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Pulsed Doppler and Two-dimensional Echocardiography: Comparison of Halothane and Isoflurane on Cardiac Function in Infants and Small Children

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The combination of two-dimensional and pulsed Doppler echocardiography was used to measure determinants of cardiac function in 20 ASA physical status I infants and small children (9 days–32 months of age) during equipotent halothane (n = 10) or isoflurane (n = 10) anesthesia in oxygen. Five sets of cardiovascular data were recorded in each patient. In the awake, unmedicated state prior to induction, at three different anesthetic levels, 0.75, 1.0, and 1.25 MAC (corrected for age) and a final measurement repeated at 1.25 MAC after the intravenous infusion of 15 ml·kg^{-1} of Lactated Ringers solution. The study was completed prior to intubation and surgery. Results are expressed as mean ± SEM. Isoflurane and halothane decreased mean blood pressure from the awake level (isoflurane 76.6 ± 2.3 to 60.6 ± 3.1 mm, halothane 72.2 ± 3.9 to 60.6 ± 3.1 mm at 1.25 MAC). Isoflurane increased heart rate at all anesthetic levels (128.7 ± 4.2 to 142.5 ± 6.0 beats/min at 0.75 MAC). Halothane decreased heart rate at 1.25 MAC (124.6 ± 4.6 to 119.4 ± 3.5 beats/min). Isoflurane and halothane decreased cardiac index at 1.25 MAC. Stroke volume index decreased at 1.0 and 1.25 MAC with both isoflurane (36.9 ± 3.8 to 30.2 ± 3.5 ml/m^2) and halothane (32.7 ± 2.5 to 28.9 ± 2.5 ml/m^2). Ejection fractions also decreased significantly at 1.0 and 1.25 MAC in both groups of patients (22 ± 6% at 1.25 MAC halothane and 28 ± 8% at 1.25 MAC isoflurane). Left ventricular end-diastolic and end-systolic volumes increased in the halothane and isoflurane group to a similar degree. After 15 ml·kg^{-1} of LR, ejection fraction, and stroke volume index decreased significantly in the halothane group, but increased significantly in the isoflurane group. This response to fluid may indicate that greater cardiovascular reserve exists during isoflurane anesthesia than during halothane anesthesia in infants and small children. (Key words: Anesthesia: pediatrics. Anesthetics, volatile: halothane, isoflurane. Heart: myocardial function. Measurement techniques: Doppler echocardiography; two-dimensional echocardiography.)

ANESTHESIA-RELATED CARDIAC ARREST occurs more frequently in infants than in adults.[1] Although the etiology of this increased morbidity in infants is multifactorial, a contributing factor may be that a greater degree of cardiac depression is produced by the inhalation anesthetics in the young compared to the adult.[2–4] While greater myocardial depression is suggested by measurements of blood pressure,[5] the actual determinants of cardiac function in infants and children have been difficult to measure using current non-invasive methods. Using M-mode echocardiography in children during anesthesia, Wolf *et al.* reported that halothane increased the pre-ejection period (PEP [isovolumic contraction time]), decreased the fraction of left ventricular shortening (LVSF), and increased the systolic time-interval (STI [pre-ejection period divided by left ventricular ejection time]).[6] Isoflurane decreased the pre-ejection period, maintained the per cent of left ventricular shortening, and shortened the systolic time interval.[6] While these parameters (PEP, LVSF, and STI) indicate that halothane, but not isoflurane, anesthesia was associated with decreased contractility, these M-mode contractility measurements assume that the other determinants of cardiac function, such as preload, afterload, heart rate, and cardiac conduction, are unchanged during halothane and isoflurane anesthesia.[7]

With two-dimensional imaging of the myocardium, a more accurate measure of ventricular volumes and ejection fractions is possible than with single dimension M-mode echocardiography.[8,9] Pulsed Doppler echocardiography utilizes a directed Doppler signal to produce a measure of blood flow velocity which can be used to estimate cardiac output.[10,11] Combined two-dimensional and Doppler echocardiography permits simultaneous measures of both ventricular volumes and aortic or pulmonary blood flow velocity. Pulsed Doppler and two-dimensional echocardiography provides a non-invasive method to determine ventricular volumes, ejection fraction, stroke volume, and cardiac output. These measurements correlate with angiographic methods in a variety of clinical settings in both children and adults.[12]

