The Effect of Right-to-left Shunt on the Rate of Increase of Arterial Anesthetic Concentration

Robert K. Stoelting, M.D.,* and David E. Longnecker, M.D.†

Right-to-left shunt was produced in dogs by placing a bronchial blocker in the left main-stem bronchus. Compared with the arterial concentrations attained with both lungs ventilated, right-to-left shunt significantly slowed the rate of increase of arterial cyclopropane. Arterial cyclopropane concentrations at 1, 3, 5, 10, and 20 minutes were 30, 27, 26, 22, and 14 per cent less than the concentrations present at the same times with both lungs ventilated. The rate of increase of arterial methoxyflurane was not altered, while halothane’s rate of increase occupied an intermediate position. Increases in arterial halothane concentrations were slower in three patients with tetralogy of Fallot prior to closure of the ventricular septal defects. At 1, 3, 5, 10, and 20 minutes, arterial halothane concentrations were 23, 17, 13, 11, and 8 per cent less than the corresponding concentrations after elimination of the right-to-left shunts. (Key words: Uptake; Right-to-left shunt; Tetralogy of Fallot; Arterial anesthetic concentration; Cyclopropane; Halothane; Methoxyflurane.)

In the presence of right-to-left shunt, a reduced proportion of the cardiac output is exposed to alveolar anesthetic gas. This acts as a barrier to the passage of anesthetic gas from alveoli to pulmonary capillary blood, and may decrease the rate of induction of anesthesia. Eger and Severinghaus² used an analog computer to predict the effects of ventilation-perfusion abnormalities on the rate of increase of arterial anesthetic concentration. They concluded that right-to-left shunt would slow the rate with poorly-soluble anesthetics, while soluble anesthetics would be affected only slightly. To date no study has confirmed or quantitated these predictions in vivo. This study reports the effects of right-to-left shunt on the rates at which the arterial concentrations of cyclopropane, halothane (Fluothane) and methoxyflurane (Penthrane) approached constant inspired concentrations in the dog and man.

Methods

Eight mongrel dogs (10–15 Kg) were anesthetized with pentobarbital (20–30 mg/kg, iv.). A bronchial blocker was passed through a bronchoscope into the left main-stem bronchus. The bronchoscope was removed and auffed endotracheal tube inserted into the trachea. When the cuff on the bronchial blocker was inflated only the right lung was ventilated, while both lungs were perfused. Proper placement of the bronchial blocker was confirmed by direct vision of the left lung through a left lateral thoracotomy prior to any measurement.

The dog was placed supine, breathing oxygen from an anesthetic machine, and ventilation was controlled with a Harvard animal ventilator. A Fink valve was placed at the endotracheal tube to insure a nonbreathing system. An esophageal temperature probe was inserted and body temperature maintained near 37°C by use of a heating pad. A femoral artery and vein cutdown was performed. Cardiac output was determined by dye dilution using cardiogreen and a Beckman cardio-densitometer. $P_{aO_2}$ and $P_{aCO_2}$ were determined with an Instrumentation Laboratory Model 113 blood-gas analyzer and corrected to body temperature. After 30 minutes the dog was attached to a second anesthetic machine and system which had been equilibrated with cyclopropane and methoxyflurane. Cyclopropane was metered from the anesthetic...

* Clinical Associate, Anesthesiology Department, National Institutes of Health, Bethesda, Maryland 20014. Present address: Department of Anesthesiology, Indiana University School of Medicine, Indianapolis, Indiana 46202.

† Clinical Associate, Anesthesiology Department, National Institutes of Health, Bethesda, Maryland 20014. Present address: Department of Anesthesiology, University of Missouri School of Medicine, Columbia, Missouri 65201.

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Fig. 1. Ratios of end-tidal to inspired concentrations (\(F_E/F_I\)) of the three inhalation anesthetics studied in the dog experiments, for 20 minutes after the start of anesthetic administration. Inspired cyclopropane, halothane, and methoxyflurane concentrations were 2.1, 1.0, and 0.55 per cent, respectively.

Fig. 2. Arterial concentrations (±SE) of cyclopropane, halothane, and methoxyflurane as indicated by the gas chromatographic peak heights when one lung was ventilated, plotted as average per cent change from corresponding arterial peak heights with both lungs ventilated (dog studies). Halothane data represent three experiments, and SE were not calculated.

A mechanical ventilator (8 l/min oxygen plus 200 ml/min cyclopropane) and methoxyflurane vaporized from a Pentec vaporizer with the concentration dial setting at 0.4 per cent. In studies of three of the dogs a Fluotec Mark 2 vaporizer was placed in series with the Pentec vaporizer and about 1.0 per cent halothane was added to the gases delivered. Flows and settings were maintained for at least 5 minutes prior to attaching the dog to the anesthetic machine and system.

