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The Effects of Halothane and Cyclopropane on Left Ventricular Volume Determined by High-speed Biplane Cineradiography in Dogs

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The effects of halothane and cyclopropane on left ventricular end-diastolic volume (LVEDV) were examined in dogs using high-speed biplane cineradiography. LVEDV was increased 1, 9, and 16 per cent above the control (conscious) value by 1, 1.5, and 2 per cent end-tidal halothane, respectively. Larger increases in LVEDV were observed during cyclopropane anesthesia. These were 14, 25, and 37 per cent for 20, 30, and 35 per cent end-tidal cyclopropane, respectively. The effect of increased heart size on myocardial wall tension is discussed. (Key words: Anesthesia; Cyclopropane; Left ventricular end-diastolic volume; Halothane; Myocardial wall tension.)

FEW DATA describing the effects of anesthetics on left ventricular volume are available. Ventricular size is important since it and ventricular pressure are determinants of ventricular wall tension. Wall tension is, in turn, a major determinant of myocardial energy consumption.[1-4] For these reasons, this study of left ventricular volume was undertaken. We used high-speed biplane cineradiography to determine left ventricular end-diastolic volumes in trained, unanesthetized dogs, for comparison with volumes determined at several end-expired concentrations of halothane and cyclopropane.

Methods

Healthy mongrel dogs weighing 12 to 16 kg were studied. Using pentobarbital anesthesia with mechanical ventilation, right thoracotomy and pericardiotomy were performed aseptically. A polyethylene catheter (PE 330 or 350) was implanted in the left atrium by the method of McQuarrie.[5] The catheter was exteriorized through the skin between the scapulae. The pericardium was not closed. After closure of the chest the dogs were allowed to convalesce for at least a week, most often longer, during which time they were trained to lie on their sides in the laboratory.

During an experiment, left ventricular pressure (LVP) and the electrocardiogram, lead II, were monitored continuously. LVP was obtained via a Statham P23-Db pressure transducer connected to a Teflon catheter which was inserted through the implanted atrial catheter into the left ventricle. In three animals LVP was measured with a Statham P23-H differential pressure transducer, the other chamber of which was connected to the right pleural space via a plastic needle and catheter. These data were recorded by an Electronics for Medicine PR-7.

Left ventricular volumes at end-diastole were determined by high-speed biplane cineradiography. The technique has been described elsewhere.[6] Two oblique views, approximately anteroposterior and lateral, were employed. Pictures were taken of both views simultaneously at 270 frames/sec during and immediately after the administration of 10 ml of sodium iothalamate (Angio-Conray) warmed

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to body temperature and injected in ½ second through the left atrial catheter using a Viamonte/Hobbs programmed-pressure injector. LVP was recorded on the cine-film as well as on the PR-7. These data were obtained from the conscious dog resting on its side as well as during the administration of 1, 1.5, and 2 per cent (end-tidal) halothane and 20, 30, and 35 per cent cyclopropane in oxygen. In a given animal, experiments with different anesthetics were separated by at least two days. The anesthetics were administered from a nonrebreathing system (Ruben valve) through a cuffed endotracheal tube. Succinylcholine, 20 mg, was given intravenously at the start of the procedure to facilitate intubation and to prevent spontaneous movement and respiration which occurred at the lowest anesthetic concentrations. Respirations were controlled with a Bird Mark 4 automatic ventilator. End-expired P_{CO_2} was held between 25 and 35 mm Hg. Anesthetic concentrations in end-expired air were determined by Beckman infrared gas analyzers. Following the establishment of an end-tidal plateau at a given anesthetic concentration, the plateau was held for at least 15 minutes before data were collected. Data were not recorded until at least 30 minutes after the injection of succinylcholine.

The A-P and lateral films were analyzed in a system[7] consisting of two Vanguard cine-projectors, a Thompson Digitizing Table, and a LINC-8 computer. The computer was programmed to compute volume according to Simpson's rule for numerical integration, assuming the ventricular cavity to be elliptical in cross sections perpendicular to the long (apex-to-base) axis.[8] The end-diastolic volumes for the control and the anesthetized states were compared statistically using Student's t test for paired samples.

Results

The effect of halothane was studied in ten dogs, seven of which were also used for the study of cyclopropane.