This study used pulsed Doppler and two-dimensional echocardiography to measure how halothane and isoflurane effect ventricular volumes, ejection fractions, and cardiac indices in infants and small children. In a second part of the study, a fluid bolus was given to determine whether fluid deficits created by fasting might contribute to impaired cardiovascular performance, or if myocardial responses to volume

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TABLE 1. MAC Values for Halothane and Isoflurane

Age	Agent*	
	Halothane 1 MAC	Isoflurane 1 MAC
0–1 month	0.87%	1.6%
1–6 months	1.20%	1.87%
6–12 months	1.01%	1.8%
12 months–3 yr	0.96%	1.6%

* MAC adjusted for age.[13,14]

loading were different during halothane or isoflurane anesthesia.

Methods

Twenty ASA physical status I children (mean age 12 months [range 9 days–32 months]), who required elective surgery, were evaluated after the protocol was approved by the hospital's Human Studies Committee. Informed written consent was obtained from the parent(s). The infants received no anesthetic premedicants and were NPO for 4–8 h preoperatively. Parents accompanied the children to a pre-surgical care unit where pre-induction heart rates, blood pressures (oscillotonometry by non-invasive automated cuff [Omega 1600®]), and echocardiographic data were measured in a quiet room 10–30 min prior to induction. The children were alternately assigned to receive either halothane (n = 10) or isoflurane (n = 10). The echocardiography technician was unaware of the anesthetic agent used.

In the operating room, anesthesia was induced *via* a mask with halothane or isoflurane using a semiclosed circle system with 5 liters of O_2. Intraoperative monitors included precordial stethoscope,blood pressure (Omega 1600®), heart rate by EKG, oxygen saturation (Nellcor® pulse oximeter), and rectal temperature. Beckman LBII® infrared gas analyzers were calibrated using test gas concentrations of 0.8 and 2.0% halothane or isoflurane. During induction, the maximum inspired anesthetic concentrations of halothane and isoflurane were 2% and 3.5%, respectively. After intravenous access was achieved, the inspired concentrations were reduced to establish and maintain end-expired concentrations of 0.75 MAC from under a tight-fitting Rendell-Baker mask (see Discussion). This concentration was maintained for at least 5 min prior to collection of the first cardiovascular data during anesthesia (approximately 15–20 min after induction). The two-dimensional and pulsed Doppler echocardiographic data collected during anesthesia was measured over a 2-min period at each anesthetic level. After the inspired concentration was gradually increased to achieve and maintain a 1.0 MAC end-expired concentration of halothane or isoflurane for at least 3 min (see Discussion), a second set of cardiovascular data during anesthesia was collected. After the inspired concentration was increased and the end-expired concentrations maintained at 1.25 MAC for 3 min, the cardiovascular measurements were repeated (see Discussion). Immediately following the measurement at 1.25 MAC, a fluid bolus of 15 $ml \cdot kg^{-1}$ of Lactated Ringer's solution was administered over 2 min with the end-expired anesthetic concentrations maintained at 1.25 MAC, and a final set of the hemodynamic measurements were repeated. The study was completed prior to tracheal intubation and the start of surgery. Ventilation was controlled throughout the study period, and intravenous fluids were withheld until the Lactated Ringer's fluid bolus (15 $ml \cdot kg^{-1}$). The study period lasted approximately 35–40 min from the induction of anesthesia. MAC values for halothane and isoflurane (adjusted for age) were selected from Gregory *et al.* and Cameron *et al.* (table 1).[13,14]

Ultrasound studies were performed with patients in a supine position with the Ultra Imager 2600® (Biosound, Inc., Indianapolis) mechanical sector scanner utilizing a 5 MHz single element transducer combined with a 3.5 MHz Doppler interrogation frequency. Short axis views at the high papillary muscle level and the great vessel level, and apical four-chamber views were obtained in each subject. Left ventricular cross-sectional area was measured at the level of papillary muscles. Left ventricular cavity length was measured in the apical four-chamber view. Pulmonary artery diameter was measured immediately above the level of the semilunar valve.