Inspired and end-tidal gas samples and arterial blood samples were obtained at zero time and 1, 3, 5, 10, and 20 minutes following the addition of the three inhalation anesthetics. Gas samples were collected into glyce-
TABLE 1. Cardiac Output and Blood—Gas Values in the Eight Dog Experiments

<table>
<thead>
<tr>
<th></th>
<th>One Lung Ventilated (Mean ± SE)</th>
<th>Two Lung Ventilated (Mean ± SE)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (l/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2.0 ± 0.4</td>
<td>2.1 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>6 min</td>
<td>1.7 ± 0.6</td>
<td>1.5 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>16 min</td>
<td>1.3 ± 0.6</td>
<td>1.1 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Paco₂ (torr)</td>
<td>102 ± 22</td>
<td>118 ± 49</td>
<td>0.01</td>
</tr>
<tr>
<td>Pₐco₂ (torr)</td>
<td>21 ± 4.3</td>
<td>27 ± 2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Esophageal temperature (C)</td>
<td>37.4 ± 0.07</td>
<td>36.4 ± 0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

* NS = not significant.

erinized glass syringes through a small catheter placed near the tip of the endotracheal tube. Anesthetic concentration was determined using a Beckman GC-2A gas chromatograph with a flame ionization detector and a 3-foot column containing Flexol 8N8 (5 per cent) and Apiezol (30 per cent) on Chromosorb-W at 100 C. Peak height was converted to concentration in volumes per cent by comparison with the peak heights of known gas concentrations.

The inhalation anesthetic in arterial blood (2 ml) was extracted into equal volumes of tetrachloroethylene.² Since the three anesthetics had different retention times on the column, it was possible to detect them all with a single injection of 5 μl tetrachloroethylene and appropriate changes in attenuation. Peak height was used as an index of arterial anesthetic concentration. No attempt was made to calculate the actual arterial anesthetic concentrations represented by these peak heights. The reproducibility of peaks with previously-prepared tetrachloroethylene solutions containing the three anesthetics confirmed that gas chromatographic responses did not change between samples.

After 20 minutes, the dog was again attached to the first anesthetic machine and breathed oxygen. The bronchial blocker was removed and the left lung expanded. After at least two hours, cardiac output was determined and adjusted to a value similar to that found with one lung being ventilated by adding isoproterenol or deepening anesthesia with pentobarbital. Paco₂ was adjusted to the first control value by changing the tidal volume. The dog was then attached to the second anesthetic machine and system at the same flows and vaporizer settings for cyclopropane, halothane, and methoxyflurane that had been used when one lung was ventilated. Inspired, end-tidal, and arterial samples were obtained as before.

Three cyanotic patients with tetralogy of Fallot were studied before and after closure of the ventricular septal defects. All were anesthetized with morphine-oxygen (10 l/min) and d-tubocurarine, utilizing a Fink valve at the endotracheal tube to insure a nonrebreathing system. Ventilation was controlled with an Air Shields ventilator, and halothane was acutely added by turning the concentration dial of a Fluotec vaporizer to 0.5 per cent. Inspired and end-tidal gas samples and arterial bloods were obtained at 0, 1, 3, 5, 10, and 20 minutes for analysis of halothane concentrations as described above. Halothane was again added about 120 minutes later at the same anesthetic flows and vaporizer settings and similar alveolar ventilation, but after elimination of the right-to-left shunt.

**Results**

Average inspired anesthetic concentrations (dog experiments) with one or two lungs ventilated were 2.1 ± 0.1 (SE) per cent cyclopropane, 0.55 ± 0.05 per cent methoxyflurane, and 1.0 per cent halothane. The rates at which end-tidal concentrations approached inspired concentrations were not significantly different for any of the anesthetics regardless of whether one or both lungs were ventilated (fig. 1).

The arterial anesthetic concentration as indicated by the gas chromatographic peak height with one lung ventilated was plotted as per cent difference from control (fig. 2). Control was the gas chromatographic peak height of the arterial sample at the same time and inspired concentration and similar alveolar ventilation and cardiac output but with both lungs ventilated. At 1, 3, 5, 10, and 20 minutes, arterial cyclopropane concentrations were 30, 27, 26, 22, and 14 per cent less than the peak heights with both lungs ventilated (P < 0.01). At 1 minute arterial halothane was 21 per cent less than control. Between 3 and 20 minutes arterial halothane was not greatly different from the control value. The
average arterial methoxyflurane peak height with one lung ventilated was not significantly different from control at any time.

Cardiac output and blood-gas data from the dog studies are presented in Table 1.

