Title: NEOSTIGMINE ANTAGONIZES A PROFOUND NEUROMUSCULAR BLOCKADE MORE RAPIDLY THAN EDROPHONIUM

Authors: S.M. Rupp, M.D., J.W. McChristian, M.D., R.D. Miller, M.D.

Affiliation: Department of Anesthesia, University of California, San Francisco, California 94143

Introduction. Edrophonium has gained increased popularity as an antagonist of nondepolarizing muscle relaxants because of its faster onset and reduced atropine requirement when compared to neostigmine.[1,2] However, previous studies have suggested there may be difficulty in edrophonium's ability to antagonize profound neuromuscular blockade induced by pancuronium or d-tubocuraine.[3,4] In this study, we compared edrophonium with neostigmine in their ability to antagonize various degrees of pancuronium-, vecuronium-, or atracurium-induced neuromuscular blockade.

Methods. We obtained informed consent and approval from the local committee on human research to study 82 ASA I or II adult elective surgical patients. Morphine sulfate, 0.15 mg/kg i.m., and diazepam, 10 mg p.o. were administered one hour preoperatively. Anesthesia was induced with thiopental, 4-6 mg/kg i.v., and inhalation of nitrous oxide, 60%, with halothane (N=53) or enflurane (N=29). The trachea was intubated without the use of muscle relaxants. The end-tidal concentration of the volatile anesthetic was then adjusted to 0.65 MAC (halothane 0.50%, enflurane 1.10%) as determined continuously by mass spectrometry. Ventilation was controlled to maintain end-tidal pCO_2 between 30 and 40 mmHg. Esophageal temperature was maintained above 35.5 C. Neuromuscular function was monitored by measuring force-of-thumb adduction with a GRASS FT10 force displacement transducer in response to supramaximal single twitch (.15Hz) stimulation of the ulnar nerve via two steel needle electrodes placed 2 cm apart at the wrist. After a stable twitch tension recording was obtained, atracurium, vecuronium, or pancuronium was administered to induce neuromuscular blockade. After recovery phase had begun (at least 2-4% recovery), edrophonium, 0.5 mg/kg, with atropine, 0.5 mg, or neostigmine, 0.04 mg/kg, with glycopyrrolate, 0.01 mg/kg was administered as an i.v. bolus. Antagonist was administered at varying degrees of recovery: Range 2%-80% of control twitch tension. We determined reversal time (the time from injection to 90% recovery of control twitch tension). Reversal times for each relaxant-antagonist combination were divided into two groups: blockades reversed when twitch height (TH) was greater than 10% of control and blockades reversed when TH was less than or equal to 10% of control. Neostigmine and edrophonium were compared in their ability to antagonize each relaxant by comparing mean reversal times using the Mann-Whitney U test. Statistical significance was considered to be $P < 0.05$.

Results.

Group	Time (min) to 90% of control TH			
Relaxant-Antagonist	N	TH > 10% at reversal	N	TH < 10% at reversal
Atra-Edro	4	2.9 ± 0.8	6	9.8 ± 7.0
Atra-Neo	12	4.8 ± 2.4	6	8.5 ± 3.3
Vec-Edro	11	2.9 ± 2.7	8	15.0 ± 12.5 *
Vec-Neo	5	2.2 ± 1.0	9	5.6 ± 1.7
Pan-Edro	5	3.7 ± 2.1	5	20.0 ± 8.0 #
Pan-Neo	5	4.2 ± 1.7	6	7.0 ± 2.2

All values Mean ± S.D.
* Different from Vec-Neo $P < 0.05$
# Different from Pan-Neo $P < 0.05$

Discussion. Edrophonium is more variable than neostigmine in its ability to quickly antagonize deep neuromuscular blockades (when TH < 10% of control) induced by atracurium, vecuronium and pancuronium. This is demonstrated not only by the longer mean reversal times for edrophonium in the vecuronium and pancuronium groups but also by the much larger standard deviations for all the relaxant-edrophonium groups than the relaxant-neostigmine groups when antagonist is administered at TH < 10% of control. On occasion edrophonium took more than 30 minutes to reverse deep blocks induced by vecuronium and pancuronium. The reason for the apparent difference between atracurium vs. pancuronium and vecuronium is unknown. Both neostigmine and edrophonium easily reversed neuromuscular blockade produced by all three relaxants when antagonism was attempted with TH > 10% of control. In these instances, edrophonium was faster (N.S.).

We conclude that when antagonizing profound neuromuscular blockade (TH < 10% of control), neostigmine provides a more rapid and predictable antagonism as compared to edrophonium.

References.

1. Cronnelly R, Morris RB: Antagonism of neuromuscular blockade. Br J Anaesth 54:183-194, 1982
2. Cronnelly R, Morris RB, Miller RD: Edrophonium: duration of action and atropine requirement in humans during halothane anesthesia. Anesthesiology 57:261-266,1982
3. Katz RL: Neuromuscular effects of d-tubocurarine, edrophonium and neostigmine in man. Anesthesiology 28:327-336,1967
4. Kopman AF: Edrophonium antagonism of pancuronium-induced neuromuscular blockade in man. Anesthesiology 51:139-142,1979