Alteration of vascular capacitance and blood flow distribution during halothane anesthesia

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Abstract: We examined the effect of halothane on systemic vascular capacitance as well as on systemic vascular resistance using cardiopulmonary bypass in dogs. Venous outflows from two different vascular beds, the splanchnic and extrasplanchnic beds, were also measured. Under constant perfusion flow and constant central venous pressure, a change in reservoir blood volume inversely represented a change in systemic blood volume and then in systemic vascular capacitance, and a change in mean arterial pressure directly reflected a change in systemic vascular resistance. Administration of 1% and 2% halothane produced the blood concentrations of 0.58±0.14 mM and 1.34±0.06 mM, respectively. Systemic vascular resistance decreased by 12±6% and 40±4% during 1% and 2% halothane, respectively. Systemic blood volume increased by 7±2 ml·kg⁻¹ and 15±4 ml·kg⁻¹ during 1% and 2% halothane, respectively. Halothane did not cause significant blood flow redistribution between the splanchnic and extrasplanchnic vascular beds. These results suggest that halothane causes an increase in systemic vascular capacitance as well as a decrease in systemic vascular resistance. This increase in vascular capacitance may contribute in part to a decrease in cardiac output during halothane anesthesia.

Key words: Halothane—Vein—Splanchnic—Vascular capacitance—Blood volume—Blood flow distribution

Introduction

Cardiac output is determined by four principal factors such as myocardial contractility, heart rate, preload, and afterload. Halothane has been shown to decrease cardiac output due primarily to depression of myocardial contractility [1,2]. However, the effect of halothane on preload has not yet been clearly determined. Preload is defined as ventricular end-diastolic volume or pressure, and it is influenced by circulating blood volume, ventricular filling time, ventricular diastolic compliance, and vascular capacitance. The purpose of this study was to examine the changes in vascular capacitance during halothane anesthesia. Vascular capacitance is defined as the blood volume contained in the systemic circulation, especially in the venous system at a given venous pressure [3]. An increase in vascular capacitance can be derived largely from venous dilatation, leading to a contained blood volume in the venous system and thus a decrease in venous return.

To elucidate the effect of halothane on vascular capacitance, we used cardiopulmonary bypass in dogs, where a change in vascular capacitance can be evaluated as an inverse change in reservoir blood volume under constant venous pressure and constant perfusion flow. Venous outflow from the systemic circulation was divided into two compartments; the splanchnic and extrasplanchnic vascular beds, which are considered to have different time constants for venous drainage, as described by Caldini et al. [4] and others [5,6].

Methods

Five mongrel dogs weighing 20–30 kg were anesthetized with 30 mg/kg of pentobarbital sodium. Supplemental doses of the anesthetic were given as necessary to maintain the basal anesthetized state of the experimental animals. The trachea was intubated with a cuffed endotracheal tube and connected to Bird Mark 7 respirator for mechanical ventilation with 100% oxygen until cardiopulmonary bypass was instituted. Paco₂ was maintained between 30 and 40 mmHg and kept constant during mechanical ventilation. Catheters were

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placed in the thoracic aorta via the left axillary artery to measure arterial pressure and the superior vena cava via the left axillary vein and the inferior vena cava via the femoral vein to measure central venous pressure. The catheters were connected to Statham pressure transducers (Statham Instruments, Los Angeles, CA, USA). Body temperature was maintained by external warming with a heating pad, and also by a heat exchanger during cardiopulmonary bypass.

