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Isoflurane Anesthesia and Arterial Oxygenation during One-lung Ventilation

ALVEOLAR HYPOXIA, whether caused by a low ventilation-to-perfusion ratio or atelectasis, causes pulmonary vasoconstriction, and the phenomenon is called hypoxic pulmonary vasoconstriction (HPV). If the alveolar hypoxia is regional, then the vasoconstriction is limited to just the hypoxic region, and there is an increase in pulmonary vascular resistance in just the hypoxic region. The selective increase in hypoxic lung pulmonary vascular resistance causes a diversion of blood flow away from the hypoxic lung to better ventilated normoxic or hyperoxic lung. The blood flow diversion decreases the amount of shunt flow that can occur through the hypoxic lung. Thus, the regional HPV response is an autoregulatory mechanism that protects the arterial oxygen tension.

This issue of ANESTHESIOLOGY contains a well-controlled study of the effect of isoflurane on regional canine HPV.[1] The authors found, in qualitative agreement with several other previous studies,[2] that when all nonanesthetic drug variables that might change regional HPV are kept constant, isoflurane inhibits single-lung HPV in a dose-dependent manner. The authors offer the reader an easily comprehensible, quantitative summary of the relationship between dose of isoflurane administered and degree of inhibition of the single-lung canine HPV response. If the summary can be extrapolated or applied to the clinical one-lung ventilation situation (at least as an approximation), then the summary is important because it can provide valuable insight as to what to expect with regard to arterial oxygenation when such patients are anesthetized with isoflurane. In order to put this insight into sharp clinical focus, it is necessary to first understand what should happen to each lung blood flow, shunt flow, and arterial oxygenation as a function of a normal amount of HPV when two-lung ventilation is changed to one-lung ventilation in the lateral decubitus position. Once the stable one-lung ventilation condition has been described, it is then possible, using the data from the article in this issue of ANESTHESIOLOGY,[1] to see how isoflurane administration would affect the one-lung ventilation blood flow distribution, shunt flow, and arterial oxygen tension.

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Two-lung Ventilation: Blood Flow Distribution

Gravity causes a vertical gradient in the distribution of pulmonary blood flow in the lateral decubitus position for the same reason that it does in the upright position. Consequently, blood flow to the dependent lung is significantly greater than blood flow to the nondependent lung. When the right lung is nondependent, it should receive approximately 45% of total blood flow as opposed to the 55% that it received in the upright and supine positions; when the left lung is nondependent, it should receive approximately 35% of total blood flow as opposed to the 45% that it received in the upright and supine positions (closed-chest data with normal pulmonary artery pressure).[3,4] If these blood flow distributions are combined (both the right and left lungs being nondependent an equal number of times), average two-lung ventilation blood flow distribution in the lateral decubitus position

