Isoflurane-induced hypotension does not cause impairment in pulmonary gas exchange

J.F. Nicholas MD, A.M. Lam, MD FRCP(C)

Induced hypotension during anaesthesia can result in deterioration in gas exchange with increases in intrapulmonary shunting and physiological deadspace. Cardiovascular stability has been previously demonstrated with isoflurane-induced hypotension but the effects on gas exchange have not been carefully studied. We have examined the shunt fraction ($\dot{Q}s/\dot{Q}T$) and physiological dead space to tidal volume ratio (VD/VT) before, during and following deliberate hypotension in twelve patients. Group I (n= 6) received an isoflurane–oxygen–air mixture with an FIO_2 of 0.5 while Group II (n = 6) received an isoflurane–oxygen mixture with an FIO_2 of 1.0. Mean blood pressure was reduced from 76 ± 2 mmHg to 47 ±2 mmHg in the combined group. Neither $\dot{Q}s/\dot{Q}T$ nor VD/VT changed significantly during the hypotensive state in either group. We conclude that isoflurane induced hypotension is associated with minimal pulmonary derangement.

Key words

ANAESTHETICS, VOLATILE: isoflurane; ANAESTHETICS TECHNIQUES: hypotension, induced; VENTILATION: shunting, deadspace.

From the Department of Anaesthesiology, University Hospital and University of Western Ontario, London, Canada.

Address correspondence to: Dr. A.M. Lam, Department of Anaesthesia, University Hospital, P.O. Box 5339, Postal Stn. A., London, Canada. N6A 5A5.

Supported in part by a grant from Ohio Medical Products.

Induced hypotension can improve surgical operating conditions and decrease operative blood loss. Moreover, in cerebral aneurysm surgery it decreases the risk of aneurysm rupture at the time of clipping. Isoflurane has been previously demonstrated to be an effective hypotensive agent[1] but its effects on gas exchange during hypotension have not been carefully studied. It was the purpose of the study to investigate the effect of isoflurane-induced hypotension on gas exchange during elective surgery.

Methods

The study protocol was approved by the Health Sciences Standing Committee on Human Research at the University of Western Ontario. Twelve patients free of cardiovascular and pulmonary disease, scheduled for elective cerebral aneurysm clipping were included in the study. Preoperative capillary blood gases were determined in all patients. Preanaesthetic medication was either omitted or consisted of oral diazepam 10 mg. All patients were induced with intravenous fentanyl, $1\ \mu g \cdot kg^{-1}$, and thiopentone $5\ mg \cdot kg^{-1}$, and intubated under isoflurane anaesthesia following lidocaine $1.5\ mg \cdot kg^{-1}$ and succinylcholine $1\ mg \cdot kg^{-1}$. An arterial catheter and a triple lumen pulmonary arterial catheter were then inserted percutaneously. All patients had a subarachnoid catheter inserted in the lumbar space for cerebral spinal fluid drainage. Mannitol $1\ gm \cdot kg^{-1}$ was administered intravenously at the beginning of the procedure, after which no other intravenous medications were given.

Patients were randomly assigned into two groups of six each, with Group I receiving an oxygen–air–isoflurane mixture with FIO_2 of 0.5, and Group II receiving 100 per cent oxygen and isoflurane. All

patients were mechanically ventilated using a non-rebreathing circuit. Tidal volume and minute ventilation were maintained constant by monitoring expired volumes using pneumotachography (heated Fleisch #3 head). ECG and body temperature were continuously monitored.

Maintenance intravenous fluid therapy was administered as described in a previous report.[1] Briefly, Lactated Ringer's Solution (maximum 1000 ml) was administered during induction to maintain the systolic blood pressure at approximately 75 per cent of the ward value. Five per cent dextrose and 0.2 per cent NaCl was then infused at a rate of approximately 125 $ml \cdot hr^{-1}$. Blood transfusion was not required in any of the procedures.

