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Title : HALOTHANE AND ENFLURANE EFFECTS ON SA NODE CELLS

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Introduction. Clinical observations indicate that a number of potent volatile anesthetic agents may produce sinus bradycardia, prolonged A-V conduction and arrythmias resulting from disturbances in automaticity and or conduction. Studies of the direct effects of halothane and methoxyflurane on cardiac muscle fibers have indicated that these agents in clinically useful concentrations are capable of producing primary pacemaker suppression and secondary pacemaker stimulation.[1] The purpose of the present investigation was to study the effects of halothane and enflurane in clinically useful concentrations on the electrophysiologic characteristics of guinea pig and cat sino-atrial node cells in vitro.

Methods. Guinea pigs and young cats were decapitated and their hearts immediately removed and placed in a perfusion chamber. The right atria were removed and superfused with Krebs solution at pH 7.4, 37±0.5°C, and continuously oxygenated with a mixture of 97% O_2 and 3% CO_2. Transmembrane potentials were recorded using 3M KCl filled glass microelectrodes with submicron tip diameters (40-80 M ohm resistance) and a WPI amplifier. The data was accumulated on magnetic tape and later analyzed with a Nicolet digital oscilloscope and X-Y recorder. Only those cells were selected for study which sastisfied the following criteria: a minimum diastolic potential -60 to -65 mV, spontaneous phase 4 slow diastolic depolarization with slow transition to phase 0, action potential overshoot less than 5 mV and absence of phase 2 or plateau. Six guinea pig hearts and three cat hearts were studied with satisfactory recordings from 3 to 6 SA node cells in each preparation. Anesthetics were introduced by switching to perfusate equilibrated for 10 min with either halothane (Draeger vaporizer) 0.5, 1.0 and 2.0% or enflurane (Ohio vaporizer) 1.12, 2.25 and 4.50%. All anesthetics were administered with control periods (no anesthetic) interspersed between each anesthetic exposure. Anesthetics were studied for effects on spontaneous rate of discharge of SA node cells, phase 4 duration and slope, phase 0 slope and action potential duration. Statistical differences were determined using the student t-test. (P values = .05 were significant).

Results. Introduction of halothane at 0.5% and initial exposure of spontaneously beating SA node cells to 1.0% halothane resulted in hyperpolarization of the diastolic transmembrane potential from -65 mv to -70 mv in all preparation studied. Initial exposure to 1.12 and 2.25% enflurane did not produce the same effect. Halothane 1.0% and 2.0% produced a significant decrease in spontaneous rates of discharge of SA node cells, significant increase in duration of phase 4, and a significant decrease in slope of phase 4 diastolic depolarization. Phase 0 slope was decreased significantly at 2% halothane and action potential duration significantly prolonged. Enflurane 2.25% and 4.50% produced a significant decrease in spontaneous rates of discharge of SA node cells, an increase in the duration of phase 4 and a significant decrease in the slope of phase 4. The slope of phase 0 was decreased and action potential duration increased at the highest concentration of enflurane (4.5%).

Guinea Pig N=6	H.R.	Phase4 Slope mv/ms	Phase0 Slope mv/ms	A.Pot. Dur. ms.
Control	180	92	1648	201
1.0% H	166*	89	1538*	214*
2.0% H	134*	47*	905*	257*
Control	220	130	2415	173
2.25% E	212*	125*	2299*	178
4.50% E	205*	107*	2250*	189*

*(P<.05)

Discussion. The direct chronotropic effects of various agents on primary pacemaker cells may be predicted on the basis of their effects on resting membrane or minimum diastolic potential, slope of phase 4 distolic potential and threshold potential. In general agents which have direct negative chronotropic effects may be expected to produce hyperpolarization of the resting or minimum diastolic potential, an increase in threshold, or a decrease in the slope of diastolic depolarization (or any combination). In the present study both halothane and enflurane were shown to have a direct negative chronotropic effect on SA node pacemaker cells. There were no differences between guinea pig vs. cat hearts. The effects of enflurane on SA node cells were less marked than the effects of halothane on the same cells. Thus halothane (2%) produced a 49% decrease in the slope of phase 4 depolarization while enflurane (2.25% and 4.50%) produced much smaller changes in the same parameter (-4% and -18%).

References.

1. Reynolds, AK, Chiz JF, Pasquett AF: Halothane and methoxyflurane - A comparison of their effects on cardiac pacemaker fibers. Anesthesiology 33:602-610, 1970.