After the heart and great arteries were imaged, a Doppler sample volume was positioned within a 75° sector sampling arch.[15] A line on the sample volume cursor documented the flow angle estimated by the ultrasonographer, and the velocity was then corrected (velocity/cos θ). The sample volume axial dimension was kept to 3 mm, and the lateral width was constant at 1.5 mm. The sample volume was placed in the pulmonary artery immediately above the pulmonic valve, and positioning for maximal flow velocity was confirmed by both the intensity of the audio signal and the spectral display of the Doppler shift frequency obtained from fast Fourier transformed spectral analysis. Peak velocity was measured to the top with the most dense signal on the velocity curve and 3 beats/min averaged.[15] Continuously updated two-dimensional images, Doppler profiles, and simultaneous electrocardiographic tracings were displayed on a monitor and recorded on video tape. Selective frozen images were recorded on strip chart recorder for measurement.

Left ventricular endocardial enclosed volumes were measured separately at end-diastole and end-systole

from two orthogonal planes: parasternal short axis and apical four-chamber views. Using a microsonic CAD-886 image processing and video quantifications system (Microsonics®, Inc., Indianapolis), images were traced along the endocardium utilizing the leading edge method.[16]

The two-dimensional recordings of left ventricular area at the papillary muscle level and left ventricular length at end-systole and end-diastole were used to calculate left ventricular end-systolic and left ventricular end-diastolic volumes (LVESV and LVEDV) at each study level. Volume was calculated from:

$$\text{Volume} = 5/6 \text{ area} \times \text{length}$$[8,9]

This formula assumes the ventricular configuration to be a hemisphere cylinder. This measurement correlates with a more sophisticated algorithm calculation (Simpson's Rule) used to measure two-dimensional left ventricular volumes, and also with angiographically determined left ventricular volumes in various clinical situations, including left ventricular overload.[8,9] The five pulmonary artery diameters determined for each patient were consistently reproduced and showed little variation (<8%) between measurements.

The Doppler determined mean velocity of pulmonary artery blood flow and echocardiographically determined pulmonary artery diameter were used to calculate cardiac output.[10] Where cardiac output is determined: C.O. = mean pulmonary blood flow velocity × pulmonary artery area · $\cos \theta^{-1}$.

Data were analyzed using a two-factor repeated measures design, with the factors being dosage level and anesthetic agent. Two-way analysis of variance was performed to determine significance and define interaction. Significance was corrected using Duncan's procedure and accepted at $P < 0.05$. When significant interaction was present, Tom's MACRO test was used to compare halothane and isoflurane at equipotent end-expired levels. All values are expressed as the mean ± standard error of the mean.

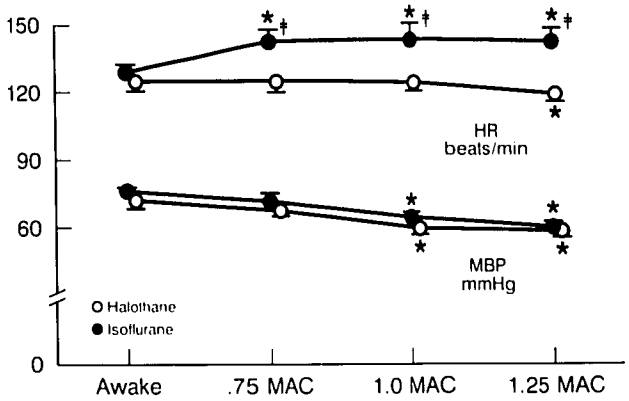

FIG. 1. Heart rate (HR) and mean blood pressure (MBP) with increasing doses of halothane (O) and isoflurane (●). Values are mean ± SEM. Significant changes from awake (*$P < 0.05$) and from halothane (†$P < 0.05$) are noted.

Results

The age (isoflurane = 12.2 ± 3.1 months, halothane = 12.35 ± 3.0 months), weights (isoflurane = 9.3 ± 1.4 kg, halothane = 8.3 ± 1.5 kg), and body surface areas (isoflurane = 0.46 ± 0.10 m^2, halothane = 0.40 ± 0.10 m^2) were not different between the two study groups.

