Effects of anaesthesia and surgery on the solubility of volatile anaesthetics in blood

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To determine the effects of anaesthesia and surgery on the solubility of volatile anaesthetics in blood, we measured the blood/gas partition coefficients of enflurane, halothane, isoflurane, and methoxyflurane in vitro *in blood obtained from six healthy unpremedicated adults at three different times during isoflurane anaesthesia: (1) awake; (2) 20 minutes after induction of anaesthesia, but before surgical incision; and, (3) 90 minutes after surgical incision. The blood/gas partition coefficients of the four volatile anaesthetics decreased significantly after induction of anaesthesia and after surgical incision ($p < 0.05$). Values for haematocrit and the serum concentrations of albumin, globulin, and cholesterol decreased parallel to the decrease in blood/gas partition coefficients.*

Key words

ANAESTHETIC: VOLATILE: enflurane, halothane, isoflurane, methoxyflurane; BLOOD: solubility.

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The rate at which the alveolar anaesthetic partial pressure increases is inversely related to the solubility of volatile anaesthetics in blood (the blood/gas partition coefficient).[1] Because the concentrations of serum constituents decrease during anaesthesia and surgery, we speculated that the solubility of volatile anaesthetics in blood may be affected by anaesthesia and surgery.[2–4] To test this thesis, we determined the blood/gas partition coefficients of four volatile anaesthetics before and during anaesthesia and surgery, and simultaneously measured the haematocrit and serum concentrations of four blood constituents.

Methods

With approval from our Committee on Human Research, informed consent was obtained from six adults scheduled for elective minor surgery. All patients were 30–45 years of age, ASA physical status I or II, fasting, and unpremedicated. Anaesthesia was induced with thiopentone and followed by isoflurane, nitrous oxide, and oxygen. The trachea of each patient was intubated and the lungs were ventilated to maintain an end-tidal carbon dioxide partial pressure (as determined by mass spectrometry) between 35 and 45 mmHg. Either lactated Ringer's solution or five per cent dextrose in lactated Ringer's solution (as chosen by the anaesthetist) was administered. Venous blood specimens of 15 ml were obtained from each patient at three times: (1) prior to anaesthesia (AWAKE); (2) 20 minutes after induction of anaesthesia, but before surgical incision (ANAESTHESIA); and, (3) 90 minutes after surgical incision (SURGERY). Each specimen was divided into a 7 ml sample anticoagulated with EDTA and an 8 ml clotted sample. The former was used to determine the blood/gas partition coefficients of enflurane, halothane, isoflurane and methoxyflurane, and to measure haematocrit; the latter to determine the serum concentrations of albumin, globulin, cholesterol, and triglycerides. Blood/gas partition coefficients were determined at 37° C using gas chromatography.[3] The serum concentrations of albumin, globulin, cholesterol and triglycerides were determined by automated (SMA 12) analysis.

Statistical significance ($p < 0.05$) was determined

using repeated-measures ANOVA, and the Student–Newman–Keuls multiple range test.

Results

The AWAKE values for the blood/gas partition coefficients agreed with previous data.[1,3] Those obtained during ANAESTHESIA and SURGERY decreased significantly below AWAKE values (Figure and Table). Except for isoflurane, the partition coefficients during SURGERY did not differ significantly from those during ANAESTHESIA.

The AWAKE values for haematocrit, and the concentrations of serum albumin, globulin, cholesterol, and triglycerides were consistent with normal estimates for these blood constituents[5] (Table). Haematocrit values during ANAESTHESIA and SURGERY decreased significantly compared with AWAKE values. Values for the serum concentrations of albumin, globulin, and cholesterol during ANAESTHESIA were significantly lower than AWAKE values and decreased further during SURGERY (Table). The serum concentration of triglycerides did not change significantly throughout the study.

The mean (± SD) volume of crystalloid administered during the 20 minutes after induction of ANAESTHESIA was 600 ml (± 200) and the volume administered during the 90 minutes after skin incision was 580 ml (± 50).

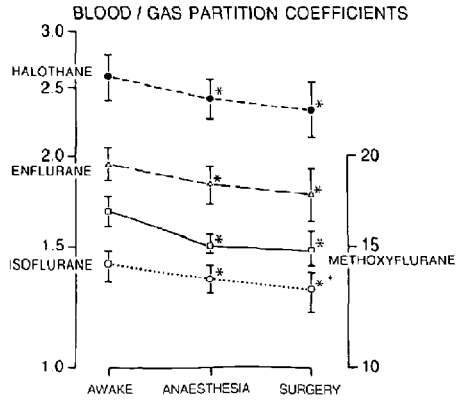

FIGURE The blood/gas partition coefficients (mean ± SE) for enflurane, halothane, isoflurane, and methoxyflurane decrease significantly during ANAESTHESIA and SURGERY compared to AWAKE values ($p < 0.05$). The blood/gas partition coefficient for isoflurane during SURGERY decreased significantly compared to that during ANAESTHESIA.
*Significantly different from AWAKE values.
†Significantly different from ANAESTHESIA values.