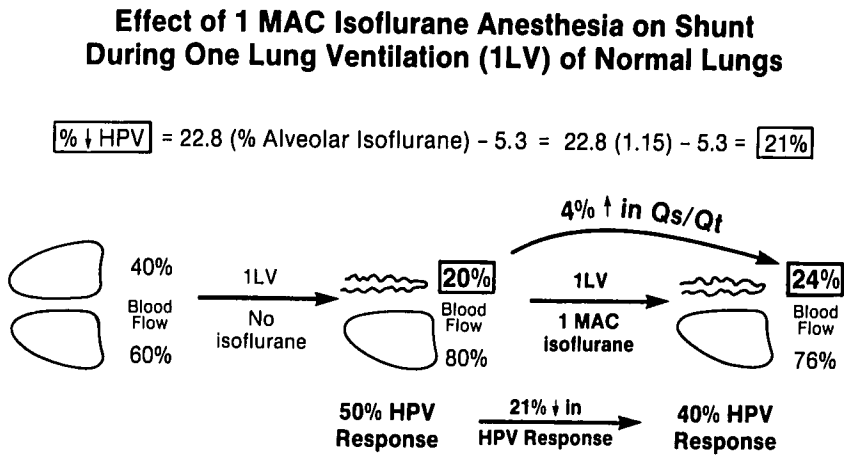

FIG. 1. Schematic shows the theoretical distribution of blood flow between the nondependent and dependent lung for patients with normal lungs for three conditions: two-lung ventilation (*left panel*); one-lung ventilation and no isoflurane anesthesia (*middle panel*); and one-lung ventilation and 1 MAC isoflurane anesthesia (*right panel*). The one-lung ventilation 50% blood flow reduction HPV response without isoflurane anesthesia is decreased to a 40% blood flow reduction HPV response (*i.e.*, inhibited by 20%) by 1 MAC isoflurane anesthesia. Consequently, the one-lung ventilation shunt increases from 20% to 24%. MAC = minimum alveolar concentration; HPV = hypoxic pulmonary vasoconstriction.

would consist of 40% of total blood flow perfusing the nondependent lung and 60% of total blood flow perfusing the dependent lung (fig. 1, *left panel*).

It is possible that nondependent lung blood flow may increase slightly when the nondependent hemithorax is open, for two reasons.[5] First, if the compliance of the nondependent lung increases so much that nondependent lung alveolar pressure decreases significantly, nondependent lung blood flow may increase relative to dependent lung blood flow. Second, if the nondependent lung falls away from the open chest wall, the vertical distance between the heart and the nondependent lung may decrease, which, in the face of a constant pulmonary artery pressure, might result in an increased perfusion of the nondependent lung. Consequently, the 40%/60% nondependent/dependent lung blood flow ratio during closed-chest two-lung ventilation may be a slight underestimation of the ratio during open-chest, two-lung ventilation.

One-lung Ventilation: Blood Flow Distribution, Shunt Flow, and Arterial Oxygen Tension

When the nondependent lung is nonventilated (made atelectatic), HPV in the nondependent lung will increase nondependent lung pulmonary vascular resistance and decrease nondependent lung blood flow. In the absence of any complicating factors, a single-lung HPV response should decrease the blood flow to that lung by 50%.[6] Consequently, the nondependent lung should be able to reduce its blood flow from 40% to 20% of total blood flow, and the nondependent/dependent lung blood flow ratio during one-lung ventilation should be 20%/80% (fig. 1, *middle panel*).

All of the blood flow to the nonventilated nondependent lung is shunt flow and, therefore, one-lung ventilation creates an obligatory right-to-left transpulmonary shunt flow that was not present during two-lung ventilation. If no shunt existed during two-lung ventilation conditions (ignoring the normal 1–3% shunt flow due to the bronchial, pleural, and thebesian circulations), then we would expect the ideal total shunt flow during one-lung ventilation to be a minimal 20% of total blood flow, and with a normal hemodynamic and metabolic state, the arterial oxygen tension with fractional inspired O_2 concentration (FI_{O_2}) equal to 1.0 should be approximately 280 mmHg (fig. 2).

Effect of Isoflurane on One-lung Ventilation Blood Flow Distribution, Shunt Flow, and Arterial Oxygenation

Domino *et al.* found:

% inhibition of regional HPV response

$$= 22.8\ (\%\ \text{alveolar isoflurane}) - 5.3^{1}$$

As described previously, under normal conditions collapse of the nondependent lung in the lateral decubitus position causes a nondependent lung HPV response to decrease nondependent lung blood flow by 50%; that is, from 40% to 20% of total flow (fig. 1). Using these values as a model of the normal two-lung to one-lung ventilation conversion process, we can construct a table that sequentially relates per cent alveolar isoflurane to: 1) per cent inhibition of the nondependent lung HPV response; to 2) the resultant nondependent lung HPV response (expressed as a per cent decrease in nondependent lung blood flow); to 3) the resultant increase in atelectatic nondependent lung blood flow (which is the shunt during one-lung ventilation); to 4) an absolute increase in shunt; and finally, to 5) a decrease in arterial oxygenation during one-lung ventilation (from 280 mmHg to some lower value).