Data were collected before induction of hypotension, during hypotension, and after hypotension. Measurements were only recorded after stable conditions had been achieved for a minimum of ten minutes. Inspired, mixed expired and end-tidal concentration of isoflurane, O_2 and CO_2 were measured using a Perkin-Elmer #1100 mass spectrometer. Cardiovascular variables recorded included systemic blood pressure, heart rate, pulmonary arterial pressure, pulmonary wedge pressure and central venous pressure. Cardiac output by thermodilution (Hewlett-Packard Module 78231C) was determined in at least duplicates. Blood samples for determination of arterial and mixed venous blood gases were capped immediately, stored on ice, and analyzed within ten minutes using a Radiometer BMS 3 MK 2 system and corrected for body temperature. To allow for possible inaccuracy at high oxygen tensions, the PO_2 electrode was calibrated with tonometered blood samples equilibrated with gas mixtures of known oxygen concentration. Arterial lactate levels were also determined before and after the period of hypotension.

Hypotension was induced by increasing the inspired isoflurane concentration. Both inspired and end-tidal isoflurane concentrations were monitored using mass spectrometry. In the posthypotensive period, we attempted to restore the prehypotensive anaesthetic depth by matching the end-tidal isoflurane concentrations.

The shunt fraction ($\dot{Q}S/\dot{Q}T$) was calculated according to the standard equation, and the dead-space to tidal volume ratio (VD/VT), which included apparatus dead space of 7 ml, determined by the modified Bohr's equation (Appendix I). Other derived cardiovascular parameters were calculated according to the formulae in Appendix II. Due to technical difficulties, two patients in Group I and one in Group II did not have all variables measured in the recovery period. All data were complete during the normotensive and hypotensive periods.

For statistical analysis, analyses of variance were employed for within group comparisons, and unpaired t-tests were utilized for between group comparisons. A p value of less than 0.05 was considered statistically significant. To estimate the type II error of failing to detect significant changes in $\dot{Q}S/\dot{Q}T$ and VD/VT with hypotension, we consider an increase in $\dot{Q}S/\dot{Q}T$ of 0.05 and an increase in VD/VT of 0.1 to be clinically important, and calculate the β error accordingly.[2]

Results

The mean age of Group I patients was 52 ± 8 years (SD), and for Group II 46 ± 9 years. Preoperative oxygen tension during room air breathing was 72 ± 4.4 mmHg for Group I and 74 ± 9.5 mmHg for Group II.

The respiratory parameters measured and derived are summarized in Table I. In both groups gas exchange was stable throughout the measurement periods and arterial oxygen and carbon dioxide tensions remained constant irrespective of change in blood pressure. The shunt fraction correspondingly did not increase during the period of hypotension. The shunt fraction was higher in Group II compared to Group I in all measurement periods but statistical significance was only reached in the recovery period. In both groups, the VD/VT ratio following induction of anaesthesia was approximately 0.4 and stayed constant throughout the measurement periods. Because of the small sample size, the β errors calculated for $\dot{Q}S/\dot{Q}T$ and VD/VT for the change with hypotension were 0.2 and 0.07 respectively. These were the same in both groups.

There was no significant difference between the groups in the mean end-tidal isoflurane concentrations although they tended to be higher in Group II.

Cardiovascular parameters are presented in Table II. These were essentially the same as previously reported,[1] showing a significant decrease in peripheral vascular resistance during the period of

TABLE I Gas exchange data

	Group I (n=6) (FIO_2 0.5)			*Group II (n = 6) (FIO_2 1.0)*		
	Control	*Hypotension*	*Recovery†*	*Control*	*Hypotension*	*Recovery‡*
PaO_2 (mmHg)	200 ± 21	200 ± 23	205 ± 15	495 ± 40	479 ± 41	447 ± 41
(kPa)	26.6 ± 2.8	26.6 ± 3.1	27 ± 2.0	65.8 ± 5.3	63.7 ± 5.5	59.5 ± 5.5
P(A-a)O_2 (mmHg)	121 ± 23	126 ± 10	120 ± 14	152 ± 39	164 ± 42	199 ± 43
(kPa)	16.1 ± 3.1	16.8 ± 1.3	15.9 ± 1.9	20.2 ± 5.2	21.8 ± 5.6	26.5 ± 5.7
$\dot{Q}s/\dot{Q}T$	0.10 ± 0.02	0.10 ± 0.01	0.09 ± 0.01	0.14 ± 0.02	0.14 ± 0.02	0.17 ± 0.01*
$PaCO_2$ (mmHg)	34 ± 1	34 ± 1	35 ± 1	34 ± 1	32 ± 1	32 ± 1
(kPa)	4.5 ± 0.1	4.5 ± 0.1	4.7 ± 0.1	4.5 ± 0.1	4.3 ± 0.1	4.3 ± 0.1
VD/VT	0.39 ± 0.03	0.40 ± 0.02	0.39 ± 0.03	0.37 ± 0.03	0.39 ± 0.03	0.40 ± 0.02
R	0.95 ± 0.13	1.18 ± 0.12	1.14 ± 0.11	0.92 ± 0.02	1.06 ± 0.09	0.88 ± 0.06

*$p < 0.05$ (between groups).
†n = 5 except VD/VT where n = 4.
‡n = 5.
All values means ± S.E.M.