TABLE 2. Hemodynamic Data

	Awake	0.75 MAC	1.0 MAC	1.25 MAC
Heart rate (beats · min^{-1})				
Halothane	124.6 ± 4.6	124.8 ± 5.0†	124.4 ± 4.5†	119.4 ± 3.5*†
Isoflurane	128.7 ± 4.2	142.5 ± 6.0*	143.3 ± 8.1*	142.7 ± 6.7*
Mean blood pressure (mmHg)				
Halothane	72.2 ± 3.9	67.8 ± 2.4	59.9 ± 3.1*	58.9 ± 2.9*
Isoflurane	76.4 ± 2.3	71.9 ± 4.4	64.9 ± 3.0*	60.6 ± 3.1*
CI (l · min^{-1}/m^2)				
Halothane	3.99 ± 0.3	3.35 ± 0.31	3.42 ± 0.24	3.43 ± .29*
Isoflurane	4.7 ± 0.5	4.91 ± 0.55	4.47 ± 0.59	4.32 ± .54*
SVI (ml/m^2)				
Halothane	32.7 ± 2.5	26.8 ± 2.0	27.8 ± 2.0*	28.9 ± 2.5*
Isoflurane	36.9 ± 3.8	34.2 ± 3.4	30.9 ± 3.5*	30.2 ± 3.5*
LVEDV (ml)				
Halothane	15.1 ± 2.2	15.9 ± 1.9	16.4 ± 2.0*	16.9 ± 2.0*
Isoflurane	16.7 ± 2.6	17.3 ± 2.7	17.8 ± 2.7*	18.5 ± 2.7*
LVESV (ml)				
Halothane	7.7 ± 1.0	8.4 ± 1.0*	8.8 ± 1.1*	9.9 ± 1.2*
Isoflurane	8.1 ± 1.4	8.7 ± 1.4*	9.0 ± 1.5*	9.4 ± 1.4*

Values are expressed as mean ± SEM.
* $P < 0.05$ from awake.
† $P < 0.05$ from isoflurane.

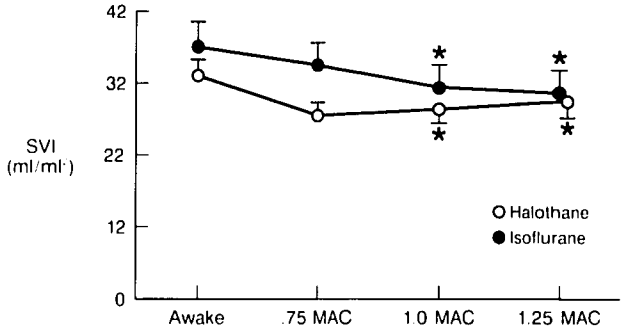

FIG. 2. Stroke volume index (SVI) with increasing doses of halothane (O) and isoflurane (●). Values are mean ± SEM. Significant changes from awake (*$P < 0.05$) are noted.

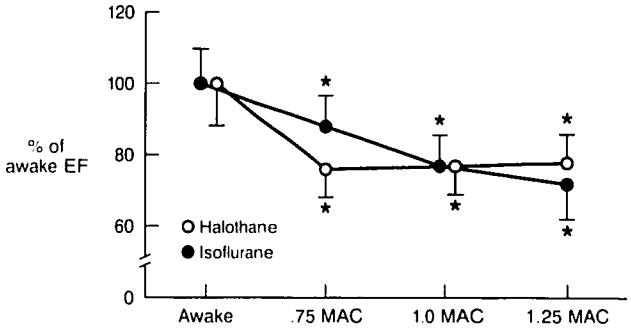

FIG. 4. Per cent change in ejection fraction (EF) with increasing doses of halothane (O) and isoflurane (●). Values are mean ± SEM. Significant changes (*$P < 0.05$) from awake are noted.

MAC Effects of Isoflurane and Halothane

The awake and first three measurements made during anesthesia (.75, 1.0, and 1.25 MAC) were used to assess how these equipotent end-expired levels of halothane and isoflurane effect cardiac function.

Isoflurane increased heart rate significantly from awake levels at all anesthetic concentrations evaluated, while halothane decreased heart rate significantly at 1.25 MAC (fig. 1, table 2). Mean blood pressure decreased in both groups at both 1.0 and 1.25 MAC (fig. 2, table 2).

The decrease in cardiac index from awake values with both drugs was significant at 1.25 MAC (table 2). Stroke volume index decreased significantly at 1.0 and 1.25 MAC with both halothane and isoflurane (table 2, fig. 2).

