Title : COMPARATIVE CARDIOVASCULAR AND NEUROMUSCULAR EFFECTS OF ORG NC 45, d-TUBOCURARINE, PANCURONIUM AND METOCURINE

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Introduction. Org NC 45, a homologue of pancuronium, produces a neuromuscular blockade which is shorter in both onset (time from injection until maximum effect) and duration of action than that of pancuronium or d-tubocurarine. Also, Org NC 45 was found to have less autonomic blocking activity than that of pancuronium. (Durant et al: Europ J Pharmacol (In press).

Methods and Results. We compared the neuromuscular and cardiovascular effects of Org NC 45 with those of d-tubocurarine, pancuronium and metocurine in five dogs anesthetized with halothane. Only one relaxant was studied each day. All dogs were studied with each relaxant and consequently serve as their own control. Paralysis was quantitated by measuring twitch tension in response to supramaximal stimulation of the sciatic nerve. From cumulative dose response curves, the ED_{90} (dose resulting in 90% depression of twitch tension was derived. Org NC 45 has a potency similar to that of pancuronium (Table 1). However, when three times the ED_{90} was given, the duration of action (time from relaxant administration until return of 50% of the original twitch tension) was considerably shorter (Table 1). Immediately before, 1, 5, 10, 20, 30, 40, 50, 60 and 75 minutes after administration of neuromuscular relaxant, cardiac output (CO) and pulmonary capillary wedge pressure (PCWP) were measured, and from continuous recordings other parameters were calculated including mean arterial blood pressure (MAP), mean pulmonary artery pressure (MPAP), central venous pressure (CVP), heart rate (HR), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR).

Conclusions.

1. Org NC 45 is 1.2 times as potent as pancuronium, 14.5 times as potent as d-tubocurarine, and 2.8 times as potent as metocurine (Table 1).
2. At three times the ED_{90} dose, Org NC 45 has a duration of only 39% of pancuronium, 32% of d-tubocurarine, and 26% of metocurine (Table 1).
3. Org NC 45 produced no significant changes in the cardiovascular parameters measured. The other muscle relaxants all produced significant cardiovascular changes (see Table 1 for details).

The authors conclude that Org NC 45 has advantages over currently used nondepolarizing muscle relaxants in its shorter duration of action, and freedom from cardiovascular side effects.

Table 1

Comparison of Neuromuscular Blockade and Maximum Cardiovascular Changes

Drug	HR (%)	MAP (%)	CO (%)
Org NC 45	+0.5±1.1	+2.0±2.9	+2.6±1.3
Pancuronium	+19.2±4.9	+18.1±3.2	+40.1±9.9
dTc	+17.3±4.2	-44.0+11.6	+24.0±10.9
Metocurine	+8.2±5.1	-4.0±1.2	+17.6±5.6

Drug	ED_{90} (mg/kg)	Mean Duration of Block (min)
Org NC 45	0.050±010	43±6
Pancuronium	0.062±.008	109±8
dTc	0.725±.061	134±10
Metocurine	0.142±.032	167±14