TABLE II Haemodynamic data

	Group I (n = 6)			*Group II (n = 6)*		
	Control	*Hypotension*	*Recovery†*	*Control*	*Hypotension*	*Recovery†*
BP (mmHg)	77 ± 1	47 ± 2*	77 ± 6	78 ± 4	45 ± 1*	79 ± 6
(kPa)	10.2 ± 0.1	6.3 ± 0.3	10.2 ± 0.8	10.4 ± 0.5	5.9 ± 0.1	10.5 ± 0.8
CI $L \cdot min^{-1} \cdot m^{-2}$	2.64 ± 0.33	2.51 ± 0.28	2.56 ± 0.18	3.00 ± 0.30	2.86 ± 0.27	2.89 ± 0.25
SVR dyne $\cdot sec \cdot cm^{-5}$	1384 ± 180	848 ± 82*	1416 ± 190	1246 ± 142	731 ± 72*	1253 ± 73
PVR $dyne \cdot sec \cdot cm^{-5}$	98 ± 10	96 ± 6	92 ± 6	84 ± 6	59 ± 11	65 ± 14
PAP (mmHg)	11 ± 1	11 ± 1	10 ± 1	15 ± 2	11 ± 1	9 ± 1*
(kPa)	1.5 ± 0.1	1.5 ± 0.1	1.3 ± 0.1	2.0 ± 0.3	1.5 ± 0.1	1.2 ± 0.1
PCWP (mmHg)	7 ± 1	7 ± 1	6 ± 1	9 ± 1	8 ± 2	4 ± 1
(kPa)	0.9 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	1.2 ± 0.1	1.1 ± 0.3	0.5 ± 0.01
FET Isoflurane %	1.09 ± 0.17	2.20 ± 16*	1.11 ± 0.19	1.23 ± 0.06	2.40 ± 0.17*	1.20 ± 0.07

*$p < 0.05$ (compared to control).
†n = 5.
All values means ± S.E.M.

induced hypotension with minimal changes in cardiac index. In Group I pulmonary vascular resistance (PVR) was not affected by the induction of hypotension. The PVR appeared to be lower in Group II compared to Group I and there was a tendency to decrease during the period of hypotension. In Group I, mean pulmonary artery pressure showed no significant change throughout the measurement periods. In Group II, there was no significant change between normotension and hypotension, but a significant decrease from normotension occurred during recovery in mean pulmonary artery pressure. There was no significant increase in arterial lactate levels with hypotension. In Group I, arterial lactate was 1.7 ± 0.2 mEq/L (SEM) before hypotension and 1.9 ± 0.2 mEq/L after hypotension. The corresponding values for Group II were 2.0 ± 0.5 mEq/L and 2.7 ± 0.7 mEq/L respectively. Haemoglobin values for Group I were 118 ± 4 gm/L, 115 ± 4 gm/L, 114 ± 3 gm/L and Group II values were 118 ± 7 gm/L, 121 ± 6 gm/L and 125 ± 7 gm/L for control, hypotension, and recovery respectively.

Discussion

There are many indications for induced hypotension during surgery, and various agents have been utilized for this purpose. The main indication

during cerebral aneurysm surgery, however, is to maintain a stable, low pressure head with no fluctuation so that the risk of aneurysmal rupture, during dissection and clipping, is minimized. To this end, we have found isoflurane to be the most satisfactory agent for this purpose and its stable cardiovascular effects have been reported previously.[1]