The surgical preparation and experimental apparatus for measurements of regional venous outflow and blood volume changes are described previously in detail [7,8]. Briefly, the chest was opened through a median sternotomy, and animals were placed on cardiopulmonary bypass using a Sarns roller pump (Sarns 3M Health Care, Model 3500, Annarbor, MI, USA) and Shiley reservoir oxygenator (Sorin Biomedical, Irvine, CA, USA). The reservoir was primed with a mixture of lactated Ringer’s (2000 ml) and Dextran 40 (1000 ml) containing 10000 units of sodium heparin. An oxygenator was bubbled with 5-6 L·min⁻¹ of oxygen and 250-300 ml·min⁻¹ of CO₂ to maintain Paco₂ at 35–40 mmHg. Systemic perfusion was performed through cannulas placed in both femoral arteries. Venous outflow was divided into two compartments; splanchnic and extrasplanchnic. The splanchnic venous outflow was collected through a cannula placed in the inferior vena cava at the level of the diaphragm, and this region was isolated by a ligation on the inferior vena cava below the renal veins. The splanchnic outflow, therefore, includes renal outflow in the present experiments. The extrasplanchnic venous outflow was collected through four cannulas placed in the superior vena cava, the right ventricle, the left ventricle, and the femoral vein. The azygos vein was ligated. The cardiopulmonary bypass pump was adjusted so that arterial blood pressure was approximately equal to the level before bypass and maintained constant throughout the experiment. Venous pressures in the extrasplanchnic and splanchnic vascular beds were measured via the catheters placed into the superior and inferior vena cava above the renal veins, respectively. The height of the opening of the tube draining venous return into the reservoir was adjusted so that the mean central venous pressure measured 5-6 mmHg. The splanchnic and extrasplanchnic venous outflows were measured using a multichannel Biotronex electromagnetic flowmeter and in-line flow probe (Biotronex Laboratory, Chester, MD, USA).

The arterial pressure, splanchnic and extrasplanchnic venous pressure, and splanchnic and extrasplanchnic venous outflows were recorded simultaneously on a Grass Model 7 polygraph (Grass Instrument, Braintree, MA, USA).

Changes in blood volume within the animal were assessed by changes in the reservoir volume. The reservoir volume was measured by reading the blood level on the reservoir scale to the nearest 10 ml. After each experiment, the relationship between real blood volume change and the volume change measured by graduation on the reservoir was examined by adding blood of known volume to the reservoir. Subsequently, the real blood volume change was obtained by correction of the measured volume change. Average correlation was as follows: real blood volume change = 0.75 × blood volume change measured by the reservoir scale.

Measurements were done under three conditions in series: control, 1% halothane, and 2% halothane. Under each condition, 20 min were allowed for hemodynamics to stabilize before measurements were done. Halothane was provided using a Fluotec 2 vaporizer (Pyprane, Keighley, England) installed in-line with a gas mixture supply to the oxygenator. Halothane concentrations in blood were measured on a Perkins-Elmer Cetus (Norwalk, CT, USA) Sigma 3B gas chromatography at 5, 10, and 15 min after the application of halothane. Sodium bicarbonate was added to the reservoir to maintain optimal pH and base excess if necessary.

All data are expressed as the mean ± standard deviation (SD) of the mean. Statistical analysis was performed using analysis of variance (ANOVA), and if the F value was significant, a paired t-test was done. A P value of less than 0.05 was considered significant.

Table 1. Arterial blood gas analysis and hemoglobin concentration

<table>
<thead>
<tr>
<th></th>
<th>Before CPB</th>
<th>20 min after CPB</th>
<th>End of CPB</th>
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</thead>
<tbody>
<tr>
<td>Hgb (g·L⁻¹)</td>
<td>157 ± 58</td>
<td>88 ± 10*</td>
<td>85 ± 8*</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 ± 0.06</td>
<td>7.36 ± 0.06</td>
<td>7.40 ± 0.06</td>
</tr>
<tr>
<td>Pao₂ (mmHg)</td>
<td>261 ± 200</td>
<td>393 ± 88</td>
<td>375 ± 110</td>
</tr>
<tr>
<td>Paco₂ (mmHg)</td>
<td>34 ± 14</td>
<td>38 ± 2</td>
<td>36 ± 4</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol·L⁻¹)</td>
<td>21 ± 4</td>
<td>21 ± 4</td>
<td>22 ± 2</td>
</tr>
<tr>
<td>BE (mmol·L⁻¹)</td>
<td>22.2 ± 1.6</td>
<td>23.4 ± 4.0</td>
<td>22.6 ± 2.2</td>
</tr>
</tbody>
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CPB, cardiopulmonary bypass; Hgb, hemoglobin; BE, base excess.
Mean ± SD, * P < 0.05 vs before CPB.