Title: INHALATION ANESTHETICS AND SINUS NODE FUNCTION: COMPARISONS WITH THE CONSCIOUS STATE IN DOGS

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Introduction. While the potent volatile anesthetics (HAL-halothane, ENF-enflurane, ISO-isoflurane) have been shown to depress sinus node automaticity (heart rate) in the isolated, superfused guinea pig heart [1], no data exist for their effects on sinus node function in the intact heart. Electrophysiologic evaluation of sinus node function includes, in addition to automaticity, conduction into and out of the node, and zones of sinus node response to premature electrical stimulation in close proximity to the node. Possible responses include: 1) reset of sinus automatiticity (zone 2), 2) interpolation/nonpenetration with no effect on automaticity (zone 3), 3) sinus node reentry manifest as echo beats (zone 4), or 4) repetitive atrial firing (zone 5).[2] The purpose of this investigation was to determine the direct and indirect effects of clinically relevant levels of HAL, ENF, and ISO on sinus node function utilizing chronically instrumented dogs and the conscious state for control.

Methods. Mongrel dogs (N=10) were instrumented for cardiac electrophysiologic investigation, which included bipolar, epicardial recording/stimulating electrodes located on the right atrial appendage, and at the right atrial junctions with both the superior and inferior vena cavae. Dogs recovered for at least three weeks prior to electrophysiologic study, by which time reproducible data (weekly testing) relating to sinus node function could be obtained. Awake testing preceded testing with anesthetics (1.2 and 1.6 MAC). Both direct and indirect effects of the anesthetics (in presence or absence of autonomic blockade) were assessed. Autonomic blockade (BLOCK) included atropine, hexamethonium and propranolol. That blockade was complete was demonstrated (pilot studies) by less than 10% variation in heart rate or direct arterial pressure values during challenges with acetylcholine, isoproterenol or nicotine at various times during experiments, which lasted up to 4 hours. Anesthesia was induced with the anesthetic in O_2, and maintained at the desired, end-tidal level (Beckman LB-2) for at least 20 minutes prior to electrophysiologic testing of sinus node function.[2] Other than BLOCK or anesthetics, no drugs were administered. Randomized were the order of anesthetics (once weekly test occasions) and levels tested, and testing with or without BLOCK. Normothermia (37^{o}-39^{o}C) and mild hypocarbia (end-tidal CO_2 33 to 38 mmHg, Beckman LB-2) were maintained. Data are reported as mean ± standard error. Statistical analysis was ANOVA for repeated measures design (Scheffe F-test). Significance was P<0.05.

Results. Arterial blood gas and serum electrolyte values were within normal limits for all test conditions. No BLOCK: HAL increased (P<0.05) maximum sinus node recovery time (SRTmax, msec), corrected SRT (CRST, msec), sinoatrial conduction time (SACT, msec). ENF increased (P<0.05) SRTmax (awake vs. 1.2 MAC, only), and decreased CRST and SACT. ISO had no effect on SRTmax, and decreased CRST and SACT. For all anesthetics, as defined by width of zones (msec), there was no effect on zone 2 responses. When zone 3, 4, or 5 responses were present in awake dogs (HAL-1/7, ENF-3/6, ISO-3/7), the effect of anesthesia (either level) was always to abolish such responses; that is, only zone 2 responses could be obtained with anesthesia. With BLOCK: Data are provided in the TABLE. Note that results did not vary between individual agents. All anesthetics increased SRTmax and the width (msec) of zone 2 responses. There were no effects of any agent on CRST or SACT. No zone 3, 4 or 5 responses were observed in conscious or anesthetized dogs.

Discussion. The direct effect of any of the anesthetics at clinically useful levels was to depress sinus node automaticity (SRTmax and width of zone 2), in agreement with previous findings.[1] Sinus node conduction (CRST, SACT) was not directly affected by any of the anesthetics. Without autonomic blockade, the effects of each agent were quite variable, likely more reflecting individual anesthetic effects on autonomic regulation of sinus node function. [Supported by NIH GM25064 and a grant-in-aid from Anaquest.]

References.

1. Bosnjak ZJ, Kampine JP: Effects of halothane, enflurane and isoflurane on the SA node. Anesthesiology 58:314-321, 1983.
2. Josephson ME, Seides SF: Clinical Cardiac Electrophysiology. Philadelphia, Lea and Febiger, 1979, pp 64-74.

TABLE. Sinus Node Function in Dogs with BLOCK

		SRTmax	CRST	SACT	ZONE 2
HAL(7)	AWAKE	478±25	37± 5	15±2	199±29
	1.2 MAC	649±36*	35± 4	17±2	336±45*
	1.6 MAC	656±53*	39± 7	17±3	298±39*
ENF(7)	AWAKE	447±20	26± 3	11±2	189±22
	1.2 MAC	623±58*	24± 6	12±3	357±36*
	1.6 MAC	618±42*	24± 5	10±3	307±28*
ISO(7)	AWAKE	457±41	37± 5	17±3	204±18
	1.2 MAC	603±57*	40±10	19±5	379± 5*
	1.6 MAC	620±50*	43± 7	20±4	379±55*

*P<0.05 compared to AWAKE