Volumes calculated from two-dimensional imaging in systole and diastole increased from awake levels with both halothane and isoflurane. The increase in left ventricular end-diastolic volume (LVEDV) was similar and significant at 1.0 MAC for both drugs (fig. 3, table 2). Left ventricular end-systolic volume (LVESV) increased significantly with both halothane and isoflurane at 0.75 MAC (fig. 3, table 2). Ejection fraction ($SV \cdot LVEDV^{-1}$), measured from stroke volume determined by pulsed Doppler, and end-diastolic volume, determined by two-dimensional echocardiography, decreased a similar and significant amount from awake values with both halothane and isoflurane at all anesthetic levels (fig. 4). The greatest decreases in ejection fraction (EF) for halothane was at 0.75 MAC (24 ± 6%); for isoflurane, EF decreases were greatest at 1.25 MAC (28 ± 6%).

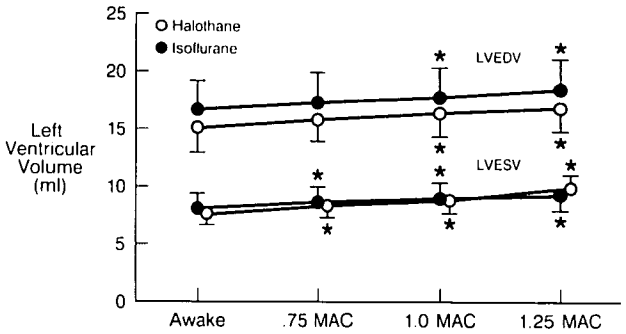

FIG. 3. Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) with increasing doses of halothane (O) and isoflurane (●). Values are mean ± SEM. Significant changes from awake (*$P < 0.05$) are noted.

Before Versus After Fluid

The response to a volume of crystalloid (15 $ml \cdot kg^{-1}$ Lactated Ringer's) infused at 1.25 MAC isoflurane or halothane anesthesia was compared to cardiovascular data measured just prior to the fluid at 1.25 MAC (table 3). Both LVEDV and LVESV increased to significant and similar degrees following the fluid with halothane and isoflurane (table 3). Ejection fraction improved with isoflurane, while, with halothane, a significant decrease in EF occurred when fluid was administered (fig. 5). Stroke volume index increased after the fluid in the isoflurane patients; in contrast, in the halothane group, a significant decrease in stroke volume index occurred following fluid administration (table 3). Blood pressure and pulse remained unchanged following fluid in the halothane group; however, in the isoflurane group, mean blood pressure decreased with no significant effect on heart rate (table 3).

Discussion

To compare the two inhalation agents at equipotent concentrations, a standard method to measure anesthetic levels is required. End-tidal anesthetic measurements are believed to reflect alveolar anesthetic levels. The time required for alveolar levels to approach levels in the vessel-rich group depends on many factors, including the solubility of the anesthetic in the tissue and

the perfusion of the tissue.[17] In this study, a 3-min period of stable end-expired levels was used prior to the measurements at 1.0 and 1.25 MAC.

While a faster rate of rise of end-tidal to inspired anesthetic levels, as well as a greater ratio of alveolar to inspired anesthetic levels, occurs in infants and children relative to adults,[17–19] 3 min would represent only one and one-third time constants for halothane (2.2 min = 1 time constant in infants).[18] Because equilibrium is not complete between end-tidal anesthetic levels and anesthetic levels in the vessel-rich tissue group, the end-expired levels we measured would be greater than CNS and myocardial anesthetic levels that were present, and lead to an underestimate of the cardiovascular effects of halothane and isoflurane. With a greater tissue solubility and a longer time constant for equilibrium, the cardiovascular effects of halothane would be underestimated more than the cardiovascular effects of isoflurane.

End-expired levels of halothane and isoflurane were measured by sampling from a mask. This measurement was used to reflect end-tidal anesthetic levels; however, because of the small tidal volumes, expired gas could be contaminated with inspired anesthetic gas. This would result in an overestimate of the anesthetic levels that were present at the time measurements were made, and, hence, lead to an underestimate of the cardiovascular effects of isoflurane and halothane.

