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## Anesthesia for One-lung Ventilation

*To the Editor:*—The recent paper by Benumof *et al.*<sup>1</sup> presents important data, but in the discussion and interpretation of this data, the unwary reader may be seriously misled.

The authors state that "In view of the usual efficacy of non-dependent lung CPAP, we conclude that the issue of halogenated drugs in patients undergoing one-lung ventilation is no longer a significant clinical issue." The fact that CPAP alleviates the hypoxemia does not mean that the problem is solved. In fact, resorting to CPAP has the disadvantage that the non-dependent lung is now pressurized and at least partially inflated. Thus, some of the fundamental advantages of the one-lung technique for thoracic surgery<sup>2</sup> are lost. However, it is a matter of common experience that only some patients develop hypoxemia during one-lung ventilation and so the real interest of the data obtained by Benumof *et al.*<sup>1</sup> lies in what clues they offer about the causes of this variability.

The basic observations were of changes in arterial blood gases ( $P_{aO_2}$ ) in two groups of approximately equivalent patients with mean  $P_{aO_2}$  of 484 and 442 mmHg during two-lung ventilation with oxygen, and either halothane or isoflurane, respectively. When one-lung ventilation was begun, the  $P_{aO_2}$  decreased to mean values of 116 mmHg with halothane and 232 mmHg with isoflurane. The striking difference of more than 100 mmHg between the two groups is statistically significant and yet the fact is overlooked in the presentation of these data. That the matter is of real clinical import can be estimated by considering that the mean  $P_{aO_2}$  of 116 mmHg during halothane signifies that half the population may be expected to have  $P_{aO_2}$  less than this and with the standard deviation of  $\pm 61$  mmHg, approximately one in three patients will have  $P_{aO_2}$  between 55 and 116 and for one in seven patients the  $P_{aO_2}$  will be less than 55. In practice, a  $P_{aO_2}$  of less than 100 mmHg is a cause of concern and, therefore, the first conclusion that may be drawn for these data is that the use of halothane during one-lung ventilation is associated with a large probability of arterial hypoxemia and that this incidence is significantly worse than with the use of isoflurane.

Figure 1a of Benumof *et al.*<sup>1</sup> reveals a second striking difference between the two groups in that the variability of the  $P_{aO_2}$  observed during one-lung ventilation is greater with isoflurane than with halothane; the standard deviations were 97 and 61 mmHg, respectively. An F test of the variances does not quite achieve significance, probably because of the small numbers of patients involved. But, in all but one of the patients receiving halothane, a remarkably homogeneous reduction of  $P_{aO_2}$  occurred, corresponding to a marked (perhaps 60%) inhibition of the hypoxic pulmonary vasoconstriction (HPV) response. In contrast, the isoflurane group shows a mean reduction of  $P_{aO_2}$  that is not as great, corresponding perhaps to a 20% reduction of HPV, but a much greater variability in the response with some patients.

These observations coincide closely with the observations of others. Isoflurane anesthesia shows the same inhibition of HPV and the same variability both in animal<sup>3</sup> and human<sup>4</sup> experiments. Furthermore, studies utilizing rat lungs perfused and ventilated *in vitro* show the same trends,<sup>5</sup> with halothane anesthesia causing a profound and homogeneous inhibition of HPV, while, with isoflurane, the inhibition was less profound but much more variable. The second conclusion from the data of Benumof *et al.*<sup>1</sup> is, therefore, that the extent and the variability of the inhibition of HPV is probably different between halothane and isoflurane.

Because inhalational anesthetics inhibit HPV, whereas injectable agents do not, the study design was intended to test whether, during one-lung ventilation, the arterial oxygen tension was lower with the inhalational agents than with injectable agents (fentanyl, diazepam,

and thiopental). With the halothane group, that result was demonstrated with a significant increase in the mean  $P_{aO_2}$  to 155 mmHg when the inhalational anesthetic was changed to the injectable agent. This increase is of real practical importance because it signifies that 86% of patients would have improved  $P_{aO_2}$  to values greater than 80 mmHg. This change was not demonstrated with the patients receiving isoflurane in whom the mean  $P_{aO_2}$  increased insignificantly to 245 mmHg when the isoflurane was replaced by injectable anesthetic. But in view of the extreme variability of this latter group, the result is not surprising. The third conclusion from this study is that the choice of inhalational versus injectable anesthetic agent can be a significant one, particularly in just those patients in whom it most matters.

Furthermore, two considerations suggest that the effect of injectable versus inhalational agents may have been underestimated. This study design is predicated on the assumption that the two groups are comparable and that injectable agents do not inhibit HPV. But, in both groups, when the inhalational agents were discontinued and anesthesia with the injectable agents had been established, the  $P_{aO_2}$ s during one-lung anesthesia remained more than 100 mmHg different. On first consideration, this result suggests that one or both of the study designs' assumption(s) is incorrect, in which case any interpretation becomes unconvincing. However, in the study of Benumof *et al.*<sup>1</sup> the hypoxic stimulus was not reversed between the inhalational and injectable agent phases and the order of these phases was not randomized and, therefore, the explanation for the persistence of the difference in  $P_{aO_2}$  between the two groups when both received injectable agents could simply be the maintenance of the response established in the previous phase in the presence of inhalational anesthetics. Clearly, there is much that needs to be established about this hypothesis, but a fourth tentative conclusion from this study is that the data support the concept that rapid alteration of an HPV response may require that the vascular tone be initially altered markedly, either by relaxing the vasculature or by a profound change in hypoxic stimulus.

