Title: BW A938U DOES NOT TRIGGER MALIGNANT HYPERTHERMIA IN SUSCEPTIBLE SWINE

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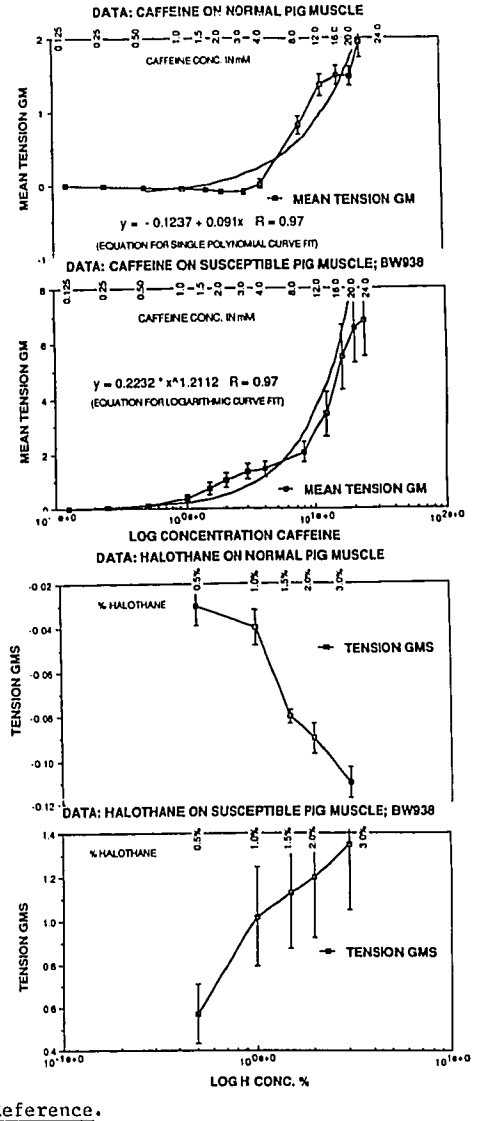
Introduction. Non-depolarizing neuromuscular blocking agents have generally been found to have little triggering potential on the occurrence of Malignant Hyperthermia (MH) in man and swine.[1] The purpose of this study was to determine whether a new non-depolarizing muscle relaxant possesses any triggering potential for skeletal muscle in swine. The halothane-sensitive Pietrain pig model was used since it is considered similar to MH positive humans sensitive to halothane.

Methods. Two groups of previously tested halothane-sensitive Pietrain pigs (N=4) were anesthetized and maintained with pentobarbital (30 mg/kg IV). Each pig was intubated without aid of muscle relaxants and ventilated with O_2-N_2O (FIO_2.4), adjusting minute volume to achieve a PCO_2 of approximately 40 mm Hg. The jugular vein and artery were cannulated. The forelimb was stabilized and the second digit attached to a force transducer via a stainless steel wire. An ulnar nerve electrode was connected to a Grass stimulator and adjusted to produce a supermaximal stimulation every 10 seconds. Twitch height, baseline tension, ECG, intra-arterial blood pressure, end tidal PCO_2, and rectal and muscle temperatures were continuously monitored. Arterial and venous blood gases, plasma glucose, potassium, lactate, and ionized and total calcium were periodically obtained and recorded. A skeletal muscle biopsy was done from the trapezius muscle for an in vitro halothane/caffeine muscle contracture test. Group I pigs (N=4) were given an IV dose of BW A938U to produce a 95% reduction of twitch height ED95 (MEAN dose 27.5 ugms/kg) while Group II pigs received a supramaximal dose (4X ED95) of 120 ugms/kg. Following return of twitch height to control and after no clinical signs of MH were observed, both groups of pigs were given halothane 2-5% for 10 minutes and then if clinically negative for signs of MH, given succinylcholine (1 mg/kg IV). Pigs were observed for signs of muscle rigidity, tachycardia, hypercarbia, acidosis, and temperature elevation. In vitro muscle testing was done utilizing a standard MH protocol exposing isolated stimulated muscle strips to increasing doses of caffeine or halothane and then observing the changes in baseline muscle tension. Results were compared with control data for non-susceptible pigs.

Results.

1. BW A938U in both ED95 and 4X ED95 doses never changed any of the measured parameters, thus indicating that the drug had no potential for triggering an episode of MH in susceptible swine.
2. Each animal was confirmed to be MH susceptible by a terminal clinical MH episode triggered by halothane and succinylcholine.
3. In vitro muscle biopsies taken from each "triggered" pig also confirmed a positive MH response when subjected to halothane/caffeine muscle contracture testing.

Conclusion. BW A938U did not trigger an MH episode when given to clinically and diagnostically proven MH positive Pietrain swine. BW A938U is a non-polarizing neuromuscular relaxant which appears safe for use in MH susceptible patients.



Reference.

1. Gronert, G.A.: Malignant Hyperthermia Anesthesiology, 53:395-423, 1980.

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