In the halothane experiments, the average control (conscious) left ventricular end-diastolic volume (LVEDV) was 30.8 ± 2.3 (SE) ml. Control heart rate was 127 beats/min. Control end-diastolic pressure measured transmurally in three dogs was +3 mm Hg. At 1 per cent end-tidal halothane, the average LVEDV was 31.3 ± 1.5 ml, a 1 per cent increase above control ($P < 0.8$). Heart rate was 125 beats/min and end-diastolic pressure was 6 mm Hg. At 1.5 per cent end-tidal halothane, LVEDV was 33.5 ± 2.5 ml, a 9 per cent increase above control ($P < 0.4$). Heart rate was 122 beats/min. End-diastolic pressure was not measured at this concentration of halothane. At 2 per cent end-tidal halothane, LVEDV was 35.4 ± 1.4 ml, a 16 per cent increase above control which was statistically significant ($P < 0.01$). Heart rate was 116 beats/min and end-diastolic pressure was 9 mm Hg. The data for volume are presented graphically in figure 1B.

In the cyclopropane experiments, the average control LVEDV was 31.4 ± 2.8 ml. Control heart rate was 140 beats/min. Control end-diastolic measured transmurally in two dogs was +3 mm Hg. At 20 per cent end-tidal cyclopropane, LVEDV was 35.9 ± 1.4 ml, a 14 per cent increase above control ($P < 0.02$). Heart rate was 150 beats/min. End-diastolic pressure was not measured. At 30 per cent end-tidal cyclopropane, LVEDV was 39.0 ± 1.2 ml, a 25 per cent increase above control ($P < 0.001$). Heart rate was 150 beats/min and end-diastolic pressure was 11 mm Hg. Measurements at 35 per cent end-tidal cyclopropane were made in only five dogs. The control LVEDV for this group was 27.6 ± 2.2 ml. At 35 per cent cyclopropane, LVEDV was 37.8 ± 1.3 ml, a 37 per cent increase above control ($P < 0.01$). Heart rate was 156 beats/min and end-diastolic pressure was 13 mm Hg. The data showing the effect of cyclopropane on LVEDV are presented graphically in figure 1A.

Discussion

The average LVEDV measured in the control (conscious) state was 31 ml. This compares well with the cineradiographic measurements of LVEDV made by Tsakiris and associates[9] and by Noble *et al.*[10, 11] in dogs of approximately the same size with similar heart rates.

We did not control cardiac rate. At 35 per cent cyclopropane heart rate rose from a control value of 140 to 156 beats/min. Increases in heart rate of this range were found to be

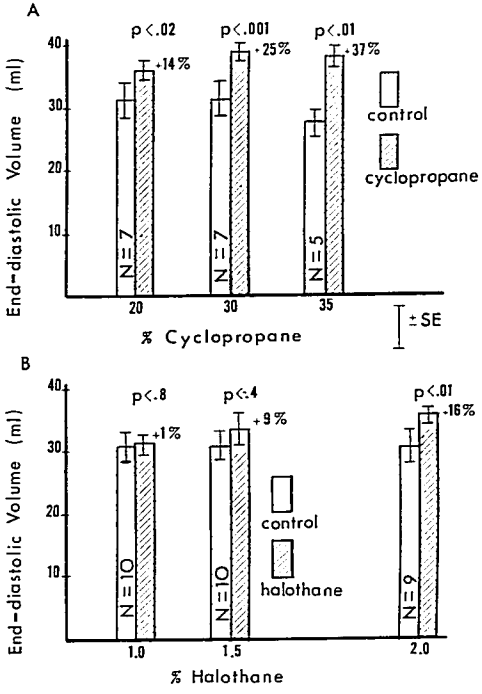

FIG. 1. Effects of cyclopropane (*A*) and halothane (*B*) on left ventricular end-diastolic volume. Open bars represent unanesthetized control values. Anesthetic concentrations refer to end-tidal values.

associated with decreases in LVEDV of approximately 5 per cent by both Tsakiris[9] and Noble[11] and their associates. Had we held heart rate constant at the control value during the administration of cyclopropane, the increase in LVEDV probably would have been somewhat greater. During halothane administration heart rate decreased. Using similar reasoning, the increase in LVEDV probably would have been slightly less had heart rate been held constant.