Despite its frequent usage, it is well-known that the technique of induced hypotension is not without risk. Eckenhoff[3] showed that deliberate hypotension may be accompanied by an increase in alveolar-arterial oxygen gradient, and increase in V_D/V_T, resulting in carbon dioxide retention. He recommended that ventilation be controlled and increased and the inspired oxygen concentration augmented during the period of induced hypotension. Griffith[4] and Wildsmith[5] similarly demonstrated decreases in arterial oxygen tension and increases in V_D/V_T with sodium nitroprusside-induced hypotension. Therefore, with induced hypotension, the anaesthetist needs to be concerned not just with the cardiovascular parameters but also with this potential deterioration in gas exchange. We have previously demonstrated that arterial oxygen and carbon dioxide tensions did not change with isoflurane-induced hypotension and suggested that this may be secondary to the preservation of cardiac output during the period of hypotension.[1] In this study, we have pursued the investigation by determining $\dot{Q}_S/\dot{Q}_T$ and V_D/V_T before, during and after the period of hypotension. We divided the patients into two groups so that we could determine the effect of isoflurane-induced hypotension on venous admixture (Group I) as well as the true shunt (Group II).

In clinical studies during anaesthesia, measurement of gas exchange is not only influenced by concurrent pulmonary disease, effect of anaesthesia and mechanical ventilation on $\dot{V}/\dot{Q}$ and changes in cardiac output, but also by failure to attain a steady state. We have attempted to achieve this steady state by collecting data only during a stable period. The validity of our data is supported by the respiratory quotient (R) which remained within a narrow range throughout the control and hypotensive periods in both groups. The lower value during the recovery period in Group II was due to the smaller number of subjects.

The induction of general anaesthesia and use of mechanical ventilation have been shown by Rehder[6] to increase $\dot{V}/\dot{Q}$ mismatch, with the development of areas with low $\dot{V}/\dot{Q}$ (effects similar to increase in venous admixture) as well as high $\dot{V}/\dot{Q}$ (effects similar to increase in dead space). The explanation of this adverse effect of general anaesthesia on gas exchange is far from clear, but it is known that the state of general anaesthesia is associated with a reduction in functional residual capacity.[7] Hence, in our present study, even during the control period (prehypotension), $\dot{Q}_S/\dot{Q}_T$ and V_D/V_T were higher than normal. Rehder has also shown that increasing anaesthetic depth with isoflurane caused no further decrease in FRC,[8] thus stability of gas exchange during isoflurane-induced hypotension may be partially explained through this mechanism.

In this study we were unable to demonstate changes in $\dot{Q}_S/\dot{Q}_T$ by hypotension induced with isoflurane. Patients in Group II tended to have greater $\dot{Q}_S/\dot{Q}_T$ than Group I, and this probably was an effect of ventilation with 100 per cent oxygen. During oxygen breathing, intrapulmonary shunting can increase[9,10] as a result of (a) development of absorption atelectasis and (b) release of hypoxic pulmonary vasoconstriction (HPV) by the high mixed venous oxygen tension ($P\bar{v}O_2$).[11,12] In the present study the difference in $\dot{Q}_S/\dot{Q}_T$ between the two groups reached statistical significance in the recovery period, suggesting that absorption atelectasis may be the most important factor. The release of HPV by a high $P\bar{v}O_2$ will tend to decrease PVR, and indeed a difference in PVR, albeit not significant, existed between the two groups. Otherwise, the observation during the control periods are similar to findings with other anaesthetic agents.[13] Importance of the present investigation lies in the fact that no deterioration was observed in either group with the increased depth of anaesthesia and reduced blood pressure. This is best illustrated by pooling the results in both groups as depicted in Figure 1. This was deemed acceptable as no statistical difference in $\dot{Q}_S/\dot{Q}_T$ and V_D/V_T exists between the two groups during the first two measurement periods, and that the β errors for these variables were identical in both groups.

Shunt fraction can be influenced by a change in cardiac output,[14] but the cardiac index was maintained during the period of hypotension. At no time was there any decrease in oxygen transport,

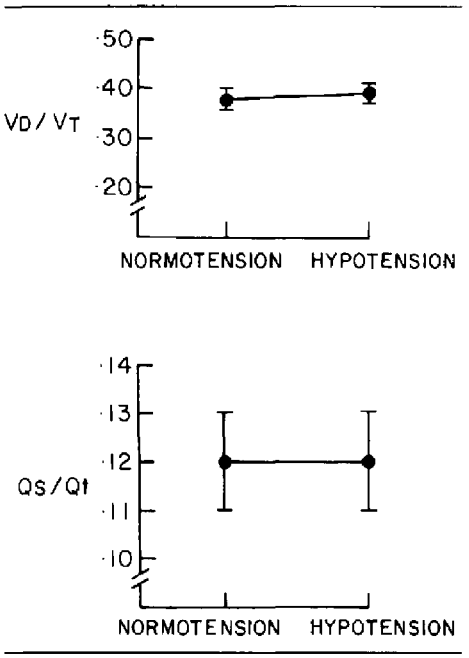

FIGURE 1 Effect of isoflurane-induced hypotension on V_D/V_T and $\dot{Q}_S/\dot{Q}_T$. Figure is drawn from the pooled results of both Groups I and II (n = 12). Vertical extension from the solid circles represents SEM. The reduction of blood pressure did not influence the magnitude of intrapulmonary shunt or physiological dead space to tidal volume ratio.

