Date : May 1, 1980

Title : HALOTHANE AND BARORECEPTOR REFLEXES

Authors : J.P. Kampine, M.D., Ph.D., J.L. Seagard, Ph.D.,J.H. Donegan, M.D. and F.A. Hopp, M.S.

Affiliation: Department of Anesthesiology, The Medical College of Wilsconsin and Wood VA Center, Wood (Milwaukee, WI 53193

Introducion. The clinical observations of hypotension and bradycardia during halothane (H) anesthesia in man have suggested that halothane impairs homeostatic mechanisms involved in reflex regulation of cardio- vascular function. The relative importance of depressant effects of halothane on carotid sinus receptors, central and peripheral autonomic pathways and end organ responses has not been investigated in terms of the observed inhibition of baroreflex function in man.[1] The present study was performed to quantitate the effects of halothane on the carotid baroreceptor reflex and examine the possibility of multiple sites of action.

Methods. To examine the effects of H on the carotid baroreceptor reflex, six dogs were instrumented for measurement of blood pressure and heart rate in the conscious and anesthetized state. For the conscious study, the dogs were suspended in a sling while blood pressure and ECG were monitored on a Grass recorder and recorded on a Tandberg FM tape recorder. Reflex changes in heart rate were initiated by pressure changes produced by infusion of nipride (100-300 μg/min) and angiotension (10-50 μg/min) through a intravenous line. The same dogs were then studied to measure the effects of halothane and sodium pentothal on the reflex changes in heart rate. Each dog was anesthetized with sodium pentothal (20-25 mg/kg) and placed on positive pressure ventilation of $50\%/50O_2/NO$ with 0.5% halothane. The dog was prepared for afferent carotid sinus nerve recordings along with arterial blood pressure and ECG recordings. The halothane was turned off and 30 minutes were allowed for the dog to eliminate halothane. Blood pressure was decreased and increased by bolus injections of nipride and angiotensin. The pressure changes were repeated at levels of 0.75% and 1.5% H. Thirty minutes were allowed for equilibration time after each change. Data analysis, performed by computer, plotted R-R interval and nerve activity versus blood pressure for the conscious dogs and for each level of H. These factors were plotted to obtain the gain (slope) of the reflex responses for each dog. To determine the direct effects of H on the response of the heart, electrical efferent stimulation of the peripheral end of the right vagus was performed with supramaximal stimuli at varying frequencies. A frequency- response curve was obtained for parasympathetic stimulation at 0%, 0.75%, and 1.5% H. The results of the stimulation studies were examined by plotting heart rate versus stimulation frequency for each H concentration. In a separate study the direct effect of H on carotid sinus nerve activity was studied utilizing a carotid artery perfusion technique while recording carotid sinus nerve activity

Results. Analysis of carotid sinus nerve activity indicated a lack of direct effects of halothane on carotid sinus afferent activity. The slope of the carotid sinus nerve activity vs. carotid sinus pressure (imp/sec/ mmHg) was not significantly different between control and 2% H. (Control- 0.347± .017 vs. 2% H-0.322±.040 N=12). Analysis of the heart rate reflex showed that halothane produced a decrease in the gain of the heart rate response to pressure changes. A decrease in reflex response was evident at 0.75% H in most dogs and was present at 1.5% in all dogs. The anesthetized dogs all showed a decrease in reflex activity compared to their conscious controls.

	Δ R-R Interval/Δ mmHg	
	Increased B.P.	Decreased B.P
0% H	4.05±1.05	1.71±0.24
0.75% H	1.76±0.63*	0.69±0.29*
1.5% H	0.96±0.64*	0.32±0.19*

Mean slopes standard errors *p<0.05 vs.0% H

The decrease in the cardiac reflex response with increasing halothane concentrations was accompanied by attenuated heart rate changes produced by direct efferent stimulation. Analysis of heart rate versus stimulus frequencies showed two effects of halothane. First, increasing levels of halothane produced a decrease in resting heart rate prior to any stimulation. Secondly, increasing halothane concentrations decreased the slopes of the heart rate-stimulation frequency curves for both sympathetic and parasympathetic stimulation at 1.5%H but not at 0.75%H

Vagal Stim.--Slope (ΔHeart rate/ΔStim.Freq.)
Control:-6.46 0.75%H:-5.37(NS) 1.5%H:-3.26*

Thus halothane directly reduced the set point as well as the gain of the stimulation curves.

Conclusions. Results from this study indicate that attenuation of the baroreceptor reflex by halothane may involve multiple sites of action. Halothane appears to depress baroreflex activity through a CNS action and a direct effect on the heart. CNS inhibition occurred at lower concentrations of H than those which produced depression of cardiac responses to direct stimulation. Direct effects on carotid sinus receptors were not observed.

References.

1. Duke PC, Fownes D, Wade JG: Halothane depresses baroreflex control of heart rate in man. Anesthesiology 46:184-187, 1977.