Our results do not agree with those of Hamilton and associates,[12] who observed a 60 per cent increase in LVEDV during the administration of 1.8 per cent (end-tidal) halothane and very little change in LVEDV during 40 per cent cyclopropane anesthesia. These workers used a thermal dilution technique for measuring LVEDV. Dilution techniques have been shown to yield higher values for volume than those obtained by angiographic means.[13-15] It should also be noted that the pericardium was open in our experiments, whereas it was intact in those of Hamilton. This may have contributed to the difference between the results, although it does not seem to have done so in the angiographic studies of Tsakiris[9] (pericardium intact) and Noble[11] (pericardium open), where approximately the same value of LVEDV was obtained by both groups. Finally, Hamilton and co-workers used thiopental for induction of anesthesia, whereas we did not.

There has been some criticism of angio-

graphic techniques related to the observation that the contrast materials employed are cardiodepressant when they reach the coronary circulation.[16] Our measurements were made during the second and third heart cycles and within 1–2 seconds after the rapid left atrial injection of a bolus of contrast medium, at a time when it would not have reached the myocardium in any appreciable amount. Contrast media are hypertonic, and injection is followed by transient increases in blood volume, heart rate, stroke volume, and cardiac output. These hemodynamic changes reach a maximum in 3 minutes and subside within 15 to 20 minutes.[17] We allowed at least 20 minutes between measurements of LVEDV so that these actions of contrast media would not appreciably influence our results.

Our results indicate that LVEDV increases during both halothane and cyclopropane anesthesia in the dog. The increase in volume appears to be greater for cyclopropane, although it cannot be stated for certain which of the end-tidal concentrations of halothane and cyclopropane we employed should be compared.[18] At 30 per cent end-tidal cyclopropane, LVEDV increased 25 per cent over control. If spherical geometry is assumed for the ventricle, this increase in volume would correspond to an 8 per cent increase in ventricular internal radius. Using the simplest form of the Laplace relationship between wall tension and intraventricular pressure ($T = PR/2$), there would be an 8 per cent increase in myocardial wall tension needed to support any given intraventricular pressure. In previous work[19] we found that the time integral of left ventricular systolic *pressure* was increased 47 per cent above the conscious control value by 30 per cent cyclopropane. Considering the increased ventricular size we found in the present study, the time integral of ventricular wall *tension* would be increased an even greater amount above control. For 1.5 per cent halothane, our previous study[19] showed a 29 per cent decrease in the integral of left ventricular systolic pressure. This is in agreement with the similar findings of Shimosato and associates.[20] Since, in our present study, we found LVEDV only slightly increased (9 per cent) by 1.5 per cent halothane, the change in the time integral of systolic wall *tension* is probably quite similar in magnitude to the change in integrated ventricular pressure, that is, decreased below the control value.

The integral of myocardial systolic wall tension has been shown to be one of the major determinants of myocardial oxygen consumption.[21] We suggest, therefore, that heart size and the integral of ventricular systolic pressure, determinants of integrated systolic wall tension, are important variables to consider when evaluating the effects of an anesthetic on the heart.

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Endocrinology

INDICES OF THYROID FUNCTION IN THYROTOXICOSIS This study was undertaken in an attempt to correlate new tests of thyroid function *in vitro* with more established, older techniques. The patients were selected from a group thought to have thyroid disease. Those with histories of prior thyrotoxicosis, thyroid surgery, or therapy with antithyroid drugs were excluded from the study. Evaluation of thyroid function was carried out in 105 patients, and included the total and free serum thyroxine fractions, thyroxine-binding globulin (TBG), thyroidal uptake of radioactive iodine, and protein-bound ^{131}I. These values were compared with a clinical diagnostic score (Wayne Index). In spite of the fact that all correlation coefficients were 0.4 or less, the serum free thyroxine concentration correlated best with the clinical diagnostic score (Wayne Index). The thyroxine–TBG ratio and total serum thyroxine levels correlated less well with the clinical score. It is significant that thyroid hormone concentrations may fall into the "normal" range, but this is usually the result of low concentrations of thyroxine-binding globulin. The level of serum free thyroxine concentration gives a slightly better correlation with the presence or absence of clinical thyrotoxicosis. (*Harvey, R. F.: Indices of Thyroid Function in Thyrotoxicosis, Lancet 2: 230–233, 1971.*) ABSTRACTER'S COMMENT: This report emphasizes the fact that accurate evaluation of thyroid function is difficult at best. Despite our extensive knowledge or the turnover and transport of thyroid hormones, clinical judgment is still the final test in borderline situations.