and there was no significant change in arterial lactate levels to suggest impairment of tissue oxygenation.

Sodium nitroprusside may cause deterioration in oxygenation by inhibiting HPV[15] and decreasing PVR, resulting in increased intrapulmonary shunting. Studies in humans and animals have demonstrated minimal influence of isoflurane on HPV.[16,17] This is consistent with our findings, in that we could detect no significant change in PVR during hypotension. There was a slight decline in PVR in Group II during hypotension and it can be argued that the higher isoflurane concentration administered to this group, particularly during the hypotensive period may also have released HPV and contributed to the decrease in PVR. This decrease, however, can be explained by the progressive release of HPV by the high $P\bar{v}O_2$ during 100 per cent oxygen breathing. These factors (stable FRC, cardiac output and minimal influence on HPV) together therefore, may account for isoflurane's lack of significant effect on intrapulmonary shunting during hypotension.

Khambatta[18] has suggested that the increase in V_D/V_T seen in surgical patients with sodium nitroprusside administration may be the result of decreased pulmonary arterial pressure (PAP), and that this change may be minimized by increasing fluid administration to maintain PAP. This is in agreement with our study, as the mean PAP did not change significantly during the period of hypotension in either group, and V_D/V_T ratio was maintained. To clarify the correlation between PAP and V_D/V_T, we performed a linear regression analysis using all the values obtained in both groups during the three study periods (Figure 2A). The correlation, although statistically significant ($p < 0.05$), was not a strong one ($r = -0.4$). This is not surprising since many factors other than PAP may determine the V_D/V_T in any one individual, and the correlation may therefore exist only within individual subjects but not among them. Accordingly, the changes in V_D/V_T were plotted against changes in mean PAP from the control period to the hypotensive period (Figure 2B). A highly significant correlation was demonstrated ($r = -0.7$, $p < 0.01$). In contrast, V_D/V_T did not correlate with either PVR or pulmonary capillary wedge pressure. This underlines the importance of maintaining PAP during any technique of induced hypotension. However, no attempts were made during this study to augment fluid administration to maintain pulmonary artery pressure during isoflurane-induced hypotension. Indeed, the slightly increased haemoglobin concentration in Group II during hypotension and recovery in the absence of transfusion suggests perhaps inadequate fluid replacement, accounting for the decline in PAP with time in this group. The V_D/V_T correspondingly exhibited a trend to increase wth time. That aggressive fluid therapy is unnecessary is of considerable clinical importance since this may result in a hypervolemic patient in the post-hypotensive period, with the attendant complications of hypertension and increased afterload on the heart.

In summary, although our numbers are small and the possibility exists that we failed to detect significant changes, our findings suggest that, in addition to providing stable hypotension which is particularly important in cerebral aneurysm sur-

