ethics Committee, 38 adult patients scheduled for elective surgery were studied. Anaesthesia was induced with thiopental 3-5 mg/kg and maintained with N20 66% in 02 and supplemental doses of thiopental 0.5-1.5 mg /kg and fentanyl 1-2 mcg/kg as required. Ventilation was assisted with bag and mask to maintain end-tidal C02 at 30-35 torr. No volatile agents were used. Train-of-four stimulation was applied to the ulnar nerve every 12 s and the force of contraction of the adductor pollicis was measured. After stabilization of muscle twitch, patients received in a random fashion either SD (.15, .20, or .25 mg/kg, n=18), CD (initial dose: .15 mg/kg, incremental doses : .10 mg/kg, n=10), or CD with an infusion (CDI) to replace eliminated drug (n=10). Incremental doses were administered when 2 consecutive equal first twitch heights were observed. Based on the dose required to maintain 90% block (2), the hourly infusion rate was set at 15 times the cumulative dose given. Linear regressions were obtained between the logit transformation of neuromuscular blockade at the adductor pollicis and log dose. For SD, each patient represented 1 data point. For CD and CDI, a regression line was calculated for each patient, from which a mean dose-response curve was constructed. Effective doses (ED) for 50, 90 and 95% block were derived from the curves obtained by each of the 3 methods, and compared using analysis of variance. Results are expressed as mean $\pm$ SEM. A p value < 0.05 was considered significant.

Results: The CD curve was flatter and to the right of the SD and CDI curves (Fig. 1), with statistically different ED 90s and ED 95s ($p < 0.05$). For CD, ED 90 was significantly greater (.42 $\pm$ .06 mg/kg, $p < 0.05$) than the ED 90s obtained with SD or CDI (.29 $\pm$ .03 and .26 $\pm$ .02 mg/kg). There were no significant differences in the ED 50, 90 or 95 between SD and CDI. Time to complete cumulative dose response curves was significantly longer with CD than with CDI (5.5 $\pm$ .5 vs 3.4 $\pm$ .3 min, $p < 0.001$). With CD, more dose increments were required to produce equivalent blockade (3.9 $\pm$ vs 2.4 $\pm$ .2, $p < 0.001$).

Discussion: Dose response curves by CD without infusion are inappropriate for succinylcholine, most likely because a significant amount of drug is metabolized during the study period. However, the potency with CDI was very close to that obtained by SD, suggesting the usefulness of the technique for short acting drugs. The data suggest that the doses of succinylcholine used clinically (1-1.5 mg/kg) are equivalent to 3-6 times the ED 90 and may explain the excellent intubating conditions provided by succinylcholine.

References:

1. Donlon JV, Savarese JJ, Ali HH, et al: Anesthesiology 53: 161, 1980.

2. Katz RL, Ryan JF: Br J Anaesth 41: 381, 1969.

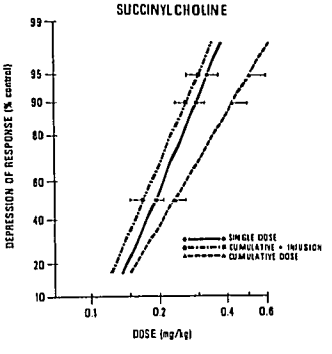

Figure 1. Succinylcholine dose response curves using 3 different methods. Error bars represent SEM.