MAC Effects of Halothane and Isoflurane

The decreases in blood pressure that occur with isoflurane or halothane are similar to those observed in prior studies of infants and children.[2,5,6,20] With halothane, a decrease in myocardial contractility is believed to be a major factor in blood pressure decreases, while, with isoflurane, a decrease in peripheral vascular resistance is believed to be the more important cause of hypotension.[6,21]

Heart rate increases with isoflurane may be dependent on resting heart rate, age, preoperative medication, and whether ventilation is spontaneous or controlled. In volunteer studies of adults and in this study, controlled ventilation with isoflurane resulted in increases in heart rate.[21] In prior studies of infants [20] and children,[6] increases in heart rate did not occur with isoflurane. Halothane, in this study and in prior studies of adults and children, maintained or resulted in small decreases in heart rate.[2,6]

Halothane and isoflurane decreased cardiac index significantly at 1.25 MAC. There was no significant difference in effect between halothane and isoflurane on cardiac index at any condition measured. The decreased cardiac index with halothane was not greater than decreases in cardiac output reported in adults [22] at 1.25 MAC halothane, and corresponds to previously reported values in older children.[2,23]

TABLE 3. Hemodynamic Data Before and Following Fluid 15 ml/kg Lactated Ringers at 1.25 MAC

	Before Fluid	Following Fluid
HR (beats/min)		
Halothane	119.4 ± 3.5†	123.0 ± 2.7†
Isoflurane	142.7 ± 6.7	135.0 ± 7.5
MBP (mmHg)		
Halothane	58.9 ± 2.9	57.9 ± 2.5†
Isoflurane	60.6 ± 3.0	49.5 ± 3.1*
LVEDV (ml)		
Halothane	16.9 ± 2.0	18.8 ± 2.2*
Isoflurane	18.5 ± 2.7	19.7 ± 2.8*
LVESV (ml)		
Halothane	9.9 ± 1.2	10.6 ± 1.2*
Isoflurane	9.4 ± 1.4	10.0 ± 1.6*
CI ($l \cdot min \cdot m^{-2}$)		
Halothane	3.43 ± 0.29	3.32 ± 0.39
Isoflurane	4.32 ± 0.54	4.72 ± 0.73
SVI (ml/m^2)		
Halothane	28.9 ± 2.5	27.1 ± 3.0*†
Isoflurane	30.2 ± 3.5	34.7 ± 4.2*

Values are expressed as mean ± SEM.
* $P < 0.05$ from before fluid.
† $P < 0.05$ from Isoflurane.

Isoflurane decreased cardiac index at 1.25 MAC despite an increased heart rate. In adults, increases in heart rate offset decreases in stroke volume and cardiac output is maintained during isoflurane anesthesia.[21] The results of this study also differ from other studies of children.[6] M-mode derived indices of contractility (PEP, LVET, STI) were reported improved or unchanged in children during isoflurane anesthesia,[6] for this reason, it has been suggested that cardiac output may be maintained.[6] Because only a single dimension of the myocardium was measured, the actual effect on cardiac output is difficult to determine from these M-mode studies.

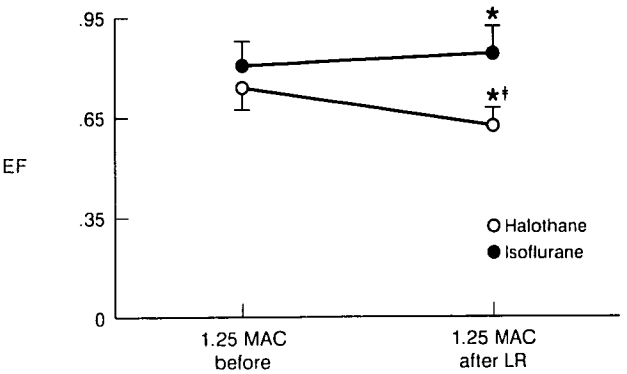

FIG. 5. Ejection fraction (EF) before and after 15 ml/kg of Lactated Ringers (LR) at 1.25 MAC halothane (○) or isoflurane (●). Values are expressed as mean ± SEM. Significant changes (*$P < 0.05$) from before and (†$P < 0.05$) from isoflurane are noted.

Left ventricular end-diastolic volume changes reflect preload changes in the intact heart. This volume increased in a dose-dependent fashion with both isoflurane and halothane. Estimates of preload in adults during isoflurane and halothane anesthesia have often used pulmonary artery wedge pressure to reflect left ventricular end-diastolic pressure measurements.[24] These pressure measurements are then assumed to reflect changes in end-diastolic volume or preload. We found increases in end-diastolic volume (LVEDV) with both agents at 1.0 and 1.25 MAC, but cannot say whether this was associated with increased left ventricular end-diastolic pressure.