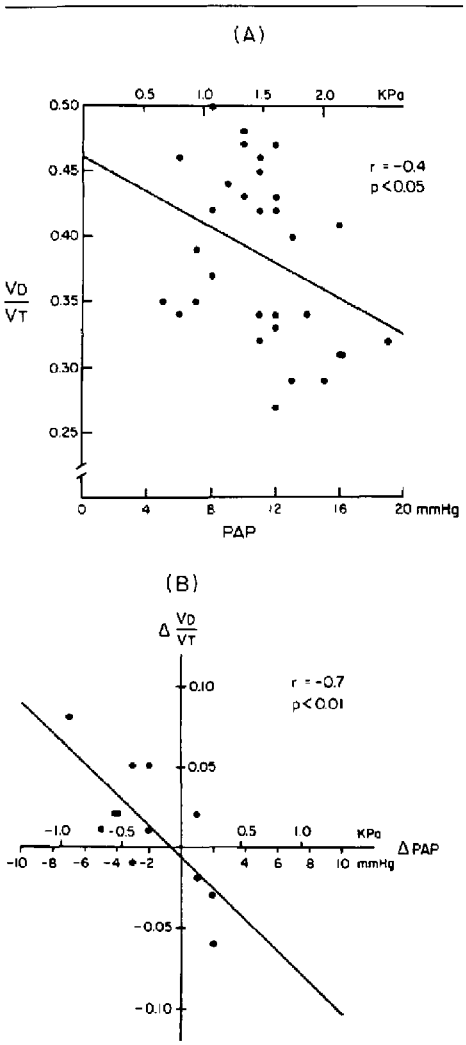

FIGURE 2 Correlation between PAP and V_D/V_T. In (A) V_D/V_T are plotted against mean PAP using the absolute values obtained during the three study states in both groups. A poor but statistically significant correlation is demonstrated. In (B) the changes in V_D/V_T and mean PAP with hypotension are used. Although the overall changes in V_D/V_T are small, a strong correlation is seen.

gery, isoflurane-induced hypotension is also accompanied by stable gas exchange. The clinical implication of these beneficial characteristics is obvious; it eliminates the need to increase inspired oxygen concentration and/or minute ventilation during the period of induced hypotension. While this does not diminish the need to monitor blood gases during induced hypotension, the technique does allow the anaesthetist to concentrate on the control of blood pressure during this critical period with an increased margin of safety.

Acknowledgements

The authors wish to thank the surgeons and nurses for their co-operation in the operating room, Dr. A.W. Gelb for his advice, Mrs. L. Nolan for secretarial assistance and Miss J. Clement for technical assistance.

References

1 *Lam AM, Gelb AW.* Cardiovascular effects of isoflurane-induced hypotension for cerebral aneurysm surgery. Anesth Analg 1983; 62: 742–8.

2 *Colton T.* Statistics in Medicine. Boston: Little, Brown 1974.

3 *Eckenhoff JE, Enderby GEH, Larson A, Edridge A, Judevine DE.* Pulmonary gas exchange during deliberate hypotension. Br J. Anaesth 1963; 35: 750–759.

4 *Griffiths DPG, Cummins BH, Greenbaum R et al.* Cerebral blood flow and metabolism during hypotension induced with sodium nitroprusside. Br J Anaesth 1974; 46: 671–9.

5 *Wildsmith JAW, Drummond GB, MacRae WR.* Blood-gas changes during induced hypotension with sodium nitroprusside. Br J Anaesth 1975; 47: 1205–11.

6 *Rehder K, Knopp TJ, Sessler AD, Didier EP.* Ventilation-perfusion relationship in young healthy awake and anesthetized-paralyzed man. J. Apl Physiol 1979; 47: 745–53.

7 *Laws AK.* Effects of induction of anaesthesia and muscle paralysis on functional residual capacity of the lungs. Can Anaesth Soc J 1968; 15: 325–31.

8 *Rehder K, Mallow JE, Fibuch EE et al.* Effect of isoflurane anesthesia and muscle paralysis on respiratory mechanics in normal man. Anesthesiology 1974; 41: 477–85.

9 *Oliven A, Abinader E, Bursztein S.* Influence of varying inspired oxygen tension on the pulmonary venous admixture (shunt) of mechanically ventilated patients. Crit Care Med 1980; 8: 99–101.

10 *Shapiro BA, Cane RD, Harrison RA, Steiner*

MC. Changes in intrapulmonary shunting with administration of 100 percent oxygen. Chest 1980; 77: 138–41.

11 *Suter PM, Fairley HB, Schlobohm RM.* Shunt, lung volume and perfusion during short periods of ventilation with oxygen. Anesthesiology 1975; 43: 617–27.

12 *Dantzker Dr, Wagner PD, West JB.* Instability of lung units with low $\dot{V}_A/\dot{Q}$ ratios during O_2 breathing. J. Appl Physiol 1975; 38: 886–95.

13 *Michenfelder JD, Fowler WS, Theye RA.* CO_2 level and pulmonary shunting in anaesthetized man. J. Appl Physiol 1966; 21: 1471–76.

14 *Cheney FW, Colley PS.* The effect of cardiac output on arterial blood oxygenation. Anesthesiology 1980; 52: 496–503.

