

Title: **COMPARATIVE NEUROMUSCULAR PHARMACOLOGY OF THE DIAPHRAGM AND THE TIBIALIS ANTERIOR**

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Comparative neuromuscular pharmacology of the respiratory and peripheral muscles provides the basis for monitoring the thumb twitch as a means of indirect assessment of the state of neuromuscular transmission of the diaphragm. The present study compares the neuromuscular effects of succinylcholine (SDC), Norcuron (NC-45), and d-tubocurarine (dTc) in the diaphragm and the tibialis anterior of the cat with an identical method. In the case of NC-45, we were interested in finding out at its current stage of development as a new drug whether it relaxes the respiratory muscles better than the peripheral muscles.

**Method:** Twenty-three anesthetized cats were tracheotomized and ventilated ( $\text{PaCO}_2$   $32 \pm 6$  (SD) torr). The left phrenic nerve was identified via a thoracotomy. The motor nerve supplying the tibialis anterior muscle was identified in the sciatic notch. Both nerves were stimulated supramaximally at a rate of 0.1 Hz. The neurally evoked compound electromyographic responses of the ipsilateral hemidiaphragm and tibialis anterior were quantified simultaneously in an identical manner. Eight cats received SDC, another 8 received NC-45, the remaining 7 received dTc intravenously. Dose-response curves were constructed for each muscle in each cat using log-probit analysis. Each cat served as its own control for comparisons between the two muscles. Group data were compared by t-tests.

**Results:** The figure below highlights:

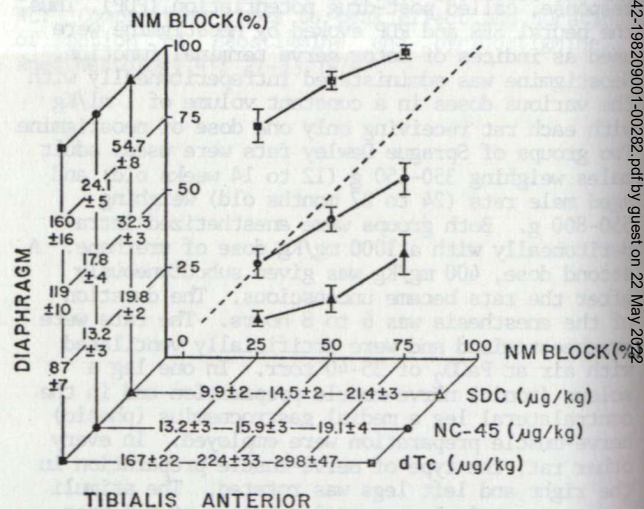
- (1)  $\text{ED}_{25}$ ,  $\text{ED}_{50}$ , and  $\text{ED}_{75}$  values of SDC, NC-45, and dTc in the tibialis anterior, shown along horizontal axis,
- (2) the corresponding ED values for the diaphragm, shown along the vertical axis, to indicate that larger doses of SDC but smaller doses of dTc were required to block the diaphragm than the tibialis anterior ( $P < 0.02$ ), and
- (3) three curves in the center one each showing that SDC ( $\blacktriangle$ ) at any dose consistently produced markedly higher percentage of block in the tibialis anterior than in the diaphragm ( $P < 0.01$ ) that NC-45 ( $\bullet$ ) had no muscle preference in small dose ( $P > 0.5$ ) but blocked the tibialis anterior slightly more profoundly in medium ( $P < 0.05$ ) and in large doses ( $P < 0.01$ ), and that dTc ( $\blacksquare$ ) consistently and markedly blocked the diaphragm more profoundly ( $P < 0.01$ ).

**Discussion:** Contrary to the so-called "respiratory sparing", dTc blocked the diaphragm with markedly increased sensitivity in the cat. In this regard, the diaphragm of the cat resembles the soleus. However, it is not proper to make generalizations that all nondepolarizing neuromuscular blockers will block the diaphragm with increased sensitivity; NC-45 did not. Therefore, differences in drug response to neuromuscular blockers between the diaphragm and the tibialis anterior may be drug specific, or NC-45 may be an atypical nondepolarizing blocker in this regard. In view of the recent understanding that clinically popular neuromuscular blockers have differential prejunctional and postjunctional affinity,<sup>1</sup> we propose that respiratory and peripheral muscles may differ in their neuromuscular sensitivity because of prejunctional factors.

**Conclusion:** While SDC blocks the tibialis anterior with greater sensitivity than the diaphragm the opposite is true for dTc. NC-45 shows least muscle preference. This new muscle relaxant might have the additional clinical advantage that the state of the diaphragm can be determined with greater accuracy by the thumb twitch.

**Reference:**

1. Bowman WC: Prejunctional and postjunctional cholinceptors at the neuromuscular junction. *Anesth Analg* 59:935-943, 1980.



All values: mean  $\pm$  S.E.M.