Title: PRELIMINARY ADMINISTRATION OF SUCCINYLCHOLINE DOES NOT INCREASE POTENCY AND DURATION OF ACTION OF PIPECURONIUM

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Introduction. It has been reported that preliminary administration of 1 mg/kg succinylcholine (SCh) decreased the ED_{50} and ED_{95} and prolonged the duration of action of vecuronium, but did not affect these parameters with other muscle relaxants (MR) [for references see (1)]. It was the purpose of the present study to determine if SCh had any effect on the ED_{50}, ED_{95} and time course of the neuromuscular (NM) effect of pipecuronium, a new long acting nondepolarizing MR now undergoing clinical trials in the USA.

Methods. Thirty ASA Class I and II patients, 18 males and 12 females signed informed consents to participate in this study approved by the IRB of our institution. Premedication consisted of 1.5 mg/kg i.m. meperidine and diphenhydramine each, administered on call. Anesthesia was induced with 0.5 µg/kg fentanyl, 0.1 mg/kg droperidol, 2 to 3 mg/kg thiopental and 2 ℓ/min O_2-4 ℓ/min N_2O and maintained with the same O_2-N_2O mixture, increments of 25 to 100 µg of fentanyl and 25 to 50 mg thiopental, as indicated. After induction, the ulnar nerve at the wrist was stimulated, through surface electrodes, with a constant current nerve stimulator, by trains of four (TOF), supramaximal, square wave impulses of 0.2 ms duration, administered every 10 s. The indirectly elicited force of adduction of the thumb (P) was quantitated by an FT10 transducer and continuously recorded. One mg/kg SCh was injected i.v. over 30 s and the trachea was intubated after the development of the maximal NM effect of SCh. After the SCh block has worn off and P became stable, the cumulative dose-response of pipecuronium was determined. The first dose of pipecuronium was 15 µg/kg, followed by increments of 5 to 10 µg/kg, administered after development of the maximal effect of the preceeding dose, until P, measured by the response to the first stimulus of TOF (T1) decreased to less than 10% of control. The ED_{50}, ED_{90} and ED_{95} were determined for each patient from the computer derived log dose-response regression line. The time for the recovery of T1 from 10% to 25% and, whenever feasible, from 25% to 75% of control was observed. At termination of anesthesia TOF was recorded before and at 2, 5 and 10 min after the start of the i.v. injection of a mixture of 40 µg/kg neostigmine and 20 µg/kg atropine administered in 60 s.

Results. The i.v. injection of 1 mg/kg SCh produced complete NM block in 1.1 ± 0.05 min (mean ± SEM). The clinical duration (time for recovery of T1 to 25% of control) was 9.7 ± 0.52 min and recovery rate (from 25% to 75% of control) was 2.7 ± 0.49 min. Maximal recovery to 122.3 ± 3.1% of control occured in 17.9 ± 0.70 min. The dose-response and time course of the NM effect of pipecuronium, administered immediately after the dissipation of the NM effects of SCh, are compared in the table with the same parameters determined in a similarly premedicated and anesthetized group of 30 patients, who did not receive SCh and who were intubated after the development of the maximal effect of pipecuronium. The data presented in this table indicate that there are no differences in the intensity, time course and reversibility of the NM effects of pipecuronium administered alone or after the preliminary administration of 1 mg/kg SCh.

Discussion. Because of its long duration of action, the NM effects of the 80 to 100 µg/kg doses of pipecuronium which would produce relaxation suitable for atraumatic intubation within a reasonable time, < 3 min, would frequently outlast the required duration of surgery. Therefore it is very likely that pipecuronium will be used for maintenance of surgical relaxation after intubation with SCh. Under our experimental conditions, when the administration of incremental doses of pipecuronium started 17 min after injection of SCh and the ED_{95} dose was administered over another 20 to 25 min, the intensity and time course of the NM effects of pipecuronium was similar to those produced by comparable doses of pipecuronium administered alone. Under clinical conditions, however, a single ED_{95} dose of pipecuronium would be administered as soon as the NM effect of the intubating dose of SCh had started to wear off. It is conceivable that under these conditions, similarly to observations made with pancuronium(2), the intensity of the pipecuronium block would be increased and its duration shortened by the preliminary injection of SCh.

References.

1. Krieg N et al.Br J Anaesth 53: 259261, 1981.
2. Nagashima H et al. Clinical experiences with Norcuron. Agoston S et al. (eds.), Current Clinical Practice Series 11. Excerpta Medica, Amsterdam 1983, pp. 127-131.

Parameters	Group I SCh+Pipecuronium		Group II Pipecuronium Alone	
ED_{50} (µg/kg)	18.6 ± 0.7(28)*		20.3 ± 1.1(30)	
ED_{90} (µg/kg)	33.6 ± 1.4		33.0 ± 1.6	
ED_{95} (µg/kg)	35.7 ± 1.5		35.1 ± 1.7	
Maximal Block(%)	95.3 ± 1.2		97.5 ± 1.2	
Time (min) for recovery of T1 from:				
10%-25%	13.0 ± 1.2(24)		13.0 ± 1.2(26)	
25%-75%	36.5 ± 7.0(7)		35.9 ± 5.8(9)	
	T1	T4/T1	T1	T4/T1
Before reversal†	55.2	0.36	39.7	0.17
After reversal				
2 min	70.6	0.67	59.1	0.49
5 min	82.8	0.81	78.0	0.70
10 min	89.6	0.88	88.1	0.83

*Values represent means ± SEM of number of observations in parenthesis.
†Mean (n=30); SEM not shown for lack of space.