Title: COMPARISON OF SPONTANEOUS RECOVERY AND NEOSTIGMINE-ACCELERATED RECOVERY FROM MIVACURIUM NEUROMUSCULAR BLOCKADE.

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Introduction

Mivacurium is a short-acting nondepolarizing muscle relaxant. It is hydrolyzed by plasma cholinesterase at a rate of approximately 88% that of succinylcholine.[1] Although mivacurium block is classically nondepolarizing, it is conceivable that administration of anticholinesterases for antagonism might slow rather than accelerate recovery, due to inhibition of plasma cholinesterase. Since mivacurium has a rapid spontaneous recovery, is there any time advantage gained by neostigmine administration during deep mivacurium block? We attempted to answer these questions by a paired comparison of spontaneous and neostigmine-induced recovery from mivacurium block.

Methods

Twenty-two ASA I-II patients of either sex, ages 18-59, weighing 45-110 kg were studied after giving institutionally approved written informed consent. Patients with known neuromuscular disease or taking medication known to interfere with muscle relaxants were excluded. Patients were premedicated with morphine (0.05-0.15 mg/kg) IM and diazepam (0.1-0.2 mg/kg) po or midazolam (0.02-0.07 mg/kg) i.v.. General anesthesia was induced with fentanyl (3.0 ug/kg) i.v. and sodium thiopental (5.0 mg/kg) i.v. and maintained with 70% N_2O in O_2. Additional narcotic and thiopental were administered to provide adequate clinical anesthesia. Bolus doses of 0.15 mg/kg mivacurium were administered intravenously to 6 patients and 0.2 mg/kg to 16. Data from these two groups were pooled. Ventilation was controlled to maintain an end-tidal PCO_2 at 35-40 mm Hg and temperature was kept in the range of 35-37°C. Evoked thumb adduction was measured using a Grass FT-10 force transducer in response to supramaximal single twitch stimulation of the ulnar nerve at 0.15 Hz via a Grass S 88 stimulator and SIU 5 isolation unit. Single Twitch responses were allowed to recover spontaneously at least to 95% of control twitch height and Train-of-Four (TOF) ratio to > 75%. Ten minutes later a second bolus of mivacurium equal to the previous dose was administered to the same patient. Neostigmine (0.06 mg/kg) and atropine (0.03 mg/kg) were injected intravenously when the single twitch response returned to approximately 5% of control baseline. The 5-95%, 25-95% and the 25-75% recovery times were measured and compared both for spontaneous and neostigmine-induced recovery using paired t-test. Values are expressed as the mean ± S.E.M. Differences were considered significant at $p<0.01$.

Results

Reversal with neostigmine resulted in recovery intervals which were shorter than spontaneous recovery. For example, the 25-75% recovery index was almost 3.5 minutes faster after neostigmine compared to spontaneous recovery (Table 1). Neostigmine administration at 88-95% mivacurium block resulted in 95% twitch recovery in 2-12 minutes (Fig. 1). There was no difference noted in the T4/T1 ratio measured within 3 minutes following recovery to control height for spontaneous and induced recovery (Table 1).

Discussion

Rapid reversal from deep mivacurium neuromuscular blockade can be achieved with neostigmine. Kopman (2) reported in a reversal study of pancuronium that the recovery time from 10% to 93% twitch height and a TOF ratio of 0.76, was 30 minutes after neostigmine administration. This compares to 7.7 min to 95% recovery and a TOF ratio of 0.79 approximately 10 minutes after neostigmine reversal of 90% mivacurium block. Neostigmine-induced recovery of mivacurium block represents an acceleration of only 7.4 mins compared with spontaneous recovery. While this difference is statistically significant, in many cases such a minor acceleration may not be clinically relevant. Antagonism, even from deep residual mivacurium block may be necessary less frequently than following the administration of other nondepolarizing agents.

References

1. Savarese JJ et al. Clinical neuromuscular pharmacology of mivacurium chloride (BW B1090U): A short-acting nondepolarizing ester neuromuscular blocking drug. Anesthesiol. 1988 (in press).
2. Kopman AF. Recovery times following edrophonium and neostigmine reversal of pancuronium, atracurium, and vecuronium steady state infusions. Anesthesiol 65:572-78 (1986).

Table 1

Comparison of Spontaneous and Induced Recovery

	25-75% Recovery Index (min) N=22	25-95% Recovery Time (min) N=22	5-95% Recovery Time (min) N=10	T4/T1 Ratio % N=13
Spon.	6.5±0.3*	11.0±0.7*	15.1±1.4*	83.9±1.1
Induced	3.0±0.2	5.9±0.4	7.7±0.7	79.1±2.4

* Statistical significance $p<0.01$

Figure 1

Correlation of Neostigmine-induced Recovery Time to 95% Twitch Height with Depth of Neuromuscular Blockade