

Title: FASTER ONSET OF NEUROMUSCULAR BLOCKADE WITH NON-DEPOLARIZING MUSCLE RELAXANTS

Authors: M.P. Mehta, M.D., W.W. Choi, M.D., S.D. Gergis, M.D., M.D. Sokoll, M.D.

Affiliation: Department of Anesthesia
University of Iowa Hospital and Clinics
Iowa City, Iowa 52242

Introduction: Non-depolarizing muscle relaxants have a slower onset of neuromuscular blockade when compared to succinylcholine, a depolarizing muscle relaxant. The purpose of this study was to determine if onset of neuromuscular blockade is shorter after a subparalyzing dose of one non-depolarizing muscle relaxant followed by a larger dose of the same or another non-depolarizing relaxant.

Method: Sixty patients, ASA I or II undergoing elective surgery were randomized into six groups of 10 patients each. Informed consent was obtained from each patient and the study was approved by the institutional human review committee. All patients were premedicated with morphine 0.05 - 0.15mg/Kg I.M. and scopolamine 0.003 - 0.004mg/Kg I.M. 45-60 mins. prior to induction of anesthesia. Anesthesia was induced with fentanyl 50-100µg, thiopental 4-5mg/Kg and maintained with 70% nitrous oxide in oxygen and incremental doses of thiopental and fentanyl. The twitch response of the adductor pollicis to ulnar nerve stimulation was elicited by supramaximal square wave pulses of 0.2msec duration, at a rate of 0.2hz and quantitated continuously by an FT-10 transducer. Once a steady state twitch was established a subparalyzing dose of 0.015mg/Kg (ED10) of pancuronium (Pan) or 0.03mg/Kg (ED10) of metocurine (Met) or 0.04mg/Kg (ED5) of d-tubocurarine (dTc) was administered. Three minutes after the subparalyzing dose, 0.08mg/Kg (2ED90) of Pan or 0.4mg/Kg (2ED90) of atracurium (Atr) was administered. The degree of neuromuscular blockade at the end of 60 secs. and time to 95% blockade were observed. At this stage all patients were intubated and time to recovery of twitch height to 50% of control was observed. Analysis of variance was used for statistical analysis. $P \leq 0.05$ was considered statistically significant.

Results: The degree of neuromuscular blockade after 60 secs. and time to 95% neuromuscular blockade following a paralyzing dose of Pan and Atr are shown in Table 1&2. At end of one minute about 80% neuromuscular blockade and by 90 secs. greater than 95% neuromuscular blockade is seen in all the groups. There was no significant difference among the groups.

Discussion: The onset to maximum neuromuscular blockade following a single bolus of Pan. (2ED90) takes about 3.5-4 mins. while for Atr. (2ED90) is about 2-3 mins. This study demonstrates that onset of neuromuscular blockade is faster when Pan or Atr are preceded by a subparalyzing dose of non-depolarizing muscle relaxants.

A subparalyzing dose of muscle relaxant may affect the neuromuscular junction by partially occupying the post-junctional receptors¹ and may

also inhibit presynaptic feedback mechanism of stimulated ACH release². Also the differing ability of muscle relaxant to inhibit neuromuscular transmission by blocking the ionophores of post junctional membrane may have some role in shortening the onset to maximum neuromuscular blockade when combinations are used³. Thus by administering a subparalyzing dose of non-depolarizing muscle relaxant prior to a paralyzing dose, a more rapid onset of adequate neuromuscular blockade may be achieved for early intubation.

Table 1 Pan 0.08mg/Kg (2ED90) preceded by			
mg/Kg	Pan 0.015 (ED10)	Met 0.03 (ED10)	dTc 0.04 (ED5)

% Block at 60 secs.	89.2±3.5	89.8±2.4	79.0±5.0
---------------------	----------	----------	----------

Time to 95% Block in secs.	72.9±5.7	69.3±4.3	85.9±9.6
----------------------------	----------	----------	----------

Recovery from max. Block to 25% Twitch (mins)	75.0±7.6	100.75±10.0*	77.5±3.7
---	----------	--------------	----------

Table 2 Atr 0.4mg/Kg (2ED90) preceded by			
mg/Kg	Pan 0.015 (ED10)	Met 0.03 (ED10)	dTc 0.04 (ED5)

% Block at 60 secs.	90.7±2.7	94.0±2.2	81.5±2.8
---------------------	----------	----------	----------

Time to 95% Block in secs.	65.1±5.7	59.1±5.3	86.1±5.9
----------------------------	----------	----------	----------

Recovery from max. Block to 25% Twitch (mins)	49.5±2.7	50.1±2.7	40.6±1.9
---	----------	----------	----------

Mean ± SE * p < 0.05

References

1. Paton, WDM and Waud, DR: The margin of safety of neuromuscular transmission. J. Physiol. 191:59-90, 1967.
2. Foldes, FF: The significance of physiological [Ca⁺⁺] and [Mg⁺⁺] for in vitro expt. on synaptic transmission. Life Sciences 28:1585-90, 1981.
3. Dreyer, F: Acetylcholine receptor, Br. J. Anaesth. 54:115-130, 1982.