Discussion

The blood/gas partition coefficients of enflurane, halothane, isoflurane, and methoxyflurane decreased significantly during ANAESTHESIA and SURGERY (Figure). These decreases paralleled significant changes in haematocrit and the serum concentrations of blood constituents. Decreases in haematocrit and in the serum constituent concentrations may be attributable in part to dilution secondary to the administration of substantial volumes of intravenous crystalloid fluids during ANAESTHESIA and SURGERY, and, in part, to a direct effect of volatile anaesthetics. The volume of crystalloid fluids administered was sufficient to decrease the haematocrit (during ANAESTHESIA) ten per cent below the AWAKE values (Table). Because the solubility of volatile anaesthetics is significantly less in aqueous solutions (such as lactated Ringer's) than in plasma or blood, the infusion of aqueous solutions will decrease the solubility of volatile anaesthetics in blood.[6,7] Evidence from animal studies suggests that administration of halothane or halothane-nitrous oxide decreases haematocrit and plasma protein concentrations by an increase in plasma volume and splenic sequestration.[8] Thus, the combination of the infusion of

TABLE Results

	AWAKE	*ANAESTHESIA*	*SURGERY*
Blood/gas partition coefficients:			
λ enflurane	1.92 ± 0.10	1.80 ± 0.10	1.74 ± 0.15*
λ halothane	2.56 ± 0.20	2.38 ± 0.15*	2.30 ± 0.21*
λ isoflurane	1.39 ± 0.07	1.33 ± 0.06*	1.28 ± 0.09*†
λ methoxyflurane	16.5 ± 0.8	14.9 ± 0.5*	14.7 ± 0.8*
Haematocrit (vol %)	39.3 ± 3.0	36.4 ± 3.0*	35.2 ± 4.6*
Serum albumin (gm %)	4.3 ± 0.2	3.8 ± 0.4*	3.5 ± 0.4*†
Serum globulin (gm %)	2.6 ± 0.4	2.25 ± 0.3*	2.15 ± 0.3*†
Serum cholesterol (mg%)	198.5 ± 40	174.5 ± 42*	161.0 ± 42*†
Serum triglycerides (mg %)	64.4 ± 32	66.8 ± 38	57.8 ± 39

Data are mean ± SD.
*Significantly different from AWAKE values ($p < 0.05$).
†Significantly different from ANAESTHESIA values ($p < 0.05$).

crystalloid fluids and the administration of volatile anaesthetics may contribute to decreases in the solubility of volatile anaesthetics in blood.

The decreases in blood/gas partition coefficients may affect the development of an anaesthetizing partial pressure of volatile anaesthetic in alveoli. Decreases in the blood/gas partition coefficients will speed the increase in alveolar anaesthetic partial pressure and thus the equilibration of alveolar and inspired anaesthetic partial pressures.

The blood/gas partition coefficient also influences the rate of increase in tissue anaesthetic partial pressure. As the blood/gas partition coefficient decreases, the tissue/blood partition coefficient increases.[3] Since the time constant for tissue equilibration is proportional to the tissue/blood partition coefficient, this prolongs the time to tissue equilibration. In the extreme, if the blood/gas partition coefficient approaches zero, both the tissue/blood partition coefficient and the time to tissue equilibration would approach infinity. However, the net effect of a decrease in the blood/gas partition coefficient on induction of anaesthesia is likely to be small.

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Résumé

Afin de déterminer les effets de l'anesthésie et de la chirurgie sur la solubilité des anesthésiques volatiles dans le sang, on a mesuré les coefficients de partition sang/gaz de l'enflurane, halothane, isoflurane, et méthoxyflurane in vitro *dans le sang obtenu de six adultes non prémédiqués à trois temps différents lors de l'anesthésie à l'isoflurane: 1) réveil, 2) 20 minutes après l'induction de l'anesthésie mais avant l'incision chirurgicale et 3) 90 minutes après l'incision chirurgicale. Les coefficients de partition sang/gaz des quatre anesthésiques volatiles diminuèrent significativement après induction de l'anesthésie et après incision chirurgicale ($p < 0.05$). Les valeurs de l'hématocrite, l'albumine sérique, la globuline ainsi que le cholestérol ont diminué parallèlement à la diminution des coefficients de partition sang/gaz.*