Stroke volume index decreased with both halothane and isoflurane. The magnitude of the decrease was similar to that observed in adults with both isoflurane and halothane.[21,22] Ejection fraction decreases were similar with halothane and isoflurane, suggesting a clinically similar impairment of myocardial function with halothane and isoflurane at the doses examined in these patients. The similar and significant increases in LVESV with both halothane and isoflurane also confirm that similar changes in the determinants of myocardial function must occur with both halothane and isoflurane in infants.

The similarities in effects on MBP, CI, LVEDV, SVI, ejection fraction, and LVESV suggest that, at these equipotent concentrations, the differences between halothane and isoflurane in infants and small children on myocardial determinants may be subtle. This study agrees with *in vitro* cat papillary muscle studies[25] and *in vivo* newborn piglet[3] studies, which suggest decreases in contractility occur with both isoflurane and halothane. Contractility measurements were reported to be maintained or improved with isoflurane, but severely depressed by halothane, when measured by M-mode echo.[6] These *in vivo* M-mode echocardiographic measurements of contractility can only be compared if halothane and isoflurane produce similar effects on heart rate, cardiac conduction, afterload, and preload. Isoflurane and halothane appear to have dissimilar effects on heart rate. Halothane is known to depress His-Bundle conduction, whereas isoflurane has minimal effects.[26,27] Isoflurane decreases systemic vascular resistance, in adults[21] and, perhaps, in older children,[6] while halothane causes only minor changes in vascular resistance. The use of M-mode measurements to determine contractility assumes that the effects of halothane and isoflurane on heart rate, cardiac conduction, and afterload are similar. For this reason, M-mode estimated contractility measurements may suggest a difference exists in contractility between halothane and isoflurane, when their effects on contractility could be similar.

Measurement of ventricular volumes with two-dimensional echocardiography correlate with angiographic methods, but these volumes may underestimate actual LVEDV and LVESV.[12] Stroke volume and cardiac output determined by this method would underestimate angiographically determined values.[12] For this reason, pulsed Doppler determined cardiac index and stroke volume index, which have been validated with thermodilution and angiographic techniques in children,[10] were used to enhance the information about cardiac performance. In this study, ejection fraction was measured by dividing stroke volume (SV) determined by pulsed Doppler into the left ventricular end-diastolic volume (LVEDV) derived from two-dimensional measurements. Because two-dimensional echocardiography underestimates ventricular volumes, the ejection fractions derived by this method are overestimated.

Before and After Fluid

Lactated ringer's was administered to correct calculated fluid deficits and determine myocardial responses to a fluid challenge at 1.25 MAC halothane or isoflurane. It has been suggested that hypotension during anesthesia in infants and children may result from the dehydration created by fasting prior to anesthesia induction. Although the NPO period was 4–8 h, the addition of fluid did not correct hypotension in either group. Volume loading to the infants in both groups resulted in increased preload (LVEDV). In the patients who received halothane, significant decreases in stroke volume index and ejection fraction occur after LR. In those patients who received isoflurane, increases in stroke volume index and ejection fraction resulted from the fluid bolus. Perhaps the patients who received isoflurane followed an expected Starling response, with increases in preload leading to improved ejection fraction and stroke volume index. Alternatively, in infants who received isoflurane, the addition of LR led to a greater decrease in afterload than in the infants who received halothane, and this resulted in the increases in SVI and ejection fraction that occurred with isoflurane. While isoflurane decreases afterload in adults and, perhaps, children,[6,21] afterload could not be directly measured by the non-invasive two-dimensional and Doppler echocardiographic technique employed in this study. Decreases in cardiac output produced by halothane or isoflurane may be of minor concern particularly in healthy patients, but the impaired myocardial responses to a fluid challenge seems an important distinction between halothane and isoflurane in clinical practice, and indicates that important differences must exist in their cardiovascular effects.

In summary, to our knowledge, this is the first study to compare cardiovascular effects in healthy unmedicated infants and small children during equipotent levels of isoflurane and halothane using two-dimensional echocardiography combined with non-invasive estimates of pulmonary blood flow velocity. Except for the increases in heart rate that occurred during isoflurane anesthesia, the changes from awake cardiovascular values were similar with halothane and isoflurane. Despite this, differences in the cardiovascular effects between halothane and isoflurane became apparent when a fluid challenge was given at 1.25 MAC. Patients who received halothane, but not isoflurane, responded to fluid by further impairment in cardiac function. This difference, apparent only after a fluid bolus, might be evidence for increased cardiovascular reserve associated with isoflurane.

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