Metabolism and Regulation

Title: PORCINE MALIGNANT HYPERTHERMIA:SUCCINYLCHOLINE INDUCED MASSETER MUSCLE CONTRACTION

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Introduction. One early indicator for onset of the malignant hyperthermia (MH) syndrome is occurrence of masseter muscle rigidity (MMR) following administration of Succinylcholine (S.ch.). Among MMR patients who subsequently have a diagnostic muscle contracture test, about 50% test positive for MH. Thus, it appears that the MMR syndrome can occur in patients without genetic predisposition to MH, raising questions about the uniqueness of masseter muscle that produces this abnormal response to S.ch. This study was designed to evaluate masseter muscle response to S.ch. in the genetically predisposed porcine MH animal model and to determine if halothane affects masseter muscle response to S.ch.

Methods. Experiments were conducted on 6 MH negative pigs and 6 MH susceptible (MHS) pigs. In the first experiment the pigs had an intravenous line started in an ear vein and were anesthetized with thiopental 25 mg/Kg IV intubated and ventilated with 100% O_2 to maintain end tidal CO_2 between 38 and 42 mmHg. Anesthesia was maintained with thiopental 2.5 mg/Kg every 5 min. A saphenous arterial catheter was used for blood pressure monitoring and sampling of blood for pH, gases and lactate every 5 min. Rectal temperature was monitored. A biopsy of the gracilis muscle was obtained for in vitro contracture studies. Forelimb muscle twitch was monitored to ensure peripheral paralysis.

A 10mm O.D. and 8mm I.D. diameter low compliance, liquid containing, tube was placed between the first and second premolars and mechanically coupled to a force transducer to measure force of masseter muscle contraction. Forty-five min after induction of anesthesia S.ch. (2 mg/Kg) was injected IV. The time from injection to onset of masseter contraction, time to maximum contraction, duration and the peak force of masseter contraction were determined. Anesthesia and monitoring continued for an additional 60 min. and the animal recovered.

In the second experiment performed 2 weeks later the basic preparation was identical to Expt I. Anesthesia was induced and maintained for 45 min with thiopental in order to establish monitoring. Following this, thiopental administration was discontinued and halothane, 3% inspired, was administered for a period of 5 min. At this time S.ch., 2 mg/Kg IV, was injected, halothane discontinued, and the masseter muscle monitored as in Expt I. Thiopental anesthesia was reinitiated and continued for an additional 60 min while blood sampling and monitoring were continued.

After a 2 week recovery period, a third experiment was performed on animals that did not develop the MH syndrome during Experiment II. The basic preparation and monitoring were identical to Expt I. 45 min was again allowed to establish monitoring and obtain baseline readings after which the thiopental was discontinued and anesthesia maintained with halothane, end tidal concentration 1.2%, for 60 min. Following this, a bolus dose of S.ch. (2 mg/Kg) was administered at 15 minute intervals while continuing with halothane anesthesia for an additional hour. Force changes in the masseter muscle and foreleg twitch were monitored throughout the experiment.

Statistical analysis: Data are expressed as mean ± standard error (S.E.) and were analyzed using students t - test. $P < 0.05$ was regarded as significant.

Results. All MHS pigs developed masseter contraction in both Expt I and Expt II, the duration of contraction was the only variable that differed; being significantly longer in Expt II compared to Expt I (767.3 ± 160.9 sec vs 220.8 ± 117.2 sec) Table 1. Two of 6 normal pigs had short duration masseter contraction to S.ch. alone (30 and 42 secs) while only one had masseter contraction to halothane and S.ch. (26 sec). No pig in Expt III, performed only on normal pigs, developed masseter contraction. All MH pigs developed clinical MH when exposed to halothane and S.ch. (increases in $ETCO_2$, temperature and lactate) but had only mild responses to S.ch. alone. In vitro contracture tests predicted MH susceptibility and in vivo masseter contraction. After the administration of halothane and S.ch. to MHS pigs, a longer duration of masseter contraction occurred in pigs which had a greater metabolic response and a greater in vitro contracture to 50 mM S.ch.

Conclusion. In MHS pigs, masseter muscle contraction always occurred following S.ch. administration but was of longer duration and associated with greater increased metabolism when S.ch. was preceded by 5 minutes of halothane. Short duration masseter contraction, not influenced by halothane occurred in two normal pigs. The relationship between masseter muscle contraction in pigs and MMR in humans is at present uncertain. Until more information is available we suggest that MMR in humans must be regarded as strong indication that MH exists.

TABLE I: Masseter Muscle Contraction

	Pig No.	Force of Contraction Kg	Onset Time (sec)	Peak Time (sec)	Duration (sec)	
Control Group Expt. I	N-5	1.3	18	26	30	
	N-6	10.5	12.5	25.5	41.5	
Expt. II	N-6	2	14	16	26	
MH Susceptible Group Expt. I	MH-1	5.4	10	25.5	44	
	MH-2	11	22	29	26	
	MH-3	1	12.5	18	11	
	MH-4	2.2	8	12	742	
	MH-5	1.8	11.5	15.5	138	
	MH-6	2.4	16	24	364	
	Mean ± SE	3.96 ± 1.53	13.3 ± 2.04	20.7 ± 2.65	220.8 ± 117.2	
						Duration MH I - MH II
Expt. II	MH-1	1.1	22	30	923	879
	MH-2	2.1	17	21.5	602	596
	MH-3	2.1	18	25	332	321
	MH-4	2.6	6.5	16	1450	708
	MH-5	3.8	20	25	503	365
	MH-6	1.9	16	23	794	430
	Mean ± SE	2.26 ± .37#	16.6 ± 2.2#	23.4 ± 1.88#	767.3 ± 160.9*	

= Not significant comparing MH susceptible Expt I with Expt II
* = $p < 0.05$ comparing MH susceptible Expt I with Expt II