Title: MECHANISM OF HALOTHANE'S MYOCARDIAL DEPRESSION: ALTERED DIASTOLIC MECHANICS VERSUS IMPAIRED CONTRACTILITY

Authors: C. Christian, II, M.D., Ph.D., L. Fagraeus, M.D., Ph.D., P. Van Trigt, III, M.D., R. Peyton, M.D., T. Spray, M.D., A. Wechsler, M.D.

Affiliation: Departments of Anesthesiology and Surgery, Duke University Medical Center, Durham, North Carolina 27710

Introduction. It is generally agreed that halothane severely depresses the contractile state of the myocardium, but the mechanism by which this depression occurs has not been clarified. This depression may be due to a direct depression of the inotropic state or to a change in the diastolic stiffness of the left ventricle. This study examined the effect of halothane (1.0% and 2.0%) on the systolic and diastolic mechanics of the left ventricle.

Methods. Seven closed-chest dogs were instrumented 7-10 days prior to each study with epicardial ultrasonic dimension transducers to measure directly the major axis, anterior-posterior minor axis, and wall thickness of the left ventricle. Pneumatic occluders were positioned around the superior and inferior venae cavae and a pacing electrode was sutured onto the right atrium. Balanced micromanometers were passed at the time of study into the left ventricle and pleural space to measure left ventricular transmural pressure. Left ventricular pressure and dimension data were recorded and computer analyzed during transient vena caval occlusion in the awake, control state and following the administration of halothane at 1.0% and 2.0% end-tidal concentration. Ventricular inotropism was assessed by the slope of the end-systolic pressure-volume relationship: Pes = IDes (Les-Ld), where Pes and Les are the end-systolic left ventricular pressure and diameter respectively, Ld is the length axis intercept and IDes is the slope of the relationship. Static diastolic diameters were normalized according to a Lagrangian strain definition (ε). The end-diastolic pressure-strain data from multiple cardiac cycles during vena caval occlusion were fitted to the equation $P = \alpha (e^{\beta\varepsilon} - 1)$ where α and β are non-linear elastic coefficients which describe the passive elastic properties of the myocardium.

Results. Analysis of the pressure-volume relationship showed a significant, dose dependent decrease of the inotropic state of the heart. Multivariant analysis of the logarithmically transformed elastic coefficients (α & β) revealed no significant change between control and the two concentrations of halothane; i.e. the end diastolic pressure-length relationship was not altered by halothane (Table).

Discussion. The depression of myocardial contractility induced by halothane may be due to either a direct depression of inotropic state or a change in diastolic compliance. One must assess each variable independantly to be able to define the mechanism of depression. Although many studies report a depression of systolic function, the effect of halothane on diastolic properties has received little attention in the literature (1,2), and conflicting results are found in the few studies completed. When parameters of contractility were analyzed (end-systolic pressure-volume ratios), a significant dose dependent depression was produced by halothane at each concentration. When diastolic indices were examined, the diastolic compliance of the left ventricle was not primarily altered by any concentration halothane. Therefore, we conclude that the negative inotropic effect of halothane is solely due to depression of systolic function and is independent of any change in diastolic mechanics.

TABLE

	Control	1.0% Hal.	2.0% Hal.
	3.95 ±1.18	5.42±2.50	5.85±1.80
	12.28±3.94	13.57±2.50	15.03±4.50
Ees	10.1 ±0.6	6.7 ±0.4+	4.2 ±0.5*

+ $p < 0.01$ * $p < 0.005$ n = 7
mean ± s.d.

References

1. Brower RW, Merin RG: Left ventricular function and compliance in swine during halothane anesthesia. Anesthesiology. 50: 409-415, 1979.

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