

Title: QUANTIFICATION OF MAGNESIUM-PANCURONIUM INTERACTION IN THE DIAPHRAGM AND THE TIBIALIS ANTERIOR

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Introduction. It is well known that magnesium (Mg) enhances nondepolarizing neuromuscular block. However, questions remain regarding the interaction in vivo. Does the dose requirement of the nondepolarizing neuromuscular blocker decrease predictably in linear relationship to the serum concentration of Mg, and if so, how much Mg is required to reduce the ED₅₀ of the neuromuscular blocker by half, and so forth? Is there a dividing point below which even some increase in the serum concentration of Mg will not significantly increase the neuromuscular sensitivity? Are the diaphragm and the tibialis anterior affected differently? The present study quantifies Mg-pancuronium interaction in the cat.

Methods. Thirteen cats averaging 3.5 ± 0.7 (S.D.) kg, were anesthetized with alpha-chloralose 50 mg/kg and pentobarbital 15 mg/kg injected into the peritoneal cavity. Ventilation with air was controlled via tracheostomy. The esophageal temperature was maintained between 35-36°C. Arterial pressure was monitored via a cutdown. All drugs except the anesthetics were injected intravenously. The left sciatic nerve was severed at the sciatic notch and stimulated distally with supramaximal electric pulses of 0.2 ms duration generated at 0.1 Hz by a Grass S88 stimulator. The twitch response of the ipsilateral tibialis anterior muscle was quantified both mechano-myographically (MMG), with a Grass FT 10c transducer, and electromyographically (EMG). With an open chest, the left phrenic nerve was stimulated and the response of the ipsilateral hemidiaphragm was quantified electromyographically. Magnesium sulfate totaling 25 (n=4), 50 (n=3), 100 (n=3), or 200 mg/kg (n=3), was injected as repeated incremental doses of 15-30 mg/kg. After completion of injection of Mg, or after complete recovery of Mg-induced neuromuscular block, if any, the preparation was stabilized for another 15-30 minutes. A blood sample was then obtained for determination of Mg concentration. The corresponding dose requirement of pancuronium was determined by construction of a cumulative dose-response curve for each muscle of each cat. The ED₅₀ of pancuronium was determined by log-probit dose-response analysis, and its relationship to the Mg concentration was determined by linear regression of group data, both performed by a computer. An additional eight cats received pancuronium under identical experimental conditions without Mg pretreatment.

Results. Figure below, each point in the Mg-group representing one cat, shows the relationship between the serum concentration of Mg and the ED₅₀ of pancuronium for the twitch response of the

tibialis anterior (taMMG). Similar results were obtained for the EMG response of the tibialis anterior (taEMG) and the EMG response of the diaphragm (dEMG). Like the ED₅₀, the ED₂₅ and the ED₇₅ show similar linear relationship to the Mg concentration. Equations below show the linear relationship between the Mg concentration (total Mg, mEq/l, y) and the ED₅₀ of pancuronium (ug/kg, x).

$$\text{taMMG } y = 19.4 - 2.1 x, r = 0.86$$

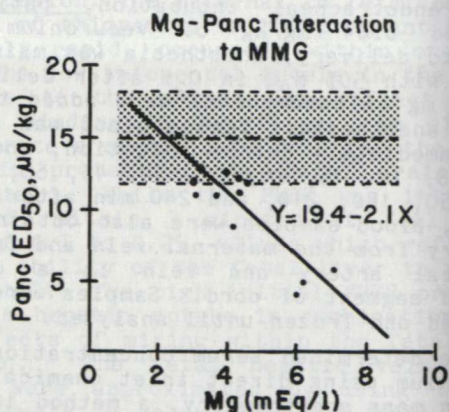
$$\text{taEMG } y = 19.3 - 2.1 x, r = 0.85$$

$$\text{dEMG } y = 17.6 - 2.0 x, r = 0.84$$

Discussion/Conclusion. Serum concentration of Mg and the dose requirement of pancuronium is linearly and inversely related in the cat. Quantification of the same interaction in humans may have clinical application. Instead of reducing the nondepolarizing neuromuscular blocker in an empirical manner, a pre-determined dose schedule may be possible in the anesthetic management of toxemic patients who receive magnesium therapy. The present study also supports the clinical validity of monitoring the thumb twitch as an index of the overall muscle power including the diaphragmatic functions in magnesium-treated toxemic patients.

References.

1. Ghoneim MM, Long JP: The interaction between magnesium and other neuromuscular blocking agents. *Anesthesiology* 32:23-27, 1970



Inverse linear relationship between serum concentration of Mg and sensitivity of the tibialis anterior to pancuronium. Shaded area and broken line indicate ED₅₀ and S.D. in normal cats not treated with Mg.