All of these remarks have been directed at the  $P_{aO_2}$  values because the  $\dot{Q}_e/\dot{Q}_t$  values reported during anesthesia were peculiarly large, especially when compared to the values for "Pre-induction Shunt." The calculated  $\dot{Q}_e/\dot{Q}_t$  is very dependent on the value for alveolar oxygen tension and in Benumof *et al.*'s study, the  $P_{aO_2}$  was calculated assuming that the anesthesia gas circuit contained 100% oxygen. It is seldom that such high levels of oxygen are achieved in a clinical anesthetic circuit and, in the absence of any reported measurements, it seems most probable that the unusually large value for the calculated  $\dot{Q}_e/\dot{Q}_t$  arose because of variable inaccuracies arising from this assumption.

In summary, the data of Benumof *et al.*<sup>1</sup> indicate that hypoxemia is a frequent cause of concern during one-lung ventilation; that the choice of anesthetic agent has a significant effect; and that much more needs to be learned before this topic can be regarded as "no longer a significant clinical issue." What has often been forgotten in the controversy about this issue is that the causes of hypoxemia are multiple. What is being sought is not a single, all-encompassing explanation, but an accumulation of quantitative understanding that finally will account for the individual variability; for that, in the end, is what clinical anesthesia is all about.

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*In Reply:*—Dr. Marshall has raised a number of points that require a response. First, Dr. Marshall states that nondependent lung CPAP pressurizes and inflates the lung and, thereby, eliminates one of the fundamental advantages of one-lung ventilation (1LV).<sup>1</sup> However, in most reports, only 5 cm H<sub>2</sub>O are required to eliminate hypoxemia. Because lung compliance near residual volume is only 10 ml/cm H<sub>2</sub>O, 5 cm H<sub>2</sub>O CPAP creates only a 50-ml volume. This is clinically a trivial volume in an open 3-liter hemithorax. Second, Dr. Marshall concludes that "the real interest of the data obtained by Benumof *et al.*<sup>2</sup> lies in what clues they may offer about causes of variability" in PaO<sub>2</sub> during 1LV and draws four conclusions concerning interpatient and intergroup variability. The first conclusion was that the use of halothane during one-lung ventilation is associated with a large probability of arterial hypoxemia (defined as PaO<sub>2</sub> < 100 mmHg). Our data do not support that conclusion. The individual PaO<sub>2</sub> values during halothane anesthesia and 1LV were 236, 116, 102, 92, 82, and 69 mmHg. Defining arterial hypoxemia as PaO<sub>2</sub> < 80 mmHg, only one of our patients was mildly hypoxemic (PaO<sub>2</sub> = 69 mmHg). Ordinarily, 5 cm H<sub>2</sub>O CPAP would have easily corrected the situation.

The second conclusion was that halothane inhibited hypoxic pulmonary vasoconstriction (HPV) more variably than isoflurane. This conclusion was based on the PaO<sub>2</sub> data in our paper<sup>2</sup> and that of a few studies that employed different experimental preparations, different species, type of hypoxia (atelectasis *versus* nitrogen ventilation), degree of hypoxia, distribution of anesthesia, etc. On the other hand, there are many studies that demonstrate the same variability for halothane and isoflurane.<sup>3</sup> Finally, our halothane group was only more variable than the isoflurane group with respect to PaO<sub>2</sub> values; it was just the opposite with respect to shunt values.

The third conclusion was that the choice of inhalation anesthetic *versus* intravenous anesthetic is most important in patients who might have the lowest PaO<sub>2</sub> during inhalation anesthesia and one-lung ventilation. Our data do not support that conclusion; the patients who had the lowest PaO<sub>2</sub> during halothane and one-lung ventilation had the smallest increase in PaO<sub>2</sub> when switched to intravenous anesthesia and one-lung ventilation, and the patients who had the highest PaO<sub>2</sub> during halothane anesthesia and one-lung ventilation had the largest increase in PaO<sub>2</sub> when switched to intravenous anesthesia and one-lung ventilation.

Dr. Marshall reaches a tentative fourth conclusion that may be valid, but is speculative in nature. However, this conclusion was reached by dismissing two thoughts, each of which, in turn, may be valid. The first thought was that the patients receiving halothane and isoflurane may not be entirely comparable, and there are data to support this contention. For example, our patients in the halothane group had a PaO<sub>2</sub> = 116 mmHg, while those in the isoflurane group had a PaO<sub>2</sub> = 232 mmHg. I do not know why there are these differences, but subtle factors such as variable double-lumen tube position may make

otherwise comparable groups dissimilar. Again, we were interested in having each patient serve as their own control rather than make interpatient and intergroup comparisons. Second, intravenous anesthetics may inhibit HPV, in which case the interpretation of the results is either inhalation and intravenous drugs both do not inhibit HPV, or they both inhibit HPV to the same extent.

Finally, Dr. Marshall comments that our calculations of  $\dot{Q}_1/\dot{Q}_2$  may be in error because the anesthesia circuit may not have contained 100% oxygen. The patients were receiving high flows of 100% oxygen for prolonged periods of time, no other gas other than either halothane or isoflurane was used, and the FI<sub>O<sub>2</sub></sub> and FET<sub>O<sub>2</sub></sub> (mass spectrometer) were typically 1.00 and 0.96-0.97, respectively.

In summary, our primary goal was to have each patient serve as his or her own control, and compare arterial oxygenation during inhalation *versus* intravenous anesthesia with the same set of one-lung ventilation conditions. Within this latter context, we<sup>2,4</sup> and others<sup>5</sup> have not found much of a difference. I agree that the problem of hypoxemia during one-lung ventilation is not unidimensional, and I join in Dr. Marshall's call for continued effort to understand the determinants of arterial oxygenation during anesthesia.

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