Table 1 (and fig. 1, *right panel*) shows that 1 MAC isoflurane anesthesia would inhibit the nondependent lung HPV response by approximately 21%, which would decrease the nondependent lung HPV response from a 50%

to 40% nondependent lung blood flow reduction, which would increase nondependent lung blood flow from 20% to 24% of total blood flow, causing shunt to increase by 4% of the cardiac output and Pa_{O_2} to decrease a moderate amount to 205 mmHg (FI_{O_2} = 1.0). Table I shows that one-half MAC isoflurane anesthesia would cause a very small increase in the total one-lung ventilation shunt and a small decrease in Pa_{O_2}, whereas 2 MAC isoflurane anesthesia would cause a moderate increase in the total one-lung ventilation shunt and a large decrease in Pa_{O_2}. It is outside the scope of this analysis to discuss extensively how isoflurane anesthesia is used today, but given the hemodynamic effects of high doses of isoflurane anesthesia (greater than 1 MAC) and the relative absence of hemodynamic effect of moderate doses of fentanyl (20 μg/kg), isoflurane anesthesia is usually administered in a 1 MAC or less concentration and is often supplemented with moderate doses of narcotics (or *vice versa*).

There are a number of important, nonanesthetic drug factors that might make the administration of isoflurane anesthesia have less of an effect on shunting and arterial oxygenation during one-lung ventilation than outlined previously. First, and most importantly, the absolute level of shunt is almost always higher in surgical patients than the minimal 20% used in the previous analysis of one-lung ventilation. The effect of a given increase in shunt on Pa_{O_2} depends on the absolute level of the initial shunt and the inspired oxygen concentration (fig. 2).[7] With an FI_{O_2} of 1.0, an increase in shunt from 20% to 24% of the cardiac output decreases the Pa_{O_2} a moderate amount. However, if the two-lung and one-lung ventilation shunt is increased, perhaps due to preexisting or anesthesia-induced lung disease, then the same isoflurane-induced increase in shunt will cause much less of a decrease in Pa_{O_2} (the larger isoshunt lines of fig. 2 are much flatter and closer together). For example, if the one-lung ventilation shunt without isoflurane is 30% and with isoflurane is 34%, then the decrease in Pa_{O_2} will be very small. In fact, in clinical one-lung ventilation studies involving intravenously anesthetized patients with this level of shunting, administration of 1 MAC isoflurane anesthesia during stable, one-lung ventilation conditions causes no detectable decrease in Pa_{O_2} (while other factors that might affect HPV, such as cardiac output, mixed venous oxygen tension, and pulmonary vascular pressures remained constant).[8,9] Considering the implications of figure 2 further,

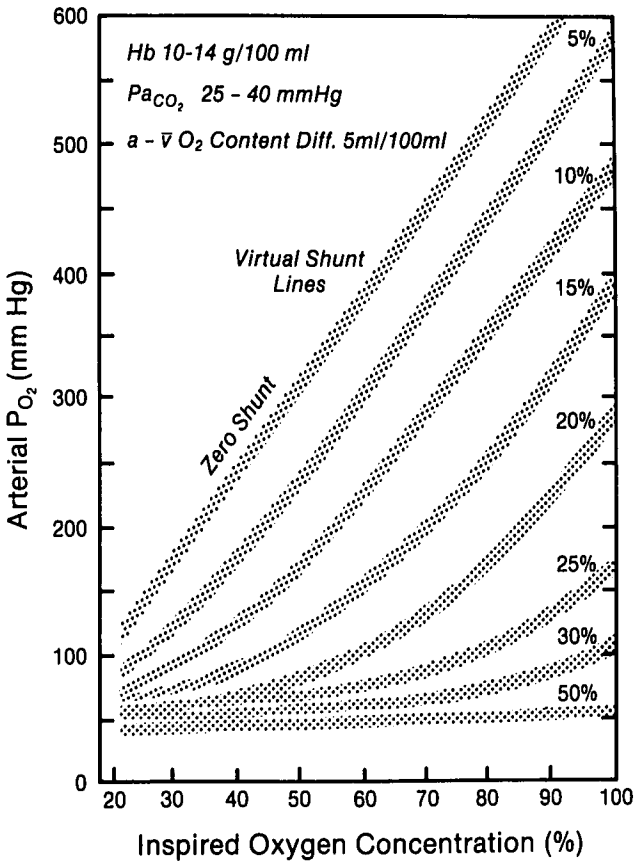

FIG. 2. The isoshunt graph relates FI_{O_2} (x-axis) to Pa_{O_2} (y-axis) for a family of pulmonary shunts. Each shunt is drawn as a band indicating the Pa_{O_2} limits caused by variation of Pa_{CO_2}, hemoglobin (Hb), and (a − $\bar{v}$)O_2 between the limits indicated in the upper left corner of the graph. Redrawn from Lawler PGP, Nunn JF: A reassessment of the validity of the iso-shunt graph. Br J Anaesth 56:1325–1335, 1984, with permission of the publisher.