15 *Colley PS, Cheney FW.* Sodium nitroprusside increase Qs/Qt in dogs with regional atelectasis. Anesthesiology 1977; 47: 338–41.

16 *Saidman LJ, Trousdale TR.* Isoflurane does not inibit hypoxic pulmonary vasoconstriction. Anesthesiology 1982; 57: A472 (Abstract).

17 *Rogers SN, Benumof J.* Halothane and isoflurane do not impair arterial oxygenation during one lung vertilation in patients undergoing thoracotomy. Anesthesiology 1983; 59: A532 (Abstract).

18 *Khambatta HJ, Stone JG, Matteo RS.* Effect of sodium nitroprusside-induced hypotension on pulmonary deadspace. Br J Anaesth 1982; 54: 1197–9.

Résumé

L'hypotension contrôlée pendant l'anesthésie peut amener une détérioration des échanges gazeux à cause de l'augmentation du shunt intra-pulmonaire et de l'espace-mort physiologique. On a précédemment démontré la stabilité cardiovasculaire de l'hypotension induite avec l'isoflurane, mais ses effets sur les échanges gazeux n'ont pas été bien étudiés. Nous avons étudié la fraction du shunt ($\dot{Q}s/\dot{Q}T$) et le rapport de l'espace-mort physiologique sur le volume courant (VD/VT) avant, pendant et après l'hypotension contrôlée chez 12 patients. Le groupe I ($n = 6$) recevait isoflurane–O_2–air pour obtenir une $FIO_2 = 0.5$ alors que le groupe II ($n = 6$) recevait isoflurane = O_2, $FIO = 1.0$. La pression artérielle moyenne fut réduite de 76 ± 2 mmHg à 47 ± 2 mmHg dans les groupes combinés. Ni le $\dot{Q}s/\dot{Q}T$ ni le VD/VT n'ont changé de façon significative durant l'hypotension dans les deux groupes. Nous concluons que l'hypotension induite par l'isoflurane provoque peu de répercussions pulmonaires.

Appendix I

$$(1)\ \dot{Q}s/\dot{Q}T = \frac{C\acute{c}O_2 - CaO_2}{C\acute{c}O_2 - CaO_2}$$

where

$C\acute{c}O_2 = (1.39 \times Hb + PaO_2 \times 0.0031)$
$CaO_2 = (1.39 \times Hb \times SaO_2 + PaO_2 \times 0.0031)$
$C\bar{v}O_2 = (1.39 \times Hb \times S\bar{v}O_2 + P\bar{v}O_2 \times 0.0031)$
$C\acute{c}O_2$ = end-pulmonary capillary O_2 content
CaO_2 = arterial O_2 content
$C\bar{v}O_2$ = mixed venous O_2 content
SaO_2 = arterial O_2 saturation
$S\bar{v}O_2$ = mixed venous O_2 saturation

$$(2)\ VD/VT = \frac{PaCO_2 - P\bar{E}CO_2}{PaCO_2}$$

where

$PaCO_2$ = partial pressure of arterial CO_2
$P\bar{E}CO_2$ = partial pressure of mixed-expired CO_2

$$(3)\ PAO_2 = PiO_2 - PaCO_2\left(\frac{PiO_2 - P\bar{E}O_2}{P\bar{E}CO_2}\right)$$

$$(4)\ P(A\text{-}a)O_2 = PAO_2 - PaO_2$$

$$(5)\ R = \frac{P\bar{E}CO_2}{PiO_2 - P\bar{E}O_2}$$

R = respiratory quotient

Appendix II

$$(1)\ SVR = \frac{\overline{BP} - \overline{RAP}}{CO} \times 80\ \text{dyne}\cdot\text{sec}\cdot\text{cm}^{-5}$$

$$(2)\ PVR = \frac{\overline{PAP} - PCWP}{CO} \times 80\ \text{dyne}\cdot\text{sec}\cdot\text{cm}^{-5}$$

$$(3)\ CI = \frac{CO}{BSA}\ \text{L}\cdot\text{min}^{-1}\cdot\text{min}^{-2}$$

where

SVR = systemic vascular resistance
$\overline{BP}$ = mean blood pressure
$\overline{RAP}$ = mean right arterial pressure
PVR = pulmonary vascular resistance
$\overline{PAP}$ = mean pulmonary arterial pressure
PCWP = pulmonary capillary wedge pressure
C.O. = cardiac output
C.I. = cardiac index
BSA = body surface area