Title: PREVENTION OF HALOTHANE-INDUCED PORCINE MALIGNANT HYPERTHERMIA BY PRETREATMENT WITH METOCURINE IODIDE


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In these experiments we examine the effect of pretreatment with metocurine iodide on the halothane-induced MH syndrome in susceptible pigs. We hypothesized that by preventing the contraction of all muscle (spontaneous and otherwise) we could prevent the development of the syndrome in response to a subsequent challenge with halothane.

Methods: Fourteen Poland China pigs were shown to be susceptible to the fulminant hyperthermia-stress syndrome when challenged with 4% halothane anesthesia. Positive pigs exhibited any two of the three following characteristics: (1) heart rate exceeding 200 beats/min; (2) an increase in rectal temperature of 10°C; (3) development of muscle rigor. We allowed at least one day for recovery. Preliminary experiments were carried out using 0.5, 1.0, and 2.0 mg/kg of metocurine. Dose-response relationships for neuromuscular junction blockade with metocurine were determined by electromyographic recording of sciatic nerve-induced activity in the gastrocnemius muscle. An intravenous dose of 2 mg/kg of metocurine was then given to an animal after a 10-15 min observation interval. Animals were ventilated with 2.5% halothane for five minutes then 1% halothane for forty-five to sixty minutes.

Direct electrical stimulation of the gastrocnemius muscle was used in three of the animals following 45-60 min of uneventful exposure to 1% halothane. Heart rate, rectal and gastrocnemius temperature, as well as subjective estimation of rigor, were monitored in all animals.

Results: Metocurine, 0.3 mg/kg, obliterated the EMG response in all animals while 2.0 mg/kg produced profound paralysis. Pretreatment with metocurine prevented the syndrome of halothane-induced MH in thirteen out of fourteen pigs. Rectal and gastrocnemius muscle temperatures were typically lowered by 0.6°C during halothane exposure. At sixty minutes post-metocurine infusion, the gastrocnemius muscle was stimulated by a direct current (150 watt-seconds). This led to a rapid onset of the syndrome with a rise in the gastrocnemius muscle temperature followed by an increase in the rectal temperature (see Fig 1).

One pig developed the syndrome despite pretreatment with metocurine (0.5 mg/kg). This particular animal had a rectal temperature of 38.5 at the time of metocurine injection, suggesting that the heat-producing phase of the syndrome may have already been initialized. Since there was no rise in temperature during the first twenty-five minutes of halothane exposure, the metocurine may have imparted some degree of protection.

Discussion: Hall et al. reported that pancuronium at 0.2 mg/kg prevented hyperthermia in three of six pigs exposed to 1.5% halothane for two ten-minute periods. The metocurine equivalent to 0.02 mg/kg ranges from 0.2-0.8 mg/kg. Our pig receiving only 0.5 mg/kg developed the syndrome, but 13 others receiving 1.0-2.0 mg/kg did not. A striking feature is that we were able to trigger MH in individual muscles, by electrical stimulation.

These experiments support the hypothesis that depolarization of the muscle membrane is an absolute requirement for inducing the MH syndrome. Metocurine, in large doses, prevents spontaneous muscle depolarization and thus prevents the halothane-induced syndrome.