TABLE 1. Effect of Isoflurane Anesthesia on Pa_{O_2} during One-lung Ventilation

MAC	Alveolar Isoflurane (%)	Inhibition of Nondependent Lung HPV Response (%)	Resultant Nondependent Lung HPV Response (% 1 in nondependent lung blood flow)	Resultant Nondependent Lung Blood Flow (% of cardiac output)	Increase in Shunt Due to Inhibition of Nondependent Lung HPV (% of cardiac output)	Pa_{O_2} (FI_{O_2} = 1.0) (mmHg)
0	0	0	50	20	0	280
0.5	0.58	8	46	22	2	250
1.0	1.15	21	40	24	4	205
1.5	1.69	33	33	27	7	140
2.0	2.30	47	26	29	9	110

HPV = hypoxic pulmonary vasoconstriction; MAC = minimum alveolar concentration; FI_{O_2} = fractional inspired O_2 concentration.

some anesthesiologists use an FI_{O_2} less than 1.0 during one-lung ventilation (which I do not recommend). As can be seen from figure 2, the family of isoshunt lines are much closer together at FI_{O_2} = 0.5 than at FI_{O_2} = 1.0, and the decrease in Pa_{O_2} with a given increase in shunt is much less.

Second, as pointed out by Domino *et al.*,[1] the secondary effects of isoflurane anesthesia may counteract the direct HPV-inhibition effect of the drug. Thus, a decrease in cardiac output, mixed venous oxygen tension, and pulmonary artery pressure, all of which may accompany isoflurane anesthesia, would intensify nondependent lung HPV at the same time isoflurane was decreasing it. Third, the presence of chronic, irreversible disease in the vessels of the nondependent lung may render these vessels incapable of an HPV response.[10,11] Fourth, the presence of disease in the dependent lung (either preexisting or anesthesia-induced), which increases dependent lung vascular resistance, will make the dependent lung less able to accept redistributed blood flow and thereby decrease the nondependent lung HPV response.[6,12-14] The smaller the HPV response, the less of an effect isoflurane anesthesia can have on the HPV response. Fifth, surgical interference with blood flow to the nondependent lung will also decrease the effect that isoflurane anesthesia can have on the one-lung ventilation shunt. Sixth, species differences[15-17] and differences in the study and clinical one-lung ventilation methodology (nitrogen ventilation *vs.* atelectasis, administration of isoflurane to the hypoxic lung *vs.* the normoxic or hyperoxic lung, and large *vs.* small alveolar to mixed venous isoflurane tension gradients, respectively) may alter the precise relationship between per cent inhibition of single-lung HPV and the alveolar concentration of isoflurane.

In summary, as demonstrated by Domino *et al.*, isoflurane anesthesia has a direct inhibiting effect on regional hypoxic pulmonary vasoconstriction.[1] In the simple case, where physiologic variables (cardiac output, mixed venous oxygen tension, pulmonary vascular pressures, and carbon dioxide tension) are normal and the amount of lung disease is minimal, the effect of isoflurane on shunting during one-lung ventilation is reasonably predictable and moderately small. In the complex case, where physiologic variables are abnormal and/or the amount of lung disease is extensive, the effect of isoflurane on shunting during one-lung ventilation is much less predictable, but almost certainly still smaller. Nevertheless, it should be remembered that it is the compromised patient who will be most intolerant of any further anesthesia-induced inhibition of HPV. For this kind of patient, the effect of isoflurane anesthesia on shunting must be carefully considered, arterial oxygenation must be closely monitored, and therapeutic measures to decrease shunting, such as nondependent lung CPAP and return to two-lung ventilation, should be quickly instituted, if necessary.

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