In the three patients with tetralogy of Fallot the arterial halothane gas chromatograph peak heights at 1, 3, 5, 10, and 20 minutes were 23, 17, 13, 11, and 8 per cent less than the peak heights at the same times, alveolar ventilation, and inspired concentrations after closure of the ventricular septal defect (Fig. 3). Inspired halothane concentrations averaged 0.6 per cent. End-tidal halothane concentrations approached the inspired at nearly the same rates before and after closure of the ventricular septal defects (Fig. 4). The average Pao2 increased from 95 to 530 torr after elimination of the right-to-left shunt. Paco2 was 29 torr before and 31 torr after closure. The ratio of pulmonary to systemic blood flow as determined at cardiac catheterization prior to operation was 0.35.

Discussion

These data indicate that right-to-left shunt slows the rate of increase of the arterial concentration of the least soluble anesthetic, cyclopropane, the most. Halothane has an intermediate solubility and is less influenced, while the increase in arterial concentration of a highly soluble anesthetic (methoxyflurane) was not altered by right-to-left shunt. Our results agree with the predictions derived in vitro from an analog computer by Eger and Serringerhaus.

The rate of anesthetic induction is directly related to the rate of increase of arterial concentration. Clinically, when a right-to-left shunt is present the inspired concentration of a poorly-soluble anesthetic will have to be greater than when a right-to-left shunt is not present to achieve the same arterial concentration and rate of induction. After 5 minutes, when one lung was ventilated, arterial cyclopropane was 26 per cent less than the arterial concentration when both lungs were ventilated. We would predict from our data that if the inspired concentration of cyclopropane is 20 per cent without right-to-left shunt, it would have to be increased to about 25 per cent to achieve the same rate of induction when only one lung was ventilated. Rate of induction will be little altered when a soluble anesthetic such a methoxyflurane is employed even if a large right-to-left shunt is present. This is not to imply that induction with methoxyflurane will be faster than induction with cyclopropane when right-to-left shunt is present. Induction with methoxyflurane will still be prolonged, but the rate of increase of the arterial concentration of the poorly-soluble anesthetic will be less rapid than normal.
Data from the patients with tetralogy of Fallot suggest that right-to-left shunt may protect against anesthetic overdose with halothane, as evidenced by the more rapid increase in arterial halothane concentration following closure of the ventricular septal defect. However, the number of patients was small and the effect of shunt probably was significant only in the first 1–3 minutes of halothane administration.

Solubility in blood affects uptake and provides an explanation for the effect of right-to-left shunt on the rate of increase of arterial anesthetic concentration.1 Uptake of a poorly-soluble anesthetic (cyclopropane, nitrous oxide) into the pulmonary capillary blood is limited, and the alveolar concentration increases rapidly regardless of whether one or both lungs are ventilated. As a result, pulmonary capillary blood from the ventilated lung contains little more anesthetic than normal, and when this blood mixes with that perfusing the nonventilated lung the resultant mean arterial anesthetic concentration is greatly lowered. Uptake of a very soluble anesthetic (methoxyflurane, ether) is considerable, and can be increased when all the ventilation is diverted to one lung. Therefore, the pulmonary capillary blood from the ventilated lung contains nearly twice as much anesthetic as when both lungs are ventilated. When this mixes with the blood from the nonventilated lung, the halving of concentration produces a mean arterial concentration which is not significantly different from control. Halothane, with an intermediate blood–gas solubility, occupies an intermediate position.

Changes in inspired anesthetic concentration, alveolar ventilation, and cardiac output may influence anesthetic uptake and rate of increase of arterial anesthetic concentration. Since inspired concentration and alveolar ventilation were nearly the same in each experiment, our results cannot be explained on this basis. We attempted to begin at similar control cardiac outputs in each experiment. The addition of the inhalation anesthetics resulted in similar progressive decreases in cardiac output at 6 and 16 minutes with and without right-to-left shunt, so the effect of changes in cardiac output should have been similar under the two conditions (table 1).

Pulmonary capillary blood flow can be diverted from nonventilated alveoli1 and the degree of right-to-left shunt decreased. It is not possible to evaluate the influence of this change in our study, although it may explain the variability in $P_aO_2$ between dogs when only one lung was ventilated. Some dogs maintained $P_aO_2$ values above 200 torr, while other values were less than 100 torr with one lung ventilated, which resulted in the large standard error for the average $P_aO_2$ values (table 1).

Doubling ventilation to a single lung should result in a more rapid increase of the alveolar concentration when a soluble anesthetic is used.1 Uptake is limited with poorly-soluble anesthetics, so differences between the alveolar concentrations with one and both lungs ventilated should be negligible. Indeed, we found no differences in the rates of increase of end-tidal cyclopropane concentrations regardless of whether one or both lungs were ventilated (fig. 1). That we were unable to demonstrate a significantly more rapid increase of end-tidal methoxyflurane (fig. 1) in the presence of right-to-left shunt is at variance with these predictions. This may represent an inability to obtain valid end-tidal samples with this soluble anesthetic. No significant change in the end-tidal concentration was found with halothane, but we would predict an intermediate effect (figs. 1 and 4).

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References